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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.

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 27427 was prepared by Technical Committee ISO/TC 121, *Anaesthetic and respiratory equipment*, Subcommittee SC 2, *Airways and related equipment*.

This second edition cancels and replaces the first edition (ISO 27427:2009), of which it constitutes a minor revision.

The following changes were made:

— a new subclause 4.1.2 (Clinical evaluation) was added;

— a new subclause 4.8 (Usability) was added and, as a result, two new references were added in Clause 2;

— 5.1.2 a) was updated;

— a new item 5.1.2 d) was added and the subsequent items were renumbered;

— in 5.1.2, a new item (o) was added;

— in 5.3.2, two new items (u and v) were added;

— a note was added to 6.1.2.

In addition, several minor editorial changes were made.

Introduction

Nebulizers are widely used to deliver drugs, in an **aerosol** form, to humans through the respiratory system. These drugs may be in the form of a solution, suspension or emulsion. **Aerosol** inhalation is the preferred route of administration of some drugs. Some drugs are intended for treatment of systemic disease and other drugs are intended to treat respiratory diseases. To achieve the intended treatment, **aerosol** particles may need to be 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** must be defined by the manufacturer and specified in the accompanying documentation. **Nebulizers** are also used for diagnostic purposes using radioisotopes, and for lung challenge tests and the delivery of vaccines.

This International Standard is based on the European Standard EN 13544-1:2007. This International Standard was developed to cover “general purpose” **nebulizers**. It was specifically written to ensure that the results of the various tests declared by the manufacturer were meaningful to the users and buyers of **nebulizers**.

The objectives of this International Standard are to ensure:

— the 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;

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

Important changes were made to the original EN standard in recognition of the advances in test devices such as lasers and low-flow impactors that allow manufacturers to use different test methods, provided these alternate methods are validated against the methods specified in this International Standard.

Terms defined in this document are set in **bold type**.

Throughout this International Standard, text for which a rationale is provided in Annex A is indicated by an asterisk (*).

Anaesthetic and respiratory equipment — Nebulizing systems and components

1 *Scope

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

This International Standard includes **gas-powered nebulizers** which can be powered by, for example, 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 International Standard does not apply to devices intended for nasal deposition.

This International Standard does not apply to devices intended solely to provide humidification or hydration by providing water in **aerosol** form.

*This International Standard does not apply to drug-specific **nebulizers** (e.g. metered dose inhalers, metered liquid inhalers, dry powder inhalers and their components).

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 594-1, *Conical fittings with a 6 % (Luer) taper for syringes, needles and certain other medical equipment — Part 1: General requirements*

ISO 594-2, *Conical fittings with 6 % (Luer) taper for syringes, needles and certain other medical equipment — Part 2: Lock fittings*

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

ISO 5356-2, *Anaesthetic and respiratory equipment — Conical connectors — Part 2: Screw-threaded weight-bearing connectors*

ISO 5359, *Low-pressure hose assemblies for use with medical gases*

ISO 5361-1, *Tracheal tubes — Part 1: General requirements*

ISO 7000, *Graphical symbols for use on equipment — Index and synopsis*

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*

ISO 9276-2, *Representation of results of particle size analysis — Part 2: Calculation of average particle sizes/diameters and moments from particle size distributions*

ISO 10524-1, *Pressure regulators for use with medical gases — Part 1: Pressure regulators and pressure regulators with flow-metering devices*

ISO 10524-3, *Pressure regulators for use with medical gases — Part 3: Pressure regulators integrated with cylinder valves*

ISO 10524-4, *Pressure regulators for use with medical gases — Part 4: Low-pressure regulators*

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

ISO 11135-1, *Sterilization of health care products — Ethylene oxide — Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices*

ISO 11137-1, *Sterilization of health care products — Radiation — Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices*

ISO 11137-2, *Sterilization of health care products — Radiation — Part 2: Establishing the sterilization dose*

ISO 11137-3, *Sterilization of health care products — Radiation — Part 3: Guidance on dosimetric aspects*

ISO 14971:2007, *Medical devices — Application of risk management to medical devices*

ISO 15001, *Anaesthetic and respiratory equipment — Compatibility with oxygen*

ISO 15002, *Flow-metering devices for connection to terminal units of medical gas pipeline systems*

ISO 15223, *Medical devices — Symbols to be used with medical device labels, labelling and information to be supplied*

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*

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

IEC 60601-1:2005, *Medical electrical equipment — Part 1: General requirements for basic safety and essential performance*

IEC 60601-1-2, *Medical electrical equipment — Part 1-2: General requirements for basic safety and essential performance — Collateral standard: Electromagnetic compatibility — Requirements and tests*

IEC 60601-1-6, *Medical electrical equipment — Part 1-6: General requirements for basic safety and essential performance — Collateral standard: Usability*

IEC 62366, *Medical devices — Application of usability engineering to medical devices*

EN 556-1, *Sterilization of medical devices — Requirements for medical devices to be designated "STERILE" — Part 1: Requirements for terminally sterilized medical devices*

ENV 737-6, *Medical gas pipeline systems — Part 6: Dimensions and allocation of probes for terminal units for compressed medical gases and vacuum*

EN 13544-2, *Respiratory therapy equipment — Part 2: Tubing and connectors*

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

3 Terms and definitions

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

3.1
aerosol
suspension of particles in gas

NOTE 1 Particles can be liquid or solid.

NOTE 2 The gas can be the driving gas or ambient air.

3.2
aerosol output
amount of **aerosol** delivered to the patient by the **nebulizing system** for the given fill volume

3.3
aerosol output rate
amount of **aerosol** delivered to the patient by the **nebulizing system** per unit of time

3.4
breath-actuated nebulizing system
nebulizer triggered by a respiratory parameter

NOTE Examples of this classification are to be found in Annex G.

3.5
continuous nebulizing system
nebulizer in which **aerosol** is delivered continuously over multiple inhalation/exhalation breathing cycles or over long periods

3.6
electrically-powered nebulizer
nebulizer that operates by means of electrical power

NOTE **Electrically-powered nebulizer** includes ultrasonic, vibrating mesh and capillary-type devices

3.7
gas-powered nebulizer
nebulizer in which the **aerosol** is generated by compressed gas

3.8
liquid container
part of the **nebulizer** that contains the liquid for nebulization

3.9
manually-powered nebulizer
nebulizer that operates by means of human power

3.10
mass median aerodynamic diameter
MMAD
maximum particle size at which 50 % of the **aerosol output** is delivered to the respiratory tract

3.11
maximum fill volume
maximum volume of liquid, expressed in millilitres, in the **liquid container** when the **nebulizer** is filled to its maximum filling level

3.12
nebulizer
device that converts a liquid to an **aerosol** of a controlled particulate size range

3.13
nebulizing system
device, including the **nebulizer** and all other components, required to make the **aerosol** available for inhalation

3.14
respirable fraction
amount of drug (in micrograms) contained in particles with sizes less than 5 µm

3.15
respirable range
aerosol particle sizes from 0,5 µm to 5,0 µm

3.16
validation
confirmation through the provision of objective evidence that the requirements for a specific intended use or application have been fulfilled

NOTE 1 The term “validated” is used to designate the corresponding status.

NOTE 2 The use conditions for **validation** can be real or simulated.

4 General requirements and requirements for test

4.1 Risk management

4.1.1 General

Nebulizing systems and **nebulizers** shall, when transported, stored, installed, operated in normal use and maintained according to the instructions of the manufacturer, cause no safety hazard which could be reasonably foreseen using risk management procedures in accordance with ISO 14971 and which is connected with their intended application, in normal and in single fault condition.

NOTE A situation in which a fault is not detected is considered a normal condition. Fault conditions/hazardous situations might remain undetected over a period of time and, as a consequence, might lead to an unacceptable risk. In that case, a subsequent detected fault condition needs to be considered as a single fault condition. Specific risk control measures need to be determined within the risk management process to deal with such situations.

4.1.2 Clinical evaluation

If applicable, a clinical evaluation shall be performed and documented in the risk management file.

Check compliance by inspection of the risk management file.

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 are specified in Annexes C and D.

4.2.2 Alternative test methods

The manufacturer may use type-test methods for **aerosol output, aerosol output rate** and particle sizing different from those specified in Annexes C and D.

Alternative test methods shall be **validated** against the test methods in Annexes C and D to demonstrate equivalency.

Demonstration of equivalency shall be included in the technical documentation of the manufacturer.

Evidence shall be provided upon request, e.g. to regulatory authorities.

4.3 Electrical safety

A **nebulizing system** that utilizes electrical power shall meet the requirements given in IEC 60601-1, in addition to the requirements given in this International Standard.

Check compliance by application of the tests of IEC 60601-1.

4.4 Mechanical safety

Nebulizing systems shall comply with Clause 9 of IEC 60601-1:2005.

Check compliance by inspection.

4.5 Pneumatic safety

If it is declared by the manufacturer that a **nebulizer** is intended to be connected directly to a pipeline system complying with ISO 7396-1 or a pressure regulator complying with ISO 10524-1 or ISO 10524-3, the **nebulizer** shall meet the requirements of this International Standard for a pneumatic power supply having a range of 280 kPa (2,8 bar) to 600 kPa (6 bar) and shall not cause a safety hazard under single fault conditions of the medical gas supply, i.e. up to 1 MPa (10 bar) inlet pressure.

4.6 Protection against inadvertent adjustments

Means of protection against inadvertent adjustment of controls which can create a hazardous output shall be provided.

NOTE Mechanical control techniques, such as locks, shielding, friction-loading and detents, are considered suitable. Pressure-sensitive finger pads, capacitive finger switches and microprocessor-oriented “soft” controls or a specific sequence of key or switch operations are also considered suitable.

Check compliance by visual inspection following the instructions for use.

4.7 Protection against infection

All parts of the **nebulizing system** subject to contamination by exhaled gases and intended to be reused by different patients shall be disinfectable or sterilizable.

4.8 Usability

The manufacturer shall address, in a usability engineering process, the risk resulting from poor usability according to IEC 60601-1-6 and IEC 62366.

Check compliance by inspection of the usability engineering file.

5 Marking and instructions for use

5.1 Marking

5.1.1 General

a) All flow-direction-sensitive components, breathing attachments or parts (e.g. facemask or mouthpiece one-way valve, etc.) shall be either clearly and durably marked with an arrow showing the direction of gas flow if operator-detachable, manufactured to prevent incorrect assembly or permanently attached.

b) If gas-specific, the inlet and outlet shall be identified by clear and durable marking.

5.1.2 Marking of devices, labels and packaging

Devices, labels and/or packaging shall contain the following:

a) the name or trademark and address of the manufacturer; for devices imported into the European Union, the following applies: the name and address of the person responsible and of the authorized representative of the manufacturer established within the European Community shall be provided with the device or with the accompanying document;

b) device identification and content information;

c) an indication that the device is sterile, if appropriate;

d) for single-use devices, the manufacturer shall disclose the risks associated with reusing in the instructions for use or upon request;

NOTE The manufacturer's attention is drawn to the regulatory provision requiring that the indication of single use must be consistent across the Community.

e) device packaging and/or labelling to differentiate between the same or similar products, both sterile and non-sterile, placed on the market by the same manufacturer;

f) the batch code, if appropriate;

g) the expiry date, if the device is sensitive to storage or shelf-life;

h) an indication that the device is for single use, if appropriate;

i) any special storage and/or handling conditions;

j) any warning and/or precaution to take, e.g. compatibility with the use of oxygen mixtures and compatibility between oxygen and administered drugs;

k) the year of manufacture, except for those covered by f);

l) the recommended method(s) of cleaning and disinfection or sterilization, if appropriate;

m) for packages containing parts made of antistatic or conductive material, the word “ANTISTATIC” or “CONDUCTIVE”, if appropriate;

n) the **liquid container** of the **nebulizer** shall be marked at the **maximum fill volume** level; this shall be defined in the instruction for use [see 5.3.2 a) i)];

o) if phthalates are incorporated in parts of the medical devices coming directly or indirectly into contact with the patient, the device shall be labelled accordingly. If such devices are used for the treatment of children or of pregnant or nursing women, the residual risk has to be identified and stated in the instructions for use.

5.1.3 Marking of controls and instruments

a) Gas supply pressures shall be displayed in kilopascals.

b) Pressures in breathing systems shall be displayed in pascals ×100.

c) Flows shall be displayed in litres per minute.

d) If supplied, air entrainment/oxygen dilution valves shall be marked in % O_2 (oxygen).

5.2 Symbols

ISO 7000, ISO 15223 and Clause 6.4 of IEC 60601-1:2005 apply.

5.3 Instructions for use

5.3.1 *General

Nebulizers, nebulizing systems and parts thereof shall be accompanied by instructions for use which shall include the information given in 5.3.2.

5.3.2 Disclosures

a) The purpose and the intended use of the device and parts thereof, including the power and/or control devices.

b) The types of liquid (e.g. solution and/or suspension and/or emulsion) the device is designed to nebulize.

c) The distribution of particles, in terms of mass, within each of the following size ranges: % > 5 µm, % 2 µm to 5 µm, % < 2 µm.

d) The **mass median aerodynamic diameter** (**MMAD**) as derived from the particle size distribution curve (see Figure D.2).

e) The **respirable fraction** performance of the **nebulizer**.

f) The **aerosol output** and **aerosol output rate** at the **maximum fill volume** under test conditions defined in C.1.1. In addition, for **gas-powered nebulizers**, the **aerosol output** and **aerosol output rate** at the minimum and maximum driving gas flows with the corresponding pressures under test conditions defined in C.1 and C.2.

g) Disclosure of the residual volume (in millilitres), when tested in accordance with the test method described in Annex C.

h) For a **breath-actuated nebulizer**, the method and relevant sensitivity.

i) A statement that using a solution, suspension or emulsion different from that recommended by the manufacturer, in particular for a suspension and/or high-viscosity solution, may alter the particle size distribution curve, the **mass median aerodynamic diameter**, **aerosol output** and/or **aerosol output rate**, which may be different from those disclosed by the manufacturer.

j) The recommended **maximum fill volume**.

k) The maximum A-weighted sound pressure level, as derived from the test method in 9.6.2.1 of IEC 60601-1:2005.

l) If hand-held, an indication of the spatial orientation (e.g. vertical, horizontal, inverted) at which the **nebulizer** continues to function as intended.

m) Whether the **nebulizer** is suitable for use in anaesthetic breathing systems or lung ventilator breathing systems.

n) If applicable, the maximum temperature above ambient reached in the nebulizing chamber in all operating conditions.

o) Interdependence of controls, if applicable.

p) The pressure and flow characteristics of any gas power outlet under the worst-case conditions stated by the manufacturer.

q) The specified range of flows required from any gas source, if applicable.

r) A statement of the composition and dryness specification for all gases to be supplied to the **nebulizer**, if relevant.

s) Details of non-return valves and pressure-relief valves and their characteristics, if fitted.

t) The lifetime of the reusable parts.

u) If the device is used in the treatment of children or pregnant or nursing women, the residual risk of using phthalates incorporated into the devices that come directly or indirectly into contact with the patient has to be identified and stated in the instructions for use.

v) The instructions for use shall contain the date of issue or the latest revision.

Check compliance by inspection.

5.3.3 Materials compatibility

a) A statement that the materials used for the components may not be compatible with solutions, suspensions or emulsions different from those recommended by the manufacturer, in particular for suspensions and high-viscosity solutions.

b) A warning that oxygen or oxygen mixtures (O_2 > 23 %) should not be used as driving gas, if applicable.

5.3.4 Driving gas supply

a) The recommended driving gas.

b) The minimum and maximum recommended driving gas pressures and flows.

5.3.5 Cleaning, disinfection and sterilization

The instructions for use shall contain information on the following:

a) Methods of cleaning, disinfection and/or sterilization prior to use.

b) The number of cycles of cleaning, disinfection and/or sterilizations the **nebulizing system** will withstand.

5.3.6 Dismantling and reassembling

The manufacturer shall recommend the following:

a) Procedures for reassembly, if applicable.

b) A functional test of operation to be carried out after reassembly and before use.

5.3.7 Monitoring, alarm and protection devices

The instructions for use shall contain:

a) a description of the methods of verifying alarm functions;

b) details of any pressure-relief valves fitted.

5.3.8 Electromagnetic compatibility

If applicable, the instructions for use shall include a warning statement to the effect that the functioning of this **nebulizer** may be affected by electromagnetic interference exceeding the levels specified in IEC 60601-1-2.

5.3.9 Device disposal

The instructions for use shall include information about any precautions to be taken if there is a specific unusual risk associated with the disposal of a device.

5.3.10 Parts not integral to the nebulizing system

The instructions for use shall include:

a) a list of the parts that are not integral parts of the system and are necessary for correct use;

b) a statement that these parts shall comply with the relevant requirements of this International Standard.

6 Construction requirements

6.1 Materials

6.1.1 Materials for construction shall be compatible with the manufacturer's recommended gas(es) or gas mixture(s) and, if applicable, in compliance with ISO 15001.

While intended to be used with drugs and cleaning agents, materials should be chosen to minimize risks due to toxicity.

6.1.2 **Nebulizer** components that come into contact with cleaning agents, sterilants, medical gases and medicaments recommended by the manufacturer shall not degrade, affect performance or present a hazard for the **nebulizer**'s intended use.

NOTE Attention is drawn to substances which are carcinogenic, mutagenic or toxic to reproduction. See also 5.3.2.

6.1.3 The recommended cleaning agents shall not affect the performance of the **nebulizer**.

6.1.4 Components that come into contact with the **aerosol** or the liquid to be nebulized shall not have any lasting visible damage from the recommended cleaning or sterilizing agents.

Check compliance by inspection.