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

EESTI STANDARDIMIS- JA AKREDITEERIMISKESKUS
ESTONIAN CENTRE FOR STANDARDISATION AND ACCREDITATION

EESTI STANDARDI EESSÕNA

NATIONAL FOREWORD

See Eesti standard EVS-EN ISO 18562-4:2024 sisaldab Euroopa standardi EN ISO 18562-4:2024 ingliskeelset teksti.	This Estonian standard EVS-EN ISO 18562-4:2024 consists of the English text of the European standard EN ISO 18562-4:2024.
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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English Version

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

Évaluation de la biocompatibilité des chemins de gaz respiratoire utilisés dans le domaine de la santé - Partie 4: Essais concernant les relargables dans le condensat (ISO 18562-4:2024)

Beurteilung der Biokompatibilität der Atemgaswege bei medizinischen Anwendungen - Teil 4: Prüfungen für herauslösbare Substanzen in Kondensaten (ISO 18562-4:2024)

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

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EUROPEAN COMMITTEE FOR STANDARDIZATION
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CEN-CENELEC Management Centre: Rue de la Science 23, B-1040 Brussels

Ref. No. EN ISO 18562-4:2024 E

European foreword

This document (EN ISO 18562-4:2024) 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 18562-4:2020.

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 18562-4:2024 has been approved by CEN as EN ISO 18562-4:2024 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, *Respiratory devices and related equipment used for patient care* 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 18562-4:2017), 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;

— clarified the stepwise test procedure;

— required determination of volume of condensate that can reach the *patient*; and

— required calculating resulting *exposure dose*.

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 is intended to protect *patients* connected to *medical devices* from harmful amounts of substances that might be dissolved in water that has condensed in the *gas pathways* of those *medical devices*. This document represents the application of the best-known science by addressing the *risks* from potentially hazardous substances in the condensate being conveyed to the *patient* by the *gas pathway*. The condensate itself will be distilled water, having condensed from the vapour phase. But substances from within the *medical device* could leach into the liquid water (condensate) present in the breathing system.

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 appropriately address the biological evaluation of the *gas pathways* of *medical devices*.

It is not within the scope of this document to address contamination arising from the source of the breathing gases entering such *medical devices*, but rather only address the potential contamination generated from within the *medical device* itself. This contamination might be from the original manufacturing *process* or generated by the *medical device* itself during use.

This document is concerned with substances that could be conveyed to the *patient* by liquid condensate forming in the *medical device* and then subsequently reaching the *patient*. Potentially harmful substances that could be found in condensate include organic compounds and elements (such as metals). Condensate management is part of most healthcare institution protocols, with the primary aim of preventing the condensate reaching the *patient* in the first place. The absolute volume of liquid reaching a *patient* by this route should therefore be low, but it might happen. This document outlines tests for substances contained in the liquid.

The methods to determine the acceptable levels of contamination are contained in ISO 18562-1.

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[16] as indicated in Annex B;

— the *Labelling Principles for Medical Devices and IVD Medical Devices,* IMDRF/GRRP WG/N52:2019[17] 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[18].

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 4: Tests for leachables in condensate

1 Scope

This document specifies tests for substances leached by liquid water condensing in *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 chemical characterization methods described in this document apply to chemical substances that could leach from the *medical device*, its parts or *accessories* into the condensate. This document establishes verifiable acceptance criteria for these tests. The identity and quantity of each chemical released is intended for toxicological *risk assessment* as described in ISO 18562-1:2024.

This document addresses potential contamination of the gas stream arising from the *gas pathways*, which deliver breathing gas to the *patient*.

This document applies over the *expected lifetime* of the *medical device* in *normal use* and takes into account the effects of any intended *processing*.

This document does not address biological evaluation of the surfaces of *gas pathways* that have direct contact with the *patient*. 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 devices, oxygen concentrators, nebulizers, low-pressure hose assemblies, humidifiers, heat and moisture exchangers, respiratory gas monitors, respiration monitors, masks, medical respiratory personal protective equipment, mouth pieces, resuscitators, breathing tubes, breathing systems filters, Y-pieces and any breathing *accessories* intended to be used with such 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*.

This document does not address contact with drugs or anaesthetic agents. If a *medical device* or *accessory* is intended to be used with anaesthetic agents or drugs, then additional testing can be required. This document is intended to quantify hazardous water-soluble substances that are leached from the *medical device*, its parts or *accessories* by condensate and then conveyed by that liquid to the *patient*.

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 10993-5:2009, *Biological evaluation of medical devices — Part 5: Tests for in vitro cytotoxicity*

ISO 10993-10:2021, *Biological evaluation of medical devices — Part 10: Tests for skin sensitization*

ISO 10993-12:2021, *Biological evaluation of medical devices — Part 12: Sample preparation and reference materials*

ISO 10993-18:2020+AMD1:2022, *Biological evaluation of medical devices — Part 18: Chemical characterization of materials within a risk management process*

ISO 10993-23:2021, *Biological evaluation of medical devices — Part 23: Tests for irritation*

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

ICH Q3D(R2):2022,[1)] *Guideline for elemental impurities*

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO 18562-1:2024 and the following 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 all defined terms and their sources used in this document are given in Annex D.

3.1
exaggerated extraction
extraction that is intended to result in a greater amount of a chemical constituent being released as compared to the amount generated under the simulated conditions of use

Note 1 to entry: It is important to ensure that the *exaggerated extraction* does not result in a chemical change of the material.

[SOURCE: ISO 10993-12:2021, 3.3]

3.2
extractable
substance that is released from a *medical device* or material of construction when the *medical device* or material is extracted using laboratory extraction conditions and vehicles

[SOURCE: ISO 10993-18:2020+AMD1:2022, 3.16]

4 General principles

All *gas pathways* that are exposed to water or that are exposed to humidified gas, and within which water vapour can condense and subsequently reach the *patient* in liquid form shall be evaluated using the principles detailed in ISO 18562-1:2024.

NOTE Some parts of the expiratory *gas pathways* can allow condensed water to settle, and subsequently flow under gravity back towards the *patient*.

1) Available at: https://database.ich.org/sites/default/files/Q3D-R2_Guideline_Step4_2022_0308.pdf