# CHAPTER III.1.2

# Sterilization of Implants and Devices

## QUESTIONS

1. Overview of major terminal sterilization modalities:
   a. What are the two dominant sterilization modalities?
   b. Why do so many device companies use them?
   c. What are their major safety concerns?
2. Please provide brief descriptions of:
   a. a gamma processing plant
   b. how gamma sterilization kills the germs on medical devices.
3. Please provide brief descriptions of:
   a. an ethylene oxide (EO) processing plant
   b. how EO sterilization kills the germs on medical devices.
4. Why does the biomaterial scientist need to be concerned about material compatibility? Provide examples of materials that react, degrade, discolor or cross-link during sterilization with EO and radiation sterilization.
5. Terminal sterilization versus aseptic processing:
   a. What is the difference between aseptic processing and terminal sterilization?
   b. Why is terminal sterilization preferred?
   c. Why would one select aseptic processing?
6. Sterility Assurance Level (SAL) issues:
   a. What is the difference between the terms "sterile" and "sterility assurance level (SAL)"?
   b. What is the most common SAL for devices with biomaterials?

## ANSWERS

1. a. Radiation sterilization and ethylene oxide sterilization are the two dominant terminal sterilization modalities.
   b. Medical device manufacturers use them extensively because both have the capability to provide robust microbial kill at reasonable costs for high product volumes, while having minimal deleterious effects on device materials.
   c. Radiation sterilization safety concerns arise since the process uses doses that are orders of magnitude higher than a human lethal dose, so shielding and interlocks are critical. Ethylene oxide safety concerns arise since it is a highly explosive and toxic gas that needs to be managed to avoid severe explosions and personnel exposure.
2. a. A $^{60}$Co gamma processing plant has three essential components:
      i. shielding to keep the lethal radiation inside the processing room away from the operators;
      ii. double encapsulated radioactive isotope, with a 20-foot deep water storage pool with an elevator system to raise and lower the isotope; and
      iii. a conveyor system and control system to bring product into the processing room, and to circulate product around the isotope to get the validated dose.
   b. Gamma sterilization achieves product sterility by penetrating through the final sterile barrier packaging of the device and inactivating microorganisms through ionization and scission of the DNA molecules.
3. a. A 100% EO processing plant has the following components:
      i. blast-limiting construction and appropriate safeguards to avoid explosions and operator exposure;
      ii. a pre-conditioning area and an aeration area;
      iii. EO process chambers into which product is loaded. These chambers are equipped for removal of air, and addition (and later removal) of EO and humidity; and
      iv. microbiological services to evaluate biological indicators.
   b. EO sterilization achieves product sterility by penetrating through the breathable sterile barrier packaging of the device along with water vapor, and inactivating microorganisms through alkylation of their DNA.
4. Sometimes the biomaterial scientist has a polymer that is suitable for a product, but the polymer cannot tolerate any terminal sterilization process. In that case it may not be possible to bring the product to market. Alternatively, the product may need to be aseptically processed which: (a) has less process control than terminal sterilization and hence yields higher patient risk; and (b) is more expensive than terminal sterilization, and hence reduces product profitability.
   **Examples** of materials that may react with EO and produce undesirable by-products:
   - Polyacrylates, e.g., polymethylmethacrylate (PMMA); some styrene resins, e.g., polystyrene (PS), and styrene acrylonitrile (SAN) are

known to have deleterious responses to a typical single EO sterilization. These materials may be acceptable in certain applications, but must be evaluated carefully after exposure to worse case EO conditions, to ensure clinically acceptable performance over the shelf-life and application of the device.

- Bioabsorbable polymers may be difficult to process with EO sterilization, in particular if structural integrity is required. EO in combination with both temperature and humidity can reduce bioabsorable material properties.
- Packaging materials need to be able to withstand the evacuation rates and pressures.

**Examples** of materials that may react badly with radiation sterilization:

- Polytetrafluoroethylene (PTFE), fluorinated ethylene propylene (FEP), and polypropylene (PP) exhibit chain scission and degradation to a significant extent following radiation sterilization. These materials may be acceptable in certain applications, but must be evaluated carefully after exposure to a maximum sterilization dose to ensure clinically acceptable performance over the shelf-life and application of the device.
- Polymethylmethacrylate (PMMA), and other polymers in the glassy state below the glass transition, may trap residual low energy electrons which can cause yellow or brownish discoloration.
- Bioabsorbable polymers, e.g., PLA and PLGA, show significant molecular weight (MW) reduction as a function of sterilization dose. This may be manageable by utilizing a higher initial MW in the product.

**5.** a. Aseptic processing of a product entails physical removal of microbial contamination by filtering, and uses clean rooms to prohibit microbial contamination. Terminal sterilization involves inactivation of microbial contamination in a product by applying a physical or chemical process that kills such contaminants.

b. It is predictive for any sterilization process, and generally follows logarithmic microbial reductions based on first order kinetics. It is much less expensive and involves less patient risk than aseptic processing.

c. When the product attributes dictate that there is no other way of providing a sterile product.

**6.** a. Sterile is a state of being free from viable microorganisms, an absolute condition, while SAL is the quantitation of the probability of a non-sterile product.

b. $1.0 \times 10^{-6}$