

security during short-term and long-term storage of stability samples. As an example, the chamber used for long-term stability studies may allocate space for a locked cage for Schedules I and II drugs, which should be situated within the confines of the larger locked cage for Schedules III to V drugs. The chamber also provides a level of security with its own lock. For Schedules III to V drugs, the larger locked cage situated within the chamber provides a second level of security. For Schedules I and II drugs, the smaller locked cage situated within the larger locked cage provides the highest level of security. In all cases, a limited number of personnel should be authorized to access the chamber and the cages containing the controlled drugs for long-term stability testing. For accelerated stability testing of drugs, a small commercially available chamber is traditionally used for the short-term studies. This chamber should allow limited access and be located in a secure area. It should be noted that the general storage requirements of stability samples are also covered in 21 CFR Parts 1301.75(b) and 1301.75(c), which allow dispersing controlled substances throughout the stock of noncontrolled substances in such a manner as to prevent the theft or diversion of the controlled substances from the stability chamber. Before designing and implementing procedures for securing controlled drugs in the accelerated and long-term stability chambers, it is essential to consult with the Drug Enforcement Administration and seek their approval.

## **SUBMISSION REQUIREMENTS**

Considering that a significant body of stability data is usually available on the branded drugs at the time of their patent expirations and well before an ANDA can be submitted, the ANDA submission requirements for stability data are less extensive than the new drug application (NDA) requirements for such data. Thus, valuable time is saved by the generic industry and also in the regulatory review by the OGD, which contributes to the process of quick introduction of cheaper generic products into the market for the benefit of all patients.

### **ANDA SUBMISSION**

#### **General Requirements for ANDA Submissions for Generic Products**

Accelerated stability data at 0, 1, 2, and 3 months on a minimum of one batch, which can be a pilot-scale batch with a minimum batch size of 100,000 capsules or tablets, are required [24]. For multiple sizes and strengths, scientifically justifiable bracketing and matrixing designs can be employed. The tentative expiration dating period of up to 24 months may be granted based on satisfactory accelerated stability data unless not supported by the available long-term stability data. Available long-term stability data should be included in the original ANDA application and subsequent amendments.

Additional stability studies (12 months at the intermediate conditions or long-term stability data through the proposed expiration date) are required if “significant change” is seen after 3 months during accelerated stability. The tentative expiration dating will be determined based on available data from the additional study.