General Discussion

This document provides guidance for validation of gamma radiation sterilization processes used to sterilize active pharmaceutical ingredients (API), drug products, medical devices, and non-product items, such as, APA gowning articles, containers, and closures with direct or potential contact with sterile raw materials (RM), APIs, drug products, or medical devices.

1. Critical Process Parameters for gamma radiation sterilization include:
   - Exposure time,
   - Timer setting (batch mode processing),
   - Conveyor speed (continuous mode processing),
   - Package size and bulk density, and
   - Dose measurement.

   These parameters should be monitored or controlled and documented on the sterilization record.

2. Compatibility Studies should be performed according to an approved protocol to demonstrate that the API, drug product, medical device, or non-product item is not adversely affected by exposure beyond the sterilization radiation dose limit. The evaluation should include the following:
   - Functionality;
   - Effects of gamma radiation on the API, drug product, or medical device (i.e., bio-compatibility);
   - Appearance; and
   - Effects of aging determined by stability testing.

3. Gamma Radiation Commissioning and/or Qualification should include, and not be limited to, documentation of the following:
   - Verification that the gamma irradiator is installed according to design criteria;
   - Identification of irradiator location within the facility and flow of materials through the facility;
   - Description of the construction and operation of the irradiator, including the conveyor system and timer;
   - Description of the irradiation carriers, including materials of construction and dimensions;
   - Identification of I/Es used to control, monitor, and record critical process parameters;
   - 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.

- 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 forwarded to the sponsor Site Quality Authority and the processed material designated Quarantine-hold until the investigation is completed and a final disposition assigned.

18. Process Documentation should include, and is not limited to, the following:
    - Accountability of API, drug product, medical device, or non-product items before and after sterilization by batch number or lot number;
    - Load pattern identification;
    - Dosimeter placement and retrieval;
    - Sterilization batch number;
    - Specified minimum and maximum dose;

