Implementation of a Calibration Wireless System in a Pharmaceutical Facility

Frances T. Berríos Meléndez
Manufacturing Engineering
Rafael Nieves Castro, Pharm D.
Industrial Engineering Department
Polytechnic University of Puerto Rico

Abstract *—Regulated industries such as Pharmaceutical, Biotechnology and Medical Devices require a Calibration Program, to guarantee the product quality. The objective of this project was to design Calibration Wireless System for the Engineering Department at a Pharmaceutical Facility. In order to achieve the objective of this project, it was required to analyze the data process and follow the Food and Drug Administration (FDA) and General Manufacturing Procedures (cGMP's) regulation. In order to design the Calibration Output report this is the Calibration Data Record. The Calibration Data Record is a regulatory document with specific requirements. The challenge for this project involves the knowledge of this regulation and adaptation to a wireless system, the decision for the better output device, taking in consideration the kind of work done by these technicians, and utilizing works system criteria. The outcome for this project is the Calibration Data Record, considering all the regulations and guidance.*

Key Terms *— DMAIC, FDA, GUIXT, SAP*

PROBLEM STATEMENT

A pharmaceutical facility needs to implement a Wireless System for the Calibration System at the Engineering Department. The calibration process is one of the highly regulatory importance processes. The Calibration area has a high volume of documentation to comply with the regulatory agency. The system must comply with the regulatory agencies and guidance. It should have the capacity to interact with actual SAP (System, Application and Product) system and maintain the schedule within the Standard Operation Procedures (SOP's).

INTRODUCTION

A Calibration is one of the most highly regulate tasks in pharmaceutical industries. Calibration is a set of operations that establish, under specific conditions, the relationship between values indicated by measuring instruments or measuring system. Values represented by material measure or reference material, and the corresponding values given by a primary standard. Regulate by the Federal Drug Agency (FDA), agency responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, products that emit radiation, and tobacco products.

The FDA [1] is also responsible for advancing the public health by helping to speed innovations that make medicines and foods more effective, safer, and more affordable. It is also responsible for helping the public get the accurate, science-based information they need to for medicines and foods to improve their health.

A leading pharmaceutical facility, tempering the times, found an opportunity implementing a wireless system in the Calibration Program of the Engineering Department. The actual calibration program consists in three technicians: calibration, clerk and a supervisor. The Calibration program has two types of orders: scheduled and unscheduled work orders. The Scheduled orders are the ones which the SAP system that generates after a maintenance schedule is placed to the desired instrument. The unscheduled orders are the ones which are generated by the Calibration Clerk after an emergency call occurs.

After the calibration work order is generated and printed, the Calibration Technician performs the calibration. Because of the high importance of the process, a calibration must be documented in place and maintained in safe for internal and external FDA audits. This last part of the process takes considerable time of the technician. This consuming process doesn't give time to attend emergency calls and training. Technicians spend approximately 33% of their time documenting in paper and entering the data to the SAP system, making the technician stay after work hours to attend the emergency calls. This overtime cost affects the engineering budget adding overhead cost.

The wireless system pretends to reduce this documentation time to 11.5%. With this reduction of time, there will be more time available to attend emergency calls, reduce paper work and lower the engineering overhead cost. The desired wireless system consists in a wireless dispositive, will receives the notification of work orders and in the same dispositive, the technician can document during a calibration. After the calibration is performed, the Calibration clerk receives the technical confirmation electronically by SAP and checks the technical confirmation and the Calibration Data Record for errors in his computer station. The Calibration Work Order and the Calibration Data Record must be maintained by the system, be available for future audits, and can be printed at any time (See Figure 1). The system must comply with the regulatory agencies and guidance. It should have the capacity to interact with actual SAP system and maintain the schedule within the Standard Operation Procedures.

METHODOLOGY

To develop the model that will support the wireless system and obtain better results during the implementation. The methodology that will be followed is the DMAIC (See Figure 2). The DMAIC cycle is the driving force behind Six Sigma process improvement projects. This methodology is use when improving existing processes. [2]

DMAIC is an acronym for the 5 key phases in a process improvement project:

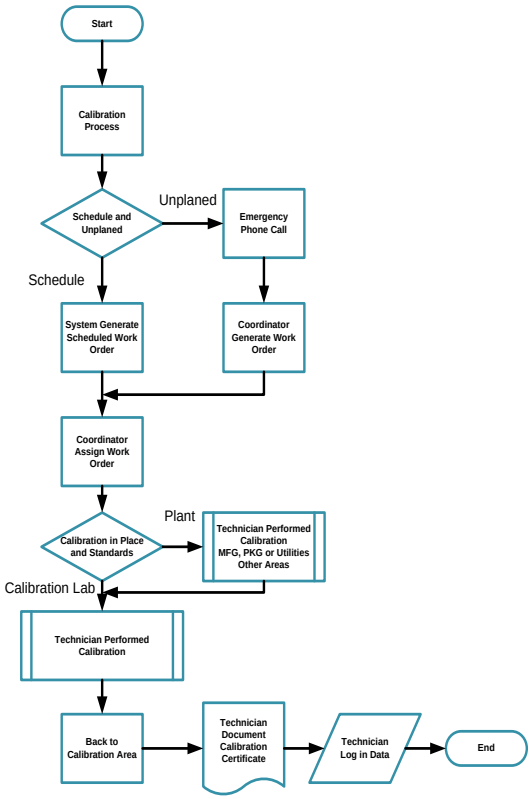

Figure 1
Calibration Process Flow Diagram

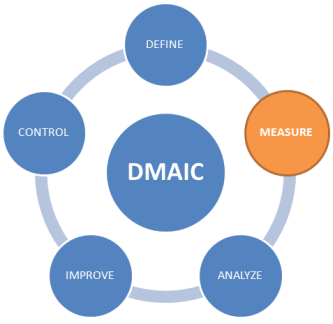

Figure 2
DMAIC Process

The DMAIC methodology is "a quality strategy for improving processes". [2]

- Define
- Measure
- Analyze
- Improve
- Control

RESULTS

DEFINING AND MEASURING PROCESS

In the Define phase, the project team clarifies the purpose and scope of the project and confirms that a DMAIC project is in fact appropriate. The key deliverable for this phase of the DMAIC process is the project Specifications.

Project Specifications

With the implementation of the wireless system: The Pharmaceutical facility expects to: Reduce documentation time and cost by 20%.

- Reducing the documentation human error.
- Improve the availability of Calibration Technicians to respond emergency calls and minimize the overtime cost.
- Reduce the documentation volume resulting in a better management of data and the beginning of a paperless environment.
- Minimize the documentation volume, resulting in a paper, time reduction.
- Evaluate the electronic dispositive to be used as wireless system utilizing evaluation criteria's.
- Evaluate the computer application to be utilized and integrated with the actual SAP software**.**
- Design input field needed to perform calibration entry to the wireless system adapted to the wireless device considering the FDA regulation and GMP's.
- Design the output report for the calibration work order known as Calibration Data Record considering the FDA regulation and GMP's.
- Make the necessaries changes to the actual SOP's and train the affected users.

ANALYZING AND IMPROVING PROCESS

The analysis phase aims to identify the critical factors such as the data based system and equipment required for the wireless project. (See Figure 3)

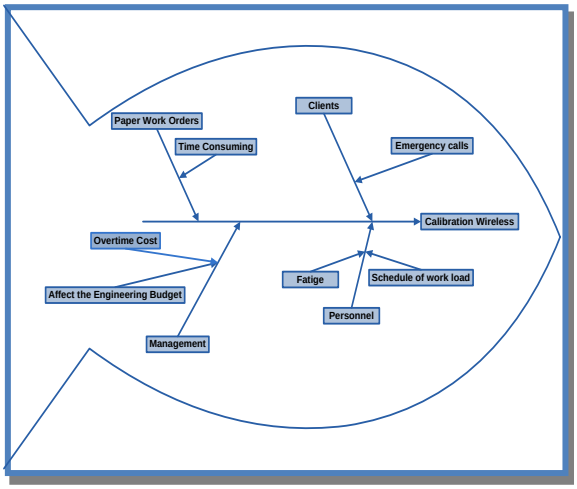

Figure 3
Fishbone Diagram

System Development

For the system development the company chooses a team with the expertise in the area. This team is part of the users and has the expertise in the related regulatory area required for the execution of the Calibration process.

Utilizing the problem- solving approach the team identify the system requirements and user requirements. Taking consideration the FDA regulations and GMP's [1] standards for pharmaceutical industries. To make a robust system and the wireless project success.

System Requirements

The wireless system must have the ability to:

- Barcode reading capability, to confirm the equipment under test.
- Create and change a Calibration notification in a wireless device.
- Create and change a Calibration work order in a wireless device.

- Confirm, display calibration points, and accept standards used and closing a calibration work order.
- Display the calibration instructions in the work order.
- Display the Calibration Work orders assignments.
- Display Calibration Data Record Report
- Maintain the Calibration Data Record report on system for future audit or references.

The wireless system design required a modern structured design. For this modern structured the team evaluates the alternatives before presented utilizing decision matrix.

Analysis of Alternatives

For the Analysis of Alternatives the team utilized an Analysis Matrix in 1-5 scale (See Table 1) to choose the Wireless Device and SAP System Interface System. [3]

Table 1
Wireless Output Device Analysis Matrix

	Weight	Tablet PC	Motorola MC70
Operational Capability	40%	2.5	4
Technical Capability	25%	4	5
Cost	20%	5	5
Compliance	15%	5	5
Ranking	100%	75	95

Based in the decision matrix we can observe that the best alternative it's the Motorola MC70. This alternative has the higher weighted score in the table. This alternatives show us that these meet with the best specification parameters.

The Symbol MC70 mobile device is designed:

- To withstand all-day everyday use in nearly any environment, this rugged compact device delivers wireless LAN voice and data communications.

Table 2
System Interface Analysis Matrix

	Weight	GUIXT SAP	Access SAP
Operational Feasibility	25%	4	4
Technical Feasibility	35%	5	3
Economic Feasibility	30%	5	4
Schedule Feasibility	10%	5	2
Ranking	100%	95	69

Based in the decision matrix we can observe that the best alternative it's the GUIXT SAP application. This alternative has the higher weighted score in the table. (See Table 2)

This alternatives show us that these meet with the best specification parameters.

- Guixt is a software technology that provides user interface customization to SAP. Extend the user interface to Net Weaver and Mobile without expensive and complicated ABAP and/or Java programming.
- Guixt lets us re-design/Customise the screens which people routinely use into a more useful, quicker and easier experience.
- The other benefit of Guixt is it allows us to reduce the screen size of the SAP transactions to fit onto the Symbol MC70.

Wireless Data Analysis

The new design most uses some portion of an existing database and is these design is an (In house development). [3]

This sequence diagram represents the As Is Calibration System and model the logic of a use case. In this diagram we can appreciate the double documentation as part of the sequence after a Calibration has done. (See Figure 3)

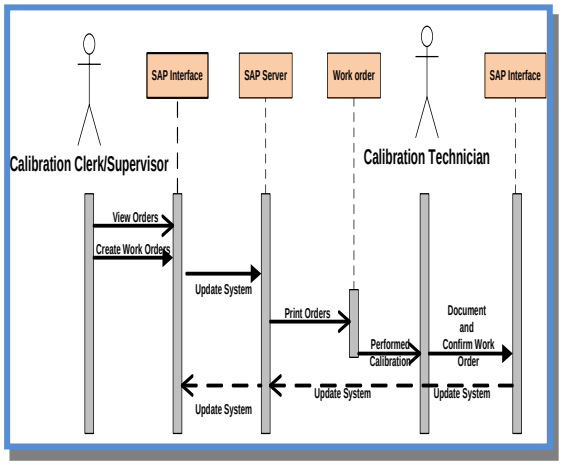

Figure 3
As Is Calibration System Sequence Diagram

This sequence diagram represents the Wireless Calibration System and model the logic of a use case. In this diagram we can appreciate the interactions between objects of the sequence after a Calibration has done. (See Figure 4) As part of the Data Analysis we used a Data Flow Diagram to represent the proposed system. This tool is used to depict the flow of the data through a system and the processing performed by the system. (See Figure 5)

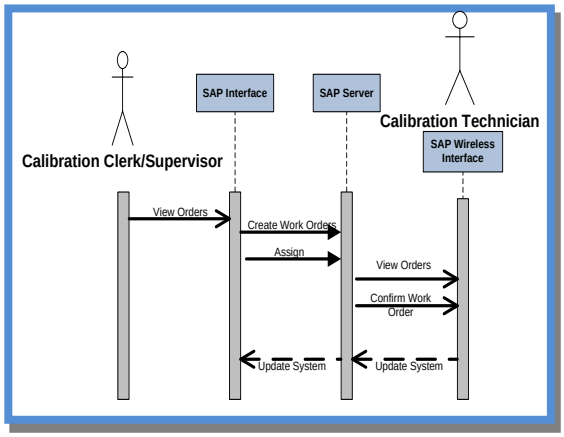

Figure 4
Calibration Wireless System Sequence Diagram

As part of the Data Analysis we used a Data Flow Diagram to represent the proposed system. This tool is used to depict the flow of the data through a system and the processing performed by the system. (See Table 3)

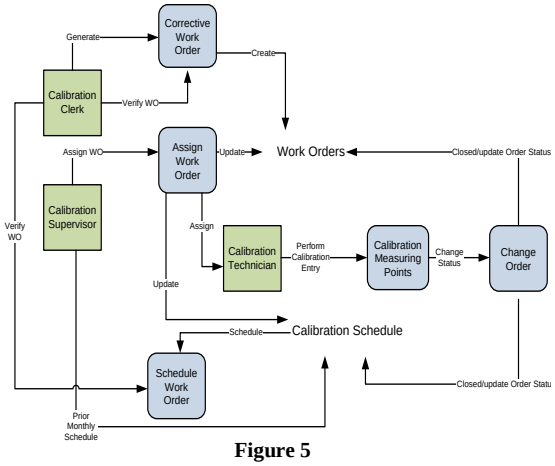

Figure 5
Calibration Wireless System DFD

Table 3
Business Entities Definition

Entity Name	Business Definition
Calibration Instrument	Instrument whereby a company associates agrees to enter in the Calibration System.
Calibration Order	It's a work order generated to complete an instrument calibration.
Maintenance Plan	An instrument plan assignment for monthly, Quarterly, semiannual or annual schedule.
Transaction	A business event to create, document and confirm a Calibration Order.

The Table 4 represents a descriptive property or characteristics of an entity.

Table 4
Attributes and types

Instrument	
Instrument ID	Number
Instrument Description	Text
Instrument Manufacturer	Text
Instrument Model	Text
Instrument Serial Number	Number
Instrument Criticality	Number
Instrument ID	Text
Instrument Parent Position	Text
Instrument Parent Department	Text
Instrument Due Date	Date
Instrument Next Due Date	Date
Instrument Range	Text
Instrument Range of use	Text
Instrument Tolerance	Text

Calibration Order	
Calibration Order Number	Number
Instrument ID	Text
Calibration Measuring Points	
Instrument Calibration Point	Value
Instrument Calibration Point	Value
Instrument Calibration Point	Value
Instrument Maintenance Plan	
Instrument ID	Number
Instrument Maintenance Plan	Text
Instrument Frequency	Number
Instrument Calibration Task List	Memo

Output Design Process

The Output Design is a data structure defining logical requirements. The Calibration Data Record is the output design. (See Table 5) This design includes all customer and regulation requirements. [3]

Table 5
Output Logical Requirement

Data Structure Defining Logical Requirements	Comments
Calibration Data Record	Field should be fixed
+ Instrument ID	
+ Instrument Description	
+ Instrument Model	
+ Instrument Manufacturer	
+ Instrument Serial Number	
+ Instrument Parent Position	
+ Instrument Criticality	
+ Calibration Procedure	
+ Calibration frequency	
+ Calibration Procedure	
+ Calibration Date	
+ Calibration Due Date	
+ Instrument Range of Use	
+ Instrument Range	
+ Instrument Tolerance	
+ Process Tolerance	
- 3 {Instrument Reading, including variable units}	Field should be fixed, data shouldn't be rounded
- 3 {Instrument Standard Reading, including variable units}	Field should be fixed, data shouldn't be rounded
- 3 {Instrument Deviation, including variable units}	Field should be fixed, data shouldn't be rounded
- 5 {Standard specification fields}	
+ Calibration Performed Technician	
+ Calibration Performed Date	
+ Review Name/Date	
+ Approved Name/Date	
+ Fully calibrated	check Field
+Out of Tolerance	check Field
+ Out of Service	check Field

COST ANALYSIS

In a regular day a technician work and 8hrs/shift.

Most Likely Calibration Duration

A technician spent approximately 72% of their time calibrating. Refer to Equation (1) and Figure 6.

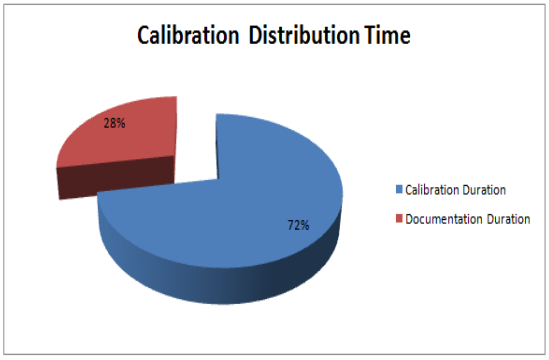

Figure 6
Calibration Distribution Time

$$\boldsymbol{Duration} = \frac{(1XOD) + (4XED) + (1XPD)}{6} = 6.5 \text{ hrs.} \quad (1)$$

OD=5 hrs.
PD=7 hrs.
RD=6 hrs.

Most Likely Documentation Duration

A technician spent approximately 28% of their time documenting. Refer to Equation (2) and Figure 6.

$$\boldsymbol{Duration} = \frac{(1XOD) + (4XED) + (1XPD)}{6} = 2.58 \text{ hrs.} \quad (2)$$

OD=1.5 hrs.
PD=3 hrs.
ED=2 hrs
OD= Optimistic Duration
PD=Pessimistic Duration
ED=Expected Duration

Calibration Distribution Time After Wireless Implementation

After the Calibration Wireless implementation the facility expect a reduction in time and documentation error. In a calibration system the documentation represents the most important output whereby the calibration action.

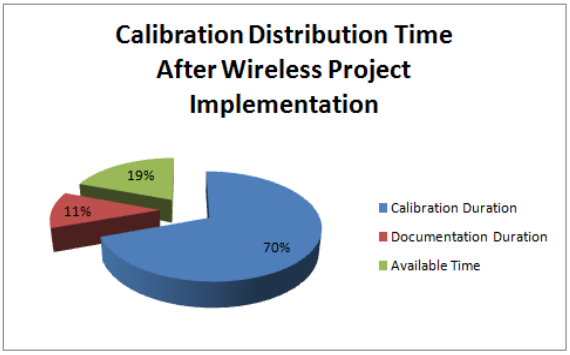

Figure 7
Calibration Distribution Time

Expected Most Likely Transaction Duration

After a project implementation technicians should spent 11.5%of time documenting.
These results represent an available time of 19% per day. Refer to Equation (3) and Figure 7.

$$\boldsymbol{Duration} = \frac{(1XOD) + (4XED) + (1XPD)}{6} = 5.5 \text{ hrs.} \quad (3)$$

OD=4 hrs.
PD=6 hrs.
ED=5 hrs.

In regular basic day a after calculated the expected duration of the documentation process. There 2,184 hrs per year per technician. Approximate $80,000 per year in man hr.

After implementation we expect an economy of $80,000 per year. [4]
Return of investment in 1.2 years.

OD= Optimistic Duration
PD=Pessimistic Duration
ED=Expected Duration

PROJECT DEVELOPMENT COST

The project development cost includes the system experts. Also include the server software, hand held and communication cost. For this project, the project development cost considers the annual operating cost and the expense of maintenance agreement for the hand held and the GUIXT system. (See Table 6)

Table 6
Project Implementation Cost

	DEVELOPMENT COST	Total Hrs	Cost/per hrs	Total Costs
Personnel				
1	System Analyst	400	50	20000
1	Programmer/Analyst	250	35	8750
1	GuiXT designer	200	50	10000
1	Telecommunication Specialist	50	50	2500
1	Databased Specialist	15	45	675
				41925
New Hardware & Software				
1	Server Software			10,000
4	Hand Held $1400			5600
	Communication Cost			50,000
	Total Development Cost			**107,525**
Projected Annual Operating Cost				
1	Programmer/Analist	125	35	4375
Expenses				
1	Maintenance Agreement for Hand held			995
1	Maintenance Agreement for GUIXT			600
				5970

Net Present Value

The Net Present Value of a project is the difference between the sum of the discounted cash and flows which are expected from the investment and the amount which is initially invested. (See Table 7)

Table 7
Net Present Value

Cash Flow Description	Year 0	Year 1	Year 2	
Development Cost	107,525			
Operation & Maintenance		5,970	5,970	
Discount factor for 12%	1	0.893	0.797	
Present Value of lifetime cost		5,331.21	4,758.09	
			Total present value	**10,089**
Benefits Derived from operation of New	0	80,000	90,000	
Discount factor for 12%	1	0.893	0.797	
Present Value of annual benefit		71,440	71,730	
			Total present value	**143,170**
			Net present value of the alternative	***133,080***

CONCLUSIONS

A Pharmaceutical industry can develop a Calibration Wireless System with the integration of the 21 CFR 211 regulations and ANSI [5] requirements.

The company should consider implementing this kind of technology in other departments. This technology will not only have economy in the technician availability, but also the wireless system will give help save paper, and management. A better management of resources allocation is one of the advantages including the minimization of human errors.

The company has to work with the employee generational issues as part of the kind of working force available. This working force is used to work with paper and there is a negative to the new system. A recommendation to solve this issue is to make them part of the process. With the objective of create sense of property and knowledge.

After this implementation the company will have the wireless infrastructure to develop other wireless systems without the initial cost.

REFERENCES

[1] National Institute of Standards and Technology. Retrieve April 28, 2012 from http://www.nist.gov/pml/wmd/.

[2] Epply, T. and Nagengast, J. *"The Lean Manufacturing Handbook".* Performance Review Institute 2011.

[3] Whitter, J., and Bentley, L."*Introduction to Systems Analysis and Designs"*. McGraw-Hill International 2008.

[4] Mantel, S. and Meredith, J. "*Project Management a Managerial Approach"*. John Wiley& Sons, Inc 2009.

[5] American National Standard Institute. Retrieve September 01, 2012 from http://ansi.org/.