TECHNICAL REPORT

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Biological evaluation of medical devices — Guidance on the conduct of biological evaluation within a risk management process

Évaluation biologique des dispositifs médicaux — Directives relatives à la conduite d'une évaluation biologique au sein d'un procédé de management du risque

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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 2.

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.

In exceptional circumstances, when a technical committee has collected data of a different kind from that which is normally published as an International Standard ("state of the art", for example), it may decide by a simple majority vote of its participating members to publish a Technical Report. A Technical Report is entirely informative in nature and does not have to be reviewed until the data it provides are considered to be no longer valid or useful.

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.

ISO/TR 15499 was prepared by Technical Committee ISO/TC 194, *Biological evaluation of medical devices*.

Introduction

0.1 General

This Technical Report provides guidance on conduct of biological evaluation of medical devices according to the requirements of ISO 10993-1. Although ISO 10993-1 provides a general framework for biological evaluation of medical devices, more detailed guidance can be helpful in the practical application of the standard. As a result, this Technical Report was developed to provide such guidance to users of ISO 10993-1. This guidance can be used to better understand the requirements of ISO 10993-1 and to illustrate some of the variety of methods and approaches available for meeting the requirements of ISO 10993-1.

Biological evaluation is a design verification activity which is set in the context of broader risk management processes. Therefore this Technical Report includes guidance on the application of ISO 10993-1 in the context of risk management processes conducted according to the requirements of ISO 14971. This Technical Report describes concepts and methods that can be considered in establishing and maintaining a risk management process for biological evaluation as part of the overall evaluation and development of a medical device.

As scientific knowledge advances our understanding of the basic mechanisms of tissue responses, biological evaluation may be based upon review of relevant established scientific data and upon chemical analysis and *in vitro* and *in vivo* testing where these are required. ISO 10993-1 specifies a framework in which to plan a biological evaluation which minimizes the number and exposure of test animals by giving preference to chemical constituent testing and *in vitro* models in situations where these methods yield equally relevant information to that obtained from *in vivo* models. The selection of which approach(es) are applicable to a particular medical device will depend on the nature of the device, the extent of available relevant scientific data and upon risk assessment.

When judging the applicability of the guidance in this Technical Report, applicable regulatory requirements and regulatory guidance should be considered.

An organization can voluntarily incorporate guidance from this Technical Report, wholly or in part, into its risk management process.

Guidance contained in this Technical Report can be useful as background information for those representing risk management process assessors, conformity assessment bodies and regulatory enforcement bodies.

0.2 Relationship with other standards, guidance documents and regulatory requirements

The relationship between ISO 10993-1, this Technical Report and the standards for biological evaluation of medical devices and general risk management is summarized as follows:

— this Technical Report provides guidance on the application of ISO 10993-1;

— biological evaluation is a component of risk management and this Technical Report includes guidance on the application of ISO 14971 to the conduct of biological evaluation.

Biological evaluation of medical devices — Guidance on the conduct of biological evaluation within a risk management process

1 Scope

This Technical Report is applicable to the conduct of biological evaluation of medical devices according to the requirements of ISO 10993-1. It does not add to, or otherwise change, the requirements of ISO 10993-1. This Technical Report does not include requirements to be used as the basis of regulatory inspection or certification assessment activities.

This guidance is applicable to all biological evaluation of all types of medical devices including active, non-active, implantable and non-implantable medical devices.

2 Normative references

The following documents, in whole or in part, are normatively referenced in this document and are indispensable for its application. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 10993-1:2009, *Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process*

3 Terms and definitions

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

3.1
biocompatibility
ability of a material to perform with an appropriate host response in a specific application

3.2
biological risk
potential for a substance to cause harm to health by virtue of its toxicity

3.3
biological safety
freedom from unacceptable biological risk

3.4
risk assessment
overall process comprising a risk analysis and a risk evaluation

[SOURCE: ISO/IEC Guide 51:1999, 3.12]

3.5
risk evaluation
process of comparing the estimated risk against given risk criteria to determine the acceptability of the risk

[SOURCE: ISO 14971:2007, 2.21]