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# Sterilization of health care products — Radiation — Substantiation of selected sterilization dose: Method $VD_{\max}^{SD}$

*Stérilisation des produits de santé — Irradiation — Justification de la  
dose stérilisante choisie: Méthode  $DV_{\max}^{DS}$*



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.

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 (see [www.iso.org/directives](http://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 (see [www.iso.org/patents](http://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.

For an explanation of the voluntary nature of standards, the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the World Trade Organization (WTO) principles in the Technical Barriers to Trade (TBT), see [www.iso.org/iso/foreword.html](http://www.iso.org/iso/foreword.html).

This document was prepared by Technical Committee ISO/TC 198, *Sterilization of health care products*.

This first edition cancels and replaces ISO/TS 13004:2013.

The main changes are as follows:

- guidance is offered for determination of an SIP for bulk materials such as powders, liquids and gels;
- [5.3.3](#) and [5.3.4](#) have been reworded to match language in ISO 11137-2;
- the NOTE in [5.4.1](#) has been removed;
- [7.2](#) has been replaced with a reference to requirements in ISO 11137-1;
- guidance has been added for when to re-substantiate the sterilization dose based on shifts in bioburden.

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](http://www.iso.org/members.html).

## Introduction

This document is intended to be used in conjunction with ISO 11137-1. One of the activities encompassed within process definition in ISO 11137-1 is the option to select and substantiate a sterilization dose to be applied to health care products.

ISO 11137-2 includes Method  $VD_{\max}^{SD}$  for the substantiation of 25 kGy as a sterilization dose (termed Method  $VD_{\max}^{25}$ ) for product with an average bioburden less than or equal to 1 000 and Method  $VD_{\max}^{15}$  for the substantiation of 15 kGy as a sterilization dose for product with an average bioburden less than or equal to 1,5.

This document extends the methods of selection and substantiation of a sterilization dose specified in ISO 11137-2. It provides a methodology for the substantiation of selected sterilization doses of 17,5 kGy, 20 kGy, 22,5 kGy, 27,5 kGy, 30 kGy, 32,5 kGy and 35 kGy, each of which is valid only for a specified upper limit of average bioburden.

**NOTE** Selected sterilization doses of 25 kGy and 15 kGy are not included in this document. The seven methods in this document follow the same technical steps as the methods given in ISO 11137-2 for selection and substantiation of sterilization doses of 25 kGy and 15 kGy. However, the descriptive text in this document has been modified to better communicate the methods and hence the text occasionally differs from that in ISO 11137-2.

The method described in this document is for substantiation of a selected sterilization dose to achieve a sterility assurance level (SAL) of  $10^{-6}$  or less at that dose (e.g. Method  $VD_{\max}^{20}$  for a selected sterilization dose of 20 kGy). The application of the method is not limited by production batch size or production frequency, and the number of product items irradiated in the verification dose experiment remains constant. The method is founded on and embodies the following three principles:

- existence of a direct link between the outcome of the verification dose experiment and the attainment of an SAL of  $10^{-6}$  at the selected sterilization dose;
- possession of a level of conservativeness at least equal to that of the standard distribution of resistances (SDR);
- for a given bioburden, use of a maximal verification dose ( $VD_{\max}$ ) corresponding to substantiation of a selected sterilization dose.

This approach to sterilization dose substantiation was first outlined by Kowalski and Tallentire<sup>[2]</sup> and, from subsequent evaluations involving computational techniques (Kowalski, Aoshuang and Tallentire<sup>[8]</sup>) and field evaluations (Kowalski et al.<sup>[9]</sup>), it was concluded that the method is soundly based. An overview of the method and aspects of implementation are provided in Kowalski and Tallentire.<sup>[10][11]</sup> Application of the Method  $VD_{\max}^{SD}$  approach to doses other than 25 kGy is discussed in Kowalski and Tallentire<sup>[12][13]</sup>.

The method described here and designated Method  $VD_{\max}^{SD}$  procedurally comprises elements that closely parallel those of dose setting Method 1 described in ISO 11137-2. One key area of difference is the number of product items used in the verification dose experiment. In the computer evaluations referred to above, changing the verification SAL value had little effect on the substantiation outcome and this finding led to a sample size of 10 product items being chosen for subsequent field evaluations and, ultimately, for inclusion in this document.

Manufacturers of health care products who intend to use this specification are reminded that the requirements contained in the ISO 11137 series apply to the manufacture and control of production batches destined for radiation sterilization. In particular, one requirement states that products have to be manufactured in circumstances such that the bioburden is controlled. The control of the quality of raw materials, the manufacturing environment, the health, hygiene and attire of personnel and for establishing the basic properties of packaging material should be maintained.