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Anaesthetic and respiratory equipment — Nebulizing systems and components

Matériel d'anesthésie et de réanimation respiratoire — Systèmes de nébulisation et leurs composants

ISO/CEN PARALLEL PROCESSING

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ISO copyright office
CP 401 • Ch. de Blandonnet 8
CH-1214 Vernier, Geneva
Phone: +41 22 749 01 11
Email: copyright@iso.org
Website: www.iso.org

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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 121, *Anaesthetic and respiratory equipment*, Subcommittee SC 2, *Airways and related equipment*, in collaboration with the European Committee for Standardization (CEN) Technical Committee CEN/TC 215, *Respiratory and anaesthetic equipment,* in accordance with the Agreement on technical cooperation between ISO and CEN (Vienna Agreement).

This fourth edition cancels and replaces the third edition (ISO 27427:2013), which has been technically revised.

The main changes are as follows:

— Alignment with the general standard for airway devices, ISO 18190;

— updating of references.

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

Nebulizers are widely used to deliver drugs and vaccines in an aerosol form to humans through the respiratory system. *Nebulizers* are also used for diagnostic purposes using radioisotopes for lung challenge tests. These drugs can be in the form of a solution, suspension or emulsion. *Aerosol* inhalation is the preferred route of administration for some drugs. Some drugs are intended for treatment of systemic diseases and other drugs are intended to treat respiratory diseases. To achieve the intended treatment, *aerosol* particles are deposited in specific parts of the respiratory tract. Different size particles tend to deposit in different parts of the respiratory system; therefore, the performance profile and the intended use of the *nebulizer* is specified by the manufacturer and in the accompanying documentation.

This document was developed to cover "general purpose" *nebulizers* and is based on adult test parameters which are likely to be different than stated when testing for paediatric or infant patient populations. It was specifically written to ensure that the results of the various tests declared by the manufacturer are meaningful to the users and buyers of *nebulizers*.

The objectives of this document are to ensure

— suitability of the *nebulizers* for the intended use as disclosed by the manufacturer;

— safety, particularly for *electrically powered nebulizers*;

— compatibility between the materials of the components and the dispensed liquid; and

— biocompatibility of the materials of the components that come into contact with the human body.

This document is written following the format of ISO 18190, which is the general standard for airways and related *equipment.* The requirements in this device-specific standard take precedence over any conflicting requirements in ISO 18190.

Throughout this document the following print types are used:

— requirements and definitions: roman type;

— informative material appearing outside of tables, such as notes, examples and references: smaller type. The normative text of tables is also in smaller type;

— *terms defined in Clause 3*: *italics*.

Anaesthetic and respiratory equipment — Nebulizing systems and components

1 Scope

This document specifies requirements for the safety and performance testing of general-purpose *nebulizing systems* intended for continuous or breath-actuated delivery of liquids, in *aerosol* form, to humans through the respiratory system.

This document includes *gas-powered nebulizers* (which can be powered by, e.g., compressors, pipeline systems, cylinders, etc.) and *electrically powered nebulizers* [e.g. spinning disc, ultrasonic, vibrating mesh (active and passive), and capillary devices] or *manually powered nebulizers*. This document does not specify the electrical requirements of *electrically powered nebulizers*.

This document does not specify the minimum performance of *nebulizing systems*.

This document does not apply to:

a) devices intended for nasal deposition;

b) devices intended solely to provide humidification or hydration by providing water in *aerosol* form.

NOTE 1 ISO 80601-2-74 and ISO 20789 cover these devices.

c) drug-specific *nebulizers* or their components (e.g. metered dose inhalers, metered liquid inhalers, dry powder inhalers).

NOTE 2 ISO 20072 covers these devices.

NOTE 3 See Annex A for rationale.

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 5356-1, *Anaesthetic and respiratory equipment — Conical connectors — Part 1: Cones and sockets*

ISO 7396-1, *Medical gas pipeline systems — Part 1: Pipeline systems for compressed medical gases and vacuum*

ISO 18190:2016, *Anaesthetic and respiratory equipment — General requirements for airways and related equipment*

ISO 18562-1, *Biocompatibility evaluation of breathing gas pathways in healthcare applications — Part 1: Evaluation and testing within a risk management process*

ISO 23328-1, *Breathing system filters for anaesthetic and respiratory use — Part 1: Salt test method to assess filtration performance*

ISO 80369-2, *Small-bore connectors for liquids and gases in healthcare applications — Part 2: Connectors for breathing systems and driving gases applications*

3 Terms and definitions

For the purposes of this document, the following terms and definitions apply.

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

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

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

3.1
aerosol
suspension of particles in gas

Note 1 to entry: Particles can be liquid or solid.

Note 2 to entry: The gas can be the driving gas or ambient air.

3.2
aerosol output
mass or volume of *aerosol* emitted by the *nebulizing system* at the *aerosol outlet port* for the given fill volume

3.3
aerosol outlet port
outlet of the *nebulizing system* through which the *aerosol* is emitted

3.4
aerosol output rate
mass or volume of *aerosol* emitted by the *nebulizing system* per unit of time

3.5
breath-actuated nebulizer
nebulizer triggered by a respiratory parameter

Note 1 to entry: Examples of this classification are found in Annex F.

3.6
continuous nebulizer
nebulizer in which *aerosol* is delivered continuously over multiple inhalation/exhalation breathing cycles or over long periods

3.7
electrically-powered nebulizer
nebulizer that operates by means of electrical power

Note 1 to entry: *Electrically powered nebulizers* include ultrasonic, vibrating mesh and capillary-type devices.

3.8
gas-powered nebulizer
nebulizer in which the *aerosol* is generated by compressed gas

3.9
liquid container
part of the *nebulizer* that contains the liquid for nebulization

3.10
manually powered nebulizer
nebulizer that operates by means of human power

3.11
mass median aerodynamic diameter
MMAD
particle size at which 50 % of the mass of the active component are contained in droplets of smaller or equal aerodynamic diameter

3.12
maximum fill volume
maximum volume of liquid, expressed in millilitres, in the *liquid container* when the *nebulizer* is filled to its maximum filling level

3.13
nebulizer
device that converts a liquid to an *aerosol*

Note 1 to entry: A *nebulizer* is also known as an *aerosol* generator.

3.14
nebulizing system
parts, including the *nebulizer* and all other components, up to and including the *aerosol outlet port*, required to make the *aerosol* available for inhalation

Note 1 to entry: Airway devices (e.g. masks, tracheal and tracheostomy tubes, supralaryngeal airways) and breathing systems are not part of the *nebulizing system*.

3.15
percentage of fill volume emitted
aerosol output expressed as a percentage of the fill volume recommended by the manufacturer that is emitted by the *nebulizer*

3.16
residual volume
estimated volume of liquid remaining in the *nebulizing system* when the *nebulizer* stops generating an *aerosol*

3.17
respirable fraction
fraction of *aerosol* droplets below 5 µm in diameter expressed as a percentage of the total *aerosol distribution*

Note 1 to entry: The *respirable fraction* can be converted to a percentage (%) by multiplying by 100.

3.18
test solution
aqueous solution used for the type-tests to characterize *aerosol output*, *aerosol output rate*, and particle sizing

Note 1 to entry: See 4.2.1.2, 9.3.2 j) and k), Annex C, and Annex D.

3.19
test substance
active ingredient contained in the *test solution*

4 General requirements and requirements for test

4.1 General

ISO 18190:2016, Clause 4 applies.

NOTE See Annex E for a list of hazards than can be used as guidance in risk assessment.

4.2 Test methods and alternatives

4.2.1 Test methods for *aerosol output*, *aerosol output rate*, and particle sizing

The type-test methods for *aerosol output*, *aerosol output rate*, and particle sizing in air are specified in Annexes C and D.

4.2.1.1 All type-test methods shall be performed on at least three representative devices of the same type.

Check conformance by inspection of the technical file/documentation.

4.2.1.2 The type-test methods shall use a *test solution* of albuterol 0,1 % (mass/mass or volume/volume (m/m or V/V)) concentration in 0,9 % sodium chloride solution or 2,5 % (m/m OR V/V) sodium fluoride in distilled water with the provision that its use is declared in the accompanying documents. See 9.3.2 j).

Check conformance by inspection of the technical file/documentation and the accompanying documents.

4.2.2 Alternative test methods

The manufacturer can use type-test methods for *aerosol output*, *aerosol output rate*, and particle sizing different from those specified in Annexes C and D, provided that any:

a) alternative test methods are validated against the test methods in Annexes C and D to demonstrate equivalency and that

b) the demonstration of equivalency is included in the technical documentation of the manufacturer.

Check conformance by inspection of the technical file/documentation.

4.2.3 Calibration and setup

To establish confidence in the test method, it is recommended that mass balance procedures be incorporated during initial determinations. It is also recommended that occasional checks for system leaks and overall efficiency of analysis be performed.

5 Materials

5.1 General

ISO 18190:2016, Clause 5 applies.

5.2 Biocompatibility

Materials used to manufacture *nebulizing systems* shall be evaluated for biocompatibility. The breathing gas pathways shall be evaluated for biocompatibility as specified in ISO 18562-1 and tested as appropriate.

Check conformance by inspection of the technical file/documentation.

6 Design Requirements

6.1 General

ISO 18190:2016, Clause 6 applies.

6.2 Inlet and outlet ports

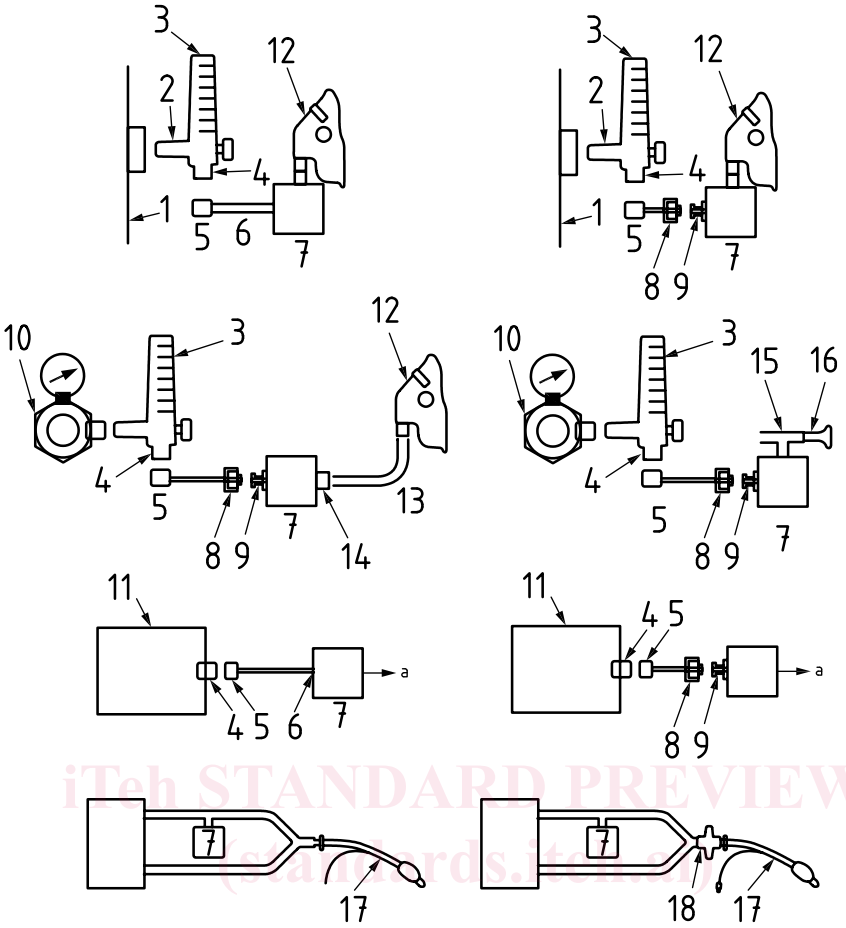
6.2.1 Inlet ports

The driving gas inlet port of a *nebulizing system* shall be compatible with the gas delivery system to which it is intended to be connected and shall be one of the following (see Figure 1):

a) a female R2 small-bore connector conforming to ISO 80369-2; or

b) permanently attached (i.e. not removable without the use of a tool).

Check conformance by inspection of the technical file/documentation.



Key

1 terminal unit conforming to ISO 9170-1
2 probe, conforming to ISO 9170-1
3 flow meter conforming to ISO 15002
4 9/16-18UNF-2A-RH male connector conforming to CGA V-5-2008, or ¾-16UNF-2A-RH male connector conforming to CGA V-5-2008 or a nipple conforming to ISO 17256
5 9/16-18UNF-2A-RH female connector conforming to CGA V-5-2008 or ¾-16UNF-2A-RH female connector conforming to CGA V-5-2008 or a funnel conforming to ISO 17256
6 permanently attached
7 nebulizer
8 male R2 connector conforming to ISO 80369-2
9 female R2 connector conforming to ISO 80369-2
10 pressure regulator conforming to ISO 10524-1
11 compressor conforming to this document (ISO 27427)
12 aerosol mask vented
13 breathing tube conforming to ISO 5367
14 connector conforming to ISO 5356-1
15 T-piece with connectors conforming to ISO 5356-1
16 mouthpiece
17 tracheal tube conforming to ISO 5361
18 HME conforming to ISO 9360-1

Figure 1 — Examples of inlet and outlet ports for *nebulizer systems*

6.2.2 Outlet port

6.2.2.1 If intended for use in breathing systems, the *aerosol outlet port* shall conform to ISO 5356-1.

Check conformance by inspection of the technical file/documentation.

6.2.2.2 If not intended for use in breathing systems, the *aerosol outlet port* shall not misconnect with connectors conforming to ISO 5356-1, or ISO 80369-1.

Check conformance by inspection of the technical file/documentation.

6.3 Flow-direction-sensitive components

Any flow-direction-sensitive, operator-detachable component shall be designed so that it cannot be fitted in such a way as to present a hazard to the patient.

Check conformance by functional testing.

6.4 Cleaning and disinfection or sterilization

Nebulizing systems and components intended for reuse shall be constructed so as to enable dismantling for cleaning and disinfection or sterilization.

NOTE See also ISO 17664 -1.

Check conformance by testing the disassembly/assembly procedure according to the manufacturer's instructions.

6.5 Rotary controls

The manufacturer should ensure consistency regarding the direction of movement of rotary controls of the device.

7 Requirement for *nebulizing systems* and components supplied sterile

ISO 18190:2016, Clause 7 applies.

8 Packaging

ISO 18190:2016, Clause 8 applies.

9 Information supplied by the manufacturer

9.1 General

ISO 18190:2016, Clause 9 applies.

9.2 Marking

9.2.1 General

9.2.1.1 Marking shall be durable following exposure to typical substances in contact during its intended use and remain legible for the intended duration of use.