closure systems. Ultimately, proof of the suitability of the container/closure system and the packaging process is obtained from shelf-life stability studies.

Shipment

Package sizes and the corresponding container/closure systems intended for marketing must be included in the ANDA application with the necessary accelerated and long-term stability data for approval by the OGD. A container/closure system (i.e., shipping containers) used for the transportation of bulk drug products to contract packaging companies should be described in the application [5]. The container/closure system should be adequate to protect the dosage form, be constructed with materials that are compatible with the product being stored, and be suitable for the intended use. The protective properties of the shipping container are verified by the practice of annual stability studies.

If a container closure/system is specifically intended for the transportation of a large quantity of a drug product to a repackaging company, it is considered to be a market package. Usually, such package sizes are well outside the range of the package sizes used in shelf-life stability testing and are not monitored in the annual stability program. For example, the large container closure/system used for bulk holding of capsules or tablets is not usually supported by shelf-life stability data and thus is not usually included in the application as a package to be marketed. It should be noted that such packages cannot be sold to repackagers.

CONTROLLED DRUGS

The Drug Enforcement Administration is the US agency that is responsible for enforcement of the regulations of the Controlled Substances Act. The regulations that are described in 21 CFR Parts 1300 to 1316 define the controls relating to the manufacture, distribution, and dispensing of controlled substances. The controlled substances have been divided into five different classes or schedules. Controlled substances under Schedules I and II require the greatest degree of security and controls. The substances under Schedules III to Schedule V require lesser degrees of control and security. Examples of drug product classifications are heroin (Schedule I), oxycodone hydrochloride tablets (Schedule II), phendimetrazine tartrate tablets (Schedule III), diazepam tablets (Schedule IV), and diphenoxylate hydrochloride and atropine sulfate tablets (Schedule V). To facilitate the use of abbreviations for the different schedules, 21 CFR Part 1302.03(c) has designated the following symbols: CI or C-I for Schedule I, CII or C-II for Schedule II, CIII or C-III for Schedule III, CIV or C-IV for Schedule IV, and CV or C-V for Schedule V.

Storage Requirements for CI to CV Drugs

The FDA regulations require accelerated and long-term stability testing for all drug products regardless of their classification as controlled substances. For such substances, pharmaceutical companies have employed additional controls to assure