When a formula for a generic drug has been finalized for an off-patent branded drug, the generic drug manufacturer is required to conduct certain studies and submit an abbreviated new drug application (ANDA) to the Office of Generic Drugs (OGD) of the FDA to demonstrate its bioequivalency and quality. Proof of bioequivalence is established through an appropriate comparative bioavailability (bioequivalence) study, which is discussed in Chapters 10 and 11. Drug quality, on the other hand, is demonstrated through implementation of extensive analytical testing procedures. The analytical testing methodologies and data are described in the Chemistry, Manufacturing, and Controls section (CMC) section of the ANDA application, which are covered in Chapters 3 and 9.

A key component of drug quality is its stability profile, which is an integral part of the Chemistry, Manufacturing, and Controls section. Drug stability is characterized by parameters such as identity, assay, degradation profile, and dissolution rate. A drug is stable when these quality characteristics remain within predetermined quality-control specifications for at least the duration of the expiration period. A stable generic drug, which has been shown to be bioequivalent to a branded drug, assures that it continues to be safe and efficacious throughout its shelf-life. Assessment of the stability of drugs is also mandated by the Code of Federal Regulations, Title 21, Part 211.166 (usually abbreviated as 21 CFR Part 211.166).

Terminology

In the pharmaceutical industry, the terms active pharmaceutical ingredient or API, drug substance, active ingredient, active substance, or simply active or drug are all used interchangeably. Drug products or drugs or products or finished products are also interchangeable. The term shelf-life is used interchangeably with expiration dating period, expiration period, expiration dating, or expiration date. An excipient is any inactive substance other than the drug substance used in the corresponding drug product.

API STABILITY

The development of the stability profile of an API is a prerequisite for approval of an ANDA application. Analytical testing to establish an API's stability profile is usually conducted by its manufacturer. Critical stability parameters include physical appearance (e.g., whether crystalline or amorphous powder for solid APIs), color, assay, degradation profile, and hygroscopic tendency. The API manufacturer's Drug Master File (DMF) submission to the FDA will not be complete without stability data. In practice, the review of the DMF by the FDA is triggered upon the submission of an ANDA application referencing the DMF.

Pharmacopeial and Nonpharmacopeial APIs

Currently, a large number of APIs are already included in the United States Pharmacopeia (USP) and its supplements. It is known that a vast majority of the pharmacopeial-grade APIs that are used by generic manufacturers are produced