objective of the annual product review program, the results of ongoing annual stability batches must be reviewed for continued justification of the shelf-lives of all products manufactured. If stability results cast any doubt with respect to the validity of the shelf-life of a particular product, the situation should be investigated in a timely manner to determine the assignable reasons for the stability problem. If warranted by the investigation, the shelf-life should be reduced until the problems, for example, marginally acceptable assay results with respect to specifications, have been identified and addressed.

Field Complaint

21 CFR Part 211.180(e) (2) requires a review of field complaints and investigations conducted for each drug product. The complaints may provide clues to the product's performance in the field and should be studied to show whether they relate to any physical or chemical changes in the product's specifications. Such changes can be caused by contamination in the plant or the field or can be caused by the packaged product's physical and chemical stability characteristics. For example, chemical discoloration of capsules or tablets due to moisture, caking of tablets, or ineffective product may indicate compromised integrity of the particular lot of the container/closure system and/or the need to tighten up on batch manufacturing parameters.

Recall

The failure of any annual stability batch to meet any specification needs to be promptly and thoroughly investigated to ascertain the reason(s) for the OOS result and to ascertain whether other batches that were not included in the annual stability program are affected. Examples of failures during annual stability would be nonconforming assay, degradant, or dissolution results. The unacceptable batches identified in the investigation should be withdrawn from the market. The FDA should be informed and a prompt voluntary recall of all affected batches should be conducted with the consent of the FDA. This will avoid possible product seizures by FDA and/or court injunctions. In addition, 21 CFR Part 314.81(b) (1) requires submission of a Field Alert Report to the local FDA district office within 3 working days of the occurrence of the OOS result.

STABILITY SOFTWARE

For over a decade, it has been a common practice by the drug manufacturers to rely on stability software to store, organize, retrieve, and analyze the vast amount of stability data generated by laboratory testing. Stability software may either be developed in-house or procured from vendors.

Computer Validation

The stability software must be validated according to the commonly accepted principles of computer software validation. If the stability software is developed in-house, it is important that internal experts are available for validation. If it is decided to outsource validation, the process will be costly because external experts will have