Clean room technologies, including the use of laminar air flow units, high efficiency particulate air (HEPA) filters, and room classification for particles were not discovered until the early 1950s to the early 1960s. Original clean rooms were used by the United States Biological Laboratories at Fort Detrick, MD, during the 1950s. The HEPA filter was first described in the early 1940s, but not applied to laminar airflow technology until W. J. Whitfield combined HEPA filters and laminar airflow units in 1961. The United States government first proposed clean room classifications in 1962 (Federal Standard 209).

It was also in 1962 that authority was given to the FDA to establish cGMPs, Parts 210 and 211 (21 CFR Parts 210 and 211), issued under section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 351(a)(2)(B) with the first proposed cGMP regulations published in 1963. In 1976 the FDA proposed to revise and expand these regulations and a final rule by the FDA commissioner was published in the Federal Register on September 29, 1978. Although some changes have occurred since 1978 (e.g., April 2008 changes that included requirement for validation of depyrogenation of sterile containers)[3], and likely minor changes will continue to occur, the great majority of GMP requirements finalized in 1978 remain enforced within the pharmaceutical industry today.

As air classifications became standard for clean rooms, developments in the equipment used in sterile product manufacture also occurred in rapid fashion. Stainless steel and its fabrication into tanks, pipes, and other equipment was refined to provide heliarc welding of joints and fittings as well as the electropolishing of surfaces to reduce potential product reactivity. Clean-in-place and sterilize-in-place technologies were developed in the 1970s that allowed larger equipment to be cleaned and sterilized without dismantling; it also greatly reduced the variability in manual cleaning.

Biotechnology emerged in the 1970s, resulting in significant growth in the development, manufacture, and use of parenteral drugs. Biotechnology, in turn, gave rise to the significant growth of controlled drug delivery systems, convenient delivery systems for home health care, monoclonal antibodies, and the advent of proteomics and genomics. To give one example, the monoclonal antibody market of commercial products is poised to double in number and estimated sales value from 2007 to 2012 (5).

It was also in the 1970s that FDA began to enforce the practice of process validation, starting with validation of sterilization processes. Today, validation of processes, methods, and computers are standard practices because validation practices are continuously being refined and updated.

The 1990s witnessed the advent of barrier isolator technology, preapproval GMP inspections, significant growth of biotechnology processes, and much increased focus and enforcement of aseptic process validation.

Advances will continue in the 21st century in the areas of parenteral drug targeting and controlled release, convenience packaging and delivery systems, aseptic processing, high-speed manufacturing, disposable technologies, rapid methods for chemical and microbiological testing, and GMP regulatory requirements.

Table 1-3 presents a list of therapeutic classes of injectable drugs and some examples of each class. This list will grow not only in number but also in clinical significance and market share. Injectable or parenteral drug science and technology is a wonderful and exciting field of study and endeavor in which to be involved and engaged. It is the author's hope that the readers of this book will readily see the truth of this belief.

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