Identification and Investigation of Test Deviations During Validation

Regulatory Basis:
FDA Quality Systems Regulations

Reference: FDA CFR - Code of Federal Regulations Title 21

General Discussion
This document provides recommendations for investigation and reporting of test deviations during a validation exercise.

Out-of-specification (OOS) results and any other deviations that may impact the acceptability of the qualification/validation should be documented, investigated, root cause determined, corrective action taken and reported. Several examples are included.

Deviations that occur during validation testing must be documented and investigated in accordance with site procedures. Additionally, a summary of all deviations, investigations or corrective actions associated with a specific validation activity need to be included, discussed, and cross-referenced in the validation report.

The documentation and investigation of a deviation and its resolution should address the impact of the deviation on the acceptability of the validation of the process or system in question. Typically, site deviation procedures are targeted towards the impact of the deviation on commercial product and may not be designed to address the specific issues that may arise during validation of a system or process. If the existing site deviation handling systems do not readily support validation deviations, it is recommended that deviations that occur during qualification/validation activities are documented separately.

The procedure for documenting validation deviations can be established in the Validation Master Plan, validation SOP or within the standard test document template. Deviation forms (see attached example in Appendix 1) can be included as part of the testing documentation.

Regardless of the system used to document a validation deviation, the principles remain the same and are summarized in the flowchart below:

Flowchart: Documenting a Validation Deviation

Protocol errors that require correction in order to allow the test to be executed as intended may include missing test instructions or incorrect acceptance criteria. In these cases, the investigation should include clear justification for the corrections, with references to any source documentation. Where a system or process error is identified as the root cause, the investigation should include an analysis of whether the system is acceptable without change. Such a conclusion should be approved by appropriate technical and QA representatives, in addition to the system/process owner.

Identification of corrective actions

Once the investigation is complete, appropriate actions should be identified, if any. These should include both corrective actions and any preventive actions required to prevent a recurrence of the deviation.

Examples of corrective actions include:

- *System/process documentation update* – where the investigation identifies that the original system/process documentation from which the protocol acceptance criteria were derived was incorrect, or the process/system does not meet the acceptance criteria but is considered acceptable by appropriate technical and QA representatives, then the system/process documentation should be updated. Where applicable, documentation update should be completed according to the relevant change management procedure.

- *Process/system changes* – where the deviation investigation concludes that a change is required to the system or process, then this should be documented and controlled through the relevant change management process. Reference to the change management documentation should be made on the deviation form.

- *Repeat testing* – where a system/process change has been completed to correct a fault, or where an operator error resulted in a test not being executed correctly, repeat testing is generally required. The level of testing to be repeated should be clearly identified and may range from the addition of another batch to a process validation study to the repeat of a single test step during system validation. In some cases, a new protocol maybe required and restarting of the validation activities may occur.

Assessment of impact on validation activities

Where the deviation and any corrective actions do not impact the intent of the original validation test, then testing should be allowed to proceed.

If corrective actions identified impact ongoing validation activities (including moving to the next phase of validation), validation testing should be stopped, the actions should be implemented and confirmed and the deviation should be closed before continuing testing. Where testing that has already been completed is impacted, consideration of the repetition of those tests should be included in the corrective actions.

samples for an API

Example 3
Deviation - During system qualification for a computerized warehouse management system (WMS), the test to confirm that the WMS could receive returned goods failed.

Investigation & corrective actions - The investigation determined that the root cause was because material being returned is automatically given a Quarantine status and is received into a (virtual) adjustment warehouse in the WMS. Inventory from the same lot already existed in the adjustment warehouse, but with Approved status. As the system requirement is that a lot cannot exist with two different statuses in the same warehouse,
the system functionality was correct. The test was re-executed, ensuring during the set-up that no inventory remained for that lot in the adjustment warehouse.

Example 4
Deviation - During system qualification of a thermoforming machine, the sealing plate temperature profile did not meet specification.

Investigation & corrective actions - Following the investigation, it was determined that the equipment installation was incorrect to achieve the required functionality. Under site change management procedures, the standoffs on top of the upper sealing tool were changed to stainless steel. The test was re-executed and met the specification.

