Study of the Effects of Improving a Process in a Pharmaceutical Laboratory

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Abstract *— Improving processes has been a key focus recently, with pharmaceutical companies exploring various approaches, particularly in laboratory settings. Enhancing processes in regulated laboratories requires compliance with regulatory agencies, standard operating procedures, and the analytical methods used. Benefits include faster results, improved quality, and reduced cycle time. This study aimed to evaluate the impact of a reporting template on laboratory metrics during chromatography data reporting. Analysts' time spent generating chromatographic reports was measured and compared before and after the introduction of the template and guidelines. Additionally, errors in reports and participant feedback were analyzed. The results demonstrated significant improvements in time efficiency and a reduction in mistakes following the implementation of the template and guidelines. However, further research with a larger sample size is needed to confirm these findings, and after confirmation, it would be possible to standardize other parts of the analysis.*

Key Terms *— Chromatographic Data, Improvement, Laboratory, Standardizing.*

INTRODUCTION

Companies that manufacture drug products must certify that the product meets specific criteria regarding identity, strength or potency, safety, release time, and other tests that ensure the product will be effective for its intended use. If they fail to prove the efficiency of the drug, patients will not receive the therapeutic effect they need, and companies could face civil and/or criminal actions. The tests or analysis processes used to prove the drug efficacy and safety need to deliver reliable results and need to meet the regulations of local and national agencies in the regions where the product will be consumed or commercialized. Some analyses are complex and require specific steps to obtain accurate and precise results and prevent product release delays. Additionally, not all product analyses require the same parameters to prove that the process was performed in a controlled and robust setup. Having worked in the pharmaceutical field for more than ten years, I know that different situations can compromise the release of results in a pharmaceutical laboratory. Having standardized processes is a way to improve release time, reduce errors, and improve quality.

By conducting this research, it will be identified how the process of reporting chromatographic data can be improved. It is expected that new tools and instructions will be developed to help standardize the work performed, reduce time, and minimize errors that can occur. It is expected that after the improvement is approved and followed by the analysts, the efficiency and quality will also improve, and cycle time will be reduced, meaning that the product will be released to market.

LITERATURE REVIEW

Current data and information present how companies evaluate and consider different mechanisms to improve quality control (QC) laboratories' processes. In the September 2004 article “Is there such a thing as a best-in-class lab? Benchmarking of QC operations” [1] presented the findings of a survey to have a better understanding of “what defines a best-in-class QC lab based on the experience of implementing operational improvement projects in world-class labs” [1]. The article mentions some challenges that Quality Control (QC) and research and development (R&D) laboratories encounter that require searching for better approaches to maximize their resources. For this purpose, they identify that there needs to be a

better understanding, as they mention, of the "operational aspects of QC" [1]. It is acknowledged that the QC laboratory's processes are not easy and require the involvement of different systems and areas for the result-releasing process. By preparing a survey, they obtained company data and identified improvement areas by comparing the findings with those of other participating laboratories. The results allowed companies, such as a biopharmaceutical manufacturing facility in Scandinavia, to improve several areas, including staffing and cycle time [1]. With the data obtained, they identified and concluded that to be a "best-in-class QC lab" [1], they must have reduced testing programs, a good planning and scheduling system, and a balance between compliance, cost-effectiveness, customer service, and constant evaluation.

Two different approaches to becoming efficient in a pharmaceutical laboratory were presented in two articles. The first approach was presented in 1995, before the survey assessment, explaining the benefits of automation in a pharmaceutical laboratory. It was demonstrated that the necessity of improvement and efficiency was an ongoing topic, and companies were making some decisions to deal with the situation. The article "Managing laboratory automation in a changing pharmaceutical industry" [2] explores why the automation process benefits the pharmaceutical laboratory. In the article, it is stated that the pharmaceutical industry's competitiveness is forcing it to "become more efficient and cost effective to remain competitive in this changing market" [2] and "providing more analytical results at a lower cost" [2]. Through the article, they analyze the opportunities for potential automation projects and how to manage them by justifying the budget and implementation process, which includes validation, training, and support. They presented how different tests can be automated, allowing a reduction in cost, an improvement in analyst safety, an increase in productivity, and a better use of human resources. It was also stated that automated equipment would require a complete validation process that may increase documentation but will "guarantee product quality" [2].

The second approach, considered by Novartis and presented in the article "Incorporating lean principles into pharmaceutical QC laboratory design" [3], was lean methodology. Lean is a Japanese method used to reduce waste associated with the process efficiently. The article presents a case study about lean principles and guidelines for a pharmaceutical QC laboratory. The articles stated that these principles "have significantly improved the internal work process, communications, customer interfaces, and operational performance" [3]. Novartis made observations on their current laboratory, and with the findings, they "developed a draft of comprehensive laboratory layout and design guidelines that would support the lean principle.". With the aid of stakeholders, they refine and improve the draft, resulting in a more solid set of guidelines that can be applied to existing and new laboratories. By having a better understanding of lean principles and identifying the "muda, mura, and muri" [3] or "wastes, workload volatility, and overloading" [3], and that the last two are significant in the laboratories, the article presents some lean opportunities. The opportunities presented are related to the design of space, inventory, and location of the laboratories, among other areas. These approaches will make us more productive by reducing the waste of motion, transport, and waiting.

QC Laboratory played an essential role in the delivery of the drug products, and it is necessary to look for efficient and productive ways to deliver the work. A better understanding of the QC laboratory's role and what areas could be improved will benefit quality metrics and the daily workload performed in the laboratories. Because QC laboratories share characteristics with manufacturing and service operations [4], not all approaches can be implemented, and more observation and studies are required. The improvement suggested must maximize the resources, standardize the process, reduce release time, and comply with local or national regulatory agencies, ultimately leading to maintaining or improving the quality of the process.

Knowing how critical it is to improve a process, an assessment of what laboratory procedures can be

improved without changing any validated processes was selected, the reporting process of chromatographic data. Improving this process is expected to affect the quality and delivery time of the products positively. Because many products are received and analyzed, having a standard format to report chromatography data is not easy. The standard operation procedure establishes the minimum requirements for each report, but the analyst must create it and add any specific requirements that the test method indicates. Because not all analysts have the same knowledge, expertise, and time to perform the reports, in addition to having different opinions on how to create the report, reviewers found a significant number of errors that must be corrected and delayed the release of the sample.

This research will compare the time analysts spend preparing a report of chromatographic data and tabulate the errors found in the process following the actual process. The process will be monitored, and suggestions will be made on the areas that need improvement. With the observations and the data acquired from the first part of the research, a new set of instructions will be proposed (and evaluated by management), and the addition of a template report to realize the second part of the study, which will consist of reporting the same set of chromatographic data. The time and error difference will be compared before and after the submitted improvement process. After performing the process with the new instructions, the analyst will be interviewed to learn any feedback about the process performed.

METHODOLOGY

The study will assess the time two analysts spend correcting and preparing chromatographic reports and the time they take to generate reports using provided templates and following work instructions (guidelines). The number of errors in each report will be evaluated, and the time spent correcting these errors will be included in the total time spent on report creation. This evaluation will use one laboratory test and the laboratory's current software to collect the chromatographic data.

The analysts selected will have different expertise in using the software, and each analyst will create two reports: one new (from the beginning) and another made from a template provided for the same sample analysis. A reviewer will also be selected to review the reports. Coordination with supervisors may be needed to ensure that the analysts involved in the experiment are available to perform it.

Each analyst will receive general instructions and requirements to create a new report of the assay test for the selected product sample. The requirements will be provided by the test method of the product, the current standard operating procedure (SOP), and the current version of the <621> Chromatography chapter of the United States Pharmacopeia (USP). In the second part of the research, the analyst will have a report template to use in addition to work instructions (guidelines) and must follow the exact requirements as in the first part. Analysts and reviewers will have one week to complete the report and review the samples. After completing the process, a survey will be provided to gather feedback from the analysts and reviewers about their experience, to be answered and returned within two days, for a total of nine working days to complete the experiment.

Quantitative data will be collected by measuring the time each analyst spends performing each report, including any rework. The number of errors found in each report, if any, will also be measured by the reviewer. Errors will be classified by type, and the frequency found in each report will be collected.

Quantitative data will be analyzed using descriptive statistics and graphic representations to show the time consumed for each report and the errors found. A comparison will be made between the time spent creating new reports and the time spent creating reports from provided templates for each test. Qualitative data will be collected from the analysts about how the guidelines and templates improve their work.

Some specific information about the research will be omitted to ensure the confidentiality of the company, its products, and its systems.

Results and Discussion

Two analysts with different knowledge and expertise in chromatographic data acquisition software created two reports, one with general instructions (report 1) and the other using a report template and work instructions or guidelines (report 2). The report provided the assay test results of a selected drug product. Analyst 1 was the analyst with less knowledge and expertise in the software, and Analyst 2 was the analyst with more experience and knowledge. Reviewers and management evaluated the report template and work instructions to create the second report to ensure they were aligned with the company policies and requirements. Table 1 summarizes the time each analyst took to make the reports and the errors encountered in each report. The types of errors found in the process and their frequencies are displayed in Table 2.

Table 1
Results of Time and Errors Obtained from Creating Reports

Analyst	Type of Report			
	Report 1		Report 2	
	Time (minutes)	Errors	Time (minutes)	Errors
Analyst 1	115	13	16	2
Analyst 2	59	4	8	1

Table 2
Type and Frequency of Errors Found in Each Report

Type of error	Analyst 1		Analyst 2		Total of errors
	Report				
	1	2	1	2	
Formatting	9	1	0	0	10
Missing information	4	3	2	1	10
Total	13	4	2	1	20

Figures 1 and 2 present the data obtained in graphic representations to better compare the results obtained from each analyst and for each report.

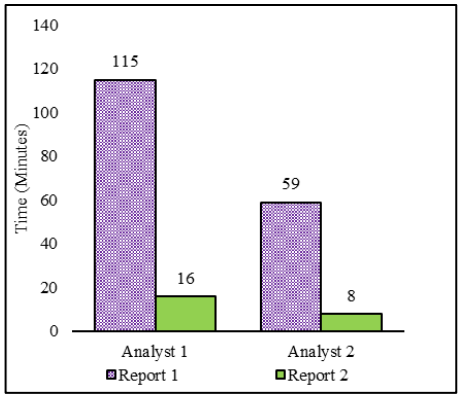

Figure 1
Comparison of Time (Minutes) to Create Reports by Two Analysts

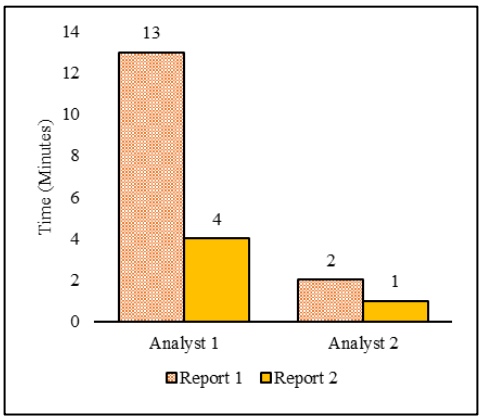

Figure 2
Number of Errors Found on Each Report After Review

As displayed in Table 2, the types of errors found were two of the most common mistakes in formatting. Formatting errors were due to the incorrect layout, tables, and significant figures necessary to display the results obtained. Missing information errors were about not having all the information required to report the results, like formulas and method specifications.

As shown in the results, Analyst 1 took almost double the time to prepare both reports as Analyst 2. Because Analyst 1 did not have much knowledge and expertise in the software for the first report (beginning), it was necessary to provide full support in creating the report. After receiving the guidelines and the template to prepare report 2, it was not required to assist as in the first report, and the analyst was able to create the report in less time and with fewer errors.

Discussion

From the results obtained, it is very clear that creating a report and following guidelines and a template reduces the time analysts take to generate the report and reduces errors. It obtained an 86% improvement in time for both analysts and a reduction of an average of 60% in mistakes when following the guidelines and template. As stated before, following the procedures and the template to create the report allows analysts with less knowledge and expertise in the software to generate the report with the standard required and minimal errors. This improvement will reduce cycle times because analysts will spend less time reporting and making corrections, and the results will be delivered in less time. It will also improve the quality of the process because it will ensure that all test results reports have the same format, and that all information required to release or reject a product batch or lot is available and reported. In addition, the guidelines, the template, and the Standard Operating Procedure (SOP) will allow any analyst to perform the reporting process, even though they don't have enough experience with the software.

Using a paired t-test analysis [5] to evaluate the results, a p-value of 0.410 and a t-value of 1.33 [6] were obtained for the time to create the reports, and a p-value of 0.430 and a t-value of 1.25 [6] for the errors found. Because the p-values are greater than 0.05 and the t-values are significantly smaller than the critical t-value (12.71) [6] with 95% confidence, it is necessary to have more data to reject or accept the null hypothesis to confirm that the results are different and significantly improved with the actions taken. As mentioned, the paired t-test will give an idea of the improvement obtained, but to have more reliable results, it would be necessary to have more data that could not be obtained because of logistical and scheduling conflicts with the analyst working in the laboratory.

From the feedback obtained from the analyst and reviewer in the process, it was a very positive response to the guidelines and the template. Both analysts share that following the guidelines and template converted the process to a very easy one of what and where must be included. Analyst 1 shared that creating the first report was very difficult and was lost in how to perform it, and also commented that with the guidelines and template, it was easy to know what to do and how to do it. The reviewer feels that it was easy to perform the process of reviewing the data and that the reports of both analysts were almost identical. The reviewer also comments that these guidelines and templates will facilitate the process, speed up the delivery of results, and minimize the corrections on the final results report. The proposed guidelines and template to create reports presented to management were well received and allowed them to make some necessary decisions to standardize how the reviewers perform the process and how analysts will present their data results.

The guidelines related to the reporting process will be included in the SOP, and all analysts will be trained in the new instructions. The general template was also created for other tests, and the guidelines were designed for all types of reports by indicating what areas are necessary for each test report.

For future work, ideas will be suggested on how to improve the SOP for reporting results of other tests to continue standardizing the process and reducing errors, in addition to implementing a new method of creating generic data folders that include generic templates of all tasks of the analysis process, to continue minimizing errors and reducing analysis time.

CONCLUSION

Improvements in a pharmaceutical laboratory are necessary but difficult to perform because of the various tests and procedures performed. The improvement must comply with local and federal regulations, internal procedures, and specific test requirements. The literature in some articles discusses the benefit of standardizing the process by automation, and the Japanese method of Lean shows the benefit of standardizing processes. This research considered all the information and suggested an

improvement process for standardizing a specific method of reporting chromatographic results that showed delays in delivering the results. The Assay test results of a particular drug product were selected to evaluate the time and number of errors that two analysts spent creating a new report and another report after providing guidelines and templates to present the results. The results showed significant improvement in the time reporting and the number of errors on the reports, and proved the necessity of having clear and specific instructions to perform a process. The guidelines and template allowed the analyst to create a report using the correct, expected, and established way to report the chromatographic data obtained, improving the quality of the process. It would also be necessary to get more data to compare the before and after results and prove the improvement obtained with more reliability. These improvements will be included in the SOP and performed in another part of the analysis to standardize it and meet the organization's quality standards. Further work will be suggested to continue improving the quality of the process of reporting results and ensuring a reduction in cycle time.

REFERENCES

[1] T. Bublitsky & A. Howards, "Is There Such a Thing as a Best-in-Class Lab? Benchmarking of QC Operations" in *Pharmaceutical Technology Europe*, vol. 16, pp. 34-42, Sept. 2004.

[2] M. L. Rutherford, "Managing laboratory automation in changing pharmaceutical industry," in *Journal of Automatic Chemistry*, vol. 17, pp. 59-63, Apr. 1995.

[3] M. Dockery, F. Gabardi, J. Garay, J. Gazvoda, L. Kimmel, P. Orombelli, C. Peytremann, T. Reynolds, T. Scharton-Kersten, G. Shoel, J. Sirovatka, "Incorporating Lean Principles into Pharmaceutical QC Laboratory Design," in *Pharmaceutical Engineering*, vol. 34, pp. 1-7, Oct. 2014.

[4] M. May, "Leaning the Quality Control Laboratory," in *Pharma Manufacturing*, Sep. 16, 2024. [Online]. Available: https://www.pharmamanufacturing.com/facilities/op-ex-lean-six-sigma/article/11323382/leaning-the-quality-control-laboratory

[5] Quality Council of Indiana, *Certified Six Sigma Green Belt Primer*, 3rd ed. West Terre Haute, IN: Quality Council of Indiana, 2014.

[6] D. C. Montgomery, G. C. Runger & N. F. Hubele, *Engineering Statistics*, 3rd ed. Hoboken, NJ: Wiley, 2004.