



SLOVENSKI STANDARD
oSIST prEN ISO 18562-1:2023
01-januar-2023

**Ovrednotenje biokompatibilnosti vdihanega plina za uporabo v zdravstvu - 1. del:
Ovrednotenje in preskušanje znotraj procesa obvladovanja tveganja (ISO/DIS
18562-1:2022)**

Biocompatibility evaluation of breathing gas pathways in healthcare applications - Part 1:
Evaluation and testing within a risk management process (ISO/DIS 18562-1:2022)

Beurteilung der Biokompatibilität der Atemgaswege bei medizinischen Anwendungen -
Teil 1: Beurteilung und Prüfung innerhalb eines Risikomanagement-Prozesses (ISO/DIS
18562-1:2022)

Évaluation de la biocompatibilité des chemins de gaz respiratoires dans les applications
de soins de santé - Partie 1: Évaluation et essais au sein d'un processus de gestion du
risque (ISO/DIS 18562-1:2022)

Ta slovenski standard je istoveten z: prEN ISO 18562-1

ICS:

11.040.10	Anestezijska, respiratorna in reanimacijska oprema	Anaesthetic, respiratory and resuscitation equipment
-----------	---	---

oSIST prEN ISO 18562-1:2023

en,fr,de

DRAFT INTERNATIONAL STANDARD

ISO/DIS 18562-1

ISO/TC 121/SC 3

Secretariat: ANSI

Voting begins on:
2022-11-04Voting terminates on:
2023-01-27

Biocompatibility evaluation of breathing gas pathways in healthcare applications —

Part 1: Evaluation and testing within a risk management process

Évaluation de la biocompatibilité des chemins de gaz respiratoires dans les applications de soins de santé —

Partie 1: Évaluation et essais au sein d'un processus de gestion du risque

iTeh STANDARD PREVIEW
(standards.iteh.ai)

ICS: 11.040.10

[oSIST prEN ISO 18562-1:2023](https://standards.iteh.ai/catalog/standards/sist/d0930d2a-8665-4ca5-9c70-e4302d0c2398/osist-pren-iso-18562-1-2023)

<https://standards.iteh.ai/catalog/standards/sist/d0930d2a-8665-4ca5-9c70-e4302d0c2398/osist-pren-iso-18562-1-2023>

This document is circulated as received from the committee secretariat.

THIS DOCUMENT IS A DRAFT CIRCULATED FOR COMMENT AND APPROVAL. IT IS THEREFORE SUBJECT TO CHANGE AND MAY NOT BE REFERRED TO AS AN INTERNATIONAL STANDARD UNTIL PUBLISHED AS SUCH.

IN ADDITION TO THEIR EVALUATION AS BEING ACCEPTABLE FOR INDUSTRIAL, TECHNOLOGICAL, COMMERCIAL AND USER PURPOSES, DRAFT INTERNATIONAL STANDARDS MAY ON OCCASION HAVE TO BE CONSIDERED IN THE LIGHT OF THEIR POTENTIAL TO BECOME STANDARDS TO WHICH REFERENCE MAY BE MADE IN NATIONAL REGULATIONS.

RECIPIENTS OF THIS DRAFT ARE INVITED TO SUBMIT, WITH THEIR COMMENTS, NOTIFICATION OF ANY RELEVANT PATENT RIGHTS OF WHICH THEY ARE AWARE AND TO PROVIDE SUPPORTING DOCUMENTATION.

ISO/CEN PARALLEL PROCESSING



Reference number
ISO/DIS 18562-1:2022(E)

© ISO 2022

iTeh STANDARD PREVIEW (standards.iteh.ai)

[oSIST prEN ISO 18562-1:2023](https://standards.iteh.ai/catalog/standards/sist/d0930d2a-8665-4ca5-9c70-e4302d0c2398/osist-pren-iso-18562-1-2023)

<https://standards.iteh.ai/catalog/standards/sist/d0930d2a-8665-4ca5-9c70-e4302d0c2398/osist-pren-iso-18562-1-2023>



COPYRIGHT PROTECTED DOCUMENT

© ISO 2022

All rights reserved. Unless otherwise specified, or required in the context of its implementation, no part of this publication may be reproduced or utilized otherwise in any form or by any means, electronic or mechanical, including photocopying, or posting on the internet or an intranet, without prior written permission. Permission can be requested from either ISO at the address below or ISO's member body in the country of the requester.

ISO copyright office
CP 401 • Ch. de Blandonnet 8
CH-1214 Vernier, Geneva
Phone: +41 22 749 01 11
Email: copyright@iso.org
Website: www.iso.org

Published in Switzerland

Contents

Page

Foreword.....	iv
Introduction.....	v
1 Scope.....	1
2 Normative references.....	2
3 Terms and definitions.....	2
4 General principles applying to <i>biocompatibility</i> evaluation of <i>medical devices</i>.....	11
4.1 General.....	11
4.2 <i>Type tests</i>	13
4.3 <i>Biocompatibility hazard</i> identification.....	13
4.4 Extent of <i>risk assessment</i>	14
4.5 <i>Biocompatibility</i> evaluation plan.....	14
4.6 Selection of tests.....	16
4.7 Subsequent evaluation.....	17
5 Contamination of breathing gas from <i>gas pathways</i>.....	17
5.1 Duration of contact.....	17
5.2 <i>Particulate matter (PM)</i> emissions.....	18
5.3 Volatile organic substance emissions.....	18
5.4 <i>Leachables</i> in condensate.....	18
6 Adjustment for different <i>patient groups</i>.....	18
6.1 General considerations.....	18
6.2 Adjustment for body weight.....	19
7 Deriving allowable limits.....	20
7.1 General <i>process</i>	20
7.2 For <i>medical devices</i> intended for limited exposure use (≤ 24 h).....	21
7.3 For <i>medical devices</i> intended for prolonged exposure use (>24 h but <30 d).....	21
7.4 For <i>medical devices</i> intended for long-term exposure (≥ 30 d).....	22
8 Risk control.....	22
9 Benefit-risk analysis.....	23
10 <i>Biocompatibility</i> evaluation report.....	23
Annex A (informative) Rationale and guidance.....	24
Annex B (informative) Reference to the IMDRF <i>essential principles</i> and labelling guidances.....	27
Annex C (informative) Reference to the <i>essential principles</i>.....	29
Annex ZA (informative) Relationship between this European standard and the General Safety and Performance Requirements of Regulation (EU) 2017/745 aimed to be covered.....	30
Bibliography.....	33
Terminology — Alphabetized index of defined terms.....	35

ISO/DIS 18562-1:2022(E)

Foreword

ISO (the International Organization for Standardization) is a worldwide federation of national standards bodies (ISO member bodies). The work of preparing International Standards is normally carried out through ISO technical committees. Each member body interested in a subject for which a technical committee has been established has the right to be represented on that committee. International organizations, governmental and non-governmental, in liaison with ISO, also take part in the work. ISO collaborates closely with the International Electrotechnical Commission (IEC) on all matters of electrotechnical standardization.

The procedures used to develop this document and those intended for its further maintenance are described in the ISO/IEC Directives, Part 1. In particular the different approval criteria needed for the different types of ISO documents should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2 (see www.iso.org/directives).

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights. Details of any patent rights identified during the development of the document will be in the Introduction and/or on the ISO list of patent declarations received (see www.iso.org/patents).

Any trade name used in this document is information given for the convenience of users and does not constitute an endorsement.

For an explanation on the voluntary nature of ISO 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 the following URL: 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 of ISO 18562-1 cancels and replaces the first edition of ISO 18562-1.

The main changes compared to the previous edition are as follows:

- reformatted according to most recent Central Secretariat editing rules;
- added informative mapping annexes to relevant regulatory requirements;
- clarified terms and definitions used in the document;
- clarified the appropriate breathing gas volumes to 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 materials in the *gas pathway* form “indirect contact” with the *patient*, and should be subjected to tests equivalent to those required for tissue contact parts of *medical devices*. This interpretation can lead to tests with questionable utility and also to 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 new 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.

In this document, the following print types are used:

- requirements and definitions: roman type;
- terms defined in [Clause 3](#) of this document or as noted and test specifications: italic type;
- informative material appearing outside of tables, such as notes, examples and references: in smaller type. Normative text of tables is also in a smaller type;

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^[15] as indicated in [Annex B](#);
- the *Labelling Principles for Medical Devices and IVD Medical Devices*, IMDRF/GRRP WG/N52:2019^[16] as indicated in [Annex B](#);
- the *essential principles of safety and performance* of a *medical device* according to ISO 16142-1:2016^[8] as indicated in [Annex C](#); and
- the general safety and performance requirements of a *medical device* according to regulation (EU) 2017/745^[17].

ISO/DIS 18562-1:2022(E)

In this document, the conjunctive “or” is used as an “inclusive or” so a statement is true if any combination of the conditions is true.

For the purposes of this document, the auxiliary verb:

- “shall” indicates a requirement;
- “should” indicates a recommendation;
- “may” indicates a permission;
- “can” is used to describe a possibility or capability;
- “must” is used express an external constraint.

Requirements in this document have been decomposed so that each requirement is uniquely delineated. This is done to support automated requirements tracking.

iTeh STANDARD PREVIEW (standards.iteh.ai)

[oSIST prEN ISO 18562-1:2023](https://standards.iteh.ai/catalog/standards/sist/d0930d2a-8665-4ca5-9c70-e4302d0c2398/osist-pren-iso-18562-1-2023)

<https://standards.iteh.ai/catalog/standards/sist/d0930d2a-8665-4ca5-9c70-e4302d0c2398/osist-pren-iso-18562-1-2023>

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, 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.

ISO/DIS 18562-1:2022(E)

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).

Future parts might be added 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, CO₂, and NO_x.

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

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:—¹⁾, *Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances*

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

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

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

ISO/TS 21726, *Biological evaluation of medical devices — Application of the threshold of toxicological concern (TTC) for assessing biocompatibility of medical device constituents*

3 Terms and definitions

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

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

- IEC Electropedia: available at <https://www.electropedia.org/>
- ISO Online browsing platform: available at <https://www.iso.org/obp>

NOTE For convenience, an alphabetized index of terms and their sources used in this document is found at the end of this document.

1) Under preparation. Stage at the time of publication: ISO/FDIS 10993 17:2022.

2) Under preparation. Stage at the time of publication: ISO/DIS 18562-2:2022.

3) Under preparation. Stage at the time of publication: ISO/DIS 18562-3:2022.

4) Under preparation. Stage at the time of publication: ISO/DIS 18562-4:2022.

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.

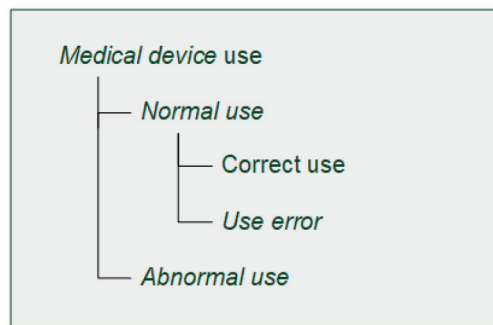


Figure 1 — Relationship of the types of use

[SOURCE: IEC 62366-1+AMD1:2020, 3.1, modified — deleted note 1.]

3.2 accessory

item, intended specifically by its *manufacturer*, to be used together with one or more *medical devices* to specifically enable or assist those *medical devices* to be used in accordance with their *intended use*

Note 1 to entry: An *accessory* is typically a consumable or separate item for use with one or more *medical devices*.

Note 2 to entry: Some *authorities having jurisdiction* consider an *accessory* to be a *medical device*.

Note 3 to entry: Some *authorities having jurisdiction* have a different definition of *accessory*.

[SOURCE: ISO 20417:2021, 3.1]

3.3 accompanying information

information accompanying or marked on a *medical device* or *accessory* for the user or those accountable for the installation, use, *processing*, maintenance, decommissioning and disposal of the *medical device* or *accessory*, particularly regarding safe use

Note 1 to entry: The *accompanying information* shall be regarded as part of the *medical device* or *accessory*.

Note 2 to entry: The *accompanying information* can consist of the label, marking, instructions for use, technical description, installation manual, quick reference guide, etc.

Note 3 to entry: *Accompanying information* is not necessarily a written or printed document but could involve auditory, visual, or tactile materials and multiple media types (e.g., CD/DVD-ROM, USB stick, website).

[SOURCE: ISO 20417:2021, 3.2, modified — deleted note 4.]

ISO/DIS 18562-1:2022(E)

3.4

authority having jurisdiction
regulatory authority

governmental agency or office assigned to oversee the regulation of a regulated product within a country, jurisdiction, or assigned territory

[SOURCE: ISO 16142-1:2016, 3.1]

3.5

benefit

positive impact or desirable outcome of the use of a *medical device* on the health of an individual, or a positive impact on *patient* management or public health

Note 1 to entry: *Benefits* can include positive impact on clinical outcome, the *patient's* quality of life, outcomes related to diagnosis, positive impact from diagnostic devices on clinical outcomes, or positive impact on public health.

[SOURCE: ISO 14971:2019, 3.2]

3.6

biocompatibility

ability to be in contact with a living system without producing an unacceptable adverse effect

Note 1 to entry: *Medical devices* may produce some level of adverse effect, but that level may be determined to be acceptable when considering the *benefits* provided by the *medical device*.

3.7

essential principles**essential principles of safety and performance**

fundamental high-level requirements that when complied with ensure a *medical device* is safe and performs as intended

[SOURCE: ISO 16142-1:2016, 3.3]

3.8

expected lifetime**expected service life**

time period specified by the *manufacturer* during which the *medical device* or *accessory* is expected to remain safe and effective for use

Note 1 to entry: The *expected lifetime* can be affected by the stability of the *medical device* or *accessory* or by the materials in the *medical device* or *accessory*.

Note 2 to entry: Maintenance, repairs or upgrades (e.g., safety or cybersecurity modifications) can be necessary during the *expected lifetime*.

Note 3 to entry: Some *medical devices* have an absolute lifetime (e.g., 5 y), whereas other *medical devices* (e.g., software) have a relative lifetime (e.g., the time between two major releases).

[SOURCE: ISO 20417:2021, 3.7, modified — added to note 1 “of the *medical device* or *accessory* or by the materials in the *medical device* or *accessory*” deleted note 4.]

3.9

exposure dose

quantity of a chemical constituent that does, or could contact the body over a specified time period
Note 1 to entry: *Exposure dose* is normally expressed as $\mu\text{g}/\text{kg}/\text{d}$ or as $\mu\text{g}/\text{cm}^2/\text{d}$.

[SOURCE: ISO 10933-17:—, 3.7]

3.10 formulation

base polymer or alloy, including additives, colours, etc. used to establish a property or the stability of the material

Note 1 to entry: This does not include *processing* aids, mould release agents, residual contaminants, or other manufacturing aids that are not intended to be a part of the material.

Note 2 to entry: The term “chemical composition” is commonly used as a synonym for *formulation*.

[SOURCE: US FDA Deciding When to Submit a 510(k) for a Change to an Existing Device, [19] reformatted.]

3.11 gas pathway

interior surfaces, over which gases or liquids that can be inspired, in a *medical device* bounded by the ports through which gases or liquids enter and leave the *medical device* including the *patient* interface or the interior surfaces of enclosures that are in contact with gases or liquids that can be inspired

Note 1 to entry: *patient* contact surfaces such as the outer surfaces of a tracheal tube or the cushion of a mask are evaluated according to the ISO 10993 series.

EXAMPLE 1 The ventilator breathing system, inlet filter, gas mixer, blower and internal piping.

EXAMPLE 2 Enclosed chamber of an incubator including the mattress or the inner surface of an oxygen hood.

EXAMPLE 3 The inner surfaces of breathing tubes, tracheal tubes or masks and mouthpieces.

3.12 hazard

potential source of harm

[SOURCE: ISO 14971-1:2019, 3.4]

3.13 infrequent use

same or similar *medical device* or *accessory* used at different treatment occasions at intervals that are expected to be long relative to the elimination time of any *leachable* harmful substance from the *patient's* body

Note 1 to entry: If the *medical device* or *accessory* is intended to be used for a recurring condition, then the determination as to whether this is treated as *infrequent use* is based on the likelihood that the *patient* recovers from any toxicological effects of the between episodes. If there is likely to be a cumulative effect then the *total exposure period* across all treatment episodes shall be considered.

Note 2 to entry: If use of the *medical device* or *accessory* is deemed to be *infrequent use*, then the *total exposure period* is determined for a single treatment episode.

3.14 intended use

use for which a product, *process* or service is intended according to the specifications, instructions and information provided by the *manufacturer*

Note 1 to entry: The intended medical indication, *patient* population, part of the body or type of tissue interacted with, user profile, use environment, and operating principle are typical elements of the *intended use*.

[SOURCE: ISO 14971-1:2019, 3.6]

3.15 leachable

substance that is released from a *medical device* or material during its clinical use

Note 1 to entry: For many *medical devices*, a *leachables* study is not practical due to the challenges with reproducing actual clinical conditions, so *simulated-use extraction* studies are often performed instead. See definition for *simulated-use extractions*.