EMPIR Call 2015 – Health, SI, Normative and Research Potential

Selected Research Topic number: **SRT-n03**
Version: 1.0

Title: Evaluation of the effect of measurement uncertainty on patient safety with respect to radiation sterilisation of medical devices

Abstract

Currently, approximately 50 % of single use medical devices are sterilised by irradiation. The safe and efficacious use of this technique therefore has a large impact on healthcare. Medical devices that are put on the European market must comply with the essential requirements of the medical directive EEC/93/42, 2007/47/EC in order to obtain CE marking. New challenges for meeting these requirements are presented to manufacturers of medical devices for new products that require tight dose tolerances in order to obtain the required Sterility Assurance Level (SAL) without negative effects on product functionality.

Standard EN/ISO 11137 allows absorbed doses to be used for obtaining the required level of sterility to be established by a manufacturer on a product-specific basis. A sterilisation dose can be determined based on microbiological evidence, or it can be selected by the manufacturer and its effectiveness substantiated. Recent revisions of the medical device radiation sterilisation standards (EN/ISO 11137-1, 2 & 3) have highlighted the lack of a unified approach to measurement uncertainty in microbiological and dosimetric aspects. Of particular concern is the uncertainty associated with microbiological aspects, where no accepted methods of uncertainty evaluation currently exist.

Keywords

Medical device, Uncertainty, Absorbed dose, Radiation, Sterilisation, Microbiology, Medical device directive.

Background to the Metrological Challenges

Determination of the sterilisation dose or selection of the sterilisation dose to be substantiated is, as a first step, based on the population of microorganisms on the product items – the bio-burden. The second step of establishing the sterilisation dose concerns verification that the radiation resistance of the product bio-burden is less than that of a standard distribution of resistances.

The international standard for radiation sterilisation EN/ISO 11137, parts 1, 2 and 3 gives requirements and guidance for establishing the sterilisation dose needed to obtain the required level of sterility given in EN 556-1. Methods for determination of dose measurement uncertainties are established, (e.g. ISO/ASTM 51707), but there is a lack of accepted methods for the interpretation and use of dose measurement uncertainties and this has led to difficulty in achieving agreement between users and regulators of radiation sterilisation. This became particularly apparent during the current revision of EN/ISO 11137-3. Work is ongoing in ISO TC198 and also in other standardisation committees such as the ASTM International committee E61 concerning this issue, but these work tasks will not be addressing the complete overall uncertainty combining microbiological and dosimetry uncertainties and their possible effect on assurance of sterility of the sterilised medical device. Regardless of the successful application of these microbiological methods, it must be noted that the uncertainties of the methods and the possible impact of uncertainties on results derived from using the methods have not been established.

Objectives

The JRP shall focus on metrology research necessary to support standardisation in both microbiological and dosimetric aspects of the radiation sterilisation process. Particular emphasis shall be given to the uncertainty associated with microbiological aspects.

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The specific objectives are

1. To establish methods for determining uncertainty related to the quantitative microbiological methods for bio-burden determination and for tests of sterility used in the radiation sterilisation of medical devices. This work will concentrate on the EN/ISO standards 11737-1 and 11737-2 that are used in the establishment of sterilisation dose required in EN/ISO 11137-1 and described in EN/ISO 11137-2 and EN/ISO TS 13004.
2. To establish methods for the determination of uncertainty in dose measurement and dose delivery in sterilisation dose establishment and routine sterilisation processing. This work will expand on the outline given in the EN/ISO 11137-3 standard.
3. To establish the effect of microbiological and dosimetric uncertainties on the uncertainty in sterilisation dose as determined by the methods given in standards EN/ISO 11137-2 and EN/ISO TS 13004. This work will involve collaboration with industrial partners, including the collection and analysis of data, and mathematical modelling of the methods.
4. To determine the effect of combined microbiological and dosimetric uncertainties on the criteria for release of product from the radiation sterilisation process.
5. To collaborate with the technical committees CEN TC204 and ISO TC198, and the users of the Standards they develop to ensure that the outputs of the project are aligned with their needs, including the provision of a report on the effect of measurement uncertainty on achieved levels of sterility and recommendations for incorporation of this information into future standards at the earliest opportunity.

The proposed research shall be justified by clear reference to the measurement needs within strategic documents published by the relevant Standards Developing Organisation or by a letter signed by the convenor of the respective TC/WG. EURAMET encourages proposals that include representatives from industry, regulators and standardisation bodies actively participating in the projects.

Proposers should establish the current state of the art, and explain how their proposed project goes beyond this.

EURAMET expects the average EU Contribution for the selected JRPs in this TP to be 0.4 M€, and has defined an upper limit of 0.5 M€ for this project.

EURAMET also expects the EU Contribution to the external funded partners to not exceed 30 % of the total EU Contribution to the project. Any deviation from this must be justified.

Any industrial partners that will receive significant benefit from the results of the proposed project are expected to be unfunded partners.

Potential Impact

Proposals must demonstrate adequate and appropriate participation/links to the “end user” community, describing how the project partners will engage with relevant communities during the project to facilitate knowledge transfer and accelerate the uptake of project outputs. Evidence of support from the “end user” community (e.g. letters of support) is also encouraged.

You should detail how your JRP results are going to:

- Address the SRT objectives and deliver solutions to the documented needs,
- Feed into the development of urgent documentary standards through appropriate standards bodies,
- Transfer knowledge to the medical device industry and health sector.

You should detail other impacts of your proposed JRP as specified in the document “Guide 4: Writing a Joint Research Project”

You should also detail how your approach to realising the objectives will further the aim of EMPIR to develop a coherent approach at the European level in the field of metrology and include the best available contributions from across the metrology community. Specifically the opportunities for:

- improvement of the efficiency of use of available resources to better meet metrological needs and to assure the traceability of national standards
- the metrology capacity of EURAMET Member States whose metrology programmes are at an early stage of development to be increased
- organisations other than NMIs and DIs to be involved in the work

Time-scale

The project should be of up to 3 years duration.

Additional information

This topic is in response to needs identified by CEN/CENELEC published at http://msu.euramet.org/pre_norm_2015/index.html#stage1-orientation (priority 2: Measurement uncertainty on patient safety related to radiation sterilisation of medical devices, microbiological methods and dosimetry).