Optimize and Automate the Documentation Process in the Manufacturing Granulation Process

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Abstract — *During the past year, the pharmaceutical industry has embraced many situations that encourage the human resource of each company to improve and develop the organization. Integrating the lean manufacturing principles can increase the ability to complete and enhance the operation in the area. This research involves the integration of the Manufacturing Execution System using Electronic Batch Records system in the documentation records process at the granulation stage. Improvement in the manufacturing area can embrace the use of electronic batch records which helps employees perform the task with accuracy and consistency during the process by increasing the productivity (none rework) since minimal risk, high quality and auditable data integrity in all leveling of the documentation was obtained.*

Key Terms — *Data Integrity, Electronic Batch Records, Lean Manufacturing, Manufacturing Execution Systems*

INTRODUCTION

The pharmaceutical industry recognized the potential to develop and changes the infrastructure which optimized the supply chain system. The importance of those processes is to empower those areas with the finality of reducing cost and begin the innovation of new ideas. The reduction of costs and the innovation of new ideas can be achieved by adding values to the performance of the areas and the efficiency of all employees. Lean manufacturing has revolutionized the pharmaceutical industries and created innovations opportunities in all leveling to the departments. Lean manufacturing focuses on waste minimization while improving manufacturing practices, which enables the company to produce higher quality products [1].

Opportunities can embrace the manufacturing area to generate products with the highest level of quality, purity, strength, and security to be received by the customer and in which they comply with FDA regulation including data integrity. In order to comply with the manufacturing area necessities, some opportunities in the granulation stage were identified where the electronic records could be an improvement. An MES is a software that connects, monitoring and controls complex manufacturing systems and data flows in the manufacturing or packaging areas [2]. The MES functionality (shown in Figure 1) consists in business integration, specs, reports, process integration, batch execution, recipe and specification management, materials management, equipment management, production order management, recipe execution, electronic batch records, and device history.

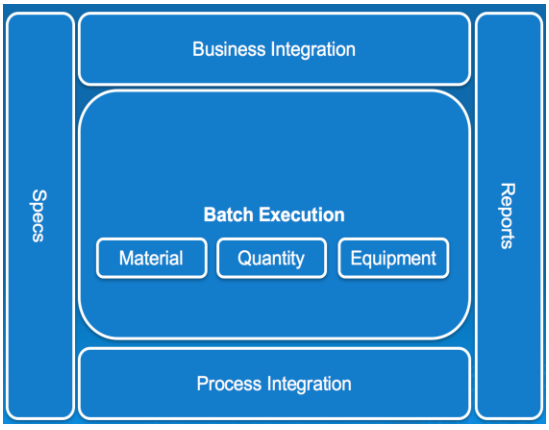

Figure 1
MES Functionality

OBJECTIVE

The principal objectives and focus in the pharmaceutical industry when implementing the

use of MES with EBR in the manufacturing area are the following:

- Improve accuracy and consistency
- Increase productivity
- Reduces manufacturing cycle time
- Reduces or eliminates data entry time
- Reduces work-in-process
- Reduces or eliminates paperwork between shifts
- Reduces lead times
- Improves product quality
- Eliminates lost paperwork
- Empowers plant operations people
- Improves the planning process
- Improve decision making
- Improves customer service
- Reduces setup costs, wait times
- More reliable and precise sequence planning

LITERATURE REVIEW

To comply with the optimization in the granulation area and full automation in the documentation is necessary to monitor and compare the activities of the process, manual and EBR documentation to evaluate the performance as the best practice. Changes in technologies in all organization can provide the means to improve performance in areas as quality, cost and the response on time. Those technologies can measure steps to reduce the cycle time, out of stocks, inventory, the number of supply, lead time, order preparation and all the non-value added.

Each EBR recipe can develop, tested, validated, and it should be approved by validation quality assurance and process engineer personnel. The process must be strict because it will be the recipe (batch) which the operators will follow to create the process and it must be correctly documented to avoid problems in data integrity in the process.

The use of problem-solving methodology is more comfortable when integrated with Lean Six Sigma Manufacturing Tools using DMAIC Methodology as an integral part of all the improvement efforts. DMAIC methodology (shown in Figure 2) refers to a data-driven quality strategy for improving processes. DMAIC stands for: Define (D), Measure (M), Analyze (A), Improve (I), and Control (C) [3].

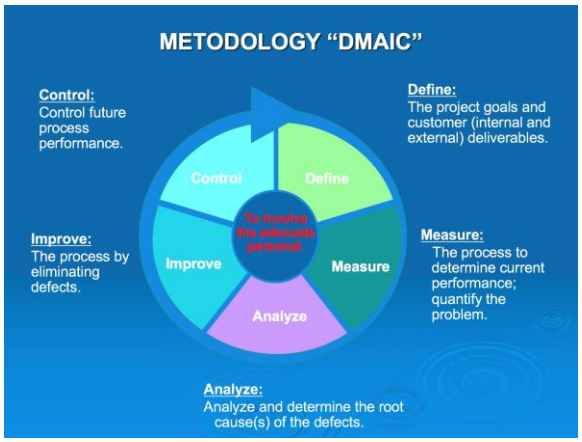

Figure 2
DMAIC Methodology

Many industries want to improve the documentation which can be done by replacing the manual exiting with better and new technologies that provide solutions and that be more cost-effective to move data. Ref. [4] establishes the guide that should be followed when maintaining or submitting information electronically. Data integrity requirements are one of the focus by different regulatory agencies as the Food and Drug Administration (FDA).

The FDA is an agency responsible for protecting and promoting public health through the control and supervision of food safety, tobacco products, dietary supplements, prescription and over-the-counter pharmaceutical drugs, vaccines, biopharmaceuticals, blood transfusions, medical devices, electromagnetic radiation emitting devices, cosmetics, animal foods & feed, and veterinary products [5].

When EBR system is used, the pharmaceutical industries must prove that they comply with all regulations established for the use of those electronic records. Many controls are required to ensure security, integrity and be trusted. The user can be identified by a unique user and password to determine who performs the task. EBR can be

designed with the different level of documentation and approval: record administration, review, and approval must be included as part of the various responsibilities to ensure the excellent practice during the design and implementation of the electronic batch recording systems. Many benefits were obtained that reduce the risk of non-compliance with the use of EBR; reducing documentation errors and the missing entries are eliminated since the system was covered with an alert to avoid those situations from the system that the user did not pass to the next steps without completed the first.

The process of each batch of products is audited and regulated to ensure quality. Some companies use paper-based processes to create batch record because is easier to use and the operators only need to read and write the information. The problem is the actual process is riskier and inefficient to make mistakes in the paper-based process. The best method is to implement an EBR to improve data integrity and all the employees working with the same streamlined process.

Data integrity was increasing at all levels in the pharmaceutical industries during the last year. FDA has increasingly observed in cGMP violations that involving data integrity. Data integrity focuses on complete, consistent, and accurate data which should be attributable, legible, contemporaneous, original, and accurate (ALCOA) [6].

The main scope is the evaluation of data generated at the granulation and process areas as manufacturing and packaging from electronic, hybrid and manual systems. When personnel arrive to work in the area, training in data integrity, access to the computer systems with a unique password that cannot be shared and the information gathering by each employee is auditable. FDA recommends that audit trails that capture changes to critical data be reviewed with each record and before final approval of the record. When generated to satisfy a cGMP requirement, all data become a cGMP record. Every employee must document and save the data at the time of performance to create a record in compliance with cGMP requirements and ensure the quality of the product that finally will be sent to the customer.

EXPERIMENT

During the research evaluation at the granulation area, it was found inefficiency in the documentation step during the process. The manufacturing area executes the granulation documentation by using two systems; manual and EBR. The objective is implemented full EBR in the granulation area. Tables 1 and 2 present the comparison for the manual and EBR process obtained during the evaluation of the batch record and the risk obtained for the approved of the lots data.

Table 1
Manual Batch Record

Lots	Error	Exceptions	Risk
1	11	Incorrect date	Medium Supervisor authorization (2)
1	1	Error without justification	Medium Supervisor authorization (2)
1	9	Incorrect date	Medium Supervisor authorization (2)
1	1	Incorrect weight	None Correct with supporting data and Supervisor authorization (0)
1	1	Wrong quantity weight	Critical. Evaluation of risk is rejected (3)
1	2	Signature in wrong space	None (0)
1	6	Incorrect weight	None Correct with supporting data and Supervisor authorization (0)

7	31		9

The manual process was evaluated using seven (7) auditable batch records of the lots in which errors were found and specified. Figure 3 summarizes each lot evaluated versus documentation error found.

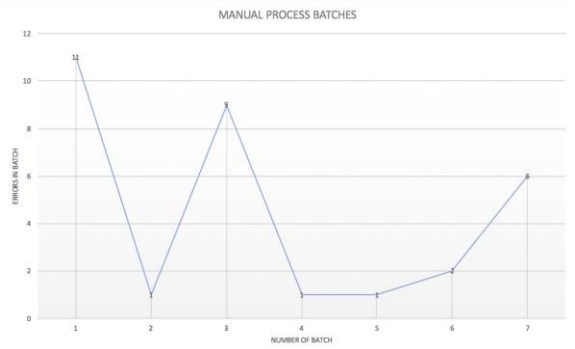

Figure 3
Manual Process

Table 2
Electronic Batch Record

Lots	Error	Exceptions	Risk
1	0	Incorrect date	None
1	0	Error without justification	None
1	0	Incorrect date	None
1	0	Incorrect weight	None
1	0	Wrong quantity weight	None
1	0	Signature in wrong space	None
1	0	Incorrect weight	None
7	0		0

The EBR process was evaluated using seven (7) auditable batch records of the lots in which none errors were found. Figure 4 summarizes each EBR batch evaluated versus documentation error found.

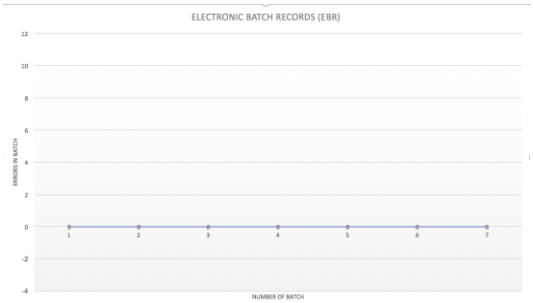

Figure 4
Electronic Batch Record Process

Once EBR is created, the probability of finding errors during the granulation process is minimal, or none since the systems were validated to avoid those and these can be strictly evaluated during the execution of the trials.

CONCLUSION

After completing the evaluation and the comparison between both documentation system (manual and EBR), it can be concluded that using the exceptions of risk obtained, the use of EBR improve the quality of the products due to the risk to obtained error was not probably. In the manual documentation, risks and errors are higher, and the supervisor needs to evaluate each error to take the risk of approving or rejecting the stages performed. In the EBR, there are no risks because the system evaluates and alerts the user to perform the task as established during the validation of them and did not permit to continue to the next step of the process. The use of EBR during the process makes it continuously and on time. As a recommendation for future research, the EBR can be implemented in other stages of the process for the same product to complete all the manufacturing and packaging stages (compression, capsule filling, and packaging).

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