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June 16, 2023

Re: Summary of SaniSure, Sparta NJ Gamma Irradiation Sterilization Validation

The purpose of this document is to provide an overview of Sanisure, Sparta's Gamma Irradiation Sterilization Validation.

The primary objective of the sterility validation was to validate that component materials used in assemblies can be supplied as sterile. Material for this sterilization validation was selected to cover a broad range of products. The gamma irradiation process was conducted at sub-contractor Sterigenics. Sterigenics performed the validation testing on the Single Use Systems Family (master product representation approach). The Single Use Systems Family master product can be assembled to consist of any number of components as described in more detail below. This study was conducted to substantiate a 27.5 kGy dose and validates the effectiveness of Gamma Radiation for sterilization of the Single Use Systems Family.

The 27.5 kGy minimum dose was selected for validation purposes based on the outcome of the initial pre-sterilization bioburden analysis.

Qualification of Irradiation Site:

The gamma irradiation process was done at a sub-contractor Sterigenics located in Itasca, IL. The installation and operational qualification (IQ/OQ) for the irradiation site was performed by the sub-contractor.

IQ demonstrated that the irradiator has installed equipment accordance with its specifications. This involves the equipment documentation, equipment testing, equipment calibration, maintenance, and training. OQ showed that the irradiator performed in accordance with its specifications. This included such items as the geometry of the course, source to product distance, cycle time, product geometry and density, dose magnitude, distribution, and reproducibility.

As part of Sanisure's Quality Process, Sterigenics was qualified as a key supplier and is audited every three years.

Single Use Systems Family Design:

The sample item portion (SIP) designed for this validation was based on the following justification:

- SIP will assess bio-burden for all current product families. A product family is described as components produced by a specific supplier from the same materials of construction, i.e. resin grade.
- SIP assembly represents the worst-case bio-burden loading due to the proximity of multiple connections (considered to be excessive handling) various materials of construction and the components produced by a variety of approved suppliers.
- The shape, size or functionality of the component was considered to contribute a minimal amount of bio-burden to the final assembly. This consideration was made as components

are produced by a variety of approved suppliers. Each supplier has established procedures to ensure bio-burden levels are kept at a minimum. This validation focused on product bio-burden that increases significantly more from the manipulations to produce the connection and not by the shape, size or function of the connector or tubing (components). The assembly design allows for accurate and reproducible bio-burden recovery.

- The SIP assembly design allows for post-gamma irradiation sterility testing which will include the effect of irradiation on product materials and packaging.

Bio-burden Characterization:

Sterigenics executed the validation testing protocol on the Single Use Systems Family per the Sterigenics protocol PR-EAS-2023-0150 Rev 0. An exhaustive bio-burden recovery validation was performed and was utilized for analyzing Sanisure's SIP. The SIP used for this testing was one (1).

Establishing the Verification Dose:

The established bio-burden testing was performed on three independent lots of one (1) for the SIP to determine the verification dose. The overall average bioburden from the three lots, including the recovery factor was 19.8 cfu/device. Based on the 19.8 cfu/device the verification dose was determined directly from Table 9 of the ANSI/AAMI/ISO TIR 13004 guidelines. The verification dose for this validation and future dose audits is 8.7 kGy.

As part of the validation, the verification dose was delivered to thirteen (13) SIP samples. These samples were dose mapped to verify the actual dose delivery. Results showed that the verification dose did not vary more than +/-10 percent.

Test of Sterility:

After the verification dose was applied to the verification samples, the samples were tested for sterility. The sterility tests showed one (1) positive in the ten (10) SIP samples. This was within the acceptance criteria of no more than one positive sample per ten verification dose samples.

Establishing the Minimum Sterilization Dose:

The verification showed one positive sterility test culture for samples irradiated at the verification dose of 8.7 kGy and was within the statistical verification of one positive in 10 systems. To establish the minimum sterilization dose at a SAL of 10^{-6}, the minimum gamma dose was selected to be 27.5 kGy from the ANSI/AAMI ISO TIR13004 guidelines with the average bioburden selected to be less than 5000 cfu/device. This was selected based on the average bio-burden results of 19.8 cfu/device found in the non-irradiated samples. Thus, this substantiated a 27.5 kGy dose and validates the effectiveness of Gamma Radiation for sterilization of the Single Use Systems Family.

In accordance with ANSI/AAMI ISO TIR13004, statistical verification was successfully completed since not more than one positive test culture was observed after irradiation at the determined verification dose for the lots tested. The average bioburden was less than 5,000 organisms, statistical verification of the bioburden resistance was accepted, and therefore the sterilization dose of 27.5 kGy was accepted as the 10^{-6} SAL dose for the Single Use Systems Family. Based on the results, material that is gamma irradiated between 27.5 – 45 kGy is considered sterile.

Dose Mapping:

1. To ensure process reproducibility within the specified range of gamma irradiation, dosimeters were used to identify the minimum and maximum zones within products. The identified minimum and maximum dose locations will be used for routine process monitoring. Dose mapping will be performed for each density range to ensure that all products will receive the irradiation dose range of 27.5 to 45.0 kGy.

2. **Sanisure's Process Monitoring Program to maintain SAL 10^{-6}:**

3. The following items will be completed to maintain the claim that Sanisure's products are at a Sterility Assurance Level of 10^{-6} built at the Sanisure, Sparta facility and irradiated at Sterigenics in Rockaway, NJ:

- This will be done by monitoring the product density prior to each sterilization cycle.
- Dose Mapping of routine production loads to determine minimum and maximum absorbance into products. The calibration and location of dosimeters will also demonstrate the degree of process control. Products will be released on these measurements by both Sterigenics and Sanisure.
- Dose audits will be performed on SIP irradiated at the verification dose of 8.7 kGy.

Verification dose audits are conducted in accordance to ANSI/AAMI/ISO 11137-1 to substantiate the continued validity of 27.5 kGy dose as a 10^{-6} SAL dose. Additionally, specific dose audit requirements are described within an approved procedures and work instructions. These procedures provide details regarding the following topics:

- Frequency (quarterly) and changes to frequency
- Master product representative selection
- Product adoption dose audits (used when new materials are added)
- Form used for new product enrollment
- Dose audit failures and interpretation

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The Gamma Irradiation Sterilization Validation was conducted in accordance with the following standards:

- ANSI/AAMI/ISO 11737-1:2018, Sterilization of health care products – Microbiological methods – Part 1: Determination of the population of microorganisms on product.
- ANSI/AAMI/ISO 11137-2:2019, Sterilization of medical devices – Microbiological methods – Part 2: Test of sterility performed in the definition, validation, and maintenance of a sterilization process.
- ANSI/AAMI/ISO 11137-1 (R) 2015 & A1:2013 & A2:2019, Sterilization of heath care products – Radiation– Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices
- ANSI AAMI ISO TIR11137-2:2013/ (r) 2019, Sterilization of health care products – Radiation – Part 2: Establishing the sterilization dose.
- ANSI/AAMI/ISO TIR13004:2013/ (R) 2016 Sterilization of health care products- Substantiation of a selected sterilization dose – Method VD_{max}
- USP/NF, U.S. Pharmacopeia <71> (current version)

If you have any further questions regarding this, please don't hesitate to contact me.

Sincerely,

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