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ISO 11137-1 “Sterilization of health care products – Radiation – Part 1: Requirements for the development, validation and routine control of a sterilization process for medical devices”

Note on differences between 2025 and 2006 versions

A second edition of ISO 11137-1 “Sterilization of health care products – Radiation – Part 1: Requirements for the development, validation and routine control of a sterilization process for medical devices” was published in April 2025, replacing the first edition that had been published in 2006. Amendments to the first edition were issued in 2013 and 2018.

Although the Scope remained unchanged and the overall outline of the two documents is very similar, there have been some significant technical changes. The guidance in the Annex to ISO 11137 has been updated.

The purpose of this document is to highlight, in general terms and without detail about the Annex, 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.

For the remainder of this document, differences between the two standards will be given, using the numbering and titles of clauses in ISO 11137-1:2025.

Normative References (Clause 2)

Quality assurance standards ISO 10012-1 and ISO 13485 were removed from the list with normative references.

ISO/ASTM 52628, Standard practice for dosimetry in radiation processing, and ISO 13004, Sterilization of health care products — Radiation — Substantiation of selected sterilization dose: Method VD_{max}^{SD}, were added.

It should be noted that ISO/ASTM 52628 is to be withdrawn and replaced by ASTM 52628, which has identical content. This might initiate a minor revision or an amendment to ISO 11137-1:2025.

Terms and Definitions (Clause 3)

This Clause introduces some new terms and symbols. On the other hand, four terms were removed.

Updates were made in accordance with ISO 11139:2018 and ISO 9001:2015 when applicable. The definition of “Measurement Uncertainty” is now taken from International Vocabulary of Metrology VIM:2012 instead of VIM:1993.

New term	**Term removed**	**New symbol**
Process load	Change control	$D_{max,acc}$ (maximum acceptable dose)
Simulated product	D value, D_{10} value	SD, D_{ster} (sterilization dose)
Sterile Barrier System (SBS)	Primary manufacturer	
Verification dose	Transit dose	

General requirements (Clause 4)

The title changed from 'Quality management system elements'

Main differences are the re-organisation of the text into three clauses, with the removal of normative references ISO 10012-1 as well as ISO 13485 and the introduction of normative reference ISO/ASTM 52628. All dosimetry processes shall meet the requirements of ISO/ASTM 52628.

ISO 13485 is now mentioned multiple times in Annex A.4. Normative requirement 4.2.2 in ISO 11137-1:2006 has been moved (and rephrased) to informative clause A.4.1. This means the 2025 version of the ISO 11137-1 standard does no longer strictly require that responsibilities and authority between parties (e.g. manufacturers and suppliers) are specified. However, roles and responsibilities must still be clear to ensure traceability and accountability under general Quality Management (QM) principles. Normative requirement 4.1.2 in the first edition of the standard was moved (rephrased + extended) to Annex A.4.2. Normative requirements 4.3.3 and 4.4 in ISO 11137-1:2006 were moved (rephrased + extended) to Annex A.4.1.

Added emphasis on identifying Quality Management processes to be established, implemented, and maintained.

Sterilizing agent characterization (Clause 5)

Most significant change in this clause is the increase in the threshold level for the electron energy above which the potential for induced radioactivity in product and packaging system shall be assessed for both electron beam and X- ray sterilization. A documented assessment is now mandatory if the energy level for electrons exceeds 11 MeV or the energy level for electrons used to generate X-rays exceeds 7.5 MeV. These values were set at 10 MeV and 5 MeV in the first edition of ISO 11137-1, respectively.

In both the clauses about induced radioactivity (5.1.2) and materials effects (5.3) “product” is extended to “product and packaging system”.

Process and equipment characterization (Clause 6)

In clause 6.1 a requirement was copied in from ISO 14937:2009 section 6.3.4 about control and monitoring functions for process variables. “Means shall be provided to ensure that failure in a control function does not lead to failure in the recording of process variables such that an ineffective process appears effective.”

Table 1 was introduced with the intent to better visualize similarities as well as differences in minimum design specifications that need to be described for gamma, electron beam and X-ray irradiators. The concept of “beam width profile” was introduced for both electron beam and X-ray irradiators.

Product definition (Clause 7)

Clarification was added to specify the configuration of product within its packaging system. This requirement was in 9.4.3 a) and 9.4.4 a) of ISO 11137-1:2006.

Clause 7.2 has been expanded to state that for products that promote microbial growth, considerations shall be given to the maximal time interval and environmental conditions between manufacture and irradiation.

Also, clarification was added that determination of bioburden includes characterization and that bioburden alert as well as action levels need to be established in accordance with ISO 11737-1. The levels need to be established for the average bioburden (see also 12.1.2.4). If bioburden exceeds the established action level, bioburden resistance needs to be verified by performing a sterilization dose audit on the same batch, if possible, or the next manufacturing batch (see 12.1.2.4).

A substantial amount of new guidance is given in clause A.7.2 around the criticality of bioburden stability both in terms of numbers and types of microorganisms. It provides considerations that competent microbiology and sterility assurance personnel could use to demonstrate bioburden stability such as establishing and periodically assessing alert and action levels, performing in-depth bioburden characterization, performing testing on raw materials and components and assessing radiation resistance. This clause also includes guidance on the circumstances when microbial identification can be advantageous, for example when positive tests of sterility are obtained from sterilization dose audits, following bioburden alert or action level excursions or when initially establishing a bioburden baseline for a new product, cleanroom or manufacturing line.

Process definition (Clause 8)

With regard to establishing the maximum acceptable dose $D_{max,acc}$, a number of clarifications were made in clause 8.1.2. First of all it is specified that both product and packaging need to be assessed, secondly it is stated that product and packaging need to be physically representative for routine production and thirdly it is mentioned that the doses need to be delivered in a manner relevant to routine processing conditions (with respect to dose rate and product temperature, see 8.4.1 and A.8.4.1).

Guidance is now given on acceptable approaches to establish $D_{max,acc}$. Most notable is the approach where instead of irradiating product samples a process load is irradiated using the maximum process target dose that can be selected for routine sterilization as defined during PQ dose mapping. Then functionality of irradiated products is tested. This can be considered as stress testing corresponding to worst conditions of normal irradiation. The limitation of the approach is that the established $D_{max,acc}$ is applicable only to the defined process. Cases are listed where this approach can be needed.

The second edition of ISO 11137-1 now allows substantiation of sterilization doses other than 15 kGy and 25 kGy using Method VD_{max}^{SD}. Through reference to ISO 13004 sterilization doses in increments of 2.5 kGy may be substantiated within the range 15 kGy to 35 kGy. Each selected and substantiated sterilization dose corresponds to an upper limit of average bioburden per product item. From a procedural perspective, VD_{max}^{SD} in ISO 13004 is the same as VDmax25.

8.2.3 and Annex A.8.2.3 clarify: When establishing a sterilization dose, the product used for validation must be representative of routine production, especially with respect to bioburden quantity and types.

As in the first edition of ISO 11137-1 transference of a maximum acceptable dose to a radiation source different from that on which the dose was originally established requires a documented assessment demonstrating that the differences in the irradiation conditions (dose rate and product temperature) of the two radiation sources do not affect the validity of $D_{max,acc}$.

On the other hand, transference of a sterilization dose or a verification dose to a radiation source different from that on which the dose was originally established is now permitted with exception of product that contains water in the liquid state. For product which contains water in the liquid state, the requirement is essentially the same as in the first version of the standard i.e. dose rate effects need to be assessed for differences in microbicidal effects. For products that promote microbial growth, new guidance was introduced in Annex A.8.4.2. Careful consideration needs to be given to control of the microbial population until the start of sterilization.

Process validation (Clause 9)

For X-ray irradiators there is an additional requirement to determine and record the characteristics of the X-ray converter.

In both the sections on Operational Qualification (OQ) and that on Performance Qualification (PQ) a note was added stating that mathematical models can be used to calculate dose distributions, and therefore supplement or complement the measurement of dose associated with dose mapping.

It is per clause 9.3.1 no longer required to use product for PQ dose mapping. Simulated product may be used instead (see definition 3.33).

A new bullet point was added (9.3.1.c) which requires defining the relationship between dose at the routine monitoring position and process parameters. This is in line with clauses 6.1 and 10.7 which require process control.

The specification how to present product for sterilization was extended in 9.3.2 to include the orientation of package(s) within the irradiation container. Further, a description shall be provided of any materials intended for use with the irradiation container, including those used for positioning the product, managing temperature during irradiation, or attenuating the radiation dose delivered to the product.

According to 9.3.6, dose mapping shall be performed not only for every conveyor path but also for each type of irradiation container intended for processing the specified product.

The process specification list in 9.4.3 was increased to include a specification of materials added together with product into the irradiation container (see 9.3.2), to specify more aspects of process monitoring (method as well as frequency of routine process monitoring; acceptable limits for the routine monitoring dose(s) and process parameters) and to define the actions to be taken in the event of interruptions of the irradiation process.

Routine monitoring and control (Clause 10)

There has been a change in the wording of the requirements for routine monitoring and control of a sterilization process. The word “dosimeter” in clause 10 of the first version of ISO 11137-1 is replaced by “traceable dose measurement” in clause 10 of the second edition.

The second edition of ISO 11137-1 then states “Traceable dose measurements, in conjunction with the monitoring of processing variables, shall be carried out at sufficient frequency to verify that the process is in a state of control.“

A note points at ISO/TS 11137-4 for guidance.

Product release from sterilization (Clause 11)

No changes with respect to the second amendment to ISO 11137-1:2006, published in 2018.

Maintaining process effectiveness (Clause 12)

The first edition of ISO 11137-1 specified in general a maximum interval of three months between determinations of bioburden as well as performance of sterilization dose audits, with the intent to challenge seasonal variability in bioburden. The second edition of ISO 11137-1 still has that challenge in mind; but clarifies the wording to state that in general both need to be performed at least four times per year, with the interval not exceeding four months from the previous sampling.

ISO 11137-1:2025 includes the requirement to not only monitor the number of microorganisms but also characterize the bioburden, examples of this can be seen in Clause 12.1.1 a) “...monitor the number and types of microorganisms present on product” and clause 12.1.2.4 “...if a bioburden result of a batch exceeds an established action level, an investigation in accordance with ISO 11737-1 shall be performed and the bioburden characterized”.

In ISO 11137-1:2006 a notable exception to the general time interval between determinations of bioburden was for product having an average bioburden less than 1.5 CFU and for which the sterilization dose has been set using Method 1 or substantiated using Method VD_{max}[15]. For those situations the maximum interval of time between determinations of bioburden was required to be one month only.

ISO 11137-1:2025 no longer has that requirement. Instead, in clause 12.1.2.2 a number of situations which may require an increased frequency for determination of bioburden were grouped together. The requirement in that clause reads “For product bioburden having a high level of variability or where there is limited data, or for bioburden associated with a sterilization dose less than or equal to 17.5 kGy, consideration shall be given to either increased frequency of bioburden determinations or increased bioburden characterization or both, based on a risk assessment.”

Both the first and the second edition of ISO 11137-1 require a sterilization dose audit to be performed in case bioburden results differ from the normal routine bioburden. The actions to be taken if the sterilization dose audit is successful and the average bioburden continues to exceed the established action level are in ISO 11137-1:2025 no longer dependent on specific bioburden levels or the sterilization dose establishment method. Sterilization may continue using the dose used prior to the sterilization dose audit. If the frequency of sterilization dose audits is less often than four times per year, a frequency of four times per year shall be implemented until either the bioburden is returned to below the established value or the sterilization dose is re-established. If the bioburden continues to exceed the established action level, more frequent monitoring of the bioburden can identify negative trends at an early stage in order to initiate corrective actions.

Tables A1, A2 and A3 were removed from ISO 11137-1:2006. They did provide guidance on qualification of changes of irradiators. Instead, references are made to ASTM 51649 and ASTM E3270. The former contains table A.2 from ISO 11137-1:2006 and the latter contains an updated version of table A.1 from that standard.

Additional guidance was added in A.12.5.2 (and a new Table A.1) regarding change to product, its packaging system or the presentation of product for sterilization.

Bibliography

ISO 11137-1: “Sterilization of health care products – Radiation – Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices”.

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

ISO/TS 11137-4: “Sterilization of health care products – Radiation – Part 4: Guidance on the establishment and control of the irradiation process”.

ISO 11139: “Sterilization of health care products – Vocabulary of terms used in sterilization and related equipment and process standards”.

ISO/ASTM 52628: “Standard practice for dosimetry in radiation processing”.

ISO 13004: “Sterilization of health care products — Radiation — Substantiation of selected sterilization dose: Method VD_{max}^{SD}”.

ISO 10012-1: “Measurement management systems”.

ISO 13485: “Medical devices — Quality management systems — Requirements for regulatory purposes”.

ISO 14937: “Sterilization of health care products — General requirements for characterization of a sterilizing agent and the development, validation and routine control of a sterilization process for medical devices”.

ISO 9001: “Quality management systems – requirements”.

ISO 11737-1: “Sterilization of health care products — Microbiological methods Part 1: Determination of a population of microorganisms on products”.

ASTM E3270: “Standard Guide for Operational Qualification of Gamma Irradiators”.

ASTM 51649: “Standard Practice for Dosimetry in an Electron Beam Facility for Radiation Processing at Energies Between 300 keV and 25 MeV”.

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