- Stability data will be included in the annual report (AR) submission to the OGD.
- Any batch with nonconforming stability data will be recalled from the market with the required notification to the FDA.

Shelf-Life Development

Shelf-life is the time period during which a drug product is expected to remain within its specifications, provided that it is stored under the conditions defined on the container label. An expiration or expiry date is the date on the container label of a drug product, designating the time period before the end of which a batch is expected to remain within the approved shelf-life specification, if stored under the labeled conditions, and after which it must not be used. Regulation 21 CFR Part 211.137 requires that a drug product must bear an expiration date determined by appropriate stability testing in accordance with 21 CFR Part 211.166. The expiration dates must be related to the storage conditions stated on the labeling as determined by the stability studies conducted as described in 21 CFR Part 211.166. If the drug product is to be reconstituted at the time of dispensing, its labeling must bear expiration date information for both the reconstituted and unreconstituted drug products. It should be noted that 21 CFR Part 201.17 requires that the expiration dates must appear on the container labeling.

21 CFR Part 211.166(a) specifies that the results of stability testing must be used in determining appropriate storage conditions and expiration dates. 21 CFR Part 211.166(b) requires testing of an adequate number of batches of each drug product to determine an appropriate expiration date. The regulations allow use of accelerated stability studies to support a tentative expiration date if full shelf-life stability studies are not available at the time of ANDA approval. Where data from accelerated stability studies are used to project a tentative expiration dating period that is beyond a period supported by actual shelf-life studies, long-term stability studies must be conducted, including drug product testing at appropriate intervals until the tentative expiration dating period is verified or the appropriate period is determined. In general, the use of an overage of an API to compensate for degradation during the manufacturing process or a product's shelf-life, or to extend the expiration dating period, is not acceptable [7]. Additional information on the subject of shelf-life development has been published [16,21].

Stability data should be developed for the drug product in each type of container/closure system proposed for marketing or bulk storage. Bracketing and matrixing designs, which will be discussed separately in this chapter, may be used if included in the approved stability protocol.

Action Limits

Long-term stability testing is conducted to assure that the drug product will be within its shelf-life specifications during the expiration period. Action limits tighter than the specification limits should be set to assure that any batch with