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Biological evaluation of medical devices —

Part 7: Ethylene oxide sterilization residuals

Évaluation biologique des dispositifs médicaux —
Partie 7: Résidus de stérilisation à l'oxyde d'éthylène

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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).

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This document was prepared by Technical Committee ISO/TC 194, *Biological and clinical evaluation of medical devices,* in collaboration with the European Committee for Standardization (CEN) Technical Committee CEN/TC 206, *Biological and clinical evaluation of medical devices,* in accordance with the Agreement on technical cooperation between ISO and CEN (Vienna Agreement).

This third edition cancels and replaces the second edition (ISO 10993-7:2008), which has been technically revised. It also incorporates the Amendment ISO 10993-7:2008/Amd 1:2019 and the Technical Corrigendum ISO 10993-7:2008/Cor 1:2009.

The main changes are as follows:

— allowable limits and extraction conditions have been derived based on the patient population and the duration of use;

— the use of a risk assessment to establish allowable limits has been permitted;

— additional guidance on product release has been provided;

— additional guidance on determining residuals and the factors that affect residual has been provided.

A list of all parts in the ISO 10993 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.

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Introduction

As noted in the introduction to ISO 11135, when determining the suitability of ethylene oxide (EO) for sterilization of medical devices, it is important to ensure that the levels of residual EO and ethylene chlorohydrin (ECH) pose a minimal risk to the patient in intended product use. Therefore, it is important that the use of alternative materials and sterilization processes are considered during product design and development. EO is known to exhibit a number of biological effects. In the development of this document, consideration was given to these effects, which include irritation, organ damage, mutagenicity, carcinogenicity, and reproductive effects in humans and animals. Similar consideration was given to the harmful effects of ECH and ethylene glycol (EG). ECH can be formed when EO comes into contact with free chloride ions, whereas EG is a hydrolytic reaction product of EO and water. In practice, for most devices, exposure to EO and ECH is considerably lower than the maximum allowable limits established according to this document. No allowable limits are set for EG because risk assessment indicated that when EO residuals are controlled, it is unlikely that biologically significant residuals of EG would be present.

Requirements herein are in addition to the biological evaluation requirements as indicated in ISO 10993-1. The biological evaluation, combined with the EO-sterilization process residual limits, form the justification that an EO-sterilized device is safe for its anticipated contact duration. Maximum allowable residuals for ECH, when ECH has been found to be present in medical devices sterilized with EO, are also specified. Local effects (e.g. irritation) have been considered and are incorporated in the TCL as given in 4.3.6.2 and Annex D for EO, and in 4.3.6.3 and Annex E for ECH.

In this edition of this document (i.e. ISO 10993-7:2026), an uncertainty factor approach is used to derive EO and ECH exposure duration-specific tolerable intake (TI) values (expressed in µg/kg/d). Furthermore, this edition of this document (i.e. ISO 10993-7:2026) introduces the conversion of each EO and ECH TI value into subpopulation-specific cumulative exposure-allowable limit values (expressed in milligrams per device), which are used to determine the extent that EO and ECH, extracted under clinically relevant conditions and time-periods, needs to be reduced post-sterilization.

This edition of this document (i.e. ISO 10993-7:2026) applies a different approach as compared to ISO 10993-17:2023 to establishing allowable limits to make it useful for development, validation, and routine control of ethylene oxide sterilization in the manufacture of finished medical devices with focus on the risk assessments associated with three chemical constituents that are potentially left in medical devices sterilized with ethylene oxide. This document extends this knowledge further by calculating the largest amount of EO, ECH or EG that can be present in a medical device such that it would always meet the requirements of ISO 10993-17 when that device has been exposed to the validated sterilization cycle parameters. This maximum amount or allowable limit is expressed in milligrams per device deemed acceptable when taken into the body through exposure to that medical device. These allowable limits will help determine the appropriate sterilization parameters such as sterilant gas concentration and dwell, as well as aeration temperature and hold time when validating the sterilization process to be used for a product or group of products. Furthermore, the allowable limits can be used by regulatory bodies, manufacturers, and processors to optimize processes and aid in the selection and qualification of alternative materials in order to protect patient health.

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Biological evaluation of medical devices —

Part 7:
Ethylene oxide sterilization residuals

1 Scope

This document specifies allowable limits (AL) for residual ethylene oxide (EO) and ethylene chlorohydrin (ECH) in EO-sterilized medical devices, procedures for the measurement of EO and ECH, and methods for determining conformity so that devices can be released. Additional background, including guidance and a flowchart showing how this document is applied, are also included in Annexes A, B, C, D, E, F, G, H, I, J and K.

EO-sterilized devices or components that have neither direct nor indirect body or user contact (e.g. in vitro diagnostic devices) are out of scope of this document. This document does not apply to devices that have been demonstrated to not absorb or retain EO or its degradation product ECH, such as medical devices made exclusively of metal alloys and glass, see Clause C.5[228].

NOTE This document does not specify limits for ethylene glycol (EG). No device limits are specified for EG because the risk assessment in Annex F indicates that calculated allowable levels are higher than those likely to occur in a medical device.

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 10993-1:2025, *Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process*

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

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO 10993-1 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/

3.1
aeration
part of the sterilization *cycle* (3.5) during which the sterilizing agent and/or its reaction products desorb from the health care product until predetermined levels are reached

Note 1 to entry: Aeration can be performed within the sterilization chamber or in a separate chamber or room.

[SOURCE: ISO 11139:2018, 3.7, modified — Note 1 to entry has been added.]

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