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Biological evaluation of medical devices—

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Part 1:
Requirements and general principles for the evaluation of biological safety within a risk management process

Évaluation biologique des dispositifs médicaux —

Partie 1: Exigences et principes généraux pour l'évaluation de la sécurité biologique au sein d'un processus de gestion des risques

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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~~ document 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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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, ~~*Biocompatibility*~~*Biological and clinical evaluation of medical* ~~*and dental materials and*~~ *devices,* in accordance with the Agreement on technical cooperation between ISO and CEN (Vienna Agreement).

This sixth edition cancels and replaces the fifth edition (ISO 10993-1:2018), which has been technically revised.

The main changes compared to the previous edition are as follows:

— ~~The standard~~this document has been completely reorganised and the title ~~was changed to align~~has been aligned with the risk management framework described in ISO 14971~~.~~;

— ~~—~~ additional content has been added to provide more guidance and clarification of calculation of exposure duration~~.~~;

— ~~—~~additional content has been added to provide more guidance on ~~characterisation~~characterization of the device and identification of biological hazards~~.~~;

— ~~—~~the identification of biological effects (previously referred to as biological ~~endpoints~~end points) has been modified~~.~~;

— ~~—~~the term “externally communicating” has been replaced ~~in the normative text~~ by language which reflects the specific tissue contact of device components~~.~~;

— ~~—~~ the term “effects after implantation” has been changed to “local effects after tissue contact” as some non-implanted devices also will need this type of assessment~~.~~;

— Annex A ~~Annex A~~ has been revised to ~~move much of the content to the normative text. The remaining text in Annex A is now confined to provision of~~only provide guidance on materials ~~characterisation.~~characterization, the rest of its former content has been incorporated into the main text.

— Annex B ~~New Annex B explains~~ has been added to explain the rationale for the changes to biological effects listed in Table 1 to Table 4~~Table 1 Table 4~~.

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

Any feedback or questions on this document should be directed to the user's national standards body. A complete listing of these bodies can be found at www.iso.org/members.html.

Introduction

The primary aim of this document is to provide guidance and requirements for the biological evaluation of a medical device within a risk management process to protect humans from biological risks arising from the use of medical devices and the materials from which they are made. Biological risk evaluation compares the estimated biological risk against given risk criteria to determine the acceptability of the biological risk as part of the overall risk management.

Biological evaluation is primarily concerned with medical device biological safety, through consideration of risks associated with biological hazards. Nonetheless, some activities undertaken in the course of biological evaluation in addition to assessments of long-term safety can also generate information on device performance, for example the use of functional implant models to assess long-term responses such as tissue ingrowth. Biological evaluation, as described in this document, is synonymous with biocompatibility evaluation.

Biological evaluation is conducted on the finished medical device as it is intended to be used. The principles and methods described can also be useful in the evaluation of candidate materials or prototype devices during a medical device development process, and data obtained from such evaluations can be of value in the assessment of the finished medical device.

Medical device design is wide-ranging, and, at one extreme, a medical device consists only of a single material, which can exist in more than one physical form, while at the other extreme, is a complex article consisting of numerous components made from multiple materials. Biological safety cannot be considered in isolation from the overall medical device design and can require the balancing of conflicting requirements. For example, the choice of the best material with respect to its biological safety can result in a less functional medical device.

The evaluation of biological safety is conducted in the context of the specific intended use of a particular medical device. Materials can be safe in one medical device and not in another. It is impossible to make ~~generalised~~generalized conclusions about the safety of a particular material for all medical applications. Biological responses that are regarded as adverse, caused by a material in one application, ~~might~~are not ~~be~~necessarily regarded as adverse in a different situation.

Physical and chemical information supports the overall biological evaluation and can be used to inform testing needs if any. When biological testing is required, such testing is based upon in vitro, ex vivo~~,~~ or in vivo models. The interpretation of the results of biological tests requires caution because the inherent variability in biological responses between species and individuals means that the biological response observed in animal or cell culture models can differ from those observed in clinical use. Differences in response to the same material among individuals means that some individuals can have adverse reactions, even to well-established materials. Thus, biological evaluation is an exercise in risk management. When applied in the evaluation of candidate materials or prototype devices during a medical device development process, it allows the informed and timely consideration of risk control measures such as use of alternative materials, manufacturing processes or designs.

The biological evaluation processes described in this document draw on all available sources of information relevant to biological safety of the medical device, including post-market information. This allows a comprehensive review of the medical device, the identification of biological hazards and the biological harms which can arise and estimation of the associated risks. This comprehensive approach allows the identification of any gaps in the existing data set and the consequent need for conduct of supplementary assessments (e.g~~.~~, chemical analysis and hazard identification~~;~~, biological testing to refine a biological risk estimate).

This document is supported by a wide range of test methods and other guidance published in other documents in the ISO 10993 series as well as other standards. Those who use this document can also consider more specific guidance contained in device specific standards where available. For some complex or novel materials

or technologies, it can be difficult to use the established methods described in the ISO 10993 series. This document allows for the use of alternative procedures where scientifically justified.

The welfare of animals is very important and the selection of test methods and evolution of testing within the ISO 10993 framework is directed to continue to reduce, refine and, where possible, replace the use of animals for biological testing.