

# 1 | Introduction, scope, and history of sterile products

Sterile dosage forms have always been an important class of pharmaceutical products in disease diagnosis, therapy, and nutrition. Certain pharmaceutical agents, particularly peptides, proteins, and many chemotherapeutic agents, can be administered only by injection (with or without a needle), because they are inactivated in the gastrointestinal tract when given by mouth. Administration of drugs by the parenteral (parenteral and injectable will be used interchangeably) route has skyrocketed over the past several years and will continue to do so. A primary explanation for this enormous growth lies with the advent of biotechnology, the products of which are biomolecules that cannot be readily administered by any other route because of bioavailability and stability reasons. Since human insulin became the first biotechnology drug approved by the Food and Drug Administration (FDA) in 1982, over 100 drug products of biotechnological origin have been approved and hundreds more will be approved in the years ahead. Most biotechnology drug products are administered only by the parenteral route. Science is advancing to a time when it is likely that some of these drugs can or will be administered by other routes, primarily pulmonary and perhaps someday even orally, but the mainstay route of administration for these biopharmaceutical drugs will be by injection.

Any statistic given at the time of writing this section will quickly be outdated by the time this book is printed and will continually need to be updated. However, it is safe to state that the number of injectable products being developed, being studied in the clinic, being approved for commercial use, and being administered to humans and animals will significantly increase in the years to come. Perhaps by 2020, the market share of sterile drug products will be approximately the same as that for oral solid dosage forms<sup>1</sup>.

This chapter will address some of the basic questions about the sterile dosage form and the parenteral route of administration.

Various definitions and end uses of sterile products will be discussed throughout this book. This book will also address many aspects of formulation development of these dosage forms, how they are manufactured, how they are packaged, how they are tested and what are the acceptable conditions during manufacture, and the uses that assure these unique products maintain their special properties.

There are three terms used interchangeably to describe these products—parenteral, sterile, and injectable. Parenteral and injectable basically have the same meaning and are used interchangeably. Sterile dosage forms encompass parenteral/injectable dosage forms as well as other sterile products such as topical ophthalmic products, irrigating solutions, wound-healing products, and devices. The coverage of devices in this book will be minimal.

Here is a definition of sterile dosage forms:

A product introduced in a manner that circumvents the body's most protective barriers, the skin and mucous membranes, and, therefore, must be "essentially free" of biological contamination.

Ideally, a sterile dosage form is absolutely free of any form of biological contamination, and, of course, is the ultimate goal of every single unit of sterile product released to the marketplace, either commercial or clinical. Perhaps some day manufacturing procedures and in-process microbiological analysis will guarantee that each and every unit of sterile product will indeed be absolutely free of biological contamination. However, the modifier words "essentially free" are added to this definition because most small-volume ( $\leq 100$  mL per container)

<sup>1</sup> Among many resources for keeping current with new drug products and trends are Burrill & Company ([www.burrillandco.com](http://www.burrillandco.com)); Pharmaceutical Research and Manufacturers of America ([www.phrma.org](http://www.phrma.org)); Tufts Center for the Study of Drug Development (<http://csdd.tufts.edu>); Onesource.com; EvaluatePharma.com; IMS; and Datamonitor, to name a few.