**Regulatory Basis:**
FDA Quality Systems Regulations

Reference: FDA CFR - Code of Federal Regulations Title 21

**General Discussion:**
This document provides document for qualification and validation activities that take place as a result of the Technology Transfer for approved commercial Active Pharmaceutical Ingredient (API) and Drug Product (DP) processes. Other aspects of Tech transfers such as regulatory changes, stability impact, etc must also be considered as described in relevant document, but these other activities are outside the scope of this document.

While overall Technology transfers often include many aspects (e.g. validation, stability, regulatory, safety considerations), this document focuses on the validation aspects of technology transfers. Qualification and validation requirements for processes, cleaning, analytical methods, and systems (equipment, facilities, utilities etc) should be documented in Site Quality Standards.

Document for qualification and validation activities necessary at the receiving site is described in the following sections.

Technology transfers of existing APIs or DP processes to a different site often involve a change in registration documentation for the product, to include the new location. This will likely prompt a regulatory inspection at the receiving site and/or regulatory scrutiny (e.g. of analytical methods, critical process parameters, etc) of the registration documents. Therefore, validation requirements for production and support systems at the receiving site should be considered at an early stage of the technology transfer process. The Site Validation Master Plan should also be updated accordingly.

It is recommended that the transferring facility compile a knowledge information package to set the foundation for knowledge transfer to the receiving facility. An overall Technology Project Plan is typically utilized to define what information is needed, by whom, and at what point in the transfer process.

Validation personnel at the receiving site should be represented in initial interdisciplinary knowledge sharing meetings to assess the scope of work and estimate time requirements and plans.

Typical contents of a knowledge information package include or reference:

__ Regulatory Process Description
__ Process Flow Diagrams
__ Equipment List
__ Bill of Material
__ Master Batch Records or Manufacturing Instructions
__ Cleaning Procedures or Instructions
__ Raw Material Specifications (where appropriate)
__ Intermediate Specifications (where appropriate)

 

__ Information on cleaning deviations related to the cleaning process and resulting investigations at sending site, if relevant to the cleaning procedure used at the receiving site.
__ Cleaning Process change control reports / documentation, if relevant to receiving site
__ Whether cleaning validation for Biopharma products will occur prior to, or concurrently with process validation batches.

**Analytical Method Qualification and / or Validation Considerations:**

When transferring analytical sampling and test methods, it should be determined what the analytical method is utilised for (e.g. quality of product, EHS purposes, etc.), as well as the current validation status.

Some methods (e.g. related to operational efficiency only) may not require validation. One can then prioritise which methods may require a more formalised analytical transfer and/or validation. A comparison of the originating and receiving laboratory instruments and capabilities would likely need to be performed.

The following information should be provided to the receiving site:

__ The analytical sampling and test method, including description of method, reagents and instrumentation used at the sending site laboratory.

__ Method development and validation documentation and reports. If methods require validation and there is no validation documentation available, or the method was not originally validated to current standards, the method may need to be revalidated.

__ Information about critical analytical method parameters and / or procedural steps, deviations related to the method, and resulting investigations at the sending site.

__ Procedures to prepare analytical standards that are not readily available, for example, API Impurities or Intermediates.

__ Microbiological method validation (e.g. Endotoxin, Bioburden) if applicable.

**Process Validation Considerations:**

Processes used in the manufacture of API or Drug Product require validation. The timing and strategy for validating the process at the receiving facility will typically be influenced by the following factors:

__ Prerequisite activities such as facility, equipment, and system qualification, cleaning validation strategy and analytical method validation requirements.
__ The number of pre-validation (e.g. engineering or demonstration) lots (if required) and the intended use and disposition of this material.
__ The extent to which existing supporting studies and matrixing and bracketing approaches can be used to reduce the validation workload. Rationale for utilizing existing information to cover requirements of a validation should be documented.

 

__ When required information is contained in other GMP documents (e.g. site Validation Master Plan, SOPs, etc) it does not have to be repeated in the VP. The other documents may simply be referenced in the relevant section of the VP. Where additional detail specific to the project is required, this information should be discussed in the VP.

__ Confirmation that critical inter-related systems at the receiving site, such as utilities, environmental control systems, equipment, etc are qualified, or are identified as requiring qualification or validation.

__ Schedule of critical validation activities, which may be by reference to a separate document, plan, or schedule.

__ The sequence of validation of different systems and processes, along with any interdependencies should also be outlined. If some activities must be completed before a given validation can be initiated these should be identified.

__ Reference to programs that support validation and qualification activities, such as: change control, SOPs, document retention, calibration, preventative maintenance, periodic review and training.

__ The VP should specify what activities may be needed outside of the normal quality systems that are specific to support a given tech transfer validation. For example, if special training is required to execute a given tech transfer validation, this may be specified in the plan.

__ Related document references, such as procedures, the site Validation Master Plan and/or guidelines used in the validation and qualification activities of the technology transfer.

**Validation Project Plan Report**

Upon successful completion of the validation and on approval of the supporting validation reports, a Validation Project report may be written and approved by the signatories of the plan (or their designee).

This report summarises conclusions from:

__ Process validation batches and references the process validation report.
__ Systems Qualification and respective report references
__ Cleaning Validation Strategy as outlined in the protocol
__ Analytical Method Qualification and / or Validation and reference to the reports

The report should also state whether or not the process is acceptable for regulatory submission and commercialisation.

 