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Biological evaluation of medical devices — Requirements for interlaboratory studies to demonstrate the applicability of validated in vitro methods to assess the skin sensitization of medical devices

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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 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*.

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.

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Introduction

International Standards can be used to demonstrate the safety and compliance of medical devices. ISO 10993-10 specifies the procedure for the assessment of medical devices and their constituent materials with regard to their potential to induce skin sensitization (Type IV hypersensitivity reaction). The methods included in ISO 10993-10 are based on animal or human testing, with an annex on in vitro and in chemico tests for skin sensitization that have been validated for neat chemicals. The effort to reduce or replace the use of animals in toxicity testing has led to the development of many new non-animal methods. The test guidelines in References [56] and [57] include alternatives to animal testing methods for skin sensitization that have been previously validated to confirm their equivalence/superiority to the current in vivo methods. However, currently, none of the OECD test guideline methods are considered sufficient stand-alone replacements for in vivo tests that assess the skin sensitization potential of chemicals[1].

Current OECD test guideline methods are validated with neat chemicals and not with more complex mixtures such as medical devices or medical devices extracts. In order to use these methods in the specific context of medical devices, an evaluation is needed to verify their applicability for assessing skin sensitization of medical devices. Given the number of candidate test methods and the time that is required to assess them, it is important to ensure that the same science-based evaluation process and criteria are consistently applied to any new candidate test method. The purpose of this document is to provide a framework for the conduct of prevalidation and interlaboratory studies to assess the applicability of candidate test methods for assessing one or more key events related to OECD's adverse outcome pathway (AOP) for skin sensitization when evaluating medical devices[2].

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Biological evaluation of medical devices — Requirements for interlaboratory studies to demonstrate the applicability of validated in vitro methods to assess the skin sensitization of medical devices

1 Scope

This document specifies the framework and the methodology to evaluate and demonstrate the applicability of a validated non-animal method from an OECD test guideline to assess the skin sensitizing potential of a medical device or a medical device material. This document addresses:

— the database of reference chemical skin sensitizers and non-skin sensitizers;

— reference materials;

— feasibility testing of candidate test methods, including any method optimization for use with extracts of medical devices;

— prevalidation of candidate test methods;

— the interlaboratory study:

  — sample preparation and coding;

  — spiking of the extracts from the negative control medical device material;

  — data collection;

  — statistical analysis to assess reliability and reproducibility.

The use of the approaches described in this document to assess the applicability of a candidate test method does not imply that the candidate test method can be used as a stand-alone test for evaluating the skin sensitization potential of medical devices. For certain candidate test methods, integrated approaches and/or defined approaches are needed.[1] The evaluation of skin sensitization potential of a medical device is described in ISO 10993-10.

2 Normative references

The following documents are referred to in the text in such a way that some or all of their content constitutes requirements of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

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

3 Terms and definitions

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

ISO and IEC maintain terminology databases for use in standardization at the following addresses:

— ISO Online browsing platform: available at https://www.iso.org/obp

— IEC Electropedia: available at https://www.electropedia.org/

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