May 29, 2019

Summary of SaniSure's Gamma Irradiation Sterilization Validation

Dear Valued Customers,

The sterility validation goal was to be in full compliance with ISO 11137 where SaniSure could claim a Sterility Assurance Level of 10^{-6} for Single Use Systems built at SaniSure and irradiated at Sterigenics in Corona, CA over its shelf life. The validation process steps included qualification of the irradiation site, designing the sample item portion (SIP) that represents the worst-case bio-burden level, bio-burden characterization of the SIP, verification dose experiments, establishing the minimum and maximum irradiation dose; performing dose mapping of various product densities. In addition, SaniSure will implement a process monitoring system to further ensure the SAL of 10^{-6} for Single Use Systems.

Qualification of the Gamma Irradiation Site:

The gamma irradiation process was done at a sub-contractor Sterigenics located at 344 Bonnie Circle, Corona, CA.

As part of SaniSure's Quality Process, Sterigenics was qualified as a critical supplier and will be audited every three years. SteriPro Laboratory performed the sterility testing for this validation. This lab was also qualified as a critical supplier to SaniSure.

Sample Item Portion:

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

- SIP will assess bio-burden for all product families. A product family is described as components produced by a specific supplier from the same exact materials of construction (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 SaniSure's 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). This assembly design allows for accurate and reproducible bio-burden recovery.
- The SIP assembly design allows for post-gamma irradiation sterility testing which include the effect of irradiation on product materials and packaging.

Bio-burden Characterization:

SteriPro Labs executed the validation testing protocol on the Single Use Systems Family. 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 ten (10) for the SIP to determine the verification dose. The overall average bio-burden from the three lots, including the recovery factor was 1284.8 cfu per device. Based on the 1284.8 cfu per device the verification dose was determined directly from Table A.6 of the AAMI TIR33 guidance.

As part of the validation, the verification dose was delivered to ten (10) SIP systems. 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 placed on sterility. The sterility tests showed no positives in the ten (10) SIP systems. 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 no positive sterility test culture for samples irradiated at the verification dose 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 AAMI TIR33 guidelines with the average bio-burden selected to be less than 5000 cfu. This was selected based on the average bio-burden results of 1284 cfu 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.

Dose Mapping:

To ensure process reproducibility with 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 45kGy.

SaniSure's Process Monitoring Program to maintain SAL 10^{-6}:

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 facility and irradiated at Sterigenics in Corona, CA:

- 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 a quarterly basis.
- Product Adoption dose audits will be performed when the need arises to add new components.

Product Adoption Dose Audits:

Product adoption dose audit is a process of formally including a candidate product into an existing validated radiation product family. The product adoption dose audit approach requires more extensive testing and number of samples than the standard dose audit. These dose audits have been successfully performed to add new components and materials.