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ISO TC 121/SC 2

Secretariat: ~~ANSI~~

Anaesthetic and respiratory equipment — Nebulizing systems and components

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

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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 compared to the previous edition are as follows:~~

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.

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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 ~~have to be 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* ~~have to be is~~ specified by the manufacturer and ~~specified~~ 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, ~~General~~ *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 Clause 3:~~ *italics*.

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Anaesthetic and respiratory equipment — Nebulizing systems and components

1 Scope

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 whole or in part, and are normatively referenced in all of their content constitutes requirements of this document and are indispensable for its application. 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 9170-1](#), *Terminal units for medical gas pipeline systems — Part 1: Terminal units for use with compressed medical gases and vacuum*

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~~ISO 18082, Anaesthetic and respiratory equipment — Dimensions of non-interchangeable screw-threaded (NIST) low pressure connectors for medical gases~~

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

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

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

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

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~~ISO 80369-3, Small bore connectors for liquids and gases in healthcare applications — Part 3: Connectors for enteral applications~~

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~~ISO 80369-5, Small bore connectors for liquids and gases in healthcare applications — Part 5: Connectors for limb cuff inflation applications~~

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~~ISO 80369-7, Small bore connectors for liquids and gases in healthcare applications — Part 7: Connectors for intravascular or hypodermic applications~~

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~~IEC 60601-1:2005+AMD1:2012+AMD2:2020, Medical electrical equipment — Part 1: General requirements for basic safety and essential performance~~

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~~CGA V 5-2005, Diameter Index Safety System — Noninterchangeable Low Pressure Connections for Medical Gas Applications~~

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3 Terms and definitions

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

ISO and IEC maintain ~~terminological~~**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/><https://www.electropedia.org/>

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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.

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3.2

aerosol output

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

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aerosol outlet port
aerosol outlet port

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

3.4

aerosol output rate
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.

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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

Clause 4 of 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.

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

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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

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

Clause 5 of 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

Clause 6 of ISO 18190:2016, Clause 6 applies.

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