- Dated certificate of the gamma radiation source including type, activity, and location of individual source capsules within the source rack;
- Calibration of I/Es and dosimetry systems;
- Qualification of alarm and safety device(s) operation;
- For continuous mode processors, qualification of conveyor operation and establishment of the conveyor speed for each item to be irradiated;
- For batch mode processors, qualification of timer settings for each item to be irradiated;
- Dose mapping studies to confirm Dose Uniformity; and
- Establishment of sterilizer load configuration for each API, drug product, medical device, or non-product item.

4. Performance Qualification (PQ) Studies for Gamma Radiation Sterilization should include, and not be limited to, documentation of the following:

   - A minimum of three (3) consecutive, successful runs for each irradiation cycle using dosimeters and production cycle parameters for load configuration, conveyor speed, exposure time, timer setting, and minimum absorbed dose to provide evidence of reproducibility;
   - Confirmation that the required sterilization dose was delivered; and
   - Meeting all validation acceptance criteria.

5. Association for the Advancement of Medical Instrumentation (AAMI) Method 1 should be used when the minimum absorbed dose is based on drug product, API, medical device, and/or non-product item bioburden.

6. An Overkill Sterilization Cycle may be used provided that at least three (3) prospective validation cycles are run using biological indicators (BI) (Bacillus pumilus) to demonstrate acceptable sterilization.

7. Establishment of a Sterilization Dose Using AAMI Method 1 for a Single Production Batch includes the following steps:

   a. Determine the average indigenous bioburden of the API, drug product, medical device, or non-product item using ten (10) randomly collected samples;
   b. Determine the verification dose for a Sterility Assurance Level (SAL) of 10^{-2} from an AAMI table using the average bioburden (see ANSI/AAMI/ISO 11137-2:2006);
   c. Verify that the verification dose does not exceed the established maximum sterilization dose limit;
   d. Irradiate one hundred (100) samples of the product batch at the verification dose;
   e. Perform a sterility test on each of the one hundred (100) samples
   f. If there are no more than two (2) samples with positive sterility tests, then accept the verification dose; and
   g. Using the AAMI table, determine the sterilization dose for the required SAL (e.g., 10^{-6}) based on the average bioburden for the batch.

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h. If there are no more than one positive sterility test from the ten (10) sterility test, then accept the verification dose and substantiate the 15kGy;
i. If there are two (2) positive sterility tests out of the ten (10) sterility tests, a conformity verification dose experiment should be performed; and
j. If there are more than two (2) positive sterility tests, the verification dose should not be accepted.

11. Radiation Sterilization Systems should be subject to a maintenance program and include, and not be limited to:
- Calibration of I/Es, including dosimeters, at least annually; and
- Radiation source addition, redistribution, or replacement, based on weekly performance monitoring.

12. Process Interruptions During Sterilization that delay the completion of sterilization beyond the specified time limit should be investigated and the effect on the API, drug product, medical device, and/or non-product item determined and documented.

13. Dosimeters should be used during routine sterilization to provide a measure of absorbed dose within specified limits. Selection of dosimeters should be based on the following:
- Temperature sensitivity;
- Humidity sensitivity;
- Dose rate dependence; and
- Stability of the absorbance reading after irradiation.

14. Dosimeters should be:
- Used within the calibration date;
- Placed in a location having a known dose relationship to the minimum and maximum doses; and
- Read within a defined time interval after gamma radiation sterilization and documented in the sterilization record.

15. Continuous Mode Irradiation Processors should have:
- Dosimeters placed so, at least, two (2) are exposed to the irradiation source at all times, including in the first and last container;
- Dosimeters placed in at least one irradiation container for each pathway during the irradiation cycle;
- Positive indication of correct position of the source and an interlock between the source position and conveyor movement; and
- Continuous monitoring and recording devices for conveyor speed.

16. Batch Mode Irradiation Processors should have:
- At least two (2) dosimeters exposed in positions related to the minimum and maximum dose; and
- Monitoring and recording of source movement and exposure time.

17. Absorbed Dose Readings Outside Specified Limits should be investigated by the contract facility Quality Authority. A copy of the investigation should be

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