Change of type of radiation in Radiation Sterilization of Medical Devices – Normative Requirements and Aspects in ISO 11137-1:2025

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Scope

In January 2020 a paper has been published by the Irradiation Panel in order to summarize normative requirements in ISO 11137-1 when changing between types of radiation, especially from gamma to X-ray, for radiation sterilization of medical devices. Scope of the current paper is to update the 2020 paper following publication of a second edition of ISO 11137-1 in April 2025.

Normative requirements in ISO 11137-1:2025 **[1]** are discussed and summarized in this paper.

Basically, four points are of interest for a change in type of radiation for sterilization and need to be evaluated:

- Requirements on the radiation source (sterilizing agent)
- Establishing or transferring the sterilization dose
- Establishing or transferring the maximum acceptable dose
- Performance Qualification (PQ) dose mapping

In each of the following sections one of these points is discussed. Since PQ dose mapping always needs to be performed in the irradiator the transfer is considered to, this point is not specifically elaborated on below.

Requirements on the radiation source

There is a requirement in ISO 11137-1:2025 (clause 5.1.2) that for electron beam and X-ray sterilization the energy level of the electron beam shall be specified. This clause also requires an assessment of the potential for induced radioactivity in the product and packaging system when the energy level for electrons exceeds 11 MeV or the energy level for electrons used to generate X-rays exceeds 7.5 MeV. While electron beams for radiation sterilization generally operate at 10MeV or below, X-ray irradiators for radiation sterilization typically operate at 7 MeV in order to benefit from greater conversion efficiency. The guidance section of A.5.1 refers to literature available about measurement and modeling of induced radioactivity.

Transfer of an Established Sterilization Dose

ISO 11137-1:2025 clearly states in clause 8.4.2 that transference of a sterilization dose (and corresponding verification dose) to a radiation source different from that on which the dose was originally established is permitted provided that the product does not contain water in the liquid state. It implies for such products not containing water in the liquid state, which are sterilized with different sources of radiation, that there is no need to perform a verification dose experiment using all applied sources of radiation.

For product that contains water in the liquid state, transference of the verification dose or sterilization dose is not permitted unless data are available to demonstrate that differences in operating conditions of the two radiation sources have no effect on microbicidal effectiveness.

In guidance section A.8.4.2.2 it is stated that a verification dose experiment carried out at the radiation source to which the product is being transferred can be a means to demonstrate that the sterilization and verification doses are still valid or to document that they should be re-established.

Additionally, for products that promote microbial growth, it is necessary to ensure that the condition of product presented for sterilization, including its bioburden, is controlled until the time of sterilization. Therefore, if transferring verification and sterilization doses to different sources, the effects of variables known to influence microbial growth (e.g. time, temperature and humidity) should be carefully considered and controlled. When control is not effective, new controls are required or transfer is not allowed.

Transfer of an Established Maximum Acceptable Dose

Clause 8.4.1 of ISO 11137-1:2025 states that transferring a maximum acceptable dose to a different radiation source from that on which the dose was originally established requires a documented assessment that the differences in irradiation conditions do not affect the validity of the established maximum acceptable dose.

Guidance to this clause refers particularly to dose rate during irradiation, with the remark that higher dose rates may lower the unwanted effects on product's critical performance attributes. Since gamma irradiators generally represent the lowest dose rate of all irradiators, this fact may ease the transfer from gamma to e-beam or X-ray to some extent. Industry guidances have been published for verifying the performances at the originally established maximum acceptable doses **[2,3]**.

Existing literature provides data on irradiation effects of different types of radiation **[4-10]** but leaves a significant amount of work to a medical device manufacturer or bioprocessing system supplier who is considering a change of radiation technology for sterilization due to logistic, economic or any other reason.

To try to support such assessments of transferring maximum acceptable dose, initiatives have been started and several groups are conducting experiments (see e.g. **[11,12]**) which will provide extensive data on radiation effects and material compatibility among different radiation types.

Databases might not be able to provide sufficient information about the product's "specified functional requirements", and in the absence of sufficient evidence to show the established maximum acceptable dose remains valid, the maximum acceptable dose will need to be re-established on the new radiation source using the process outlined in clause 8.1 of ISO 11137-1:2025.

Conclusion

This paper summarizes the regulatory requirements for changing the type of radiation for radiation sterilization of medical devices and discusses guidance provided in ISO 11137-1:2025. The assessment of the maximum acceptable dose has been identified as the main technical hurdle.

References

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