International

ISO 10993-3

Biological evaluation of medical devices —

Part 3: Evaluation of genotoxicity, carcinogenicity, reproductive toxicity and developmental toxicity

Évaluation biologique des dispositifs médicaux —

Partie 3: Évaluation de la génotoxicité, de la cancérogénicité, de la toxicité sur la reproduction et de la toxicité sur le développement

Fourth edition
2026-08

Reference number
ISO 10993-3:2026(en)

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Published in Switzerland

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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 fourth edition of ISO 10993-3 cancels and replaces ISO 10993-3:2014 and ISO/TR 10993-33:2015.

The main changes are as follows:

— this document has been entirely revised to emphasize evaluation of genotoxicity, carcinogenicity, reproductive toxicity and developmental toxicity instead of testing;

— chemical characterization and toxicological risk assessment have been added as an approach to address genotoxicity, carcinogenicity, reproductive toxicity and developmental toxicity;

— the follow-up evaluation has been changed when an in vitro genotoxicity test is positive and the flowchart for follow-up evaluation has been removed;

— reproductive toxicity and developmental toxicity have been described separately;

— the annex on cellular transformation has been deleted;

— ISO/TR 10993-33 has been merged into this document as Annex B on genotoxicity test methods.

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

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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 toxicity 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 edition of this document, 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 of the medical device.

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 toxicity and developmental toxicity.

This document presents test methods and evaluation strategies for the identification of specific biological harms. Testing is not always necessary or appropriate in evaluating biological 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 ISO 10993-18[7] are provided.