Improving the flow of Sampling Analysis of Manufacturing Batches to reduce time and Increase the Capacity of the Process

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Abstract *— This research will focus on analyzing the flow of sample analysis of manufacturing batches to reduce time and increase the capacity of the process in the laboratories. A laboratory in the pharmaceutical industry receives many samples from manufacturing daily. This research aims to find how to mitigate waste time factors in the flow of sample analysis in laboratories. With the incorporation of the new software, the laboratory can analyze many samples and use the equipment at a higher capacity and in less time. A significant improvement in the "takt time" of the process was observed from 50 minutes to 30 minutes. In turn, the flow of analysis of laboratory tests had a 47% increase. Regarding the annual cost of licenses, $3,777 were saved.*

Key terms *— data integrity, laboratory analysis, lean manufacturing, sample flow*

INTRODUCTION

This project supports and contributes to maximum efficiency in sample analysis in laboratories at an industrial level. In a company whose one of its goals is to provide quality products to its patients, it is essential to have an excellent quality department, and the Quality Control (QC) laboratories are part of that department. The contribution of these QC laboratories is of the utmost importance to provide quality products to clients or patients. With this project, the laboratory can analyze many samples and use the equipment at a higher capacity and in less time. This would represent significant improvement in the flow of processes and decrease in waiting time. As overview, the project seeks to install new software on specific laboratory equipment that was previously selected in order to maximize efficiency, reduce batch analysis time, and reduce costs. These are some of the advantages that this project will bring:

- **Create individual user accounts:** It will make possible to enter new samples by different analysts without affecting the analysis of the other samples.
- **Mitigate time waste:** The flow of sample analysis in laboratories can be improved.
- **Lower costs:** Licenses for using this software are cheaper than the current software version available on the computer.
- **Data integrity:** With individual accounts for each user, the data is protected, and an individual analysis can be done (audit trail).

To achieve this project's objectives, we will use a software (Transparent Screen Lock) that will be integrated into laboratory equipment to increase its capacity. This equipment is used to analyze manufacturing samples in the pharmaceutical industry; for this reason, this software must comply with pharmaceutical industry regulations. The pharmaceutical company in which this project will be carried out is regulated by the 21 CFR Part 11 code of federal regulations [1]. In the US, the Food and Drug Administration (FDA) uses the rules in 21 CFR Part 11 to evaluate and enforce data integrity requirements for electronic records and signatures in drug manufacturing operations.

PROBLEM

This research will focus on analyzing the flow of sample analysis of manufacturing batches to reduce time and increase the capacity of the process in the laboratories. A laboratory in the pharmaceutical industry receives many samples from manufacturing daily. Many of these samples need to be analyzed quickly in order to not affect

the flow of manufacturing. This project seeks to find software that allows for the creation of an individual account, so that, if an analyst receives a sample and, afterwards, a second analyst needs the computer to enter their new samples into the equipment, both analysts may access their individual accounts without affecting the run or altering the results of either analyst.

This research aims to find how to mitigate the waste time factors in the flow of sample analysis in laboratories. With the incorporation of the new software, the laboratory can analyze many samples and use the equipment at a higher capacity and in less time. Implementing the Lean methodology can identify areas of improvement in our processes. After implementing our new software, it is expected that our Takt time will decrease by approximately 15 minutes. Currently, this is the minimum time for improvements to meet the demands of our analytical processes.

LITERATURE REVIEW

21 CFR Part 11 code

In March 1997, the FDA issued the final Part 11 regulations [1], which provide acceptance criteria that electronic records, electronic signatures, and handwritten signatures executed on electronic records must meet as equivalent to paper records and handwritten signatures executed on electronic records. The primary goal of these regulations is to allow the widest possible use of electronic technology consistent with the FDA's responsibility to protect public health.

Data Integrity

The selected software must comply with data integrity. For example, access to the software must be limited. Individual accounts must be created and will include a username and password in order to control access. Provide an audit trail in which access to the software is shown and let us know if any change has been made within the established parameters. [2]

To further understand what data integrity is, a series of literature searches related to the topic of computer system data integrity was conducted. Based on the information analyzed, term data integrity refers to the integrity, consistency, and accuracy of the generated data. Ensuring the integrity of the data generated in the pharmaceutical industry is of paramount importance. With data integrity compliance, the quality of manufactured products can be guaranteed. When the acquired data is generated, recorded, and stored in a computer, the computer system becomes part of the data. [2]-[5]

Lean Manufacturing

In addition to compliance with data integrity regulation, our new software should bring improvements to the productivity of the analytical processes in our laboratories. Bearing this in mind, an investigation of Lean Manufacturing concepts was carried out to verify which lean tools we can implement.

Lean manufacturing is a production system whose main focus is to reduce waste, create value for the customer, and seek continuous improvement of processes. This is achieved through the application of Lean project management principles, techniques, and tools. The lean methodology helps to improve production systems, that is, it simplifies the operational structure to understand, carry out, and manage the work environment. [6]-[7]

With the implementation of the Lean Manufacturing methodology, we seek to create improvements in our process. Among the improvements, the following should be highlighted:

- **Unnecessary transportation:** The unnecessary transportation of employees, tools, materials, or equipment is a waste that must be eliminated by optimizing processes.
- **Waiting:** This type of waste occurs when employees cannot work because they are waiting for materials or equipment, or otherwise there may be idle equipment waiting for maintenance.

- **Overproduction:** This leads to excess inventory and other problems in the manufacturing process. That is why Lean manufacturing implements the just-in-time production method that consists of producing only what customers demand.
- **Overprocessing:** This waste consists of adding components or features to a product that are not required by the customer, making them unnecessary. For Lean project management to be most effective, all types of waste must be identified and eliminated. [6]-[7]

METHODOLOGY

In the first steps of this project, statistical studies will be performed to analyze the current flow of laboratory sample analysis versus time. To determine the flow, we will use Lean methodology's "standard work" to identify improvements in the process of sample analysis in the laboratories

With the data obtained, we will be able to analyze if our project will be an effective one. In addition, we ensure compliance with one of the objectives, which is to increase the flow of analysis of laboratory samples.

Another factor that will be analyzed is the economic factor, calculations will be made to determine the decrease in costs of acquiring new software versus current software licenses.

Once the proposal has been analyzed and approved, we proceed to the acquisition of the new software. With the acquisition, we proceed to carry out qualification exercises. In this process, it is required to generate the necessary documentation such as Validation Plan, IOQ protocol, Summary Report, SOP, and Data Integrity Report. [8] This step will test compliance with the 21 CFR Part 11 code of federal regulations. The computerized system's compliance with data integrity will be tested.

The initial plan is to implement this new software on some laboratory analysis equipment. In this phase of the project, the selected laboratory analysis equipment is the total organic carbon (TOC) used to analyze the purity of the water used in the manufacturing process. [9] In the case of obtaining a significant increase, the use of this software will continue to be implemented in other laboratory equipment.

Statistical analyses will be performed after the implementation of the new software to analyze the flow of samples in the laboratory and find out if there was indeed an increase.

RESULTS AND DISCUSSION

In this project, 20 samples were obtained to carry out their analysis. For 20 days, the number of samples (manufacturing batches) received in the laboratory were recorded daily versus the number of samples analyzed. These analyses were carried out in June and July (tables 1 and 2). These months will represent the control group before integrating our new software (Transparent Screen Lock).

Table 1

Sample of batches received vs analyzed (June)

Day	Quantity Received	Quantity analyzed
Day 1	34	14
Day 2	21	15
Day 3	50	26
Day 4	12	13
Day 5	24	17
Day 6	35	12
Day 7	40	16
Day 8	28	15
Day 9	40	26
Day 10	15	40
Day 11	35	27
Day 12	42	16
Day 13	20	15
Day 14	19	24
Day 15	27	15
Day 16	12	10
Day 17	24	47
Day 18	13	12
Day 19	15	14
Day 20	14	15

**Data based on what was obtained during the three shifts with a 24-hour representation*

Table 2

Samples of batches received vs analyzed (July)

Day	Quantity Received	Quantity analyzed
Day 1	20	10
Day 2	19	12
Day 3	50	25
Day 4	15	19
Day 5	35	20
Day 6	24	15
Day 7	21	16
Day 8	22	15
Day 9	36	40
Day 10	27	18
Day 11	60	50
Day 12	45	20
Day 13	18	15
Day 14	27	19
Day 15	14	20
Day 16	11	16
Day 17	23	20
Day 18	16	13
Day 19	14	17
Day 20	12	25

**Data based on what was obtained during the three shifts with a 24-hour representation.*

Figures 1 and 2 show that, comparatively, the batch samples received in the laboratory are substantially large than the ones analyzed. With the data obtained, we can identify that there are indeed areas of opportunity to increase productivity in laboratory sample analysis.

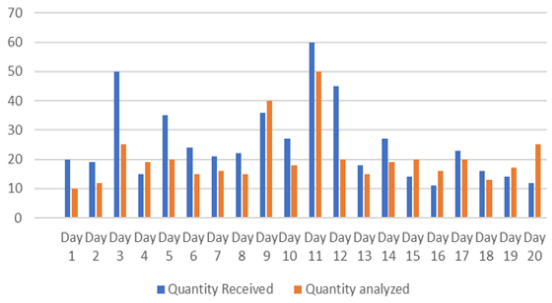

Figure 1

Quantities of sample received vs. analyzed (June)

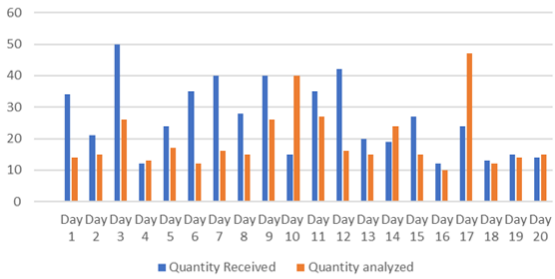

Figure 2

Quantities of sample received vs. analyzed (July)

Based on all the previously presented data, we will implement Lean methodology's "standard work" for a better analysis of the process. With the implementation of this methodology, we can have an idea of how our laboratory can improve the sample analysis process, maximizing its performance, and obtaining the least amount of waste (waste time). The "standard work" provides the basis for measuring improvement. Improving the "standard work" is a process that never ends, and these improvements are essential to creating stability in laboratory sample analysis processes.

Table 3 lists the content of the work that must be done in sequence. It also contains the manual job duration and the job duration for each step. These data represent the flow of "takt time" before integrating the new software.

Table 3

"Takt time" pre-implementation

Process	Start time	End time
Receive sample	0	3
Sample analyzed	3	18
Clean area	18	23
Sample Release	23	27

The total time from when the samples are received until they are released is 50 minutes (figure 3). This time shows the "takt time" of the process. It must be clear that this "takt time" must meet the demands of the product. If the time involved in carrying out the entire process does not meet the demands of the product, improvements will need to be made to the process. With the implementation of our new software, we expect to obtain a significant reduction in our "takt time" to meet the demands of the product. Figures 1 and 2 show the amounts received vs. analyzed in June and July; the number of samples received is more significant than those analyzed. For this reason, it is understood that the current "takt time" does not meet the demand for the product.

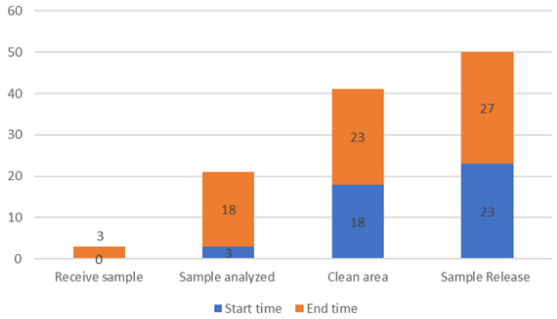

Figure 3
Standard work of samples analyzed

Post-implementation

The same analysis strategy presented above was used for our analysis phase after the implementation of our new software. For 20 days, we analyzed the number of samples (manufacturing lots) analyzed in the laboratory day by day in August versus the number of samples analyzed day by day in July. The data for August (table 4) presents the information obtained after the implementation of the new software. With the implementation of this new software, we expect to see a significant increase in the number of samples analyzed to reduce the amount of backlog in the samples to be analyzed by the laboratory (figure 4).

Table 4
Samples of batches analyzed in July vs. August

Day	Quantity analyzed (July)	Quantity analyzed (August)
Day 1	14	34
Day 2	15	45
Day 3	26	30
Day 4	13	32
Day 5	17	29
Day 6	12	27
Day 7	16	33
Day 8	15	43
Day 9	26	40
Day 10	40	56
Day 11	27	34
Day 12	16	33
Day 13	15	30
Day 14	24	42
Day 15	15	30
Day 16	10	31
Day 17	47	55
Day 18	12	32
Day 19	14	34
Day 20	15	20

**Data based on what was obtained during the three shifts with a 24-hour representation.*

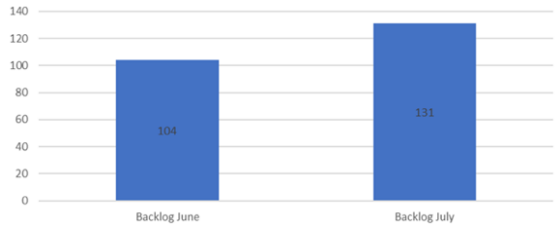

Figure 4
Sample backlog

Figure 5 shows that the number of samples analyzed by the laboratory in August exceeds those analyzed in July. Based on the data presented, the increase in the flow of sample analysis was a significant one.

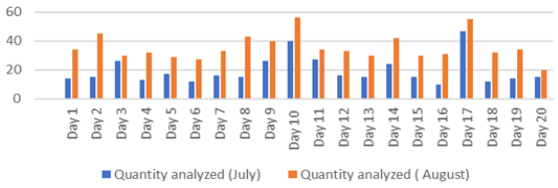

Figure 5
Quantity of sample analyzed (pre- vs. post-implementation)

Figure 6 shows a significant increase in the flow of analysis of samples received by the laboratory. We can see that the mitigation plan for the samples in the backlog was successfully completed. The number 321 represents the difference between the samples analyzed in July and those analyzed in August. In August, 321 more samples were analyzed compared to July.

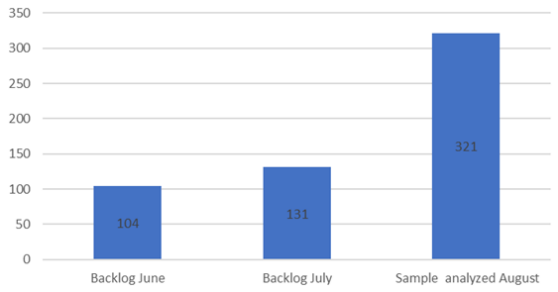

Figure 6
Backlog June and July vs. samples analyzed in August

Figure 7 shows that the flow of analysis presents a significant increase of 47% in the flow of analysis of samples in our laboratory (tables 1, 2, and 4). The data is obtained based on the three shifts, which is equal to 24 hours of work in the laboratories.

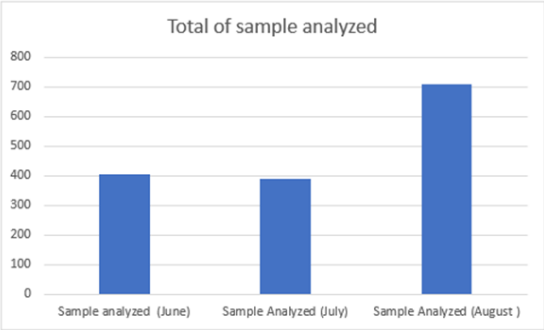

Figure 7
Sample analyzed pre- and post-software implementation

With our new software implemented, we will carry out our analysis at the "takt time" of the sample analysis to identify if there was any reduction after the incorporation of the new software.

Table 5 lists the content of the work that must be done in sequence. It also contains the manual job duration and the job duration for each step.

Table 5
Software post-implementation "takt time"

Process	Start time	End time
Receive sample	0	3
Sample analyzed	3	11
Clean area	11	14
Sample Release	14	16

Figure 8 shows that the total time from when the samples are received until they are released is 30 minutes; this shows us the "takt time" of the process. Here we can observe a decrease in time compared to the data obtained before the implementation of our new software. We can observe a decrease of 20 minutes in our "takt time" (table 3, figure 4). This reduction in time favors the fulfillment of the demand for our products. By reducing our "takt time," we increase the number of samples analyzed daily (figures 5 and 7).

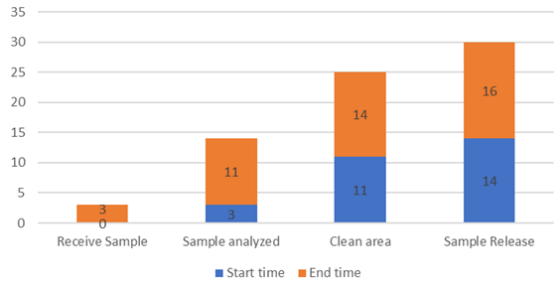

Figure 8
Software post-implementation "takt time"

Economic Effect

In addition to the improvements in the flow process of analysis of samples of manufacturing batches carried out in the laboratories, the aim was to obtain software at a lower cost that complied with the specifications stipulated by the regulatory agencies (21 CRF part 11).

A comparative analysis was carried out between both software to see if the upgrade provided a positive financial impact (table 6). Based on the calculations obtained, our new software not only complied with the regulations required by the pharmaceutical industry, but it also had a positive economic effect, since the company saved of $3,777 annually.

Table 6
Annual economic effect

Annual license fee	
Old Software	New Software
$ 580.00 each	$ 67.45 each
x 10 (license) = $ 5,800	x 10 (license) = $2,023
Total Annual Savings	$ 3,777

**Data based on licenses purchased for TOC instrument.*

CONCLUSION

The purpose of carrying out this project was to create an evaluation of productivity in the analysis laboratories of the pharmaceutical industry. It seeks to identify if there is indeed a need for improvements in the sample analysis flow process. To achieve this, statistical analyses were carried out to identify the improvements that could be made in our processes.

Implementing the "standard work" Lean methodology, we performed our analyses to identify improvements in the process of sample analysis in the laboratories. With the implementation of this methodology, it was possible to obtain specific data on the time of the sample analysis process (manufacturing batch) in our laboratories. Based on the data obtained, we were able to identify that some process improvements could be made.

As an improvement, we identified a new software to implement (Transparent Screen Lock). The advantages of implementing this new software are as follows:

- Software implementation is more cost-effective.
- Unauthorized access to analysis systems is prevented.
- Multiple user accounts can be created.
- All these accounts are 21-CFR-Part-11-compliant code of federal regulations, which guarantees a quality standard and compliance with data integrity.
- By being able to generate multiple user accounts individually, analysts can configure their analysis specifications without affecting the runs of their other colleagues. With this advantage, the time in the analysis flow decreases.

Analyses were carried at post-implementation of our new software to see if there were indeed improvements in our laboratory sample analysis flow. A comparison of the number of samples analyzed pre- and post-implementation of our new software showed there was a significant increase of 47% in the number of samples analyzed after the implementation of the new software. Another factor analyzed was the “takt time” of the sample analysis process. Initially, our “takt time” was 50 minutes. After the implementation, our “takt time” was decreased to 30 minutes. Both the increase in the flow of analysis and the decrease in “takt time” observed in our data allow us to conclude that indeed our software created improvements in our process as expected. The processes must be analyzed to seek continuous improvements, so that we will be able to meet the demands of our processes and products.

In addition to improvements to our sample analysis flow processes, our process had a significant economic effect. By obtaining more efficient and lower-cost software, a positive economic effect was obtained through annual savings of $3,777. With this project we were able to cover the waste of time and money, we were able to increase productivity in the sample analysis flow and, therefore, we were able to meet the demands of our analytical processes.

FUTURE WORK

Based on the satisfactory results for the next year, it is expected that the software will be integrated into 5 additional units of TOC equipment. In addition, in the future, an analysis of the laboratory equipment compatible with our software will be carried out in order to implement a new productivity project in the same way.

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