EN ISO 11137-3 “Sterilization of health care products - Radiation – Part 3: Guidance on dosimetric aspects of development, validation and routine control”

Notes on differences between 2006 and 2017 versions

Introduction

An updated version of document EN ISO 11137-3 “Sterilization of health care products - Radiation – Part 3: Guidance on dosimetric aspects of development, validation and routine control” was published in 2017, replacing the original version that had been published in 2006. Although the Scope and overall outline of the two documents are similar, there have been significant changes in terms of the amount of guidance provided, particularly with respect to measurement uncertainty and the use of dosimetry in the OQ, PQ and routine control aspects of the radiation sterilization process. The purpose of this document is to highlight, in general terms, areas of difference between the two versions of the standard. It is not intended as a substitute for reading the standard itself and does not attempt to provide any additional guidance.

Contents of EN ISO 11137-3:2017

Figure 1 shows the contents of EN ISO 11137-3:2017. The overall structure is very similar to that of EN ISO 11137-3:2006, but Sections 4 (Measurement of Dose) and 5 (Selection and Calibration of Dosimetry Systems) in the 2006 version have been combined into one Section (Measurement of Dose) in the new standard. Three new informative Annexes have been added: Annex B (Tables of references for dosimetry-related testing during IQ/OQ/PQ), Annex C (Tolerances associated with doses used in sterilization dose setting/substantiation in ISO 11137-2 and ISO/TS 13004) and Annex D (Application of dose measurement uncertainty in setting process target doses).

In the remainder of this document, specific differences between the two standards are given, using the numbering and titles of clauses in EN ISO 11137-3:2017.

Scope (Clause 1)

The Scope has been widened to include guidance relevant to ISO/TS 13004 “Sterilization of health care products — Radiation — Substantiation of a selected sterilization dose: Method $VD_{max}{}^{SD}$”

Terms Definitions and Symbols (Clause 3)

This Clause has been expanded considerably to include many standard terms used in radiation sterilization. It also introduces two new terms:

“direct dose measurement” where dose at a given location is determined by a dosimeter measuring at that position, and

“indirect dose measurement” where dose at a given location is determined by a dosimeter measuring at another position. This typically applies to situations where dose at a separate monitoring location is used to determine minimum and maximum doses in an irradiation container by applying previously determined dose ratios.

Both terms are used in the new standard and it is necessary to differentiate between these two cases.

A list of symbols is given for doses at specific positions (e.g. maximum, minimum and monitoring) and their ratios, as determined during dose mapping. Symbols and meanings are also given for “target doses” that are introduced in Clause 4 and Annex D.

Measurement of Dose (Clause 4)

This Clause expands on the guidance given in Clauses 4 and 5 of EN ISO 11137-3:2006. The main difference is expanded guidance on dose measurement uncertainty, with emphasis on the methodology outlined in the “Guide to the expression of uncertainty in measurement”, commonly known as the GUM. The GUM document forms the basis of all statements about measurement uncertainty in ISO standards. Guidance is given both on general concepts and also on radiation dosimetry specific aspects. Using the GUM methodology, all measurements are considered to have an associated uncertainty. A given dose measurement can be taken to be the best estimate of the dose, but there will be a finite probability that the “true” dose lies in a region of uncertainty above or below the measured value. The measured dose does not require correction for uncertainty. The concept of “process target doses” is also introduced in Clause 4 and taken up in more detail in Annex D. The “target dose” concept involves the application of information on measurement uncertainty and process variability to ensure that the delivered doses are within specification during routine processing.

Establishing the Maximum Acceptable Dose (Clause 5)

Additional guidance is given on carrying out irradiations to establish the maximum acceptable dose. Clarification is given about the interpretation of data from samples irradiated to a range of doses.

Establishing the Sterilization Dose (Clause 6)

Some additional guidance is given on the allowable tolerances for irradiations carried out for establishing the sterilization dose and on the treatment of dose measurement uncertainty. The dose tolerances in ISO 11137-2 and ISO/TS 13004 are summarized in Annex C.

Installation Qualification (Clause 7)

No significant changes.

Operational Qualification (Clause 8)

No significant changes, but the importance of repeat OQ measurements to demonstrate consistent and stable operation is emphasised.

Performance Qualification (Clause 9)

Specific guidance is given about situations which require PQ measurements to be repeated. Additional guidance is given on dosimetry for inhomogeneous product, for example metal implants, irradiated in Gamma and X-ray irradiators. Guidance for Gamma and X-ray irradiators has been split into separate sections.

Routine Monitoring and Control (Clause 10)

Introduces the concept of an acceptable range of doses at the monitoring location based on consideration of the measurement uncertainty and process variability, in conjunction with user defined decision rules. It is clarified that these derived acceptance doses should be included in the process specification and that doses measured during routine processing should not be subject to correction for measurement uncertainty.

Annex A Mathematical Modelling

No significant changes.

Annex B Tables of references for dosimetry-related testing during IQ/OQ/PQ

This new annex contains three tables detailing the cross-references of clauses in ISO 11137-1:2006 and ISO 11137-3:2017 relating to dosimetry activities for IQ, OQ and PQ, respectively.

Annex C Tolerances associated with doses used in sterilization dose setting/ substantiation in ISO 11137-2 and ISO/TS 13004

This new annex summarises the tolerances associated with doses used in sterilization dose setting and substantiation in ISO 11137-2 and ISO/TS 13004.

Annex D Application of dose measurement uncertainty in setting process target doses

This new annex expands on the concept of “Target Doses” introduced in Clause 4. A combination of all information on measurement uncertainty and process variability is used to derive a standard deviation, designated $\sigma_{process}$. This can be used in the calculation of target doses at the monitoring location that correspond to doses to product in irradiation containers that are within specifications at a given level of confidence. Pictorial representations of these concepts are also given. These topics are expected to be developed further in the forthcoming ISO/TS 11137-4.

Figure 1 Contents of EN ISO 11137-3:2017