SLOVENSKI STANDARD
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Biološko ovrednotenje medicinskih pripomočkov - 3. del: Ovrednotenje genske toksičnosti, kancerogenosti, toksičnosti za razmnoževanje in toksičnosti za razvoj (ISO/DIS 10993-3:2025)

Biological evaluation of medical devices - Part 3: Evaluation of genotoxicity, carcinogenicity, reproductive toxicity, and developmental toxicity (ISO/DIS 10993-3:2025)

Biologische Beurteilung von Medizinprodukten - Teil 3: Bewertung der Genotoxizität, Karzinogenität, Reproduktionstoxizität und Entwicklungstoxizität (ISO/DIS 10993-3:2025)

Évaluation biologique des dispositifs médicaux - Partie 3: Évaluation de la génotoxicité, de la cancérogénicité, de la toxicité sur la reproduction et le développement (ISO/DIS 10993-3:2025)

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Contents

Page

Foreword ..... **iv**
Introduction ..... **v**
1 Scope **1**
2 Normative references **1**
3 Terms and definitions **2**
4 Assessment strategies **3**
4.1 General 3
4.2 Other considerations 3
5 Genotoxicity assessment **3**
5.1 General 3
5.2 Testing strategy 4
5.2.1 General 4
5.2.2 Test battery 4
5.2.3 In vivo genotoxicity testing 5
5.2.4 Follow-up evaluation 5
5.3 Test sample preparation 5
6 Carcinogenicity Assessments **6**
6.1 General 6
6.2 Evaluation strategy 6
6.2.1 General 6
6.2.2 Genotoxic carcinogens 6
6.2.3 Non-genotoxic carcinogens 7
7 Evaluation of reproductive and developmental toxicity **7**
7.1 General 7
7.2 Evaluation methods 8
8 Test report **9**
Annex A (informative) **Test sample preparation procedure for genotoxicity testing** **10**
Annex B (normative) **Tests for genotoxicity** **16**
Annex C (informative) **Carcinogenicity Tests in animals** **26**
Annex D (informative) **Genotoxicity assessment of nanomaterials** **29**
Annex E (informative) **Recipe for S9 mix** **30**
Annex F (informative) **Endocrine Disruptors** **31**
Annex G (informative) **Evaluation of reproductive and developmental toxicity** **32**
Annex ZA (informative) **Relationship between this European standard and the General Safety and Performance Requirements of Regulation (EU) 2017/745 aimed to be covered** **36**
Bibliography **40**

Foreword

ISO (the International Organization for Standardization) and IEC (the International Electrotechnical Commission) form the specialized system for worldwide standardization. National bodies that are members of ISO or IEC participate in the development of International Standards through technical committees established by the respective organization to deal with particular fields of technical activity. ISO and IEC technical committees collaborate in fields of mutual interest. Other international organizations, governmental and non-governmental, in liaison with ISO and IEC, also take part in the work. In the field of information technology, ISO and IEC have established a joint technical committee, ISO/IEC JTC 1.

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).

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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, *Biocompatibility of medical and dental materials and devices,* in accordance with the Agreement on technical cooperation between ISO and CEN (Vienna Agreement).

This fourth edition of ISO 10993-3 cancels and replaces the third edition (ISO 10993-3:2014), which has been technically revised.

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

— Deletion of the Annex on Cellular Transformation;

— Restructure of Annex A on Guidance on selecting an appropriate test sample preparation procedure for genotoxicity testing;

— Addition of Annex C on in vivo carcinogenicity assays that includes the Annex on solid state carcinogenesis;

— Addition of Annex D on Genotoxicity Assessment of Nanomaterials;

— Expanded Annex B on genotoxicity test methods;

— Addition of Annex E on Recipe for S9 mix;

— Addition of Annex G on the evaluation of reproductive and developmental toxicity;

— Update of normative references and bibliography.

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

Introduction

The basis for biological evaluation of medical devices is often empirical and driven by relevant concerns for human safety. The risk of serious and irreversible effects, such as cancer or second generation abnormalities, is of particular public concern. It is inherent in the provision of safe medical devices that such risks be minimized to the greatest extent feasible. The assessment of mutagenic, carcinogenic, reproductive, and developmental toxicity hazards is an essential component of the control of these risks. Not all test methods for the assessment of genotoxicity, carcinogenicity, reproductive toxicity, and developmental toxicity are equally well developed, nor is their validity well established for the testing of medical devices.

Significant issues with test sample size and preparation, scientific understanding of disease processes and test validation can be cited as limitations of available methods. Since the previous document revision, many genotoxicity test methods have been updated with revised OECD guidelines. However, these generally provide clearer recommendations but little alteration in test methods. Scientifically sound alternatives to the proposed testing can be acceptable insofar as they address relevant matters of safety assessment.

In the selection of tests needed to evaluate a particular medical device, a careful assessment of expected human uses and potential interactions with biological systems is important, particularly in such areas as reproductive and developmental toxicology.

This document presents test methods and evaluation strategies for the identification of specific biological harms. Testing is not always necessary or helpful in managing toxicological risks associated with exposure to medical device materials but, where it is appropriate, it is important that maximum test sensitivity is achieved.

In view of the multitude of possible outcomes and the importance of factors such as extent of exposure, species differences and mechanical or physical considerations, risk assessment is typically performed on a case-by-case basis. Suggestions for risk consideration and integration of ISO 10993-17 and -18 are provided.