17 Sterilization methods in sterile product manufacturing

The entire field of discipline of sterile product science and technology is based on the ability to render finished dosage forms sterile. Sterility is defined theoretically as the complete absence of microbial life. Achieving sterility is the subject of this chapter.

There are four main methods that sterilize items used in parenteral manufacturing, testing, and administration.

1. Heat
2. Gas
3. Radiation
4. Filtration

There is a fifth possibility—bright light—but at the time of writing this text, light sterilization had not yet reached a status where it can be considered a standard sterilization technique. More discussion of bright light sterilization will be given at the end of this chapter. This chapter will cover heat, gas, and radiation sterilization while chapter 18 will cover filtration sterilization.

Another way to classify sterilization methods can be the following:

1. Thermal
   (a) Moist
   (b) Dry
2. Nonthermal
   (a) Filtration
   (b) Radiation
3. Chemical
   (a) Gaseous
   (b) Liquid

Before describing each of these sterilization methods, basic microbiology principles are presented. Both the United States aseptic processing guidelines and the European Union manufacture of sterile medicinal products documents require all personnel working with sterile products to have formal training on basic microbiology principles. In addition, prior to providing the basics of sterilization methods, the basics of microbial death kinetics will be covered.

SOME BASIC MICROBIOLOGY PRINCIPLES

Terms used frequently in discussing sterilization procedures in sterile product manufacturing include the following:

- Sterility—Absolute freedom from biological contamination
- Asepsis—Freedom from microbial infection potential (sepsis)
- Sterilization—Elimination of all viable microorganisms
- Disinfection—Renders objects noninfectious
- Sanitizing agent—Reduces the microbial population
- Spore—Resistant hibernation state of microorganisms
- Vegetative cell—capable of multiplication.

Most information developed on the growth, survival, and death of microorganisms comes from work performed under ideal conditions of a laboratory. Microorganisms found in a sterile production area are typically under nutritional, chemical, dehydration of other form of stress. Therefore, what is known ideally about microorganisms may not predict actual situations.

Sterilization procedures destroy or eliminate bacterial, fungal (yeast and mold), and viral contamination. Some brief instructions about each of these life forms: Bacteria can be gram positive or gram negative. Whether a bacterial life form is gram positive or negative depends