initial test results close to the action limits is evaluated through an appropriate course of action. By definition, action limits are the maximum or minimum values of a test result that can be considered to be the boundaries of acceptability without requiring further actions. Results less than the minimum or greater than the maximum action limit indicate that an action must be taken. For example, if an assay or degradant or dissolution result is near but outside the action limits, an appropriate action would be to monitor this batch by long-term stability testing to assess whether the batch will meet the shelf-life specifications. Conforming stability results for this batch also builds up a database in the sense that a future batch with a similar result need not be subjected to stability. That is, a worse-case approach can be taken in deciding whether a future batch would require long-term stability testing. From among all of the batches of the product on long-term stability, the worse-case batch, which must still conform to specifications, is defined as that batch with results that are outside and farthest from the action limits. If the test results of a future batch are outside the action limits but are superior to the results of the worse-case batch, this batch should not require long-term stability studies. However, if the test results pass but are marginal with respect to the shelf-life specifications with no allowance for analytical variability, that batch should be rejected to avoid the risk of a stability failure and consequent recall. It should be noted that anytime an atypical batch is produced, a separate manufacturing investigation should be conducted to determine and correct the root causes for the production problem.

Expiration Date Assignment

The computation of the expiration dating period of a drug product batch should begin not later than the date of the quality-control release of that batch and the date of release should not exceed 30 days or 1 month from the date of production regardless of the packaging date. If the quality-control release date of the batch exceeds 30 days or 1 month from the date of production, the expiration date should be calculated from 30 days or 1 month after the date of production. The date of production of a batch is defined as the first date that an API was added to the excipients during manufacturing.

The data generated in support of the assigned expiration dating period should be obtained from stability studies conducted under the long-term stability condition consistent with the storage environment recommended in the labeling. If the expiration date includes only a month and year, the product should meet specifications through the last day of that month.

A stability protocol should also include the statistical methods for analysis of stability data in addition to the design of the stability study. The draft guidance [5] on stability testing contains acceptable statistical approaches for the analysis of stability data and for deriving an expiration dating period. Generally, an expiration dating period should be determined based on statistical analysis of long-term stability data.

If the reworking of a drug product is approved in an application, the expiration dating period of a reprocessed batch should not exceed that of the parent batch and the expiration date should be calculated from the original date of production [7].