Change of Irradiation Modalities in Radiation Sterilization of Medical Devices – Normative Requirements and Aspects in EN ISO 11137-1

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Scope

This paper has been proposed by the X-ray Working Group of the Irradiation Panel in order to summarize normative requirements in EN ISO 11137-1 when changing of radiation sterilization modalities, especially from gamma to X-ray, for radiation sterilization of medical devices.

Background

Approximately half of the single-use medical devices manufactured today are sterilized using ionizing radiation **[1**]. Radiation sources are either isotope based (gamma irradiation from Co-60 decay) or machine based (electron beam or X-rays from high energy electron accelerators).
While all three irradiation modalities are treated equally in the applicable standard EN/ISO 11137-1 **[2]**, gamma irradiation continues to dominate the radiation sterilization market (~90%), followed by electron beam (~10%) **[1]**. X-ray technology currently has a share below 1 percent.
However, recently we have seen a growing interest in machine based radiation sources and discussion on measures required when changing the sterilization modality arose. Normative requirements exist in EN/ISO 11137-1 which are discussed and summarized in this paper.

Basically three points are of interest for a modality change 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

Requirements on the radiation source

There is a requirement in EN/ISO 11137-1 (clause 5.1.2) that for electron beam and X-ray sterilization the energy level of the electron beam shall be specified. This clause requires an assessment of the potential for induced radioactivity in the product for electron beam energies greater than 10 MeV and X-ray energies exceeding 5 MeV. While electron beams generally operate at 10MeV or below, X-ray systems typically operate at 7 MeV in order to benefit from higher conversion efficiency. The guidance section of A5.1 refers to a document by Gregoire et al. **[3]** which may represent such an assessment for non-metallic and most metallic elements. Materials not covered in that publication could require more detailed evaluation.

Transfer of an Established Sterilization Dose

EN/ISO 11137-1 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 shall not be permitted unless data are available to demonstrate the differences in operation conditions of the two radiation sources have no effect on the microbicidal effectiveness.

Guidance to this clause raises the concern that a source with a widely differing dose rate (related to the time period over which the sterilization dose is applied) can provide different microbicidal effects. To demonstrate that microbicidal effectiveness is not altered, a successful dose verification experiment using the radiation source to which it is intended to transfer is considered sufficient.

Following this guidance, a transfer of the established sterilization dose from one radiation source to another is permitted once a dose verification experiments has been successfully accomplished. Dose verification experiments typically involve the irradiation and tests of sterility of a specified number of samples (see EN/ISO 11137-2).

Transfer of an Established Maximum Acceptable Dose

Clause 8.4.1 of EN/ISO 11137-1 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 and temperature during irradiation, with the remark that higher dose rates may lower the unwanted effects upon product. 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.

Existing literature provides some data on irradiation effects of different sterilization modalities **[4, 5]** but it is currently not extensive and leaves a significant amount of work to a medical device manufacturer who is considering a change of radiation sterilization modality 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. **[6]**) which will provide a more extensive database on radiation effects and material compatibility among different radiation sterilization modalities.

However, 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 EN/ISO 11137-1.

Conclusion

This article summarizes the regulatory requirements for changing radiation sterilization modalities and discusses guidance provided in EN/ISO 11137-1. The assessment of the maximum acceptable dose has been identified as the main technical hurdle.

References

[1] Comparison of Gamma, E-beam, X-ray and ETO technologies for the industrial sterilization of medical devices and healthcare products, GIPA white paper August 2017, available from: http://gipalliance.net/wp-content/uploads/2013/01/GIPA-WP-GIPA-iia-Sterilization-Modalities-FINAL-Version-2017-October-308772.pdf

[2] International Standard EN/ISO 11137 Sterilization of health care products - Radiation.

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[4] B. Croonenborghs et al., X-ray versus gamma irradiation effects on polymers, Radiation Physics and Chemistry 67, issue 11-12, November-December 2007

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[6] M. Murphy et al., Filling data gaps related to material effects in polymer medical products from e-beam and X-ray sterilization, IMRP 2019