



BSI Standards Publication

**Cardiovascular biological
evaluation of medical devices
— Guidance for absorbable
implants**

National foreword

This Published Document is the UK implementation of ISO/TR 37137:2014.

The UK participation in its preparation was entrusted to Technical Committee CH/194, Biological evaluation of medical devices.

A list of organizations represented on this committee can be obtained on request to its secretary.

This publication does not purport to include all the necessary provisions of a contract. Users are responsible for its correct application.

© The British Standards Institution 2014. Published by BSI Standards Limited 2014

ISBN 978 0 580 84352 5

ICS 11.040.40

Compliance with a British Standard cannot confer immunity from legal obligations.

This Published Document was published under the authority of the Standards Policy and Strategy Committee on 30 June 2014.

Amendments issued since publication

Date	Text affected
------	---------------

**Cardiovascular biological evaluation
of medical devices — Guidance for
absorbable implants**

*Évaluation biologique cardiovasculaire des dispositifs médicaux —
Directives pour les implants absorbables*





COPYRIGHT PROTECTED DOCUMENT

© ISO 2014

All rights reserved. Unless otherwise specified, no part of this publication may be reproduced or utilized otherwise in any form or by any means, electronic or mechanical, including photocopying, or posting on the internet or an intranet, without prior written permission. Permission can be requested from either ISO at the address below or ISO's member body in the country of the requester.

ISO copyright office
Case postale 56 • CH-1211 Geneva 20
Tel. + 41 22 749 01 11
Fax + 41 22 749 09 47
E-mail copyright@iso.org
Web www.iso.org

Published in Switzerland

Contents

	Page
Foreword	iv
1 Scope	1
2 Terms and definitions	1
3 General considerations	1
4 Sterilization considerations	2
5 Drug-device combination product considerations	3
6 Part listing and description of absorbable related issues in addition to the relevant parts of ISO 10993 series “Biological evaluation of medical devices”	4
6.1 ISO 10993-1:2009, Evaluation and testing within a risk management process	4
6.2 ISO 10993-2:2006, Animal welfare requirements	4
6.3 ISO 10993-3:2003, Tests for genotoxicity, carcinogenicity and reproductive toxicity	4
6.4 ISO 10993-4:2002, Selection of tests for interactions with blood	4
6.5 ISO 10993-5:2009, Tests for <i>in vitro</i> cytotoxicity	5
6.6 ISO 10993-6:2007, Tests for local effects after implantation	6
6.7 ISO 10993-7:2008, Ethylene oxide sterilization residuals	8
6.8 ISO 10993-9:2009, Framework for identification and quantification of potential degradation products	8
6.9 ISO 10993-10:2010, Tests for irritation and delayed-type hypersensitivity	8
6.10 ISO 10993-11:2006, Biological evaluation of medical devices — Part 11: Tests for systemic toxicity	9
6.11 ISO 10993-12:2012, Sample preparation and reference materials	9
6.12 ISO 10993-13:2010, Identification and quantification of degradation products from polymeric medical devices	13
6.13 ISO 10993-14:2001, Identification and quantification of degradation products from ceramics	13
6.14 ISO 10993-15:2000, Identification and quantification of degradation products from metals and alloys	13
6.15 ISO 10993-16:2010, Toxicokinetic study design for degradation products and leachables	13
6.16 ISO 10993-17:2007, Establishment of allowable limits for leachable substances	13
6.17 ISO 10993-18:2005, Chemical characterization of materials	13
6.18 ISO/TS 10993-19:2006, Physico-chemical, morphological and topographical characterization of materials	14
6.19 ISO/TS 10993-20:2006, Principles and methods for immunotoxicology testing of medical devices	14
Annex A (informative) Nomenclature of absorb, degrade and related terms	15
Bibliography	16

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 documents should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2. www.iso.org/directives

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights. Details of any patent rights identified during the development of the document will be in the Introduction and/or on the ISO list of patent declarations received. www.iso.org/patents

Any trade name used in this document is information given for the convenience of users and does not constitute an endorsement.

The committees responsible for this document are ISO/TC 194, *Biological evaluation of medical devices* and ISO/TC 150/SC 2, *Cardiovascular implants and extracorporeal systems*.

Cardiovascular biological evaluation of medical devices — Guidance for absorbable implants

1 Scope

The objective of this Technical Report is to provide interim Part-by-Part guidance on potential adjustments to various test methods within the 10993 series to account for the intentional release of soluble components or degradation products from absorbable medical devices. The content is intended to add clarity and present potentially acceptable approaches for reducing the possibility of erroneous or misleading results due to the nature of the absorbable material. All suggestions should be considered as preliminary and subject to change, with final dispositions implemented through direct modification to the respective parts of ISO 10993. Thus, interim adoption of any of the described adjustments requires an accompanying written justification.

2 Terms and definitions

For the purposes of this document, the following terms and definitions apply.

2.1

absorb

<biomaterials> action of a non-endogenous (foreign) material or substance passing through or being assimilated by cells and/or tissue over time

2.2

degradation product

<byproduct> any intermediate or final result from the physical, metabolic, and/or chemical decomposition of a material or substance

2.3

degrade

to physically, metabolically, and/or chemically decompose a material or substance

2.4

leachable

substances that can be released from a medical device or material during clinical use

Note 1 to entry: In absorbable devices, leachables can be substances released from the as-manufactured product or substances generated and released as a consequence of its degradation (i.e degradation products).

[SOURCE: ISO 10993-12:2012, 3.10 modified — Note 1 to entry has been added.]

3 General considerations

Biological evaluation is the assessment of the ability of a device, device component, or a material to be present in the body without creating an adverse systemic impact and/or local effect on the surrounding cells and/or tissue. Biological evaluation of an absorbable material should be conducted in accordance with ISO 10993-1:2009 and other relevant parts (see ISO 10993-1:2009, Table A.1).

NOTE 1 General guidance regarding evaluation of devices in accordance with ISO 10993 series can be found in ISO/TR 15499.

By design, polymeric, ceramic, or metallic absorbable materials inherently produce relatively low molar mass degradation products when *in vivo*. The relatively elevated presence of these same products within the culture media can potentially impact the results of some biocompatibility tests. For example, in rare