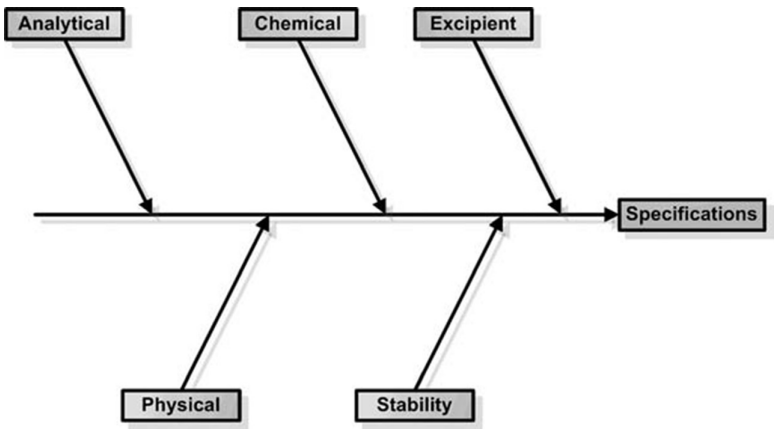
are specifically designed into the drug substance (e.g., crystal engineering, botanical extraction conditions, and protein yields at folding stages) should be identified and discussed. However, the type of properties of the drug substance to be studied is highly dependent on the source of the drug. While most of the new drugs are still derived by chemical synthesis, more drugs are now beginning to be sourced from biological sources, particularly through recombinant DNA manufacturing, and the recent acknowledgment by the regulatory authorities that botanical (herbal in Europe) drugs should be controlled has resulted in an organized sourcing through botanical means as well. This chapter describes the characterization of drug substances derived by chemical synthesis, wherein the molecules are well defined. The general characteristics described here may also apply to biological and botanical drugs; the specific differences will be discussed in a later chapter devoted to those drugs.

8.2 Scheme of Characterization

Systematic development cycles are more likely to be efficient and should result in a definite specification for the lead compound. Scheme 8.1 shows a typical flow chart for the characterization that leads to the development of specifications for the lead compound.

Examples of properties that are routinely examined include solubility, water content, particle size, crystal properties, biological structure, chirality, and so on. The compatibility of the drug substance with excipients should be discussed. For products that contain more than one drug substance, the compatibility of the drug substances with each other should also be evaluated. Although the dosage form considerations are still to evolve, based on a prospective dosage form, the specifications should include those parameters that may be relevant. For example, if the final dosage form intended is an injectable product, solubility and thermal stability (to autoclaving) are important considerations. Table 8.1 lists some common study protocols for different dosage forms.



SCHEME 8.1 Steps that lead to the development of specifications for new lead compounds.