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Biological evaluation of medical devices —

Part 6: Tests for local effects after implantation

Évaluation biologique des dispositifs médicaux —

Partie 6: Essais concernant les effets locaux après implantation

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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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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 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 10993-6:2016), which has been technically revised.

The main changes are as follows:

— new definitions for “comparative control”, “coupon”, “euthanasia”, “local effect”, “location marker”, “steady-state” and “reference control” have been added to Clause 3;

— a new paragraph on the use of smaller compositionally representative samples or coupons has been added to 4.2.2;

— a new subclause 4.3 “Selection of control materials” has been added;

— the discussion of assessment of lymph nodes for certain materials has been expanded;

— a new Annex E “Test methods for devices contacting peripheral nerve tissue” and Annex G “Microscopic evaluation of tissue responses to implanted materials” have been added;

— tissue and pathological terminology has been updated throughout this document;

— bibliographical entries have been updated.

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

The objective of the implantation test methods is to characterize the local tissue response after implantation of a medical device or material (test sample) including integration, degradation, or absorption in an appropriate animal model.

The test sample is implanted into an anatomical site appropriate for the evaluation of the local effects of the medical device (or portion of) in an animal.

The medical device or material local effects are evaluated by a comparison of the tissue response caused by a test sample to that caused by comparative or reference control samples used in medical devices whose clinical acceptability and biocompatibility characteristics have been established.

Careful study design can include other relevant biological effects to reduce the number of animals used to evaluate safety and efficacy while accomplishing all study objectives. Additionally, a long-term systemic toxicity study that is designed to incorporate the methods, biological effects, additional timepoints and outcomes of implantation testing can satisfy the requirements of this document and ISO 10993-11.

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Biological evaluation of medical devices —

Part 6:
Tests for local effects after implantation

1 Scope

This document specifies requirements for implantation test methods for preclinical assessment of the local effects after implantation of medical devices or materials intended for use in medical devices. This document is applicable to the evaluation of local tissue responses from medical devices that are intended to be used where skin or mucosal tissue is breached, when required.

This document is applicable to medical device or materials that require implantation evaluation and can be solid or non-solid (such as porous materials, liquids, gels, pastes, powders, and particulates), absorbable, degradable, non- absorbable, or can be tissue-engineered medical products (TEMPs).

These implantation tests are not intended to evaluate or determine the performance of the test sample in terms of mechanical loading or functional performance. This document also does not provide guidance on methods and study design to satisfy requirements for systemic toxicity, carcinogenicity, teratogenicity or mutagenicity. However, the study designs can be modified to also assess other biological effects.

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, *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 10993-4, *Biological evaluation of medical devices — Part 4: Selection of tests for interactions with blood*

ISO 10993-9, *Biological evaluation of medical devices — Part 9: Framework for identification and quantification of potential degradation products*

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

ISO 10993-16, *Biological evaluation of medical devices — Part 16: Toxicokinetic study design for degradation products and leachables*

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO 10993-1, ISO 10993-2, ISO 10993-4, ISO 10993-9, ISO 10993-12, ISO 10993-16 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/

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