liquid form, is noncorrosive and requires relatively low temperatures (20–35°C). The concentration used for VPHP sterilization of isolators depends on the internal surface area of the isolator. Typically, a 30% solution of liquid peroxide is pressurized in a VPHP generator (example shown in Figure 27-3 with the generator next to the sterility test isolator) to produce vapor peroxide at a concentration of 1 to 2 mg/L. The fact that VPHP sterilization occurs at ambient temperature is a major advantage of this sterilant over other gaseous sterilants (chlorine dioxide, peracetic acid). Among the disadvantages of using VPHP is its tendency to be absorbed by plastic and other types of materials.

RADIATION STERILIZATION

Radiation sterilization may be achieved by gamma radiation, beta particle (electron beam; accelerated electrons), or ultraviolet light. Microwave radiation has been the studied as a sterilization method for empty vials, in-line glass ampoule solution products, and hydrophilic contact lenses, but is not considered a major radiation sterilization method. Gamma radiation, typically cobalt 60 high-energy photons, is the most penetrative and effective radiation sterilization method. Beta particles are ionizing radiations, not electromagnetic like gamma rays, and, thus, are less penetrative. Electrons are generated from a radioactive element, for example, Strontium 90, and accelerated mechanically to extremely high energy levels in the range of 5 to 30 kilogray (kG) (0.5–3.0 mRad). Ultraviolet light is considered a surface sterilizing method only, as its energy level is insufficient to penetrate materials. Gamma sterilization is overall the method of choice although beta particle radiation being more closely evaluated, especially as a possible terminal sterilization method for finished products.

Items sterilized by radiation sterilization are essentially the same items that can be sterilized by gaseous methods—plastic materials, heat-labile materials, powders.

Radiation will damage the nucleoproteins of microorganisms. Effectiveness of radiation is dependent on the dose of radiation and time.

The 12 *D* overkill approach is always used in radiation sterilization. What this means is that whatever the *D* value of the most resistance microbial spore form in the material to be sterilized, the typical radiation dose is sufficient to produce a 12-log reduction in the spore population. For example, typical *D* values for the most resistant bacterial spore (*Bacillus pumulis*) to radiation is 1.7 to 2.0 kG [or megarad (mRad)] (remember that the *D* value determination for radiation uses dose rather than time). The typical radiation dose is 25 kG, greater than the 12-fold the *D* value of *B. pumulis.* In addition, during the radiation sterilization treatment, dosimeters are placed at strategic locations in order to monitor radiation doses received throughout the load.

A schematic depiction of a radiation sterilization conveyor system is seen in Figure 17-10. The product enters the entrance to the conveyor, then travels through different sections where different doses of radiation are given. The total dose may be 25 kG, but that dose is distributed throughout the conveyor system in order not to apply overwhelming and perhaps damaging dose of radiation at any given segment. A major concern when attempting to sterilize finished products or active pharmaceutical ingredients is the formation of radiolytic byproducts (e.g., *OH) that in turn may cause damage to the raw material and/or the packaging system.

Validation of radiation sterilization follows the guidelines of the Association for the Advancement of Medical Instrumentation (AAMI). Validation involves the radiation dose required to destroy 10^8 spores of the biological indicator in a maximum load size. Validation also requires determination of the radiation absorbed (using dosimeters) in the material being sterilized. Factors that affect radiation sterilization validation include the *D* value of the biological indicator in the item being sterilized, the radiation strength, the radiation dose rate, and the conveyor speed.

BRIGHT LIGHT (OR PULSED LIGHT) STERILIZATION

Bright light has been developed as a possible terminal sterilization method for drug products in final containers, specifically polyethylene containers produced from form-fill-finish operations. Maxwell Technologies developed pure pulsed light to inactivate all microbial life. Light is produced by ionizing xenon gas in a quartz lamp using a high voltage pulse of short duration (specifically, a few hundred millionths of a second). Light produced is claimed to be 20,000 times more intense (brighter) than sunlight (initially estimated to be 90,000 times brighter). A single