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# Biological evaluation of medical devices —

## Part 33: Guidance on tests to evaluate genotoxicity — Supplement to ISO 10993-3

*Évaluation biologique des dispositifs médicaux —*

*Partie 33: Directives sur les essais pour évaluer la génotoxicité — Supplément à l'ISO 10993-3*

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# Foreword

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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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For an explanation on the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the WTO principles in the Technical Barriers to Trade (TBT), see the following URL: Foreword — Supplementary information.

The committee responsible for this document is ISO/TC 194, *Biological and clinical evaluation of medical devices*.

ISO 10993 consists of the following parts, under the general title *Biological evaluation of medical devices*:

— *Part 1: Evaluation and testing within a risk management process*

— *Part 2: Animal welfare requirements*

— *Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity*

— *Part 4: Selection of tests for interactions with blood*

— *Part 5: Tests for in vitro cytotoxicity*

— *Part 6: Tests for local effects after implantation*

— *Part 7: Ethylene oxide sterilization residuals*

— *Part 9: Framework for identification and quantification of potential degradation products*

— *Part 10: Tests for irritation and delayed-type hypersensitivity*

— *Part 11: Tests for systemic toxicity*

— *Part 12: Sample preparation and reference materials*

— *Part 13: Identification and quantification of degradation products from polymeric medical devices*

— *Part 14: Identification and quantification of degradation products from ceramics*

— *Part 15: Identification and quantification of degradation products from metals and alloys*

— *Part 16: Toxicokinetic study design for degradation products and leachables*

— *Part 17: Establishment of allowable limits for leachable substances*

 

— *Part 18: Chemical characterization of materials*

— *Part 19: Physico-chemical, morphological and topographical characterization of materials (Technical specification)*

— *Part 20: Principles and methods for immunotoxicology testing of medical devices (Technical specification)*

— *Part 33: Guidance on tests to evaluate genotoxicity - Supplement to ISO 10993-3 (Technical Report)*

# Introduction

Genotoxicity tests are designed to detect compounds which induce genetic damage directly or indirectly by various mechanisms. These tests should enable hazard identification with respect to genetic damages. Expression of gene mutations, large scale chromosomal damage, recombination, and numerical changes are generally considered to be essential for heritable effects and the multi-step carcinogenesis. A positive genotoxicity test provides an indication that further testing can be warranted to determine the carcinogenic potential of the compound. Because the relationship between exposure to particular chemicals and carcinogenesis is established for man, while a similar relationship has been difficult to prove for heritable diseases, genotoxicity tests have been used mainly for the prediction of carcinogenicity. Nevertheless, because germ line mutations are clearly associated with human disease, the suspicion that a compound can induce heritable effects is considered to be just as serious as the suspicion that a compound can induce cancer. In addition, the outcome of such tests can be valuable for the interpretation of carcinogenicity studies.