Molecular Weight Test Method Validation and HPLC System Qualification

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Abstract

There are four (4) product families manufactured at an un-named company which contains Poly-4-hydroxybutyrate (P_4HB) monofilament as part of their mesh structure. The Phasix Mesh (Flat mesh) product is knit with P_4HB monofilament to form a surgical mesh. On the other hand, the Phasix ST product combines two market-leading technologies into one product; Phasix Mesh (resorbable monofilament) and a proven HA/CMC PEG hydrogel barrier based (Sepra Technology or ST). The P_4HB is a strong biosynthetic material with remarkable mechanical, biocompatibility and biodegradability properties. As P_4HB is a bioresorbable material, it is susceptible to degradation over time prior to implant and that is the reason to monitor its Molecular Weight prior sending the product to the costumer.

As with all bioresorbable polymers, the P_4HB exhibits a typical degradation characteristic that is tracked by measuring the average molecular weight (M_w) decrease over time. M_w is a key performance characteristic of the device and is used to determine the product shelf life. The rate of degradation (i.e. M_w loss) is affected by the exposure to the moisture, temperature, and humidity. The M_w specification is a critical to quality attribute (CQA) that must be measured on a lot by lot basis for the Phasix ST Mesh, Phasix Mesh, Phasix ST with Echo 2 and Phasix ST with OPS products.

Figure 1: Phasix ST and Phasix Flat Mesh

Introduction

Currently, the Mw Test Method is performed by a contract laboratory. Performing the method externally affects the product release timeframe and represents additional costs when the results are required to be expedite. It is the intent of the company to validate the Molecular Weight (in-house testing) in order to avoid the waiting time associated to the samples travel time and to the test processing lead time. Qualifying this test in-house will allow to process results in three (3) days instead of two (2) weeks (current timeframe for contract laboratory to provide the results upon processing). There will not be associated costs to expedite results once the test is qualified at the company laboratory. Additionally, the company will be implementing a data acquisition software (Empower) which will allow the automatic processing of the samples as well as the results to avoid data transcription. Empower software is FDA 21 Part 11 compliance fully traceable through an audit trail configuration. This feature will avoid security opportunities (data manipulation).

Problem

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Methodology

The research conducted was outlined through the DMAIC methodology. The DMAIC methodology helped to develop the research of the methods and defined the steps followed to reach the results.

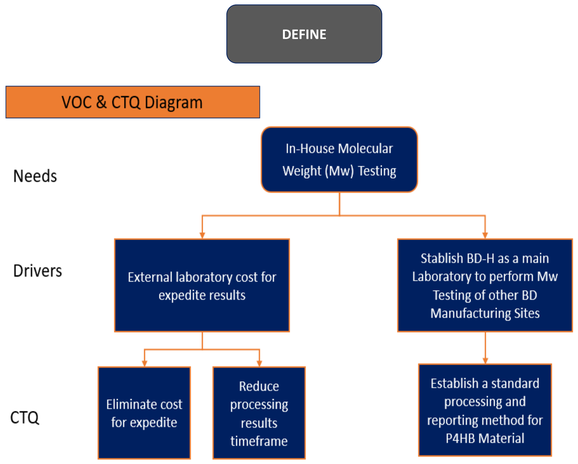

Figure 3: VOC & CTQ Diagram

Table 1: Performance and Financial Metrics

Performance Measures		
Metric	Baseline	Goal (If Applicable)
Equipment and Software Qualification	There is no data acquisition software (full 21-part 11 compliance) and a separation system (HPLC) available at BD-H	Qualify and released for production (software and equipment) within six months. IQ, OQ and PQ for software and IQ, OQ and PQ for equipment.
Test Method Qualification	Full transfer of method characteristics (no leverage of an already qualified characteristic)	Complete Test Method Qualification within a one-month period including laboratory to laboratory correlation assessment.
Financial Measures		
Cost Reduction	Contract Laboratory doubles the base rate when results are expedited. External Laboratory Base Cost = $700 per lot External Laboratory Cost for expedite results = $1.4k	N/A
Revenue	BD-Humacao will served as the main laboratory for the Molecular Weight testing for Delran (mesh supplier) Equipment acquired will be paid-off in 0.8 months. Savings are expected at $500k annually.	N/A

Table 2: In-house Mw Testing Advantages

In-house M_w Testing	Advantages
	Eliminates external laboratory transit and test time.
	Eliminates extra charges due to expedite the testing results (rush delivery).

Table 3: New Equipment and Validation Costs

Equipment and Service Cost	
Description	Cost
Equipment	$96,483
Consumable Materials for Validation	$6,354
External Testing for Validation (Including Materials)	$9,000
Services	$13,850
Freight Charges (6.0% of Total Equipment Cost)	$5,789
Sub Total	$119,733
Contingency 10% of Sub Total	$13,147.61
Grand Total	$144,624

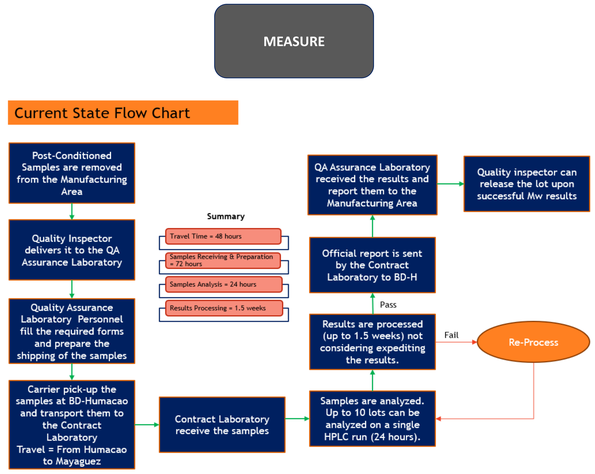

Figure 4: Current State Diagram

Project Schedule			
Phase	Start Date (Month/Year)	Completion Date (Month/Year)	Activities
1	10/2019	01/2019	AFE Approval / Equipment acquisition and pre-installation
2	02/2019	08/2020	Equipment and Software Qualification
3	09/2020	11/2020	Test Method Validation which covers the following activities: - Test Method Validation Protocol generation - Molecular Weight Test Method document generation - Test Method Validation execution - Test Method Validation Report generation - Release Molecular Weight Test Method at BD-H

Table 4: Validation Activities Schedule

Results and Discussion

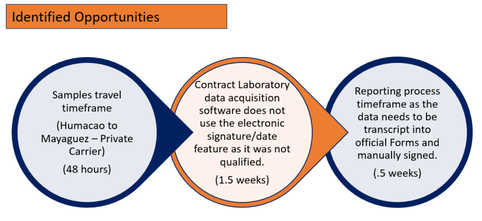

Figure 5: Identified Opportunities

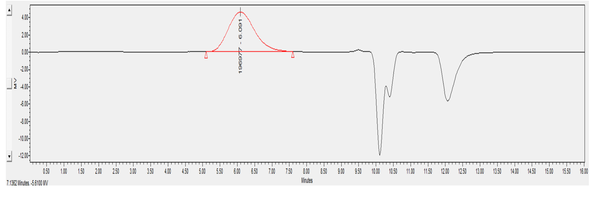

Figure 5: Sample Chromatogram Analysis

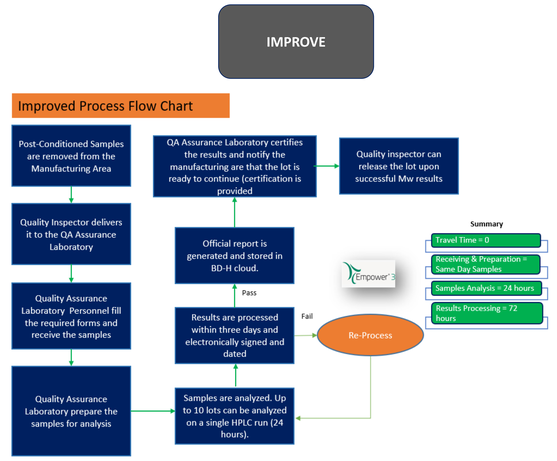

Figure 6: Improved Diagram

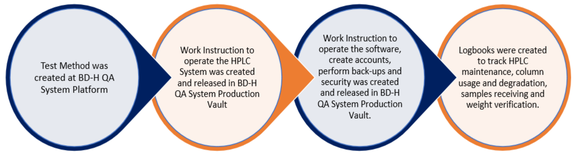

Figure 7: Controls

Conclusions

The qualification activities for the software were conducted considering the requirements for the qualification of a computerized system capable of performing electronic signature/date. The equipment (separation system) itself was qualified in order to challenge each function. After qualifying the equipment and the software, a method validation was conducted in order to validate each required parameter for an analytical method. The processing time was reduced from two (2) weeks to three (3) days. Also, there is no associated cost related to expedite samples results; therefore, lots can be released in a faster way.

Future Work

This project will allow the establishment of a critical to quality trending in were Mw could be trend or analyze to determine any opportunities within the process.

Acknowledgements

Special thanks to Professor Maria Garcia for her continue support during the project design.

References

1. Wu, Chi-san, Column Handbook for Size Exclusion Chromatography. Academic Press c. 1999.
2. USP <621>
3. 21 CFR Part 11, FDA Code of Federal Requirements
4. 21 CFR 820, Quality System Regulation