INTERNATIONAL STANDARD

**ISO 27427**

Second edition
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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.

## 6.2 Connectors

### 6.2.1 Driving gas inlet connectors

The driving gas inlet connector 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) the nut and nipple of a non-interchangeable screw-threaded (NIST) connector complying with ISO 5359;

b) the nut and nipple of a DISS connector complying with ISO 5359 (CGA V-5-2005 diameter index safety system non-interchangeable connectors for medical gas applications);

c) a probe complying with ISO 9170-1, ENV 737-6 or the relevant national standard;

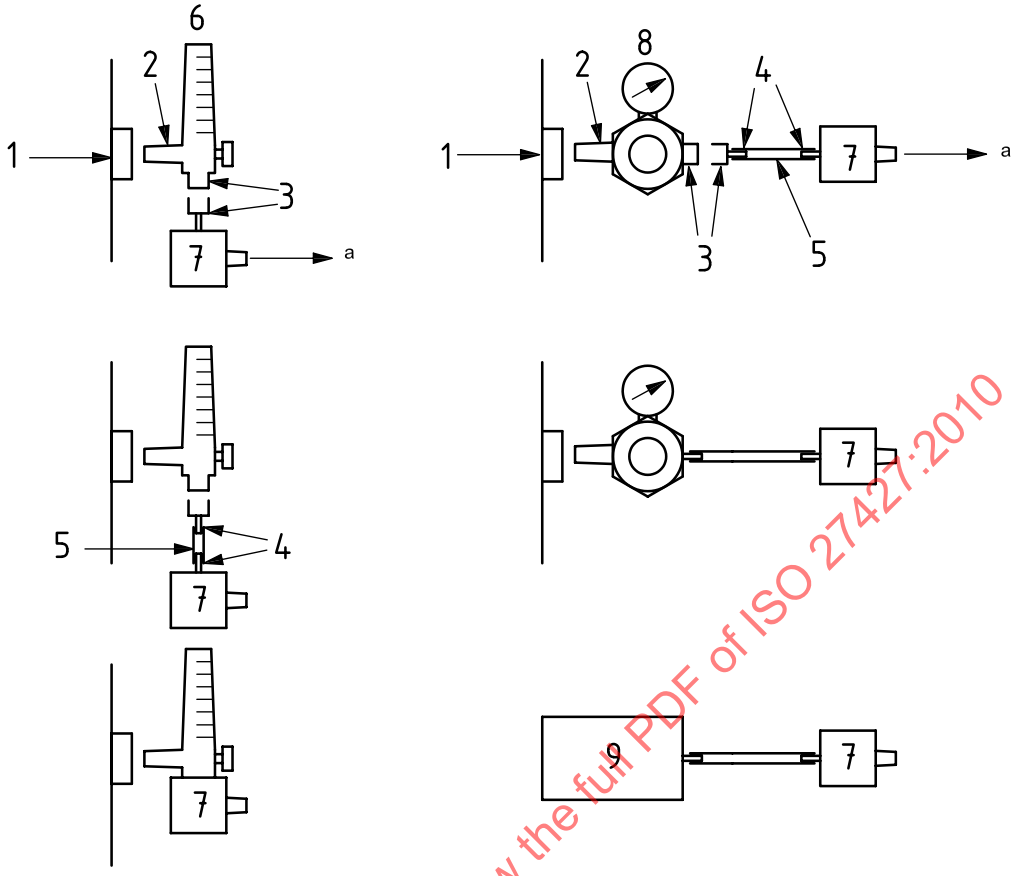
d) a threaded connector complying with EN 13544-2;

e) a nipple complying with EN 13544-2.

### 6.2.2 Nebulizer breathing system connectors

a) If conical, these shall be 8,5 mm, 15 mm, or 22 mm size connectors complying with ISO 5356-1 or ISO 5356-2.

b) If proprietary, these shall not engage with conical connectors complying with ISO 5356-1 or ISO 5356-2 unless they comply with the engagement, disengagement and leakage requirements of ISO 5356-1 or ISO 5356-2.

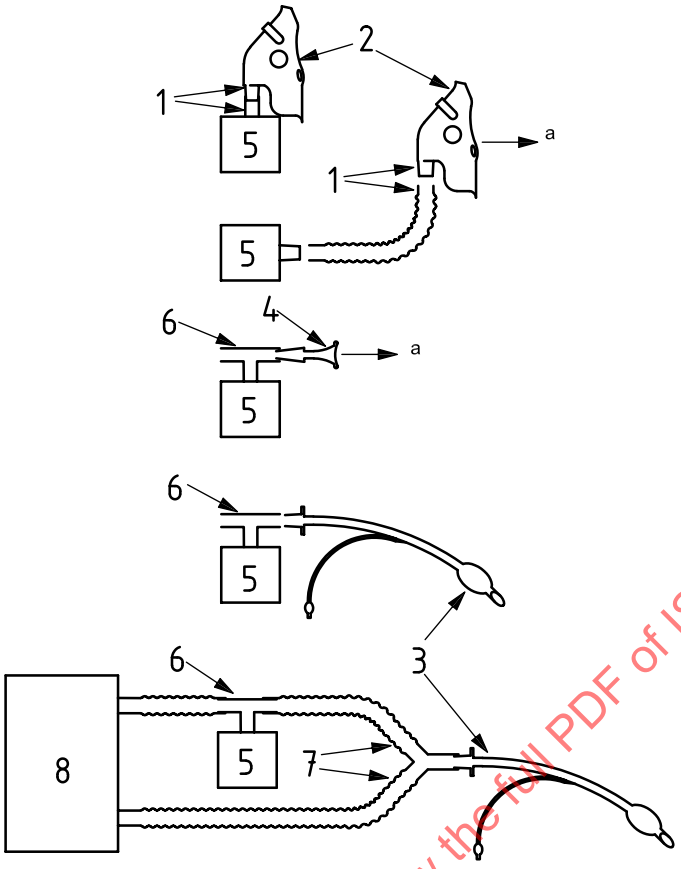



**Key**

1 terminal unit complying with ISO 9170-1 (on a pressure regulator or on an MGPS)
2 probe or DISS or NIST – ISO 9170-1, ENV 737-6, ISO 5359
3 threaded connector – EN 13544-2
4 nipple – EN 13544-2
5 hose – EN 13544-2
6 flowmeter – ISO 15002
7 nebulizer
8 pressure regulator – ISO 10524-4
9 compressor

[a] To the patient.

**Figure 1 — Examples of driving gas inlet connectors for nebulizer systems**




**Key**

1 ISO conical connectors – ISO 5356-1
2 aerosol mask, vented
3 tracheal tube connector – ISO 5361-1
4 mouthpiece
5 nebulizer
6 tee piece
7 ventilator breathing circuit
8 ventilator

[a] To the patient.

**Figure 2 — Examples of breathing system connectors for nebulizer systems**



### 6.2.3 Nebulizer outlet connector

The outlet connector of the **nebulizer** shall be one of the following.

a) If intended to be connected to a breathing system or breathing tube, it shall be a 22 mm connector complying with ISO 5356-1.

b) Proprietary **nebulizer** connectors shall not be compatible with conical connectors complying with ISO 5356-1 or Luer connectors complying with ISO 594-1 and ISO 594-2.

#### 6.2.4 Flow-direction-sensitive connectors

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.

#### 6.2.5 Small-bore nebulizer connector

Any small-bore connector of the **nebulizing system** shall not be compatible with 6 % conical (Luer) connectors as defined in ISO 594-1 and ISO 594-2.

### 6.3 Rotary controls

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

## 7 Cleaning, sterilization and disinfection

a) If provided sterile, the **nebulizing system** and components shall have been sterilized using an appropriate, validated method described in: ISO 11135-1, ISO 11137-1, ISO 11137-2, ISO 11137-3, ISO 17665-1, EN 556-1.

b) Evidence about the method(s) to ensure the intended level of cleanliness of the **nebulizing system** components during production and supply shall be given by the manufacturer upon request.

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

d) The relevant performance tests such as **aerosol output, aerosol output rate** and particle size testing shall be repeated after the given number of cleaning and/or sterilization cycles to validate the **nebulizer** performance.

## 8 Biocompatibility

a) Parts of the **nebulizing system** intended to come into contact with biological tissues, cells, body fluids or breathing gases shall be assessed and documented according to the guidance and principles given in ISO 10993-1.

b) All parts of the **nebulizer** shall be designed and manufactured to minimize health risks due to substances leached from the device during use.

c) **Nebulizing systems** shall be free of volatile organic compounds and particulate matter throughout the operating life of the equipment.

d) **Nebulizing systems** shall comply with volatile organic compounds and particulate matter testing, if required by regional or national competent authorities.

Check compliance by inspection of the relevant **validation** reports. Subclause 11.7 of IEC 60601-1:2005 applies.

# Annex A
(informative)

# Rationale

## General

This annex provides a concise rationale for the important requirements of this International Standard and is intended for use for those who are familiar with the subject of this International Standard but who have not participated in its development. An understanding of the reasons for the main requirements is considered essential for its proper application. Furthermore, as clinical practices and technologies change, it is believed that a rationale for the present requirements will facilitate any revisions of this International Standard necessitated by those developments.

The clauses in this annex have been so numbered to correspond to the clauses in this International Standard to which they refer. The numbering is, therefore, not consecutive.

## A.1 Scope

The essence of this International Standard is to describe the characteristics and requirements of a general purpose **nebulizer** that can be used with a variety of medicinal substances. It is expected that the selection of the **nebulizer** be based on the requirements and characteristics developed in this International Standard and declared in the manufacturer's instructions for use.

Nasal deposition devices are also excluded, as they are not considered general purpose **nebulizers**.

There may be times when a device falls under the scope of either ISO 27427 or ISO 20072. The committee envisions that the intended use of the product and the risk assessment of the device will derive which standard the manufacturer chooses to qualify the device.

### A.4.2 Test methods and alternatives

Various methods are in use for presenting the particle size distribution of **nebulizers** (see Annex B).

#### A.5.3.1 General

The **respirable fraction**, as defined in 3.14, is an important parameter because, along with the **aerosol output**, it gives a single physical characteristic that allows the comparison of the performance of **nebulizing systems**.

#### A.C.2.2 Test principles

A treatment session using a **nebulizer** requires the patient to breathe in and out of the **nebulizer** for a duration of between approximately 5 min and 15 min (depending on the medication used) while the **nebulizer** is running. During this time, the **nebulizer** is continuously producing **aerosol**. When the patient inhales **aerosol**, it is taken up in the lungs. However, when the patient exhales, some **aerosol** is driven out of the **nebulizer** and lost. Thus, only a certain fraction of **aerosol** produced by the **nebulizer** can be taken up by the patient. The test described in this section collects the amount of **aerosol** exiting at the **nebulizer** mouthpiece while the **nebulizer** is subjected to a simulated breathing pattern.

### A.C.2.3 Test equipment

A sine pump is used when determining **aerosol output** from a **nebulizer** in order to reasonably estimate the mass of aerosolized active pharmaceutical ingredient provided at the exit of the **nebulizer system** under simulated conditions of breathing.

### A.C.2.4 g) Test method

Measurements of mass (weight) rather than volume alone correct for evaporative losses.

## A.D.2 Test principle

A continuous suction pump is used for nebulized **aerosol** size testing as impactors for performing these measurements operate at a constant “inhalation” flow rate in order to reasonably estimate **aerosol** size.

# Annex B
(normative)

# Diameters of respirable fraction particles

In general, it is considered that **aerosol** particles with an aerodynamic diameter of

— > 5 µm will result in deposition in the upper airways,

— 2 µm to 5 µm will result in deposition in the lower airway, and

— 0,5 µm to 2 µm will result in deposition in the alveoli.

**Aerosol** particle sizing can be defined in terms of **Mass Median Aerodynamic Diameter** (**MMAD**) and Geometric Standard Deviation (GSD). These values can be interpolated from the cumulative particle size distribution curve as follows.

**MMAD** – Note the particle size at which the line crosses the 50 % mark.

GSD – This should be calculated only if the particle size distribution curve is reasonably straight between 10 % and 90 %, showing that the **aerosol** is log-normally distributed. Where a straight line is a good fit to the data, the calculation of GSD is performed by noting the particle size X at which the line crosses the 84,13 % mark and the particle size Y at which the line crosses the 15,87 % mark.

Then the GSD = $(X/Y)^{0,5}$.

Methods of deriving information from data that are based on interpolation from a graph are inevitably subject to some degree of approximation.

Rigorous mathematical methods of analysis are described in ISO 9276-2. These methods are readily performed by computer, including the generation of the particle size distribution graph.

# Annex C
(normative)

# Test methods for aerosol output and aerosol output rate

## C.1 Aerosol output

### C.1.1 Test conditions and test equipment

The ambient conditions shall be:

— temperature: (23 ± 2) °C;

— relative humidity: 45 % to 75 %;

— pressure: from 86,0 kPa to 106,0 kPa.

For the test equipment, please refer to C.2.3.

### C.1.2 Test principle

The **nebulizer** under test is connected to the same equipment as in C.2.3, filled with albuterol 1 % (10 mg/ml) (M/V), which is equivalent to albuterol sulfate 1,2 % (M/V) and operated until nebulization ceases. A quantitative chemical analysis is then applied and the output is expressed as millilitres of albuterol 1 % (M/V).

### C.1.3 Test equipment

For the test equipment, please refer to C.2.3.

### C.1.4 Test method

Use the test method described in C.2.4, but continue until nebulization ceases. If necessary, interrupt the test and replace the filter before saturation occurs.

The **aerosol output** shall be taken:

— for **gas-powered nebulizers** 1 min after the beginning of sputtering, or

— for **electronic nebulizers** at the end of the operation.

### C.1.5 Test results

The test results shall include:

— for **gas-powered nebulizers**, the test gas employed;

— the fill volumes and flow rates used;

— the **aerosol output** expressed as millilitres of albuterol 1 % (M/V) solution.

## C.2 Aerosol output rate

### C.2.1 Test conditions

Ambient conditions as given in C.1.1.

### C.2.2 *Test principles

The **nebulizer** is filled with a solution of known concentration of albuterol, connected to a sine pump (to simulate respiratory flow) and operated for a known time, during which the **aerosol** is collected on a filter. The amount of albuterol on the filter is then quantified by chemical analysis.

This figure, divided by the time of the test, provides the **aerosol output rate**.

### C.2.3 Test equipment

The test equipment (see the schematic diagram given in Figure C.1) shall comprise:

— a filter holder;

— a sine pump, which creates a cycle of: frequency, $f$, = 15 breaths/min; I/E ratio = 1/1; tidal volume ($V_t$) = 500 ml measured at the output of the filter;

— solution of albuterol 1 % (M/V) concentration;

— a breathing system filter complying with ISO 23328-1 with a filtration efficiency > 98 % of particles less than 10 µm;

NOTE Suitable filters are high-efficiency polypropylene filters (product K248 of 3M) [1)].

— a dead space of the equipment 10 % or less of the tidal volume (between the patient interface and the filtering surface);

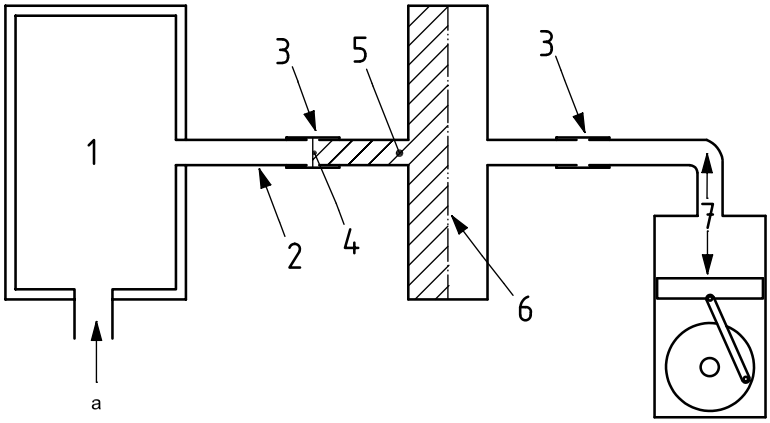
— for **gas-powered nebulizers**, a driving gas of medical air unless the **nebulizer** is exclusively designed to be powered by a compressor at ambient conditions described in C.1.1, as defined in ISO 7396-1;

— a means of extracting albuterol from filters and other components and quantitative analysis apparatus calibrated in 1 % albuterol (M/V) to an accuracy of ±5 % of reading.

The **aerosol** and **aerosol output** test for a pneumatic **nebulizer** shall be driven by the gas and at the flow rate recommended by the manufacturer.



1) This information is given for the convenience of users of this International Standard and does not constitute an endorsement by ISO of the product named.




**Key**

1 nebulizer system filled with 1 % albuterol solution (see note)
2 connection to the patient interface
3 dismountable connectors
4 patient interface
5 dead space
6 collection filter
7 sine pump

[a] Recommended driving gas inlet.

NOTE The recommended delivery system can terminate e.g. in a mouthpiece or facemask. The dismountable connector (3) at the inlet to the filter holder should provide a matching adaptor to make a leak-free joint.

**Figure C.1 — Schematic diagram showing the equipment for testing the aerosol output and aerosol output rate**



### C.2.4 Test method

a) Stabilize all parts of the **nebulizer system**, fluids and test equipment at the ambient conditions as described in C.1.1 before use.

b) Perform a series of tests with the **nebulizer** filled with albuterol (1 %) (M/V) solution to the fill volume of 2 ml or to the fill volume recommended by the manufacturer.

c) By means of dismountable connectors, connect the outlet of the **nebulizing system** to the filter and its holder, and the latter to the sine pump, as shown in Figure C.1.

d) Switch on the pump and, 10 s later, the **nebulizer**.

e) Run the **nebulizer** for (60 ± 1) s, switch off the **nebulizer** and, 5 s later, the pump.

f) Dismantle the filter, the filter holder and the dismountable connectors from the outlet of the **nebulizing system** to the filter holder.

g) *Extract and measure the mass of albuterol in the components downstream of the outlet of the **nebulizer**, including the filter.

### C.2.5 Test results

The test results shall include:

a) for a **gas-powered nebulizer**, the test gas employed;

b) the **filling volume** and flow rate used;

c) the **aerosol output** expressed as millilitres of albuterol 1 % (M/V) solution per minute (see also Annex E);

d) the residual volume.

# Annex D
(normative)

# Test methods for particle sizing

## D.1 Ambient conditions

Ambient conditions shall be as given in C.1.1.

## D.2 *Test principle

The **nebulizer** is filled with a specified albuterol solution.

For **gas-powered nebulizers**, the compressed driving gas is supplied through the **nebulizer** at a given flow rate. The **aerosol** is released from the **nebulizer** and drawn along a T-piece by a continuous flow suction system from which it is either sampled into the cascade impactor or collected on a filter.

After sampling the nebulized **aerosol**, the collection substrates are removed from the impactor and the amount of albuterol determined.

A multistage cascade impactor (as described in D.3) is used to evaluate the particle distribution of the **aerosol** for a type test of the **nebulizer.**

Alternative type-test methods for particle sizing may be used if **validated** as described in 4.2.

## D.3 Test equipment

The test equipment (see the schematic diagram in Figure D.1) shall comprise:

a) the **nebulizer** under test;

b) a cascade impactor[2] with:

   1) calibration data at a flow not exceeding 15 l/min;

   2) at least eight stages to estimate **respirable fraction**;

   3) sufficient loading capacity on each stage to estimate the **respirable fraction** and not overloading stages;

   4) no measurable heat transfer-related droplet evaporation;

NOTE 1 The impactor might need to be chilled to avoid this cause of inaccuracy.

2) Several types of impactor are available: Marple, Anderson and Next Generation Impactor (NGI).

5) a 22 mm internal diameter female connector from the impactor, which fits a 22 mm outer diameter T-piece;

6) a calibrated impactor specifying the $D_{50}$ (the aerodynamic diameter of a particle having a 50 % probability of impacting on the collection stage, also called the ECD); and have a $D_{84}$ (the aerodynamic diameter of a particle having an 84 % probability of impacting on the collection stage) that is less than $1{,}3 \times D_{50}$, and a $D_{16}$ (the aerodynamic diameter of a particle having a 16 % probability of impacting on the collection stage) that is greater than $0{,}77 \times D_{50}$;

NOTE 2 Calibration of the impactor must include determination of the $D_{16}$, $D_{50}$ and $D_{84}$ either by the manufacturer or user.

NOTE 3 Selection of the cut points (i.e. $D_{50}$) for the impactor must include at least two stages with $D_{50}$s greater than the **MMAD** of the **aerosol** from the **nebulizer** and two stages with $D_{50}$s less than the **MMAD** of the **aerosol** from the **nebulizer**.

c) a sampling pump and adjustable flowmeter capable of drawing through the cascade impactor a flow specified in the calibration data of the cascade impactor;

d) a tube holding the collection filter;

e) a suction pump that creates a continuous flow sufficient to raise the total flow through the T-piece (Figure D.1, key 6) to 15 l/min ± 1.5 l/min, the surplus flow above the sampling flow to the cascade impactor passing through the collection filter;

NOTE 4 This pump is not required if the cascade impactor is calibrated at 15 l/min.

f) solution of albuterol 1 % in distilled water (at stabilized temperature);

g) a breathing system filter complying with ISO 23328-1 with a filtration efficiency > 98 % of particles less than 10 µm having minimal resistance and which can collect > 98 % of fine particles;

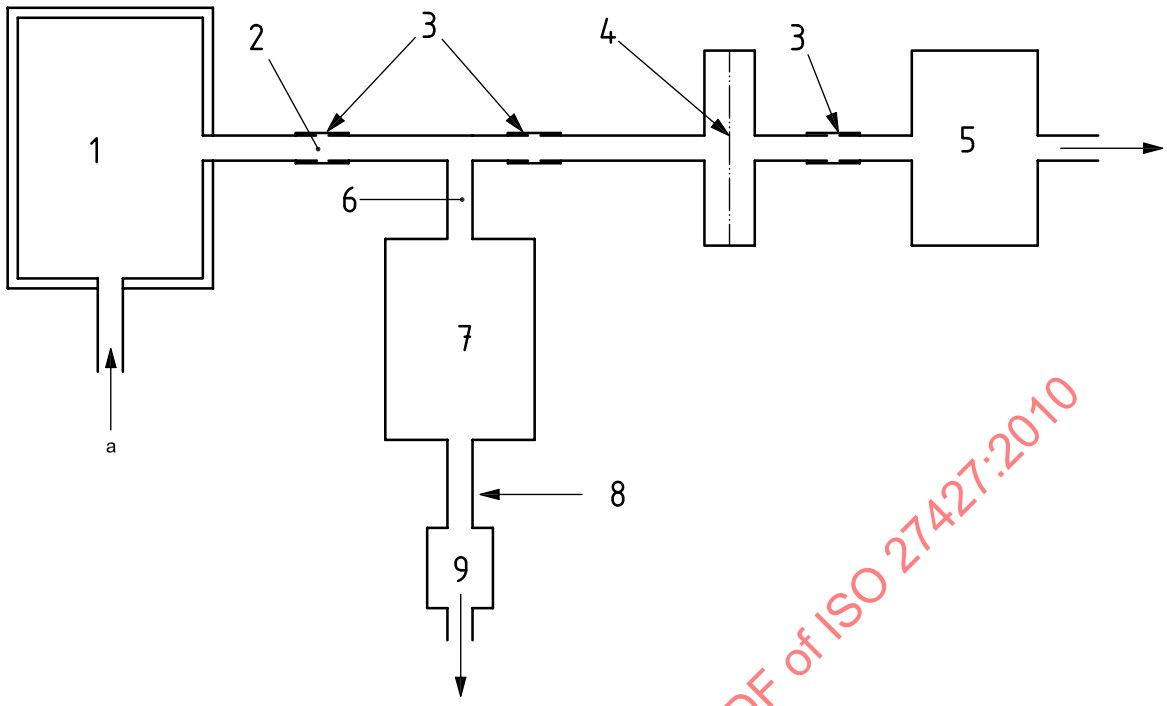
NOTE 5 Suitable filters are high-efficiency polypropylene filters (product K248 of 3M) [3].

NOTE 6 Dead space of the equipment between the patient interface and the filtering surface must be minimal.

h) for **gas-powered nebulizers,** the driving gas specified by the manufacturer (either compressed air from ambient conditions as described in C.1.1 or medical air as defined in ISO 7396-1).



3) This information is given for the convenience of users of this International Standard and does not constitute an endorsement by ISO of the product named.




**Key**

1 nebulizer system filled with albuterol 1 % (M/V)
2 patient interface
3 dismountable connectors
4 collection filter for excess aerosol
5 suction pump
6 T-piece
7 cascade impactor
8 connector to sampling pump
9 sampling pump

[a] Entrained air inlet.

**Figure D.1 — Schematic diagram showing the equipment for testing the particle sizes**

## D.4 Test method

The **nebulizer** is charged with the **maximum fill volume** (within the limits recommended by the manufacturer) of albuterol 1,0 % and connected to the test compressor or air supply in accordance with the manufacturer's instructions.

a) A T-piece is attached to the **nebulizer** chamber outlet.

b) The cascade impactor is dismantled, cleaned (e.g. with distilled water, wiped and allowed to air dry) and reassembled incorporating all the stages of impaction surfaces in accordance with the manufacturer's instructions.

c) Readily dismountable connections are made from the T-piece to the inlet of the connection attached to the cascade impactor and from the outlet of this connection to the collection filter, which is itself connected to a suction pump adjusted to produce a flow of e.g. 15 l/min ± 10 %.

d) An absolute filter (see C.2.3) is interposed between the outlet of the cascade impactor and the sampling pump, the flow of which is set to e.g. 2 l/min ± 10 %.

NOTE 1 During testing, the **nebulizer** and the cascade impactor must be in the position specified by the manufacturer.

NOTE 2 Care must be taken to prevent vibration of the impactor and to minimize perturbation of flow through the test apparatus.

e) The suction and sampling pumps are turned on and allowed to stabilize at the required flows.

f) Start the **nebulizer**.

g) Sampling times can be varied for different **nebulizers** to allow for maximum deposit on each stage without overloading the stages.

NOTE 3 Some experimentation might be needed to establish the optimum period of test, aided by visual recognition of "overload" of an impactor substrate.

h) After sampling for the required time, the **nebulizer** is switched off, followed in a few seconds by the sampling pump and then the suction pump.

i) Dismount the cascade impactor from the remainder of the apparatus.

j) Dismantle the impactor according to the manufacturer's instructions and determine the amount of albuterol on the individual stages of the impactor, the input connection and the outlet filter (see also Annex E).

## D.5 Calculations and results

### D.5.1 Calculations

a) Calculate the total mass of albuterol collected in the impactor as follows in the case of 8 stages:

$$F = m_1 \text{ (including inlet assembly)} + m_2 + m_3 + m_4 + m_5 + m_6 + m_7 + m_8 + m_{\text{filter}}$$

b) Calculate the cumulative collection (%) of albuterol of particle mass undersize as follows:

$c_8 = m_{\text{filter}}/F \cdot 100$; plot this against the $D_{50}$ of stage 8

$c_7 = c_8 + m_8/F \cdot 100$; plot this against the $D_{50}$ of stage 7

$c_6 = c_7 + m_8/F \cdot 100$; plot this against the $D_{50}$ of stage 6 and so forth

where

$F$ is the total mass of albuterol collected in the impactor including the inlet assembly and the filter;

$m_x$ is the mass collected on stage x;

$c_x$ is the cumulative collection in percent of particle undersize.

NOTE A typical set of figures is shown in Table D.1, which includes mean values from the series of tests.

c) Plot the cumulative size distribution on log-probability graph paper as shown in Figure D.2. The utility of the log-probability graph is that the cumulative size distribution can be represented by a straight line fitted through the data points. This is equivalent to the more familiar "S" curve fitted to the data on semi-log graph paper. The probability axis is a linear scale of the "$z$" values (standard deviation units associated with the cumulative area under a normal distribution). An Excel spreadsheet can be used to plot this rather than using log-probability paper by converting the cumulative frequency to $z$ values using the NORMSINV function and plotting the results on a linear axis and the diameter values on a logarithmic axis.

d) Determine the **MMAD** and the GSD as shown in Figure D.2.

The **MMAD** is the diameter vertically below the horizontal intersection of the 50 % cumulative frequency value and the size distribution line. The GSD shall be calculated using the values $D(-1)$ or $D(1)$. The diameter $D(-1)$ is the diameter vertically below the horizontal intersection of the 16 % cumulative frequency value (or the value $-1$ on the probability axis) and the size distribution line; alternatively, the $D(1)$ value [the diameter vertically below the horizontal intersection of the 84 % cumulative frequency value (or the value 1 on the probability axis) and the size distribution line].

The GSD is then the **MMAD**/$D(-1)$ or $D(1)$/**MMAD**.

It is not necessary to plot all the results from the impactor stages to determine the **MMAD** of the **nebulizer**. It is only necessary to plot the two values, one above and one below the 50 % cumulative collection efficiency value, to find the **MMAD** and plot the line representing the size distribution. Plotting more points than that could actually result in the value being determined with less accuracy. Points farther away from the 50 % cumulative value have less accuracy because they represent a smaller fraction of the total mass. Points closer to the **MMAD** will have higher mass and should be determined therefore with greater accuracy. By weighting points with less accuracy with the same weighting as points with more accuracy (i.e. by drawing a best fit line through all the points), the overall accuracy of the determination is reduced. Using only the points representing the highest amount of the mass (i.e. those above and below the **MMAD**) to draw the line ensures higher accuracy even though only two points are used.

### D.5.2 Results

The test results shall include:

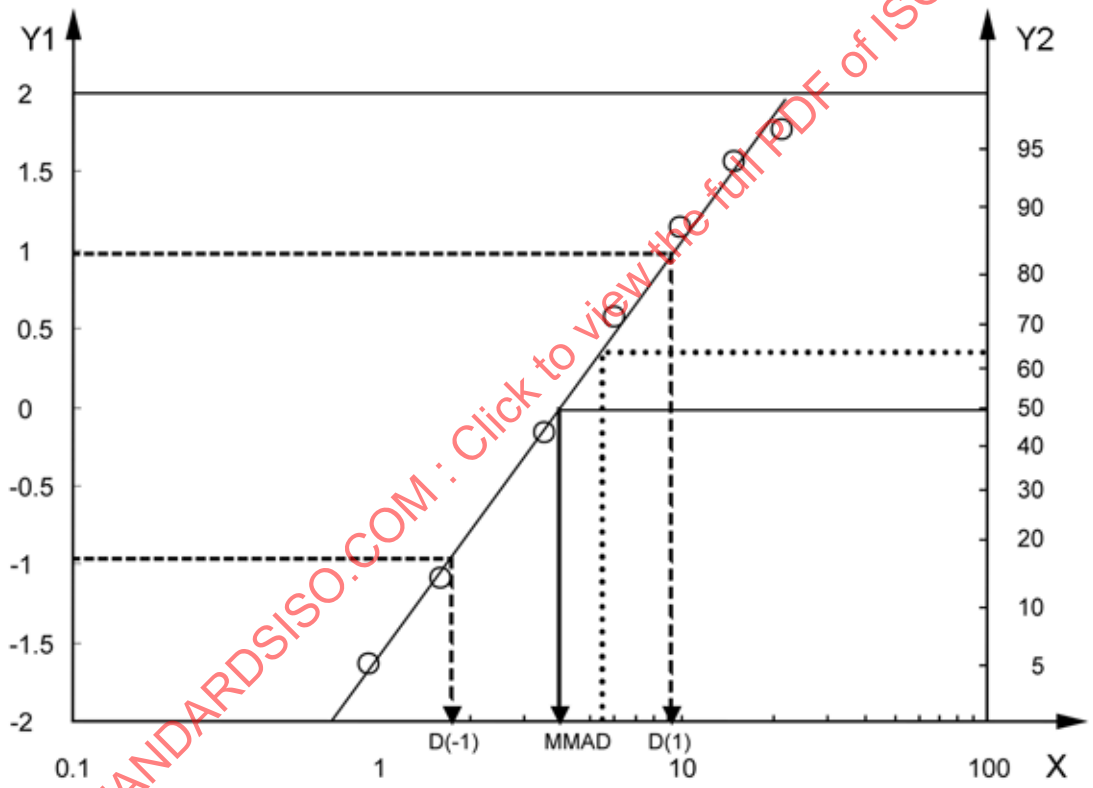
— for **gas-powered nebulizers**, the test gas employed;

— the filling volumes and flow rates used;

— the amount of albuterol deposited on the individual stages of the impactor (including the inlet assembly and the absolute filter).

**Table D.1 — Typical sets of results from repeat measurement of cascade impactor**

| Stage No. | Effective cut-off diameter (µm) | Cumulative particle mass of albuterol under size (%) | | | | |
|---|---|---|---|---|---|---|
| | | Mean | Test 1 | Test 2 | Test 3 | Test 4 |
| 8 | 0,53 | 2,1 | 2,8 | 3,2 | 1,5 | 1,1 |
| 7 | 0,93 | 5,2 | 5,6 | 6,4 | 5,4 | 3,4 |
| 6 | 1,6 | 14,0 | 13,7 | 17,0 | 13,3 | 12,1 |
| 5 | 3,5 | 43,6 | 41,4 | 47,0 | 42,9 | 43,1 |
| 4 | 6,0 | 72,0 | 69,6 | 73,2 | 70,0 | 75,3 |
| 3 | 9,8 | 87,4 | 85,0 | 87,4 | 85,2 | 92,0 |
| 2 | 14,8 | 94,1 | 93,0 | 94,1 | 92,1 | 97,1 |
| 1 | 21,3 | 96,2 | 95,4 | 96,0 | 95,6 | 97,7 |






**Key**

X diameter (µm)

Y1 probability ($z$ values)

Y2 cumulative percent

solid line – MMAD (3,9 µm)

dashed lines – MMAD/$D(-1)$ = GSD or $D(1)$/MMAD = GSD (2,6)

dotted line – cumulative % less than 5 µm (60 %)

NOTE Parameters such as the **MMAD** of 3,9 µm (shown with an arrow) and percent **aerosol** solute mass below 5 µm can be interpolated from the plot – in this case approximately 60 %.

**Figure D.2 — Plot of cumulative size distribution from results in Table D.1**

# Annex E
(informative)

# Test apparatus for leak test

## E.1 General

To establish confidence in the test method, it is recommended that mass balance procedures be incorporated during initial determinations and for occasional checks.

## E.2 Aerosol output rate and aerosol output tests

These tests are for system leaks and overall efficiency of analysis.

Arrange an additional high-efficiency filter and suction system to collect the **aerosol** emitted during the outward phase of the sine pump without imposing resistance on the flow to the sine pump.

a) Declare the fill volume and concentration of the **nebulizer** chamber.

b) After the test, determine by elution and analysis the residual volume, the volume on the inward flow filter and that on the outward flow filter, including all connection components in the elution process.

c) The fill volume of the nebulizing chamber should equal the sum of the residual volume, the volume on the inward flow filter and that on the outward flow filter.

See Figure C.1 for test equipment.

## E.3 Particle size testing

This test on the cascade impactor should be done as a more stringent check on the overall analytical accuracy, as the mass tracer will be much smaller.

Having completed and recorded the results of a series of tests in accordance with D.4 with a given **nebulizer**, repeat the test after assembling the cascade inlet connector directly to the final absolute filter stage (i.e. without any of the intermediate stages or filters).

Compare the total mass from this test with the total mass collected from all stages in the normal tests.

# Annex F
(informative)

# Hazard identification for risk assessment

NOTE This list is not intended to be comprehensive for all devices within the scope of this International Standard, but it provides guidance for risk assessment. Not all hazards will apply to each type of **nebulizer**.

## F.1 Potential hazards associated with the use of nebulizers or nebulizer systems

These hazards are based on reported Adverse Event Reports submitted to the US Food and Drug Administration (FDA) with the use of **nebulizers**. FDA CDRH MAUDE Manufacturers and Users Database Product Code:

— CAF (**Nebulizers**)

— 1996-0801 to 2007-0427

— 122 reports

— 3 deaths

— 10 injuries

a) Trauma (mechanical, neurovascular or cardiopulmonary injury related to inhalation of **nebulizer** fragments or components, fire, electrical shock) causing:

1) Soreness, minor abrasions
2) Haematoma
3) Dermal ischemia
4) Necrosis
5) Epiglottic entrapment or inflammation
6) Upper oesophageal sphincter injury
7) Tissue damage, oedema
8) Severe or prolonged sore throat
9) Neuropathy
10) Vocal cord damage
11) Dental damage
12) Bleeding
13) Infection
14) ARDS associated with smoke inhalation injury

15) Dermal burns

16) Thermal airway burns

17) Barotrauma, volutrauma, stretch injury

18) Hyperthermia, hypothermia

19) Overhydration

b) Inadequate ventilation (hypoxia, hypercarbia) due to:

1) Leakage of respiratory gases

2) Inadequate oxygen flow

3) Inadequate oxygen gas concentration

4) Airway obstruction

5) Inadequate spontaneous ventilation

6) Reactive airway disease

7) Bronchospasm, laryngospasm, stridor, hiccup, coughing, breath holding

8) Negative pressure pulmonary oedema

9) Rebreathing

10) Increased intrathoracic pressure

11) Thickened secretions, mucus plugs

c) Aspiration or regurgitation due to:

1) Aspiration of bulk **nebulizer** solutions, water or saline

2) Inadequate attachment or locking of the tracheal tube or other airway device

3) Gastric insufflation

4) Inability to evacuate gastric contents

5) Airway obstruction (kinking or narrowing) with spontaneous breathing

d) Toxicity:

1) Allergy, including latex

2) Smoke inhalation injury

3) Oxygen toxicity

4) Inhalation of cleaning and disinfection solutions

5) Radiation toxicity (due to excessive DTPA **aerosol** administration/contamination)

e) Pharmacologic injury due to excessive/inadequate **aerosol** delivery:

1) Tachycardia
2) Bradycardia
3) Cardiopulmonary failure
4) Hypertension/hypotension
5) Hypervolemia
6) Unconsciousness
7) Death

## F.2 Potential nebulizer device hazards identified by the FDA MAUDE database

a) Fire

1) Overheating
2) Electrical malfunction, short circuits, sparks

b) Fragmentation

1) Broken components
2) Detached components

c) Inadequate oxygen

1) Cracked air entrainment dials
2) Cracked oxygen gas connectors

d) Misconnection

1) **Nebulizer** connected directly to tracheal tube
2) **Nebulizer** connected to wrong port of ventilator

e) Low **aerosol output**

1) Missing components
2) Cracked or damaged components
3) Electrical failure

## F.3 Potential mitigations

a) Design

b) Instructions for use

c) Labelling

d) Pre-use checks

e) Education/training

f) Compatibility testing

g) Disclosure

h) Risk assessment

| CAUSE | REPORT |
|---|---|
| Fire | Smoke/fire – overheating/melting (28 reports) |
| Burns | Contact dermal burns caused by laying compressor against thigh (2 reports) |
| Burns | Overheated tubing 44 degrees – hot to touch |
| Contamination | Blood inside **nebulizer** in sealed package (2 reports) |
| Contamination | Bleach odour from **nebulizer** – albuterol turned yellow colour |
| Electrical hazard | Battery failure – no **aerosol** – no therapy |
| Electrical hazard | Connection cable pulls free, disconnects easily |
| Electrical hazard | Electrical shock |
| Electrical hazard | Cables break at connector |
| Electrical hazard | Electrical shorting – electrocution |
| Electrical hazard | Cracked power adaptor – exposed wires |
| Fragments | T-piece obstruction |
| Fragments | Cracked **nebulizer** – non functional |
| Fragments | Mouthpiece rubber flap disconnected – potential airway obstruction |

| | |
|---|---|
| Fragments | Cracked T-piece |
| Fragments | Foreign material – plastic particles – tubing obstruction |
| Fragments | Eye injury when **nebulizer** exploded (2 reports) |
| Fragments | Component dislodged, obstructed airway |
| Fragments | Potential airway obstruction caused by detached component (2 reports) |
| Fragments | Cracked **nebulizer** (4 reports) |
| Fragments | T-piece occlusion |
| Fragments | Inhaled plastic screen material – use error – forced **nebulizer** mouthpiece cap into spacer, rupturing screen |
| Infection | Pseudomonas pickettii (ralstonia pickettii) infection caused by contaminated solutions (4 reports) |
| Infection | Mould inside tubing |
| Injury | Tachycardia, unconsciousness, lack of breathing |
| Injury | Loss of consciousness |
| Low humidity | **Nebulizer** humidifier failed on oxygen concentrator, plugged ET, mucus becomes firm, desaturation, hypercarbia |
| Low humidity | Mucus plug to trach – no misting |
| Low output | No **aerosol** – venturi malfunction – no therapy |
| Low output | Failure to nebulize DTPA |
| Low output | Low output – low flow rate – no therapy – asthma attack |
| Low output | Hypoxia – desaturation caused by malfunction and absence of visual and audio alarms when gas flow stopped flowing |
| Low output | Airflow restriction – **nebulizer** malfunction |
| Low output | Missing components – missing venturi – no therapy |
| Low output | Low output – albuterol |
| Low output | Fails to nebulize when nylon screw is removed |

| | |
|---|---|
| Low output | Injury due to defective **nebulizer** cap |
| Low output | Death due to compressor motor failure |
| Low output | Asthma due to lack of nebulization |
| Medication error | Low-potency albuterol |
| Medication error | Foaming **nebulizer** albuterol solution on ventilator circuit – desaturation requiring paralysis to tolerate vent settings, tachycardia |
| Medication error | Medication error – sterile water for inhalation was administered IV – body rash |
| Misconnection | Reverse aerosolization |
| Misconnection | Connected directly to ET (3 reports) |
| Misconnection | Ventilator circuit misconnection – ventilator bypassed |
| Mismarking | Desaturation – hypercarbia – high breathing rate caused by inadequate $O_2$ caused by inaccurate % $O_2$ markings on air entrainment valve |
| Mismarking | Mismarking, poor labelling |
| Mismarking | Failure to properly indicate the count of MDI inhaler doses |
| Missing components | Worsening symptoms – reactive airway disease – desaturation – missing exhalation valve in aero chamber |
| Missing components | Missing components – loss of **aerosol** |
| Overfill | Water overflow from bag into nasal cannula – aspiration of water – required suctioning – desaturation requiring high $O_2$ % for days |
| Oxygen coupler cracked | Cracked $FIO_2$ collar – low $O_2$ % |
| Oxygen coupler cracked | Oxygen coupler malfunction – gas leak – bottle fell to floor – desaturation |
| Oxygen coupler cracked | Cracked oxygen connector – desaturation |
| Oxygen coupler cracked | Oxygen connector cracked – desaturation |
| Oxygen coupler cracked | Oxygen gas coupler defective |
| Oxygen restriction | Desaturation not functioning – “backing up” oxygen |
| Oxygen restriction | Oxygen restriction – bottle not opening properly |

| | |
|---|---|
| Oxygen restriction | Restricted output, restricted oxygen flow |
| Oxygen restriction | Oxygen connector malfunction – improper oxygen flow |
| Oxygen restriction | Obstructed gas flow |
| Oxygen restriction | Diaphoresis, tachypnoea – desaturation – poor oxygen flow |
| Oxygen restriction | Death – cardiopulmonary failure – **nebulizer** stem broke |
| Oxygen restriction – leaks | Leaking oxygen tubing (2 reports) |
| Use error | Auto power converter did not function – no **aerosol** – no therapy (unit did not have converter – use error) |