Implementation of Electronic Logbooks for the Utilities Area in a Pharmaceutical Manufacturing Facility

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Abstract *— Technology is an ever evolving concept, that every year incorporates new terminology appropriate to technological advances and different application domains. Industries are trying to leverage all of those new concepts to start to have major integration between their processes and their systems. One of the enablers to do this integration in the pharmaceutical industry are the Manufacturing Execution Systems. Serving as the main point for capturing manufacturing data, the Manufacturing Executions Systems can help pharmaceutical industries detect inefficiencies and problems sooner, saving time and money and support continuous business improvements. With the objective of simplifying and standardizing processes, as well as to leverage the infrastructure and systems already in place, this design project will focus in the implementation of electronic logbooks for the Utilities area, including, but not limited to the creation of requirement and design documents, development of electronic logbooks, validation and production implementation.*

Key Terms *— Pharmaceutical Industry, MES, Information Technology, DMAIC, Environmental Regulations*

INTRODUCTION

As part of the fourth industry revolution, called 'Industry 4.0', the pharmaceutical industries are evolving and starting to have a major integration between their processes and their systems. One of the enablers to do this integration are the Manufacturing Execution Systems (hereby called MES). MES needs to become the central information hub for manufacturing data.

A particular biotech bulk manufacturing facility, whose products are sold all over the world (hereby called Pharmaceutical Company X), is implementing an MES System across their processes. Company X manufacturing steps are divided in two major processes, Fermentation and Purification. In addition, Company X have other supporting areas such as Warehouse and Utilities. As of today, company X has implemented electronic logbooks as part of its MES implementation in all the Fermentation, Purification and Warehouse areas. With the objective of simplifying and standardizing processes, as well as to leverage the infrastructure and systems already in place, there is an initiative to implement electronic logbooks for the Utilities area. Company X's Utilities area performs a very important role in the operation of the site. This area manages and assist with the electric system, air conditioning system, water supplies, nitrogen, condensate, cooling water as well as operate the wastewater treatment facilities.

This design project will focus in the implementation of a total of 10 electronic logbooks, using a Commercial off the Shelf Manufacturing Execution System (MES), for the Utilities area.

RESEARCH OBJECTIVES

The objective of this design project is to implement electronic logbooks in the Utilities area, creating a paperless environment with an integration among the business and other systems by May 2018. With this implementation, the Utilities area is moving to eliminate data omission, documentation errors, second person verification and maximize resources for their process. Also, it

will provide proactive management of situations to minimize deviations as well as rapid access to current data for management to make decisions with up to the minute information. One of the main reasons for the implementation of electronic logbooks is to have all the data needed in a single place to enable future reporting capabilities for Environmental Agencies reports. This will enable environmental representatives to produce up to the minute reports with more accurate data.

RESEARCH CONTRIBUTIONS

Contributions of this research project can be summarized as reduction in data collection, data omission, documentation errors and second person verification. Data omission and documentation errors are very important due to the impact it has in data integrity. Data Integrity has been a very important topic for regulatory agencies in the last few years, specially for FDA, as required in the Code of Federal Regulations (CFR) Title 21, parts 210, 211 and 212.

In addition, if data omissions and documentation errors are reduced, deviations are reduced too, as well as any potential impact it could have in product quality. Consequently, due to the reduction of all of the concepts mentioned above, the area can optimize resources and identify other areas to attend.

Likewise, another contribution is the availability of the data at any time, anywhere. Due to the fact that the process is executed on a web application, managers and supervisors can track the process execution. This allows them to have visibility of the process and have access to current data to make decisions with up to the minute information.

During the Electronic Logbook's core team workshops, it is expected for both IT teams and Process Teams (Process Engineering, Environmental Representatives, Operators) to work together in order to deliver the correct procedures and strategy.

RESEARCH BACKGROUND

In order to better understand the concepts covered in this Design project, different terms will be covered in this chapter. Some of these terms are: Industry 4.0, Pharmaceutical Industry, and MES. Other concepts to be discussed are Information Technology and Automation, since both are very integrated when dealing with electronic logbooks and MES in general. In addition, a description for environmental regulations will be discussed due to the importance of the data to be captured for the regulations requirements. After discussing all the theoretical background, the reader will have the all the required knowledge to understand the objectives and context of this Design Project.

Industry 4.0

Industry 4.0 is the so called fourth industrial revolution. In this new industrial revolution computers and automation will come together in an entirely new way, with robotics connected remotely to computer systems equipped with machine learning algorithms that can learn and control the robotics with very little input from human operators. The initial goals in Industry 4.0 are automation, manufacturing process improvement and production optimization. However, several other benefits can be obtained as part of this such as transitioning to new business models and revenue sources with information as the main enabler.

Industry 4.0 is driven by the following four concepts:

- The incredible rise in data volumes (Big Data), computational power, and connectivity.
- Emergence of analytics and business-intelligence capabilities (Parallel Computing).
- Human-machine interaction such as touch interfaces and augmented-reality systems.
- Improvements in transferring digital instructions to the physical world, such as advanced robotics and 3-D printing.

The Industry 4.0 vision encompasses more than automation and data exchange in manufacturing technologies as it stretches beyond technologies

and looks at the end-to-end chain, including, for instance, warehousing, logistics, recycling, energy and so forth.

Automation

Automation, as defined by ISA (International Society of Automation), is "the creation and application of technology to monitor and control the production and delivery of products and services" [1] Automation is used in virtually all industries, including transportation, utilities and manufacturing. Some of the benefits of automation are:

- "Consistency. Consumers want the same experience every time they buy a product, whether it's purchased in Arizona, Argentina, Austria, or Australia." [2]
- "Reliability. Today's ultra-efficient factories can't afford a minute of unplanned downtime, with an idle factory costing thousands of dollars per day in lost revenues." [2]
- "Lower costs. Especially in mature markets where product differentiation is limited, minor variations in cost can cause a customer to switch brands. Making the product as cost-effective as possible without sacrificing quality is critical for overall profitability and financial health." [2]
- "Flexibility. The ability to quickly change a production line on the fly (from one flavor to another, one size to another, one model to another, and the like) is critical at a time when companies strive to reduce their finished goods inventories and respond quickly to customer demands." [2]

Automated processes are implemented mostly when there are tasks with high degree of difficulty, where human labor is physically hard (movement of heavy equipment, size difficulties) or dangerous or when workers are needed for other, more important tasks.

Across all the industries, there are several different types of automation tools used such as: Distributed Control Systems (DCS), Human Machine Interface (HMI), Supervisory Control and Data Acquisition (SCADA) and Programmable Logic Controller (PLC). In highly integrated industries, information gathered from the Control System is used to monitor processes and view different process trending.

Information Technology

Information technology (IT) is the area in charge of supporting all other business area in the leveraging of information management. The IT department is the one with the expertise to work with computers, networking, infrastructure and processes to create, process, store, secure and exchange all forms of electronic data. The people who work on this area, normally called IT Business Analyst, are the ones in charge of automatizing all the manual work that is done, using the available tools in order to increase productivity, accuracy and decision making.

Some relevant aspects to this particular design project is the current role of IT in the implementation and maintenance of electronic logbooks. As part of the IT group, there is a sub-group (MES Team), which is in charge of the development, testing, implementation, maintenance and support of the electronic logbooks and electronic recipes that are used in the areas. This includes creation of reports, installation of patches, server administration and more. One of the main goals of the IT group is to reduce paper-work and in turn, improve the quality and accuracy of the data.

In order to satisfy customer necessities, the IT group works very closely with the different business areas, making sure that all the requirements are gathered and analyzed to find the best possible solution for each specific need.

Manufacturing Execution System

"In recent decades, industrial companies have invested much time and money in machine and production line automation on one hand, and in ERP systems on the other hand. Between these two automation layers lies another, usually called the

MES layer." [3] A Manufacturing Execution System (MES) is an information system that "concerns the activities that take place within manufacturing department. These include preparatory activities, such as detailed production scheduling and logbook management, but also retrospective activities, such as data collection, reporting, and analysis." [3] MES is crucial in highly regulated industries, such as pharmaceuticals, due to the importance of having everything documented as a proof of all the processes and actions that were followed to produce a batch. Some of the benefits of an MES are: reduces manufacturing cycle time, reduces or eliminates data entry time, improves data quality and enable paperless processes.

The role of the MES as part of this project is an intermediary between the Enterprise Resource Planning (ERP) Software, where all the financial information and raw material inventory is tracked, and the Distributed Control System (DCS), where all the monitoring and control of the process occurs (refer to Figure 1).

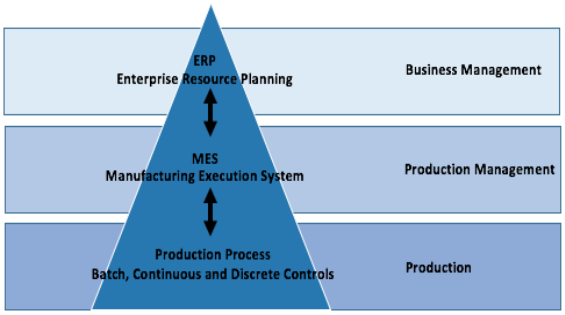

Figure 1
System Integration Model

In the MES all the process parameters (critical and non-critical) are gathered from the DCS and reported as part of the batch report, together with the bill of material used to create the specific product. All the material consumed is reported into the ERP system as well as all the different times such as when the process started and when it was completed. MES also has the capability to interact with other systems such as data historians and laboratory information management system.

Environmental Regulations

Environmental regulations are an "organized system of statutes, regulations, and guidelines that minimize, prevent, and punish those responsible for the consequences of damage to the environment. This system requires each individual—whether an engineer, physicist, chemist, attorney, or consumer—to be familiar with its concepts and case-specific interpretations. Environmental regulations deal with the problems of human activities and the environment, and the uncertainties of law associated with them." [4]

"EPA is the most far-reaching regulatory agency in the federal government because its authority is very broad. It is charged with protecting the nation's land, air, and water systems. Under a mandate of national environmental laws, it continues to strive to formulate and implement actions that lead to a compatible balance between human activities and the ability of natural systems to support and nurture life" [4]

Design Project

After presenting all the necessary and important concepts to be discussed as part of this design project, the next topic to consider is the process to be follow in order to accomplish the final goal of the project, the implementation of the electronic logbooks for the Utilities area. In the case of transforming paper logbooks to electronic, a process that allows the simplification and standardization of the process, reducing defects and increasing quality, was needed. Lean thinking, as well as Six Sigma approach, will be used as part of the methodology. In Six Sigma, one of the most effective process improvement technique is the DMAIC methodology (refer to Figure 2). The main purpose to select DMAIC is that this technique is focused in analyzing the process thoroughly before doing any kind of implementation. This approach is important in the conversion of paper logbooks to electronics due to all the simplification opportunities that can be identified such as data availability in other systems, activities that can be performed simultaneously, process improvements

and resource allocation. Other important aspect of the DMAIC methodology is that it has an analytical approach, allowing the business to use the collected data to find trends, identify opportunities in the process and facilitates the reporting to external regulatory agencies.

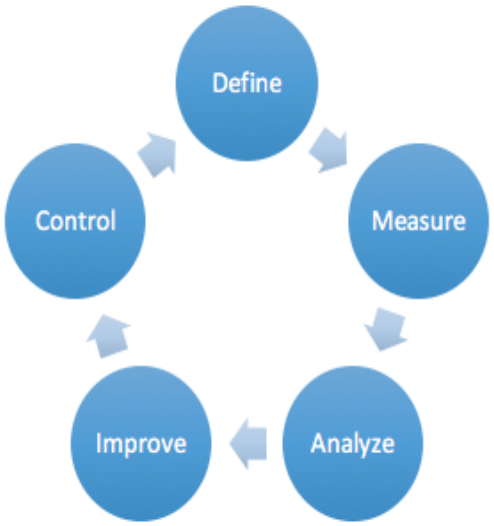

Figure 2
DMAIC Model

The DMAIC methodology is composed of five steps: Define, Measure, Analyze, Improve and Control. Each step can be defined as followed:

- **Define** – Starts by defining the process, stating the problem, knowing who the customer is, identifying the goals and existing output conditions.
- **Measure** – In this step, parameters to be quantified are chosen and key characteristics are categorized. Also measurement systems are verified and data is collected.
- **Analyze** – After the data is collected, it is analyzed as part of this next step. All the raw data is converted into meaningful information, including identifying causes of the defects or problems.
- **Improve** – In this step, solutions of problems are developed, results of process changed are seen and also it, is decided if the change is beneficial or if any other change is necessary.
- **Control** – In this final step of DMAIC, the process is monitored to assure no unexpected changes occur and, if the process after this analysis is performing as desired, it can be said is under control.

RESEARCH METHODOLOGY

As previously mentioned, DMAIC approach will be used as the project's methodology. In this chapter, all the DMAIC steps will be explained in order to establish a clear scope and milestones for the design project.

Define

During the define phase, a clear scope of the project will be defined. The project charter will be developed in order to state: Project Goal, Project Participants, Stakeholders, Requirements, Constraints, Milestones, Communication methods and Deliverables. This charter will be presented to the Company X's Governance Team in order to received their approval to proceed with the project.

Measure

As part of the measure phase, information about the problem statement will be gathered to use it as a baseline for process performance data and to identify opportunities. This step is the most complex, and will require the most time. Spending more time understanding the requirements and scope of the project during this phase, will allow for a better analysis of the data and a less time spend in the Analyze and Improve phases. During this phase, the Voice of the Customer (VOC) will be collected, overall project planning will be setup and Gantt chart will be created. In addition, during this phase, data integrity must be considered, Standard Operating Procedures (SOP) are reviewed and benchmarking with other Company X's sites is conducted to determine if replication can be an option and evaluate how others are doing things in order to have a standard against which something can be assessed.

Analyze

During the analyze phase, all the information gathered in the Measure phase will be examined in order to identify all the root causes of problems, opportunities for simplification and determine the level of effort for the next phases, especially the Improve Phase. Requirements will be analyzed and design of solution will be established. In order to comply with the established schedule, weekly meetings will be scheduled were resources from the different impacted areas (Process Engineering, Technical Services, Operations, Information Technology, Automation, Training and Procedures) will be participating.

Improve

At the Improve phase, the implementation of the project will occur. Training on the new electronic logbooks and other impacted procedures should be given to the impacted area. Also, validation of the electronic logbooks will occur as part of this phase. Once validation is completed, training is delivered and procedures are made effective, coordination with the Utilities area will be made in order to start using the electronic logbooks.

Control

As part of the Control Phase, a Stabilization Period will start the day of the Implementation of the electronic logbooks. Any issue that was not seen during the design or validation phase, will be worked during this phase. Also, on-site support (24 hours, 7 days a week) will be given to the Utilities area for the first 2 weeks after the implementation. The support is important in order to ensure a successful and seamless transition.

RESULTS AND DISCUSSION

Implementation of this project was performed using DMAIC. In this section, a discussion of the DMAIC methodology steps completed will be presented and results for the Electronic Logbook implementation will be discussed.

Define

The Utilities area has more than 30 paper logbooks to document, resulting on thousands of paper records, manual data entries, calculations and verifications. Paper records does not prevent documentation omissions or errors and require storage, handling and procedures to guarantee the documentation integrity and availability. As part of this project it was defined that 10 logbooks would be converted to electronic as an initial phase. Project team was established and it included a multifunctional team with representatives from the Utilities area, Training and Procedures, Automation, Information Technology and Environmental. The main milestones were Project Kick-off, Utilities Process Review, Electronic Logbook Application Training and Electronic Logbooks Go Live.

Measure

In order to better understand the logbooks to be converted to electronic, as well as to identify opportunities for simplification and standardization, a Process review was performed. Once the process review was completed, a Voice of the Customer (VOC) was used to gather all the inputs and requirements from the customer. “The VOC analysis gathers the customers' needs and wants as a basis for establishing objectives” [5].

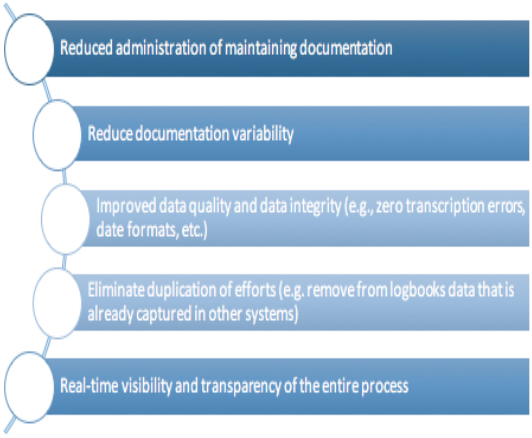

Figure 3
VOC Results

Standard Operating Procedures (SOP) were revised in this phase, to identify opportunities of simplification. Each paper logbook to be converted came from a different SOP, hence 10 SOPs were revised. In addition, a previous electronic logbook implementation was revised to identify opportunities for replication and standardization. With all the data collected, a project plan was developed, tasks were established, as well as dependencies, roles and responsibilities. Agile methodology was used as the method of planning for this Project.

Analyze

In the Analyze phase, a detailed review of each paper logbook was performed, were several simplification opportunities were identified such as: reduced documentation frequency, reduce parameters to document due to information existing in other systems, reduce parameters due to no value added, standardize documentation methods, re-organization of inspections routes and reduce amount of second person verification needed. All of the findings were discussed with the Project team in order to have all the different views and all agreed on the recommended design.

Also in this phase, requirements for Environmental reporting were gathered, to ensure that data is collected in a meaningful manner to later build reporting solutions for environmental purposes. In addition, a previously build dashboard, used in other Company X's areas, was evaluated to replicate as part of this project. One of this solution is the Pending Task Dashboard, were operators can see all the tasks from the electronic logbooks that they have pending per Calendar Day or per Shift. This view facilitates the management of resources on the team and to better distribute who is doing which task per shift.

Based on the Voice of the Customer performed as part of the Measure phase, requirements were evaluated and tangible benefits were calculated. A summary of the benefits that were analyzed and that are expected as part of this project can be view in Figure 4.

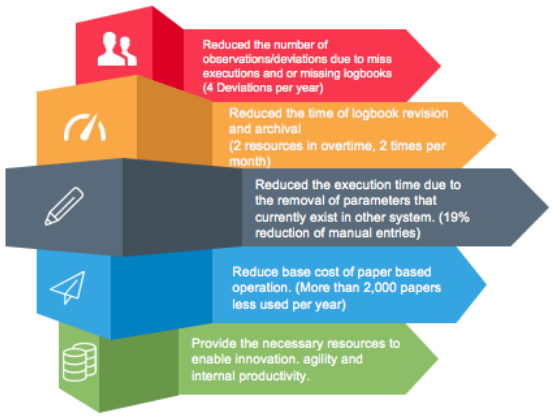

Figure 4
Implementation Benefits

Improve

During the improve phase all the validation activities started. Validation of each electronic logbook developed was performed by Utilities area operators, with the intent of integrating them and made them familiar with the solution. In parallel, al the SOPs that were being revised were send for review and approval, to ensure that documents can be effective in a timely manner. In addition, a training strategy was developed, to deliver to the Utilities operators the Electronic logbook application training, as well as training on the different SOPs being revised. As part of the training activities, several operators were identified as Power Users, to help in the support of day to day activities and be the first line of defense in case any issues arise. Several different training sections were needed to cover all the different shifts.

Once all the validation activities were completed, the SOPs approved and the training was delivered, coordination with the Utilities area was performed to implement the electronic logbooks in the production environment and start Go Live activities.

Control/Support

Once the Go Live started, a stabilization period began. An information technology resource was supporting the area on-site (24 hours, 7 days a week) for the first 2 weeks. After the initial two weeks, a Tier 1/Tier 2 support strategy was

established. Tier 1 support was covered by the previously identified Power Users. Power users are utilities operators with additional trainings that are responsible in the identification and resolution of possible issues. In case that Power Users were not able to resolve the issue, Tier 2 support is given. Tier 2 support is performed by an Information Technology Analyst and it is typically performed on an on call basis. Tier 2 support also manages future change control processes that may arise due to process changes or application upgrades.

In addition, the Project Team started to measure all the benefits that were established in the Analyze phase in order to compare in 6 months all the parameters and performance indicators, including deviations, resource management, documentation handling and execution time.

CONCLUSION

When performing an assessment of an MES implementation, the first thing that comes out of anyone's mind is to convert a paper based record into an electronic manner. However, when applying Lean Six Sigma to an MES implementation, powerful results can be expected.

Due to the highly regulated environment that controls Company X's processes, having a process that standardizes, simplifies and facilitates the documentation of process parameters is fundamental. An MES system provides a mechanism to prevent documentation omissions or errors, eliminate paper storage and archival, and guarantee a higher degree of documentation integrity and availability.

Applying Lean Six Sigma to this project helped identified opportunities to be more efficient and simplify the process such as eliminate duplication of efforts, eliminate manual entries and faster access to the data

Part of the next steps would be to fully convert all the other paper based logbooks into electronic. In addition, once all the data resides into a single source system, specific regulatory reports can be created to facilitate Environmental agencies reporting.

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