1 Introduction

Process engineering has been a central activity in pharmaceutical product development since its inception. The knowledge that key fundamentals and the processes to which they are applied were in most respects equivalent to those in other industries allowed chemical and mechanical engineering principles to be adopted, which were thoroughly understood (McCabe et al., 1997).

The first chapters of this book describe in some detail the important fundamentals of fluid flow, heat and mass transfer. The intent is not to duplicate the authority of an engineering text of which there are many to which this volume owes tribute. Rather it is hoped that the topics are covered in sufficient depth to allow professionals in the pharmaceutical sciences, without engineering training, to feel comfortable when faced with matters pertaining to these topics. The chapters immediately following the fundamentals introduce processes that either employ the principles described earlier or that relate to important aspects of pharmaceutical development. Hence, these might be considered methods of handling and conveying different states of matter, that is, solids, liquids, or gases. The heterogeneous nature of many pharmaceutical formulations leads to a degree of empiricism in the understanding of processes and their application to achieve the desired goals of uniform and reproducible drug delivery from the designated dosage form or the handling of environmental or other conditions related to their preparation. Consequently, the chapters dealing with solids (including crystallization, powders, size, mixing, and blending), filtration, sterilization, evaporation, drying, and humidity have their basis in theory but often invoke semiempirical interpretation. Figure 1.1 illustrates the relationship between the various unit processes and the underlying fundamental principles.

The value of any text in pharmaceutical process engineering is that the fundamental nature of the topics presented gives it a long shelf life since the science and engineering have not changed significantly in decades. However, the last decade has been characterized by changes in the common practices of conducting experiments to rapidly and efficiently define the process accompanied by a change in the regulatory environment in which manufacturing is conducted.

It may seem premature to introduce this evolving technical and regulatory consideration into an otherwise slowly changing foundational text. However, it appears that the important principles of statistical experimental design, risk assessment, and quality by design, including specific tools to aid with these approaches, are established elements of process engineering.

The final chapters of the book relate to these topics. In the information age, the advent of computer technology allows the collection of vast quantities of data, which can then be manipulated in real time or near real time to promote the quality of the product and to ultimately bring therapies to patients. The challenge of working in this environment is to manipulate this data to fulfill the promise shown in Figure 1.2.

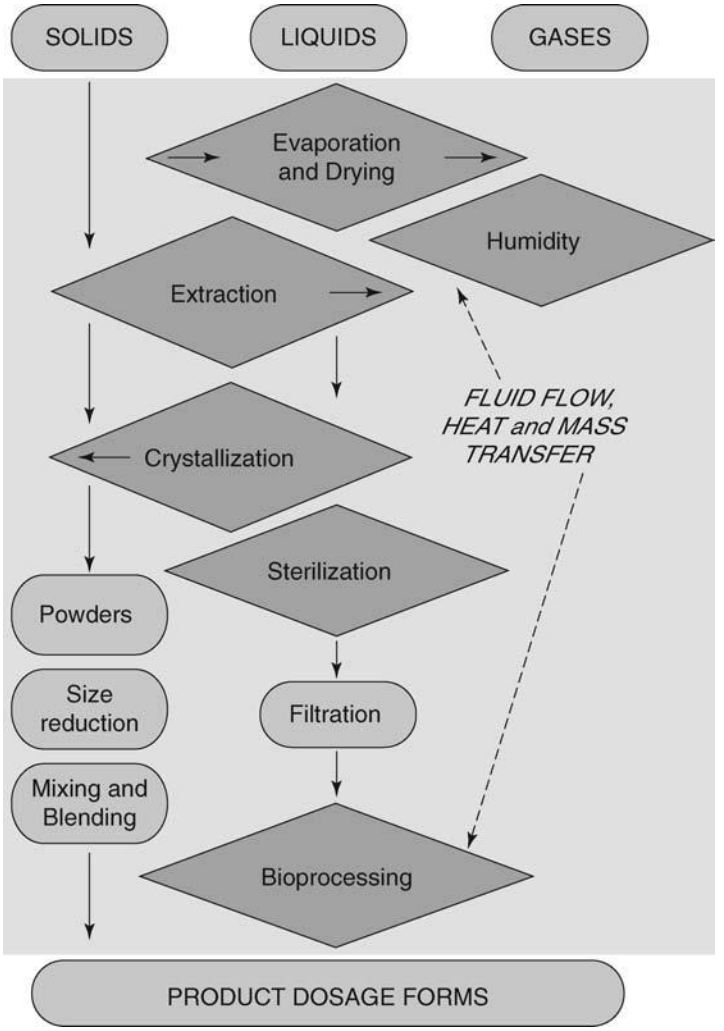

FIGURE 1.1 Relationship of unit processes in the background of fundamental principles.

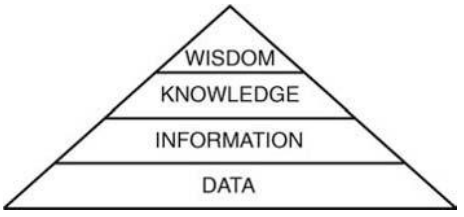

FIGURE 1.2 Schematic of levels of understanding that emanate from a comprehensive base of data.

The intent is to derive from an extensive database crucial information that increases the body of knowledge of the process or product and ultimately allows the wise intervention to bring about a desired objective. This may seem self-evident, but it could be argued that until relatively recently insufficient data could be acquired to adequately elevate our understanding through the upper levels of intelligent management. The practicalities of the experiments and their conduct in a regulated environment may not differ dramatically from previous periods in history, but the consideration of an operating framework and the facility to acquire relevant data has changed substantially. This is undoubtedly an improvement and should be embraced by all to elevate activities to a higher level of control and prediction commensurate with a 21st century industry.

In this context, the final chapters of the book cover in some detail the basis for statistical experimental design, risk assessment, and supporting tools of process analytical technology associated with quality by design. Figure 1.3 illustrates the collation of input variables that is required to predict and control the output for any process.

If successful in this endeavor, the cost and efficiency of processes in the future may be managed by informed decisions that facilitate rapid product development. In broad terms, the following sections, therefore, consider: (*i*) fundamental principles; (*ii*) unit processes; and (*iii*) experimental design, data management, and interpretation. The intent is to begin to address process engineering in a quality systems environment.

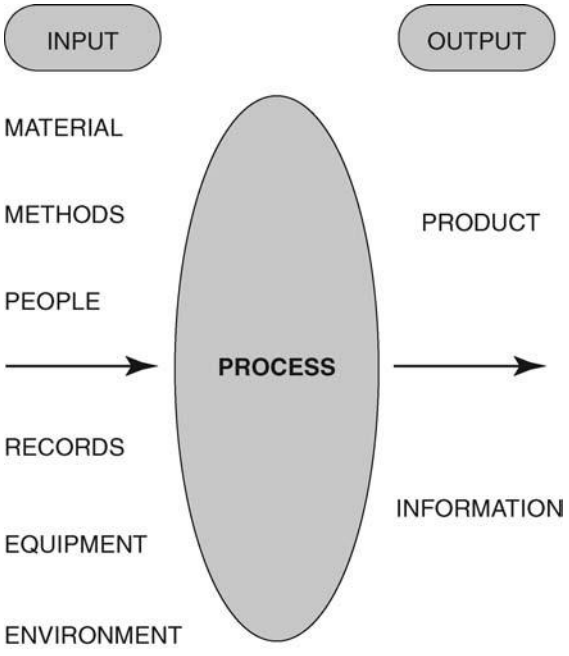

FIGURE 1.3 Process input variables and their contribution to output properties.