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Biocompatibility evaluation of breathing gas pathways in healthcare applications - Part 1: Evaluation and testing within a risk management process (ISO 18562-1:2024)

EESTI STANDARDIMIS- JA AKREDITEERIMISKESKUS
ESTONIAN CENTRE FOR STANDARDISATION AND ACCREDITATION

EESTI STANDARDI EESSÕNA

NATIONAL FOREWORD

See Eesti standard EVS-EN ISO 18562-1:2024 sisaldab Euroopa standardi EN ISO 18562-1:2024 ingliskeelset teksti.	This Estonian standard EVS-EN ISO 18562-1:2024 consists of the English text of the European standard EN ISO 18562-1:2024.
Standard on jõustunud sellekohase teate avaldamisega EVS Teatajas.	This standard has been endorsed with a notification published in the official bulletin of the Estonian Centre for Standardisation and Accreditation.
Euroopa standardimisorganisatsioonid on teinud Euroopa standardi rahvuslikele liikmetele kättesaadavaks 23.10.2024.	Date of Availability of the European standard is 23.10.2024.
Standard on kättesaadav Eesti Standardimis-ja Akrediteerimiskeskusest.	The standard is available from the Estonian Centre for Standardisation and Accreditation.

Tagasisidet standardi sisu kohta on võimalik edastada, kasutades EVS-i veebilehel asuvat tagasiside vormi või saates e-kirja meiliaadressile standardiosakond@evs.ee.

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EUROPEAN STANDARD

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English Version

Biocompatibility evaluation of breathing gas pathways in healthcare applications - Part 1: Evaluation and testing within a risk management process (ISO 18562-1:2024)

Évaluation de la biocompatibilité des chemins de gaz respiratoire utilisés dans le domaine de la santé - Partie 1: Évaluation et essais au sein d'un processus de gestion du risque (ISO 18562-1:2024)

Beurteilung der Biokompatibilität der Atemgaswege bei medizinischen Anwendungen - Teil 1: Beurteilung und Prüfung innerhalb eines Risikomanagement-Prozesses (ISO 18562-1:2024)

This European Standard was approved by CEN on 15 March 2024.

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This European Standard exists in three official versions (English, French, German). A version in any other language made by translation under the responsibility of a CEN member into its own language and notified to the CEN-CENELEC Management Centre has the same status as the official versions.

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EUROPEAN COMMITTEE FOR STANDARDIZATION
COMITÉ EUROPÉEN DE NORMALISATION
EUROPÄISCHES KOMITEE FÜR NORMUNG

CEN-CENELEC Management Centre: Rue de la Science 23, B-1040 Brussels

Ref. No. EN ISO 18562-1:2024 E

European foreword

This document (EN ISO 18562-1:2024) has been prepared by Technical Committee ISO/TC 121 "Anaesthetic and respiratory equipment" in collaboration with Technical Committee CEN/TC 215 “Respiratory and anaesthetic equipment” the secretariat of which is held by BSI.

This European Standard shall be given the status of a national standard, either by publication of an identical text or by endorsement, at the latest by April 2025, and conflicting national standards shall be withdrawn at the latest by April 2025.

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. CEN shall not be held responsible for identifying any or all such patent rights.

This document supersedes EN ISO 18562-1:2020.

This document has been prepared under a standardization request addressed to CEN by the European Commission. The Standing Committee of the EFTA States subsequently approves these requests for its Member States.

For the relationship with EU Legislation, see informative Annex ZA, which is an integral part of this document.

Any feedback and questions on this document should be directed to the users’ national standards body/national committee. A complete listing of these bodies can be found on the CEN website.

According to the CEN-CENELEC Internal Regulations, the national standards organizations of the following countries are bound to implement this European Standard: Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Republic of North Macedonia, Romania, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Türkiye and the United Kingdom.

Endorsement notice

The text of ISO 18562-1:2024 has been approved by CEN as EN ISO 18562-1:2024 without any modification.

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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 document 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).

ISO draws attention to the possibility that the implementation of this document may involve the use of (a) patent(s). ISO takes no position concerning the evidence, validity or applicability of any claimed patent rights in respect thereof. As of the date of publication of this document, ISO had not received notice of (a) patent(s) which may be required to implement this document. However, implementers are cautioned that this may not represent the latest information, which may be obtained from the patent database available at www.iso.org/patents. ISO shall not be held responsible for identifying any or all such patent rights.

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For an explanation of the voluntary nature of standards, the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the World Trade Organization (WTO) principles in the Technical Barriers to Trade (TBT), see www.iso.org/iso/foreword.html.

This document was prepared by Technical Committee ISO/TC 121, *Anaesthetic and respiratory equipment*, Subcommittee SC 3, *Lung ventilators 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 second edition cancels and replaces the first edition (ISO 18562-1:2017), which has been technically revised.

The main changes are as follows:

— added informative mapping annexes to relevant regulatory requirements;

— clarified terms and definitions used in the document;

— expanded the *patient* groups to include: premature, small child, child, and adolescent;

— introduction of inhalation dose;

— the *threshold of toxicological concern* is changed;

— expanded the range of *volatile organic substances* that are tested;

— clarified the appropriate breathing gas volumes to be used in testing for *VOS*; and

— clarified the appropriate breathing gas volumes to be used in the analysis.

A list of all parts in the ISO 18562 series can be found on the ISO website.

Any feedback or questions on this document should be directed to the user’s national standards body. A complete listing of these bodies can be found at www.iso.org/members.html.

Introduction

This document represents the application of the best-known science, in order to improve *patient* safety, by addressing the *risk* of potentially hazardous substances being conveyed to the *patient* by the gas stream.

This document is intended to cover the biological evaluation of *gas pathways* of *medical devices* within a *risk management process*, as part of the overall *medical device* evaluation and development. This approach combines the review and evaluation of existing data from all sources with, where necessary, the selection and application of additional tests.

In general, the ISO 10993 series is intended to cover the biological evaluation of *medical devices*. However, the ISO 10993 series does not sufficiently address the biological evaluation of the *gas pathways* of *medical devices*.

Before this document was developed, some *authorities having jurisdiction* interpreted the ISO 10993-1:2009, Table A.1 to mean that as materials in the *gas pathway* form "indirect contact" with the *patient*, they should be subjected to tests equivalent to those required for tissue contact parts of *medical devices*. This interpretation can lead to tests that are not optimized for evaluation of *gas pathways* including possible *hazards* not being detected.

ISO 10993-1:2018 states that it is not intended to provide a rigid set of test methods as this might result in an unnecessary constraint on the development and use of novel *medical devices*. ISO 10993-1:2018 also states where a particular application warrants it, experts in the product or in the area of application concerned can choose to establish specific tests and criteria, described in a product-specific vertical standard. This series of standards is intended to address the specific needs for the evaluation of *gas pathways* that are not adequately covered by ISO 10993-1:2018.

This document provides a guide to the development of a biological evaluation plan that minimizes the number and exposure of test animals by giving preference to chemical constituent testing and *in vitro* models.

The initial version of this series of standards was intended to cover only the most commonly found potentially harmful substances. It was felt that it was best to get a functioning document published that would test for the bulk of the currently known substances of interest. With the use of the *TTC* (*threshold of toxicological concern*) approach, this document has the potential to be used to assess the safety of essentially any compound released from the *gas pathways* of respiratory *medical devices*, with very few exceptions (e.g. PCBs, dioxins), and not just the most commonly found potentially harmful substances.

ISO 18562-1 does not address all possible biological *hazards* that can be associated with *gas pathways*. Other, additional evaluations can be appropriate. These evaluations can require further *risk control* before finishing the biological evaluation.

Future parts of this series might be added to this series to address other relevant aspects of biological testing including additional contamination that might arise from the *gas pathway* because of the presence of drugs and anaesthetic agents added to the gas stream, and potential contamination by emission of inorganic gases such as ozone, CO, CO_2, and NO_x.

NOTE Some *authorities having jurisdiction* require evaluation of these *risks* as part of a biological evaluation.

This document has been prepared in consideration of:

— the *Essential Principles of Safety and Performance of Medical Devices and IVD Medical Devices,* IMDRF/GRRP WG/N47:2018[13] as indicated in Annex B;

— the *Labelling Principles for Medical Devices and IVD Medical Devices,* IMDRF/GRRP WG/N52:2019[14] as indicated in Annex B;

— the *essential principles of safety and performance* of a *medical device* according to ISO 16142-1:2016 as indicated in Annex C; and

— the general safety and performance requirements of a *medical device* according to regulation (EU) 2017/745[15].

In this document, the following verbal forms are used:

— “shall” indicates a requirement;

— “should” indicates a recommendation;

— “may” indicates a permission;

— "can" indicates a possibility or capability.

Biocompatibility evaluation of breathing gas pathways in healthcare applications —

Part 1: Evaluation and testing within a risk management process

1 Scope

This document specifies:

— the general principles governing the biological evaluation within a *risk management process* of the *gas pathways* of a *medical device*, its parts or *accessories,* which are intended to provide respiratory care or supply substances via the respiratory tract to a *patient* in all environments;

— the general categorization of *gas pathways* based on the nature and duration of their contact with the gas stream;

— the evaluation of existing relevant data from all sources;

— the identification of gaps in the available data set on the basis of a *risk analysis*;

— the identification of additional data sets necessary to analyse the biological safety of the *gas pathway*;

— the assessment of the biological safety of the *gas pathway*.

This document covers general principles regarding *biocompatibility* assessment of *medical device* materials, which make up the *gas pathway*, in *normal use* and *normal condition*. This document does not cover biological *hazards* arising from mechanical damage.

The other parts of ISO 18562 cover specific tests that address potentially hazardous substances that are added to the respirable gas stream and establish acceptance criteria for these substances.

This document addresses potential contamination of the gas stream arising from the *gas pathways* within the *medical device*, which might then be conducted to the *patient*.

This document applies over the *expected lifetime* of the *medical device* when operated according to the instructions for use. This includes degradation arising from exposure to environmental conditions as well as cleaning, disinfection and sterilisation (i.e. *processing*). It also includes user action or inaction (omission) that leads to an unintended or unexpected outcome (result) (i.e. *use error*). It does not include conscious/intentional action or inaction that violates the instructions for use and is beyond reasonable *risk control* by the *manufacturer* (i.e. *abnormal use*).

This document does not address biological evaluation of the surfaces of *medical devices* that have direct contact with the *patient* or *user*. The requirements for direct contact surfaces are found in the ISO 10993 series.

Medical devices, parts or *accessories* containing *gas pathways* that are addressed by this document include, but are not limited to, ventilators, anaesthesia workstations (including gas mixers), breathing systems, oxygen conserving equipment, oxygen concentrators, nebulizers, low-pressure hose assemblies, humidifiers, heat and moisture exchangers, respiratory gas monitors, respiration monitors, masks, medical respiratory personal protective equipment[23][25][28-30], mouth pieces, resuscitators, breathing tubes, breathing system filters and Y-pieces as well as any breathing *accessories* intended to be used with such *medical devices*. The enclosed chamber of an incubator, including the mattress, and the inner surface of an oxygen hood are considered to be *gas pathways* and are also addressed by this document.

This document does not address contamination already present in the gas supplied from the gas sources while *medical devices* are in *normal use*.

EXAMPLE Contamination arriving at the *medical device* from gas sources such as *medical gas pipeline systems* (including the non-return valves in the pipeline outlets), outlets of pressure regulators connected or integral to a medical gas cylinder, or room air taken into the *medical device* is not addressed by ISO 18562 (all parts).

2 Normative references

The following documents are referred to in the text in such a way that some or all of their content constitutes requirements of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 10993-1:2018, *Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process*

ISO 10993-17:2023, *Biological evaluation of medical devices — Part 17: Toxicological risk assessment of medical device constituents*

ISO 14971:2019, *Medical devices — Application of risk management to medical devices*

ISO 18562-2:2024, *Biocompatibility evaluation of breathing gas pathways in healthcare applications — Part 2: Tests for emissions of particulate matter*

ISO 18562-3:2024, *Biocompatibility evaluation of breathing gas pathways in healthcare applications — Part 3: Tests for emissions of volatile organic substances*

ISO 18562-4:2024, *Biocompatibility evaluation of breathing gas pathways in healthcare applications — Part 4: Tests for leachables in condensate*

3 Terms and definitions

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

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

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

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

NOTE For convenience, an alphabetized index of terms and their sources used in this document is found in Annex D.

3.1
abnormal use
conscious, deliberate act or deliberate omission of an act that is counter to or violates *normal use* and is also beyond any further reasonable means of *user interface*-related *risk control* by the *manufacturer*

EXAMPLE Reckless use or sabotage or intentional deliberate disregard of information for SAFETY are such acts.

Note 1 to entry: An intended but erroneous action that is not *abnormal use* is considered a type of *use error*.

Note 2 to entry: *Abnormal use* does not relieve the *manufacturer* from considering non-*user interface*-related means of *risk control*.

Note 3 to entry: Figure 1 shows the relationships of the types of use.