obtained. In the case of demonstrated poor analytical understanding and accuracy, the employee should not be assigned analytical testing duties.

It is important from the CGMP perspective as well as for laboratory efficiency that training on analytical procedures, laboratory SOPs, applicable CGMP regulations for laboratory operations and record-keeping requirements, and new analytical technology should be a periodic process and formalized in an SOP on training. Trainers should not be limited to laboratory experts only. Instrument manufacturers, technical seminars, and scientific meetings are valuable external training resources, which should be sought, when necessary, in enhancing employees' analytical expertise especially on new technology such as computerized and networked HPLC and gas chromatography systems, multiwavelength photodiode array detection in HPLC analysis, particle size measurement based on laser diffraction, and Fourier transform infrared spectrometry. For training on USP monographs and general chapters and dissolution technology, USP experts provide both off-site and on-site training. Essentially, periodic training demonstrates a company's commitment to continuing improvements in laboratory quality. All certification and training records on all employees should be maintained by the QA Department and presented on request to FDA investigators.

## OOS Investigation

The procedure for investigation of out-of-specification (OOS) test results varies within the pharmaceutical industry. With the objective of developing a harmonized approach for investigation of OOS test results, the FDA published a guidance in October, 2006 [28]. The term, OOS results, includes all suspect results that fall outside the specifications submitted in ANDA applications. For products with monographs in the USP, the ANDA specifications would usually correspond to the USP specifications.

The guidance presents the FDA's current policy on evaluation of OOS results and should be viewed as an important resource in evaluating and validating or invalidating OOS stability data. To meet the FDA's requirement, an investigation should be conducted whenever an OOS stability test result is obtained. The guidance requires that the investigation should be thorough, timely, unbiased, well documented, and scientifically defensible. Because the particular annual stability batch with an OOS result represents all batches of the product manufactured in a given year, it is necessary to evaluate all batches manufactured in the year to determine whether or not the OOS result was limited to this batch only. If only one batch is affected by the OOS result and other batches are not, the investigation must show the unique circumstances responsible for the failure of the particular batch to meet specifications and, at the same time, demonstrate clearly that the annual stability program was not compromised.

## Annual Product Review

Annual product reviews are mandated in 21 CFR Part 211.180(e), which states that written records must be maintained so that data therein can be used for evaluating, at least annually, the quality standards of each drug product to determine the need for changes in drug product specifications or manufacturing or control procedures. As an important