Analytical Method Technology Transfer From Quality Control Laboratory To Manufacture Area

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Abstract

The project was developed with the intent to document the analytical transfer method to reduce In-process concentration testing cycle time. A reduction of up to 50% turnaround time (TAT) downtime was achieved. Waste reduction due to no sample preparation, gowning cost reduction, since there is no need for the operators to take the sample to the Quality Control (QC) Laboratory and transferring the In-process method to the manufacturing area allows more capability to the QC laboratory to perform another testing were other improvements obtained from the project.

Technology method transfer tools were applied to generate a successful in process method transfer from the QC laboratories to the manufacturing area. The implementation of this project complying with all the standards required by the company and the different regulatory agencies will improve the capability and competitiveness of the manufacturing area among the company sites.

Key Terms: Analytical Method Transfer, Manufacturing Process, Protein Concentration, Turnaround time (TAT) reduction

Project Description

As part of downtime reduction plan, Concentration In-process testing turnaround time was identify as a "waste" on manufacturing process. Transferring a new In-process methodology from the QC Laboratories to the manufacturing area, that can be performed by an operator will reduce the downtime, which allows having a leaner manufacturing process.

Objectives

- Reduce the downtime at a 50% of the manufacturing turnaround time for the concentration determination of in-process testing

Methodology

Analytical Method Transfer Planification and Execution

The transfer of an analytical method can happen in different ways and circumstances: from transferring only a method to a whole product specification test requirement, which contains several test methods. For this project, the transfer of a single method will be considered. Nonetheless, the transfer approach process will remain the same. Figure 1 contains the process flowchart of an analytical method transfer. To ensure a flawless activity, these nine (9) steps process should be taken into consideration and will be discussed as part of the transfer methodology.

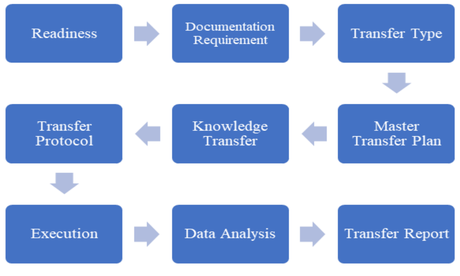

Figure 1
Analytical Method Transfer Planning Process Flowchart

Results and Discussion

To document the activities performed as part of the analytical transfer method process of the In-process concentration testing from the QC Laboratories to the manufacturing area. Figure 2 shows the current process of the In-process concentration testing flow at the QC Laboratory.

Results and Discussion, cont.

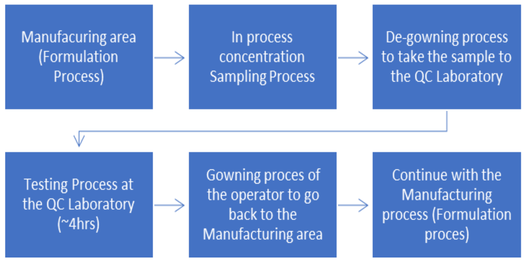

Figure 2
In-process Concentration Testing Flow at the QC Laboratory

Formulation process of the drug product is start in the manufacturing area. To achieve the desired protein concentration at the 85% of the formulation process, an In-process concentration sample is collected and needs to be deliver to the QC Laboratory. An Operator needs to de-gown to take the sample to the QC Laboratory. Sample needs to be received in a logbook by a QC Analyst. To enter to the manufacturing area a continue supporting the formulation process, the Operator needs to gown again. The QC Laboratory takes approximately four (4) hours to provide an approved concentration result of the In-process sample. Then the manufacturing area uses this value to calculate the remains buffer needed to achieve the 100% concentration formulation process.

Measure Phase

To reduce at 50% the downtime of waiting of the QC Laboratory results, analytical transfer method process of the In-process concentration testing from the QC Laboratories to the manufacturing area was proposed. To ensure a flawless transfer activity, the nine (9) steps process were consolidated into three (3) main activities and were taken into consideration as part of the transfer methodology.

- **Master Transfer Plan**
  - Readiness (documentation requirements, and knowledge transfer).
  - Roles and Responsibilities.
  - Qualification Philosophy.
- **Analytical Transfer Method Protocol**
  - Execution and data analysis.
- **Analytical Transfer Method Report**
  - Documentation of the transfer activities
  - Each of these steps are further discussed is this section.

Analyze Phase

Master Transfer Plan

This master transfer plan is to provide the basic and organizational structure for the execution of the analytical transfer method process of the In-process concentration testing from the QC Laboratories to the manufacturing area.

Readiness Process

In order to have a successful method transfer process, readiness is a fundamental key element. Table 1 summarized the readiness process that need to happen prior to start a method transfer.

Table 1
Readiness Process Element Prior to Start a Method Transfer

Documentation	Material	Knowledge Transfer
Protocol/Report	Equipment	Familiarization Run
SOP (New and/or Change)	Reagents	
Method/Form	Consumables	On the Job execution
On the Job generation		

Roles and Responsibilities

Having the roles and responsibilities established at part of the method transfer will help to ensure task are completed. Table 2 establish who is responsible of what.

Analyze Phase, cont.

Table 2
Manufacturing and QC Laboratory Transfer Plan RACI Chart

Activities /Task	Receiving Area (Manufacturing)	Project Manager	Transferring Area (QC Lab.)	Quality Assurance
Overall Project Accountability for transfer	C	A/R	I	I
Generate Instrument Procedure SOP	C	A/R	C	C
Review and Approval of SOP	R	A/R	C	R
Purchase of Equipment as needed	A/R	C	C	N/A
Provide Tech Transfer Samples	C	A/R	C	N/A
Generation of Training Documentation	C	A/R	C	C
Execution of Training	R	A/R	R	N/A
Execute Shake-Down Analysis	R	A/R	R	N/A
Generate Protocol	C	A/R	C	C
Review and approval of Protocols	R	A/R	C	R
Execution of Experiments	R	A	R	N/A
Review of Raw Data Packets	C	R	A/R	C
Generate Report	C	A/R	C	C
Review and approval of Reports	R	A/R	C	R
Provide support if any investigation occurs	R	A/R	R	R
Review and approval any investigation, if applicable	R	A/R	R	R

R = Responsible: Individuals or groups who perform an activity/task.
A = Accountable: The individual or group who is ultimately accountable for the completion of the activity/task.
C = Consulted: Individual(s) or group(s) who are to be consulted prior to completion of the activity/task or before the decision is made.
I = Informed: Individual(s) or group(s) who are to be informed of the completion of the activity/task, or of the decision result.

Qualification Philosophy

The type of transfer will let you know the amount of work that needs to be done. In addition, it will let you know what are the control are put in place, to ensure that the analytical method was transfer properly. Table 3, documents the Transfer type used and parameters that need to be tested to ensure the quality of the transfer.

Table 3
Transfer Type and Parameters

Transfer Type	Parameters to be Tested
Comparative Testing	System Suitability Repeatability Intermediate Precision

Analytical Transfer Method Protocol

In this transfer, method protocol, precision (repeatability, intermediate precision, and reproducibility), accuracy and system suitability were the parameters selected to measure the receiving area's ability to determine In-process protein concentration. Table 4 summarizes the transfer protocol parameters, objectives, and acceptance criteria.

Table 4
Technical Transfer Table

Parameter	Objective	Acceptance Criteria
Precision-Repeatability (Intra-assay) (receiving area)	To determine the precision under the same operating condition over a short interval of time.	% RSD of nine-determination sample concentration must be within ± 5.0%.
Precision-Intermediate-Precision (receiving area)	To determine if suitable precision is obtained when performed by different associates on different days.	%RSD of concentration measurements of six associates on different days must be ≤ 5.0%
Precision-Reproducibility (Inter-area) (receiving and transferring area)	To evaluate the reproducibility of the method when the same samples are analyzed in the transferring and receiving areas.	The %RSD for reportable results for all associates from the receiving and transferring areas must be ≤5.0%.
Accuracy	To determine the closeness of agreement between the concentration obtained by the receiving area and transferring sample concentration.	The % difference between the averages of each associate reportable results in the receiving area compared to the transferring sample concentration for each lot must be ±5.0%.
System Suitability	To demonstrate that the method is performing as required producing valid results.	Only valid experiments (all system suitability criteria met) will be used in this technical transfer.

Improve Phase

Analytical Transfer Method Report

Table 5 summarized the Transfer activities results In-process protein concentration determination.

Table 5
Transfer Protocol Summary Results

Test	Acceptance Criteria	Results				Pass /Fail
Repeatability (Intra-assay) (receiving area)	The % RSD of nine (9)-determination sample concentration must be within ± 5.0%.	Associates	% RSD (%)			Pass
		1	0.3			
		2	0.4			
		3	0.3			
		4	0.2			
		5	0.4			
		6	0.3			
Intermediate-Precision (receiving area)	The %RSD of the combined protein concentration measurements of six (6) associates on different days must be ≤ 5.0%.	Sample Type	% RSD (%)			Pass
		In process	1.2			
Reproducibility (Inter-area) (receiving and transferring area)	The %RSD for reportable results for all associates from the receiving and transferring areas must be ≤5.0%.	Sample Type	% RSD (%)			Pass
		In process	1.1			
Accuracy	The % difference between the averages of each associate reportable results in the receiving area compared to the transferring sample concentration for each lot must be ±5.0%.	Associate	Percent Difference			Pass
			Rep. 1	Rep. 2	Rep. 3	
		1	1.0	0.1	0.3	
		2	0.5	0.5	0.1	
		3	0.6	0.5	0.2	
		4	0.9	0.2	0.2	
		5	0.1	0.1	0.1	
		6	0.5	0.0	0.1	
System Suitability	The % difference between Standard measured concentration and standard COA must be within ± 5%	All System Suitability criteria during transfer were met.				Pass

Conclusions

Figures 3 and 4, shows that the In-process concentration testing cycle time was reduced from four (4) hours to two (2) hours.

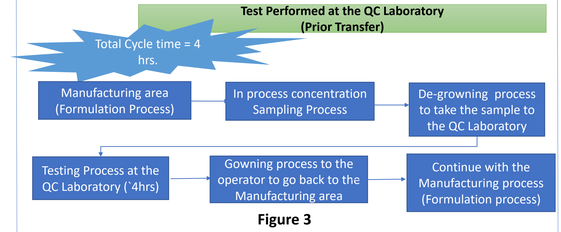

Figure 3
In-process Concentration Testing Cycle Time Prior Transfer

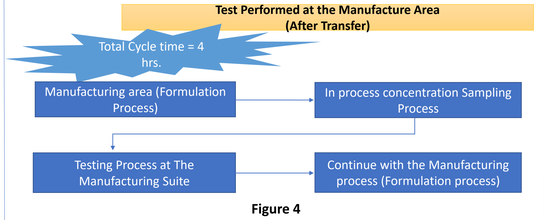

Figure 4
In-process Concentration Testing Reduction Cycle Time, After Transfer

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