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Interested committees:

Title: Draft BS EN ISO 10993-16 Biological evaluation of medical devices. Part 16: Toxicokinetic study design for degradation products and leachables.

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Introduction

This draft standard is based on national and international discussions. Your comments on this draft are invited and will assist in the preparation of the consequent standard.

For international standards, comments will be reviewed by the relevant UK national committee before sending the consensus UK vote and comments to the international committee, which will then decide appropriate action. If the international standard is approved, it is usual for the text to be published as a British Standard.

For national standards, comments will be reviewed by the relevant UK national committee and the resulting standards published as a British Standard.

UK Vote

Please indicate whether you consider the UK should submit a negative (with supporting technical reasons) or positive vote on this draft. Please indicate if you are aware of any reason why this draft standard should not be published as a British Standard.

Submission of Comments

- **Annotated drafts are not acceptable and will be rejected.**
- All comments should be submitted online at <https://standardsdevelopment.bsigroup.com/>. You will need to register in order to comment.

Template for comments and secretariat observations

Date: xx/xx/20xx	Document: ISO/DIS xxxx
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1	2	(3)	4	5	(6)	7
MB	Clause No./ Subclause No./Annex (e.g. 3.1)	Paragraph/ Figure/Table/Note	Type of comment	Comment (justification for change) by the MB	Proposed change by the MB	Secretariat observations on each comment submitted
	3.1	Definition 1	ed	Definition is ambiguous and needs clarifying.	Amend to read '...so that the mains connector to which no connection...'	
	6.4	Paragraph 2	te	The use of the UV photometer as an alternative cannot be supported as serious problems have been encountered in its use in the UK.	Delete reference to UV photometer.	



DRAFT International Standard

ISO/DIS 10993-16

Biological evaluation of medical devices —

Part 16: Toxicokinetic evaluation for degradation products and leachables

ICS: 11.100.20

ISO/TC 194

Secretariat: **DIN**

Voting begins on:
2025-12-08

Voting terminates on:
2026-03-02

This document is circulated as received from the committee secretariat.

ISO/CEN PARALLEL PROCESSING

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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 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 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 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 fourth edition cancels and replaces the third edition (ISO 10993-16:2017), which has been technically revised with the following changes:

- a) the title is changed to accommodate methods alternative to animal studies;
- b) the introduction is modified;
- c) the scope is modified;
- d) a new [clause 4](#) was added to include guidance on toxicokinetic evaluation;
- e) normative [Annex A](#) has been moved to [clause 5](#) and the title is changed to accommodate methods alternative to animal studies;
- f) a new [clause 6](#) was added to include mathematical modelling for the evaluation of toxicokinetics;
- g) a new [clause 8](#) was added to address possible outcome of toxicokinetic evaluation;
- h) a new informative [Annex A](#) was added to include additional information on mathematical modelling;
- i) [Clause 5](#) guidance on test methods, has been moved to new informative [Annex B](#).
- j) the bibliography has been updated.

A list of all the parts in the ISO 10993 series can be found on the ISO website.

Introduction

Medical devices can release leachables (e.g., residual catalysts, processing aids, residual monomers, fillers, antioxidants, plasticizers, etc.) or degradation products which migrate from the material and have the potential to cause adverse effects in the body. Toxicokinetic evaluation describes the fate of a foreign chemical in the body with time by assessing absorption, distribution, metabolism, and excretion of the chemical and can be of value in assessing the safety of medical devices. Toxicokinetic evaluation can also be applicable to medical devices containing active ingredients, in which case, pharmaceutical legislation is to be considered.

Traditionally, animal studies have been used for toxicokinetic evaluation. The need for and extent of toxicokinetic animal study should be carefully considered; it is preferably to replace animal studies with mathematical modelling or evaluation of existing toxicological and toxicokinetic data. The need for consulting toxicokinetic experts for these considerations is emphasized.

A considerable body of published literature exists on the use of toxicokinetic methods to study the fate of chemicals in the body (see Bibliography).

Biological evaluation of medical devices —

Part 16:

Toxicokinetic evaluation for degradation products and leachables

1 Scope

This document describes the considerations for inclusion of toxicokinetic evaluation in the biological evaluation of medical devices and provides principles on designing and performing toxicokinetic evaluation relevant to medical devices.

2 Normative references

The following documents are referred to in the text in such a way that some of or all 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, *Biological evaluation of medical devices — Part 1: Requirements and general principles for the evaluation of biological safety within a risk management process*

ISO 10993-2, *Biological evaluation of medical devices — Part 2: Animal welfare requirements*

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

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 terminological databases for use in standardization at the following addresses:

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

3.1

absorbable device

medical device designed to biodegrade and to be absorbed by the body over time; typically serving a temporary function

3.2

absorption

action of a material or substance, or its decomposition products passing through or being assimilated either by cells or tissue or both over time

3.3

bioavailability

extent of systemic *absorption* (3.1) of specified substance