

## TECHNICAL TIP #02

This overview covers steps and other considerations for the qualification of new medical devices that will be processed with gamma radiation. The order listed is the approximate order in which various steps will be accomplished. However, it should be recognized that there may be considerable overlap between one or more steps.

### 1. Materials Selection

When designing a medical device, materials selection should be considered as early in the process as possible. It is important that the medical device be functional after radiation sterilization. (Many radiation tolerant materials are now available through a number of suppliers.) FDA regulations require that when converting an existing product from another sterilization technology, or introducing a new product to market, all products (components) must be tested to ensure that the form, fit, and function meet the product specification after the component has been exposed to radiation.

Possible radiation effects on some materials include embrittlement, discoloration, unpleasant odor, or lack of functionality due to a compromised physical trait, such as tensile strength. Some effects may be evident immediately after exposure to irradiation, while some may develop over an extended storage period. Accelerated aging is commonly used to determine material property changes over extended periods of time.<sup>1</sup>

Early in the planning stages, it is necessary to estimate the maximum acceptable dose, the D<sub>max</sub>, or the highest dose a product is likely to receive during processing, and determine if the material(s) from which the device is constructed will retain all its critical properties and dimensions up to that irradiation level. As a general rule of thumb, the D<sub>max</sub> target should be at least 1.6 times the minimum sterilizing dose for gamma processing, and 2 times the minimum sterilizing dose for E-beam processing. However, the larger the qualified range between the minimum and maximum established doses, the better the product turn time due to improved scheduling potential. Larger dose specification ranges also reduce the likelihood for product processing deviations (often related to restrictive dose ranges). All product physical testing and accelerated aging must be performed at or above the selected maximum dose and documented according to good documentation practices.<sup>2</sup>

### 2. Manufacturing and Product Controls

Device manufacturing environments must be in a state of control. The microbial population of the manufacturing environment contributes to the microbial load on the manufactured component and therefore impacts the sterilization dose. Consequently, a consistent manufacturing environment must be maintained as a part of an overall dose maintenance program. An environmental sampling program may be appropriate to demonstrate that components are being manufactured<sup>3</sup> in a consistent manner.

### 3. Dose Establishment

Dose establishment is the determination of the minimum amount of radiation necessary to achieve a given Sterility Assurance Level (SAL; typically 10<sup>-6</sup> or 10<sup>-3</sup>). Established guidelines from AAMI/ISO/ANSI provide several methods that can be utilized to determine an appropriate minimum sterilizing dose for a given device. The most commonly utilized guidelines involve experimental methods to determine a device's microbial load. From this microbial load, the resistance to radiation is experimentally determined and compared to the resistance of a known "standard" population (around which the guidelines were designed). If the products' microbial resistance to radiation is equal to or less than that of the "standard" population, the sterilization dose utilized for the product is the same as that for the "standard" population. In short, dose setting involves:

- determination of the component's initial microbial load,
- calculation/extrapolation of the dose based on the resistance of an identified microbial population, and
- verification of the calculated dose at a sample size of 100 to see if the dose is efficacious

#### 4. Dose Mapping

Once the component has been qualified as to dose and materials, a facility (or facilities) is identified to process the product. The product, in its final packaging configuration, must be profiled to identify the high and low zones of absorbed dose in the product load in relation to the energy field it travels through. Each facility has a unique cobalt source configuration; therefore, the effects of the unique energy field on the finished product arrangement must be characterized for each location in which the product may be processed. The product density and minimum sterilization dose requirement will also be used to determine the cycle time (time spent in the energy field absorbing the dose) for processing.

#### 5. Establishing Routine Processing Specifications

After all the above has been determined and prior to processing, a specification containing the information needed for routine processing of the product at a facility is developed. This specification will include (but is not limited to):

- Product and packaging description
- Carrier loading configuration
- Minimum acceptable dose (for sterilization)
- Maximum acceptable dose (for material compatibility)
- Dosimeter placement for “monitoring” the minimum and maximum dose for the process as identified during the dose mapping
- Special handling requirements (e.g., temperature, humidity), if applicable

#### 6. Dose Auditing

For medical devices labeled sterile, the efficacy of the minimum dose must be substantiated and is subject to FDA scrutiny. Periodic reexamination of the minimum sterilizing dose is required to ensure that the dose is still adequate. Industry guidelines<sup>4</sup> have a provision to perform periodic dose audits, whereby samples are irradiated and tested at sublethal doses (as in the original sterilization dose experiment) to check for continued dose efficacy. If a dose audit “fails” (determines that the specified minimum dose is not sufficient to ensure product’s required sterility assurance level), remedial action steps are outlined in the standards. Such remedial steps range from dose augmentation to requalification of the minimum dose.

#### 7. Revalidation

Any changes in material or manufacturing location must be evaluated for their possible influence on the product’s sterility validation or physical/functional qualification. Product moved to an alternate gamma facility must be evaluated for dose monitoring positions (a new dose mapping conducted). However, no additional **dose setting** validation need be done as a result of changing gamma processing facilities. As an example, the following changes would merit an in-depth evaluation and **possible** requalification or revalidation: moving component manufacturing to a new facility; changing from one grade or supplier of polymer to another; implementing a new packaging scheme for the product (rigid tray to polybag).

#### References

1. AAMI TIR No. 17
2. 21 CFR Part 820 Medical Devices: Current Good Manufacturing Practice (cGMP)
3. 21 CFR Part 820 Medical Devices: Current Good Manufacturing Practice (cGMP)
4. ANSI/AAMI/ISO 11137-1: 2006. Sterilization of health care products-Radiation-Part 1: Requirements for development, validation, and routine control of a sterilization process for medical devices.  
ANSI/AAMI/ISO 11137-2: 2006. Sterilization of health care products-Radiation-Part 2: Establishing the sterilization dose. ANSI/AAMI/ISO 11137-3: 2006. Sterilization of health care products-Radiation-Part 3: Guidance on dosimetric aspects.

---

For more information, please contact:

STERIS Applied Sterilization Technologies  
5960 Heisley Road  
Mentor, OH 44077  
877.783.7479  
www.steris-ast.com

 **STERIS**  
Applied Sterilization Technologies