information that is globally available from published articles in scientific journals and/or in international pharmacopoeias should be utilized.

In all cases, whether pharmacopeial or nonpharmacopeial analytical procedures, it must be demonstrated that the API and any associated impurities from the synthesis of the API as well as excipients are all separated from the degradation products of the API present in the matrix of the drug product. This is achieved through method validation, which is discussed below.

Method Validation

Stability data serve as a barometer for the shelf-lives of drug products. Stable products are produced from validated production processes that are expected to be in a state of statistical control from one batch to another. It is therefore imperative that every effort be made to ensure that the analytical procedures for measurement of critical stability parameters are fully validated. HPLC has become a universal tool for stability testing because of its demonstrated capability of resolving the main component from degradants and any associated synthesis impurities. The stability-indicating capability of a particular HPLC method is governed by its degree of separation, which is established by conducting forced degradation studies of drugs under various stressed conditions of temperature, humidity, oxygen, acid, base, UV light, and visible light. The details of the development of stability-indicating analytical procedures are included in a separate chapter in this book (Chapter 3) and also in several published guidelines [9–13].

An important component of an ANDA application consists of completed analytical method validation reports. During or after approval of an ANDA application, the FDA usually requests samples and test data to conduct regulatory validation. To fulfill this request, the applicant should follow the published FDA guidance on this topic [19]. In performing the tests, the FDA laboratories will apply the regulatory methods, which are the analytical methods provided in the ANDA application.

For drugs with published monographs in the current USP, the analytical methods are those legally recognized under Section 501(b) of the Federal Food, Drug, and Cosmetic Act. In this respect, 21 CFR Part 211.194(a) (2) states that the analytical methods described in the USP do not require complete validation. The regulation, however, requires that the suitability of all testing methods must be verified under actual conditions of use. In other words, the pharmacopeial methods should be validated to establish their suitability for specific drug products manufactured by generic companies. This is understandable because stability data are critical attributes of drug products. An important advantage will be gained by conducting method validation consistently for all pharmacopeial and nonpharmacopeial products in raising a company's analytical standard in the eyes of FDA reviewers of ANDA applications as well as FDA investigators during on-site compliance inspections.

FDA and ICH Guidelines

In 1994, the Center for Drug Evaluation and Research (CDER) of the FDA accepted the ICH stability testing conditions [6] for new drugs. In a letter to all ANDA