PALL Biotech

Approach to Sterility

Gamma-Irradiation: Sterilization Validation Approach for Allegro™ Single-Use Systems with Sterile Claim

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1 Pall Biotech's Approach to Sterility for Allegro Systems

Pall's Allegro single-use systems (SUS) are sterilized by gamma irradiation following the ISO standard 11137-2 '*Sterilization of health care products – Radiation – Part 2: Establishing the sterilization dose'* and/or ISO/TS 13004 *'Sterilization of health care products – Radiation – Substantiation of selected sterilization dose: Method VDmaxSD'* to support the sterile claim as given for these products. A sterile claim can be made when a Sterility Assurance Level (SAL) of 10^{-6} has been proven.

The standards allow for a 'product family' approach to be used for establishing and maintaining the sterilization dose. The standards also give guidelines on how to establish a product family. Three options are given to establish a product family: a master product, an equivalent product, or a simulated product.

The simulated product is described in the above standards as '*a combination of components (…) that would not typically be combined for use*', and this approach has been selected for Allegro single-use systems. This master system features a design with an unusual amount of connections and handling when compared to surface area, comprising of a wide range of different materials from different suppliers. It is produced under identical production conditions as all Allegro single-use systems. As such, the Allegro master system is used to show that the components, handling and cleanroom environment result in a final product that is within specification for the relevant requirements for sterile systems.

Because Allegro systems vary from very small tube sets to very large biocontainers with complex assemblies, it is not possible for the laboratory to perform a sterilization validation on a full-scale set to account for all variations. To allow for this possibility, the standards have adopted, where required, to use a Sample Item Portion (SIP) approach. Factors like length, mass, volume, or surface area can be used to determine the SIP factor for individual final products, and from that an estimated bioburden.

Allegro systems use an SIP approach based on number of connections or surface area, whichever is the greatest contributor to bioburden levels. Each new system is compared against the Allegro master system to estimate bioburden level using the SIP factor and to determine coverage by the master system of all used components.

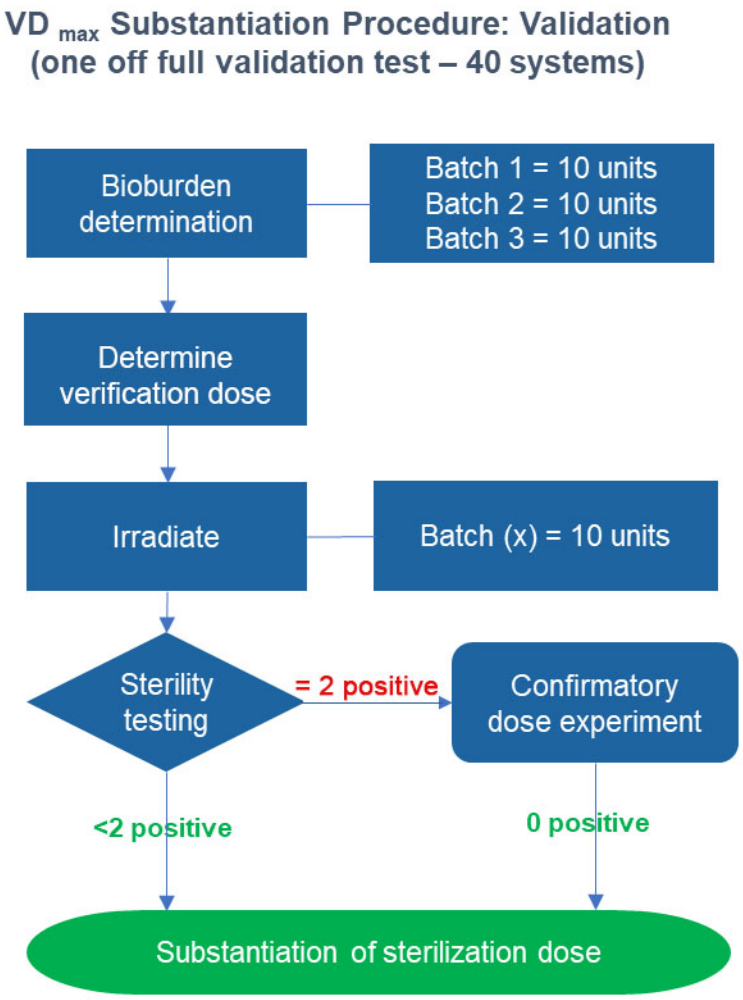
The minimum irradiation dose to obtain a sterility assurance level of 10^{-6}, the prerequisite for a sterile claim, depends on the average bioburden on the product to be sterilized. To accommodate for the variety in bioburden levels of Pall's Allegro systems, Verification Dose maximum (VD_{max}) sterilization validation approaches are used.

2 Validation

VD_{max} studies are performed using the Allegro master set as per ISO 11137-2 and/or ISO/TS 13004. Three different batches each comprising of ten samples are tested for bioburden and an average result is obtained. This average bioburden result is used to establish the verification dose (kGy) to yield a sterility assurance level (SAL) of 10^{-6}. Ten additional samples are then irradiated at the validation dose and tested for sterility. If no more than one positive result is obtained after the incubation period, then the validation is accepted.

Figure 1.

VD_{max} substantiation procedure - validation



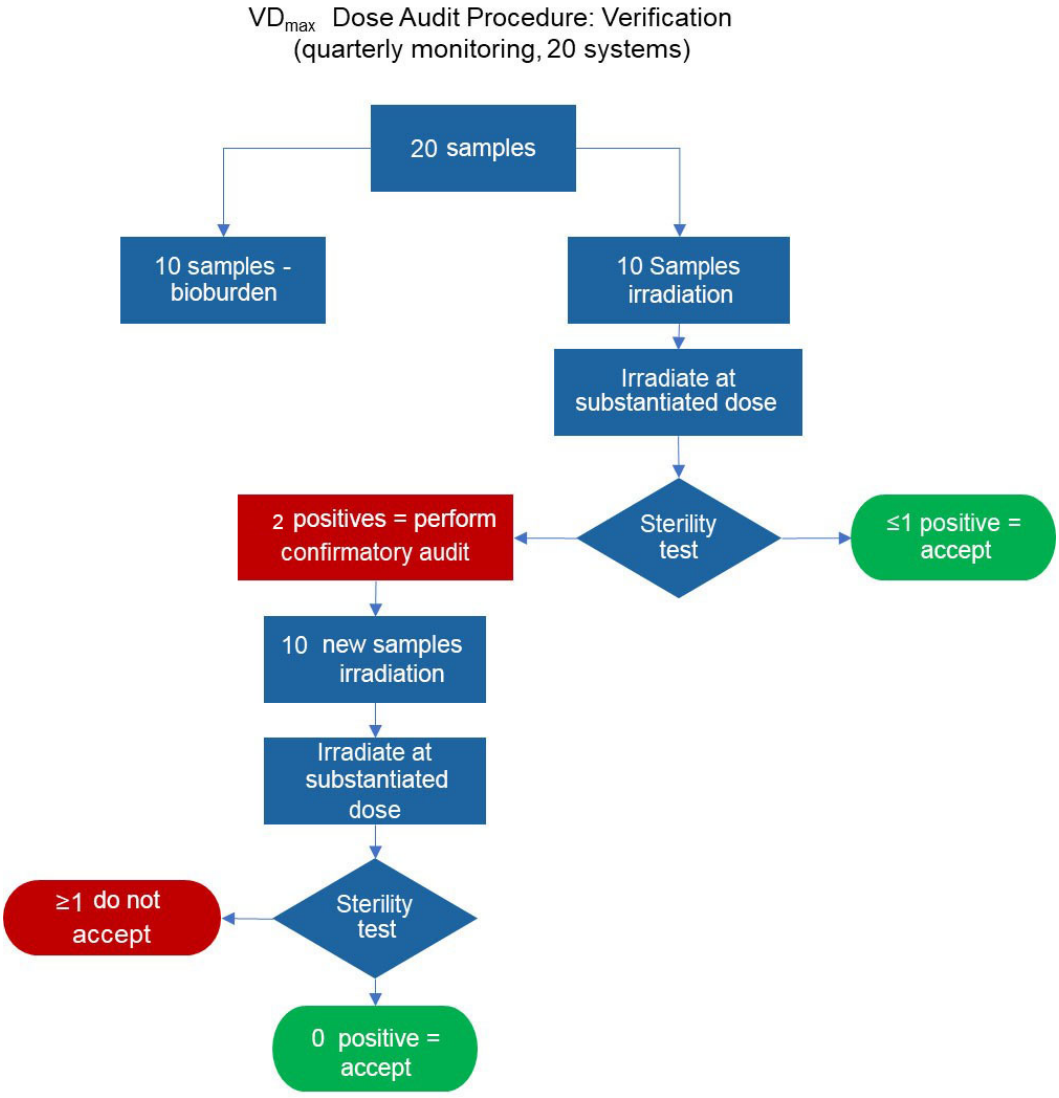
Sterilization validation, as described above, is independently performed for each Pall Biotech single-use technology (SUT) site. Each Allegro single-use system manufacturing site shall perform a similar validation independently.

3 Verification

Sterilization dose audits are furthermore repeated on a quarterly basis to demonstrate continued substantiation of sterilization dose.

Figure 2.

VD_{max} dose audit procedure - verification



Gamma dose levels to assure $SAL10^{-6}$ reduction and hence sterility, according to ISO 11137-2:

VD_{max} sterilization dose v maximum CFU count:

- $\geq$ 25.0 kGy – Bioburden of < 0.1 – 1,000 CFU
- $\geq$ 27.5 kGy – Bioburden of < 1.0 – 5,000 CFU
- $\geq$ 30.0 kGy – Bioburden of < 1.0 – 23,000 CFU

4 Dose Mapping

Assurance that minimum dose is achieved:

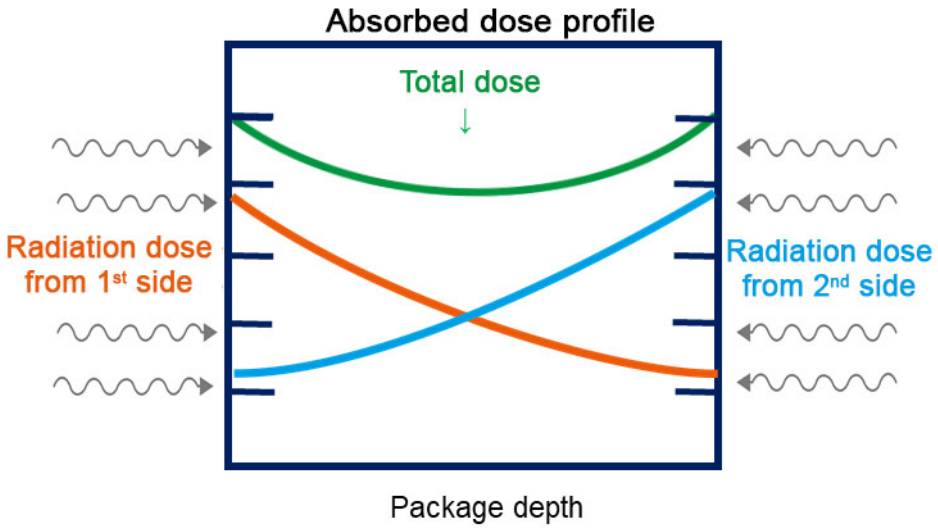
Each ‘product family’ is dose mapped, by placing dosimeters throughout the product load. This is to verify that the minimum specified dose is applied to the product, within the product packaging, and that the maximum specified dose is not exceeded.

Individual products may be dose mapped and the dose applied from two sides. The dosimeter changes color as the dose is applied. The color is measured to determine the dose applied.

A typical irradiation line will apply the dose from two sides as the product passes around the source. The total dose is the accumulated values – see Figure 3 below.

Figure 3.

Total dose applied – dose mapping



Production batches are supplied with a Certificate of Irradiation with the specified minimum and maximum dose range and the calculated actual dose received during processing.

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