sterile products are produced where the finished product is not terminally sterilized, but rather is aseptically processed. The difference in sterility assurance is far greater (generally at least 3 logs) for terminally sterilized products compared to aseptically processed products. This does not mean that aseptically processed products are frequently contaminated; rather it means that aseptically processed products cannot be validated to the same level of sterility assurance compared to terminally sterilized products. Sterility assurance is covered primarily in chapter 13 while sterilization is covered in chapters 17 and 18 and aseptic processing is covered in chapter 21.

The term "parenteral" comes from two Greek words, "par" meaning "avoid" and "enteral" meaning "alimentary canal." Therefore, the word "parenteral" literally means "beside the intestine." The only way to avoid the alimentary canal and to circumvent the skin and mucous membranes is to inject a pharmaceutical product directly into the body. Parenteral (the author prefers the term "sterile") products must be exceptionally pure and free from physical, chemical, and biological contaminants (microorganisms, endotoxins, particles). These requirements place a heavy responsibility on the pharmaceutical industry to practice current good manufacturing practices (cGMPs) in the manufacture of sterile dosage forms and upon pharmacists and other health care professionals to practice good aseptic practices (GAPs) in dispensing them for administration to patients.

Injections usually are accomplished using needles, but newer technology avoids the use of needles or use of extremely small diameter needles (covered in chap. 4). As stated already, not all sterile dosage forms are administered by injection. Sterile products that are not parenteral or injectable products include the following:

- Topical ophthalmic medications
- Topical wound healing medications
- Solutions for irrigation
- Sterile devices (e.g., syringes, administration sets, and implantable systems)

There are many terms that will be used throughout this book. A glossary of definitions of sterile product terms, not intended to be comprehensive, is given in Table 1-1.

The United States Pharmacopeia (USP)[2] contains several hundred monographs on sterile drugs or diluent preparations. Most products of biotechnology origin are not included because of confidentiality reasons. Some interesting statistics gathered after analyses of these USP monographs are as follows:

- About 22% are solid preparations that require solution constitution prior to use.
- About 9% are diluent preparations, both small and large volume.
- About 10% are radioisotope diagnostic preparations.

Sterile drug products are relatively unstable and are generally highly potent drugs that require strict control of their administration to the patient. Overcoming solubility and stability issues and achieving and maintaining sterility and other purity requirements present great challenges to those developing, manufacturing, and administering sterile drug products.

In this book, the teaching of the principles involved in the product development, product manufacture, and quality control of medicines delivered by the parenteral route will continue to be an important and relevant subject. This book is aimed to provide basic principles and practical applications of the formulation, packaging manufacture, and quality control of injectable dosage forms; in fact, all sterile dosage forms.

## HISTORY OF THE STERILE DOSAGE FORM

Avis published probably the most detailed review of the history of the sterile dosage form (1). Turco and King's last book also is a good general resource not only about history but also about clinical applications of sterile dosage forms (2). This chapter will highlight these references plus

[2] In general, referencing the USP also applies to other primary compendia, European Pharmacopeia (EP or PhEur) and Japanese Pharmacopeia (JP).