SLOVENSKI STANDARD

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Biologko ovrednotenje medicinskih pripomoļ kov - 10. del: Preskusi draģenja in zakasnjene preobļ utljivosti (ISO 10993-10:2002)

Biological evaluation of medical devices - Part 10: Tests for irritation and delayed-type hypersensitivity (ISO 10993-10:2002)

Biologische Beurteilung von Medizinprodukten - Teil 10: Prüfung auf Irritation und Allergien vom verzögerten Typ (ISO 10993-10:2002)

Evaluation biologique des dispositifs médicaux - Partie 10: Essais d'irritation et d'hypersensibilité retardée (ISO 10993-10:2002)

Ta slovenski standard je istoveten z: **EN ISO 10993-10:2002**

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11.100.20	Biologko ovrednotenje medicinskih pripomoļ kov	Biological evaluation of medical devices

SIST EN ISO 10993-10:2003 **en**

EUROPEAN STANDARD

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English version

Biological evaluation of medical devices - Part 10: Tests for irritation and delayed-type hypersensitivity (ISO 10993-10:2002)

Evaluation biologique des dispositifs médicaux - Partie 10: Essais d'irritation et d'hypersensibilité retardée (ISO 10993-10:2002)

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This European Standard was approved by CEN on 5 August 2002.

CEN members are bound to comply with the CEN/CENELEC Internal Regulations which stipulate the conditions for giving this European Standard the status of a national standard without any alteration. Up-to-date lists and bibliographical references concerning such national standards may be obtained on application to the Management Centre or to any CEN member.

This European Standard exists in three official versions (English, French, German). A version in any other language made by translation under the responsibility of a CEN member into its own language and notified to the Management Centre has the same status as the official versions.

CEN members are the national standards bodies of Austria, Belgium, Czech Republic, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Italy, Luxembourg, Malta, Netherlands, Norway, Portugal, Spain, Sweden, Switzerland and United Kingdom.

EUROPEAN COMMITTEE FOR STANDARDIZATION
COMITÉ EUROPÉEN DE NORMALISATION
EUROPÄISCHES KOMITEE FÜR NORMUNG

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Foreword

This document (EN ISO 10993-10:2002) has been prepared by Technical Committee ISO/TC 194 "Biological evaluation of medical devices" in collaboration with Technical Committee CEN/TC 206 "Biocompatibility of medical and dental materials and devices", the secretariat of which is held by NEN.

This document supersedes EN ISO 10993-10:1995.

This European Standard shall be given the status of a national standard, either by publication of an identical text or by endorsement, at the latest by March 2003, and conflicting national standards shall be withdrawn at the latest by March 2003.

This document has been prepared under a mandate given to CEN by the European Commission and the European Free Trade Association, and supports essential requirements of EU Directive(s).

For relationship with EU Directive(s), see informative Annex ZB, which is an integral part of this document.

According to the CEN/CENELEC Internal Regulations, the national standards organizations of the following countries are bound to implement this European Standard: Austria, Belgium, Czech Republic, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Italy, Luxembourg, Malta, Netherlands, Norway, Portugal, Spain, Sweden, Switzerland and the United Kingdom.

Endorsement notice

The text of ISO 10993-10:2002 has been approved by CEN as EN ISO 10993-10:2002 without any modifications.

NOTE Normative references to International Standards are listed in Annex ZA (normative).

Annex ZA
(normative)

Normative references to international publications with their relevant European publications

This European Standard incorporates by dated or undated reference, provisions from other publications. These normative references are cited at the appropriate places in the text and the publications are listed hereafter. For dated references, subsequent amendments to or revisions of any of these publications apply to this European Standard only when incorporated in it by amendment or revision. For undated references the latest edition of the publication referred to applies (including amendments).

NOTE Where an International Publication has been modified by common modifications, indicated by (mod.), the relevant EN/HD applies.

Publication	Year	Title	EN/HD	Year
ISO 10993-1	1997	Biological evaluation of medical devices - Part 1: Evaluation and testing	EN ISO 10993-1	1997
ISO 10993-2	1992	Biological evaluation of medical devices - Part 2: Animal welfare requirements	EN ISO 10993-2	1998
ISO 10993-9	1999	Biological evaluation of medical devices - Part 9: Framework for identification and quantification of potential degradation products	EN ISO 10993-9	1999
ISO 10993-12	1996	Biological evaluation of medical devices - Part 12: Sample preparation and reference materials	EN ISO 10993-12	1996
ISO 10993-13	1998	Biological evaluation of medical devices - Part 13: Identification and quantification of degradation products from polymeric medical devices	EN ISO 10993-13	1998
ISO 10993-14	2001	Biological evaluation of medical devices - Part 14: Identification and quantification of degradation products from ceramics	EN ISO 10993-14	2001
ISO 10993-15	2000	Biological evaluation of medical devices - Part 15: Identification and quantification of degradation products from metals and alloys	EN ISO 10993-15	2000

Annex ZB
(informative)

Clauses of this European Standard addressing essential requirements or other provisions of EU Directives

This European Standard has been prepared under a mandate given to CEN by the European Commission and the European Free Trade Association and supports essential requirements of EU Directive 93/42/EEC.

WARNING Other requirements and other EU Directives may be applicable to the product(s) falling within the scope of this standard.

The following clauses of this standard are likely to support requirements of Directive 93/42/EEC.

Compliance with these clauses of this standard provides one means of conforming with the specific essential requirements of the Directive concerned and associated EFTA regulations.

Table ZB.1— Correspondence between this European Standard and EU Directive 93/42/EEC

Clause/subclause of this European Standard	Corresponding Essential Requirement of Directive 93/42/EEC	Comments
6 7	7.1 of Annex I	
B.2 B.3 B.4 B.5 B.6 B.7	7.1 of Annex I 7.2 of Annex I	

INTERNATIONAL STANDARD

ISO 10993-10

Second edition
2002-09-01

Biological evaluation of medical devices —

Part 10: Tests for irritation and delayed-type hypersensitivity

Évaluation biologique des dispositifs médicaux —
Partie 10: Essais d'irritation et d'hypersensibilité retardée

Reference number
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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.

International Standards are drafted in accordance with the rules given in the ISO/IEC Directives, Part 3.

The main task of technical committees is to prepare International Standards. Draft International Standards adopted by the technical committees are circulated to the member bodies for voting. Publication as an International Standard requires approval by at least 75 % of the member bodies casting a vote.

Attention is drawn to the possibility that some of the elements of this part of ISO 10993 may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights.

ISO 10993-10 was prepared by Technical Committee ISO/TC 194, *Biological evaluation of medical devices*.

This second edition cancels and replaces the first edition (ISO 10993-10:1995), which has been technically revised.

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

— *Part 1: Evaluation and testing*

— *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 8: Selection and qualification of reference materials for biological tests*

— *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*

Future parts will deal with other relevant aspects of biological testing.

This part of ISO 10993 is a harmonization of numerous standards and guidelines, including BS 5736, OECD Guidelines, U.S. Pharmacopoeia and the European Pharmacopoeia. It is intended to be the basic document for the selection and conduct of tests enabling evaluation of irritation and dermal sensitization responses relevant to safety of medical materials and devices.

Annex A forms a normative part of this part of ISO 10993. Annexes B and C are for information only.

Introduction

This part of ISO 10993 assesses possible contact hazards from chemicals released from medical devices that may produce skin and mucosal irritation, eye irritation and delayed contact hypersensitivity

Some materials that are included in medical devices have been tested, and their skin or mucosal irritation or sensitization potential has been documented. Other materials and their chemical components have not been tested and may induce adverse effects when in contact with biological tissues. The manufacturer is thus obliged to evaluate each device for potential adverse effects prior to marketing.

Traditionally, small animal tests are performed prior to testing on humans to help predict human response. More recently, *in vitro* tests as well as human tests have been added as alternatives. Despite progress and considerable effort in this direction, a review of findings suggests that currently no satisfactory *in vitro* test has been devised to eliminate the requirement for *in vivo* testing. Where appropriate, the preliminary use of *in vitro* methods is encouraged for screening purposes prior to animal testing. In order to reduce the number of animals used, this part of ISO 10993 presents a step-wise approach, with review and analysis of test results at each stage. An animal test is usually required prior to human testing.

It is intended that these studies be conducted using Good Laboratory Practice and comply with regulations related to animal welfare. Statistical analysis of data is recommended and should be used whenever appropriate.

The tests included in this part of ISO 10993 are important tools for the development of safe products, provided that these are executed and interpreted by trained personnel.

Biological evaluation of medical devices —

Part 10:
Tests for irritation and delayed-type hypersensitivity

1 Scope

This part of ISO 10993 describes the procedure for the assessment of medical devices and their constituent materials with regard to their potential to produce irritation and delayed-type hypersensitivity.

This part of ISO 10993 includes

a) pretest considerations,

b) details of the test procedures, and

c) key factors for the interpretation of the results.

Instructions are given in annex A for the preparation of materials specifically in relation to the above tests.

Supplementary tests which are required specifically for devices used intradermally in the ocular, oral, rectal, penile and vaginal areas are given in annex B.

2 Normative references

The following normative documents contain provisions which, through reference in this text, constitute provisions of this part of ISO 10993. For dated references, subsequent amendments to, or revisions of, any of these publications do not apply. However, parties to agreements based on this part of ISO 10993 are encouraged to investigate the possibility of applying the most recent editions of the normative documents indicated below. For undated references, the latest edition of the normative document referred to applies. Members of ISO and IEC maintain registers of currently valid International Standards.

ISO 10993-1:1997, *Biological evaluation of medical devices — Part 1: Evaluation and testing*

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

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

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

ISO 10993-13, *Biological evaluation of medical devices — Part 13: Identification and quantification of degradation products from polymeric medical devices*

ISO 10993-14 *Biological evaluation of medical devices — Part 14: Identification and quantification of degradation products from ceramics*

ISO 10993-15, *Biological evaluation of medical devices — Part 15: Identification and quantification of degradation products from metals and alloys*

ISO 10993-18, *Biological evaluation of medical devices — Part 18: Chemical characterization of materials*

ISO 14155-1, *Clinical investigation of medical devices for human subjects — Part 1: General requirements*

ISO 14155-2, *Clinical investigation of medical devices for human subjects — Part 2: Clinical investigation plans*

3 Terms and definitions

For the purposes of this part of ISO 10993, the terms and definitions given in ISO 10993-1 and the following apply.

3.1
allergen
sensitizer
substance/material which is capable of inducing specific hypersensitivity such that, on subsequent exposure to the same substance/material characteristic, allergic effects are produced

3.2
blank liquid
solvent portion treated in the same manner as the identical solvent used for the preparation of test samples but without test material, and which is intended for the determination of a background response of the solvent

3.3
challenge
elicitation
process following the induction phase in which the immunological effects of subsequent exposures in an individual to the inducing material are examined

3.4
corrosion
slow destruction of the texture or material of a tissue

EXAMPLE The action of a strong irritant.

3.5
delayed-type hypersensitization
induction of specific T-cell mediated immunological memory for an allergen to which an individual is exposed, resulting in a delayed-type hypersensitivity reaction after secondary contact with the allergen

3.6
dose
quantity to be administered to the test system at one time

3.7
erythema
reddening of the skin or mucous membrane

3.8
eschar
scab or discoloured slough of skin

3.9
induction
process that leads to the *de novo* generation of an altered state of immunological reactivity in an individual to a specific material

3.10
irritant
agent that produces irritation

3.11
irritation
localized non-specific inflammatory response to single, repeated or continuous application of a substance/material

3.12
necrosis
death of one or more cells, or portion of tissue or organ, resulting in irreversible damage

3.13
negative control
material or substance which, when tested by the procedure described, demonstrates the suitability of the procedure to yield a reproducible, appropriate negative, nonreactive or background response in the test system

3.14
oedema
swelling due to abnormal infiltration of fluid into the tissues

3.15
positive control
material or substance which, when tested by the procedure described, demonstrates the suitability of the procedure to yield a reproducible, appropriate positive or reactive response in the test system

3.16
solvent
material or substance used to moisten, dilute, suspend, extract or dissolve the test substance material

EXAMPLES Chemical, vehicle, medium, etc.

3.17
test material
material, device, device portion or component thereof that is sampled for biological or chemical testing

3.18
test sample
extract or portion of the test material that is subjected to biological or chemical testing

3.19
ulceration
open sore representing loss of superficial tissue

4 General principles — Step-wise approach

The available methods for testing irritation and sensitization were developed specifically to detect skin irritation and sensitization potential. Other types of adverse affect are generally not predicted by these tests.

This part of ISO 10993 requires a step-wise approach, which shall include one or more of the following:

a) characterization of test material, involving chemical characterization and analysis of the test sample according to the general principles described in ISO 10993-9, ISO 10993-13, ISO 10993-14, ISO 10993-15 and ISO 10993-18;

b) literature review, including an evaluation of chemical and physical properties, and information on the irritation and sensitization potential of any product constituent as well as structurally related chemicals and materials;

c) consideration of *in vitro* tests in preference to *in vivo* tests, and replacement of the latter as new *in vitro* methods become available and validated. At the present time there are no validated *in vitro* tests (other than simple screens) to detect irritants or sensitizers.

d) *in vivo* animal tests;