Table 2-1 Seven Basic Characteristics of Sterile Product Dosage Forms

1.	Safety (freedom from adverse toxicological concerns)
2.	Sterility (freedom from microbiological contamination)
3.	Nonpyrogenic (freedom from pyrogenic—endotoxin—contamination)
4.	Particle-free (freedom from visible particle contamination)
5.	Stability (chemical, physical, microbiological)
6.	Compatibility (formulation, package, other diluents)
7.	Tonicity (isotonic with biological fluids)

in chap. 14), validation of aseptic processes, training and application of good aseptic practices, use of antimicrobial preservatives for multiple-dose products, and valid testing for sterility of the product and maintenance of container/closure integrity.

Freedom from Pyrogenic Contamination

Pyrogens are discussed extensively in chapters 13 and 28. Pyrogens are fever-producing entities originating from a variety of sources, primarily microbial. In sufficient amounts following injections, pyrogens can cause a variety of complications in the human body. Because of the advent of the in-vitro test, Limulus Amebocyte Lysate (LAL), for the quantitative detection of the most ubiquitous type of pyrogen called bacterial endotoxins, all marketed injectable products must meet requirements for pyrogen (or endotoxin) limits.

To achieve freedom from pyrogenic contamination, like achieving and maintaining product sterility, many factors contribute toward this goal. Depyrogenation methods will be discussed in chapter 13, which include cleaning validation, time limitations, validated depyrogenation cycles for glassware, validation of pyrogen/endotoxin removal from rubber closures and other items that depend on rinsing techniques, validated water systems, and use of endotoxin-free raw materials.

Freedom from Visible Particulate Matter

Most aspects of particulate matter will be discussed in chapters 22 and 29. Visible particulate matter implicates product quality and perhaps safety. It definitely reflects the quality of operations of the product manufacturer. Both ready-to-use solutions and reconstituted solutions are to be free from any evidence of visible particulate matter and must meet compendial specifications for numbers of subvisible particles no greater than certain sizes, those particle sizes being for most compendia no greater or equal to 10 μm and no greater or equal to 25 μm.

Like other product characteristics, several factors contribute to the presence or absence of foreign particulate matter. These include valid cleaning methods of all equipment and packaging materials, valid solution filtration procedures, adequate control of production and testing environments, adequate training of personnel in manufacturing, testing and using sterile product solutions, and employment of required compendial testing procedures for detection of both visible and subvisible particulate matter.

Stability

All dosage forms have stability requirements. All dosage forms are required to be stable under predetermined manufacturing, packaging, storage, and usage conditions. Sterile dosage forms, like all other dosage forms, need to maintain both chemical and physical stability throughout the shelf-life of the product. The achievement of chemical and physical stability is the greatest challenge of scientists responsible for developing sterile dosage forms. With the exception of overcoming solubility challenges, often related to long-term physical stability, addressing and solving stability problems occupies most of the time and effort of scientists in the product development process. With much more complicated chemical structures and vulnerabilities to environmental conditions (temperature, light, pH, shear, metal impurities, oxygen, etc.) stabilization of therapeutic peptides and proteins offer enormous challenges. Achieving and maintaining chemical and physical stability starts with the active ingredient and how it is stored, shipped, and handled. Stability challenges continue with the compounding, mixing, filtration, filling,