Standardize the Documentation for the Water Analysis for Wastes Elimination in the Raw Material Laboratory

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Abstract *– During the reviewing data of water analysis in the Raw Material Laboratory, the reviewer finds many documentation discrepancies between laboratory analysts, making this task difficult affecting the cycle time due to the waiting of corrections. To improve the documentation process, it plans to create a standardized process for water analysis documentation to improve the documentation procedure to prevent data integrity failure and to establish a new form for the water analysis in the Raw Material Laboratory. The strategy used to reach this goal in this research was support Kaizen method with the PDCA Cycle to standardize a process for the water analysis documentation to monitor and prevent data errors in the Raw Material Laboratory. The PDCA cycle was used to modify a reconciliation sheet used in the Raw Material Laboratory. Once the new reconciliation sheet was implemented a standardized process was created for the water analysis documentation to monitor and prevent data errors. The results of this project contribute to improve the data integrity, to eliminate wastes and, to create a standardized process to maintain in control the water analysis documentation errors.*

Key Terms *— Data Integrity, Kaizen, PDCA cycle, Standardize Process.*

PROJECT STATEMENT

Often during the reviewing data of water analysis in the Raw Material Laboratory, the reviewer finds many documentation discrepancies between laboratory analysts, making this task difficult affecting the cycle time due to the waiting of corrections. In the Raw Material Laboratory does not exist a standardized process for the water analysis documentation to monitor and prevent data errors. Moreover, without a documentation procedure this situation can lead to data integrity failure.

Research Description

The purpose of this research is to create a standardized process for water analysis documentation. The water analysis in the Raw Material Laboratory has many tests that generate a lot of documentation and discrepancies in documentation between laboratory analysts are found. The importance of this research is to create a standardized process for the water analysis documentation to monitor and prevent data errors that can lead in data integrity failure and cycle time overdue. Data integrity and cycle time are two important components of quality control laboratories' responsibility to ensure the efficacy, safety and quality of drugs.

Research Objectives

The objectives of this research work are:

- To develop a standardized process for the water analysis documentation to prevent data errors by June 2018.
- To improve the documentation procedure to prevent data integrity failure.
- To establish a new form for the water analysis in the Raw Material Laboratory.

Research Contributions

This research project supports the Company's goal of Data Integrity, to prevent Federal Drug Administration (FDA) observations related to Current Good Manufacturing Practice (CGMP) issues. During recent years, FDA has observed that CGMP violations involving data integrity increased during CGMP inspections. This situation represents a problem because ensuring data integrity is an important component of industry's responsibility to

ensure the efficacy, safety and quality of drugs. The development of a standardized process for the water analysis documentation would prevent data errors in the Raw Material Laboratory. The creation of a new form will reduce the cycle time from two days to one due to the waiting of corrections. The results of this project will contribute to improve the data integrity, to eliminate wastes and, to create a standardized process to maintain in control the water analysis documentation errors.

LITERATURE REVIEW

CGMP refers to the Current Good Manufacturing Practice regulations enforced by the US Food and Drug Administration (FDA) [1]. Adherence to the CGMP regulations assures the identity, strength, quality, and purity of drug products by requiring that manufacturers of medications adequately control manufacturing operations [1]. Often during the reviewing data of water analysis in the Raw Material Laboratory, the reviewer finds many documentation discrepancies between laboratory analysts, making this task difficult affecting the cycle time due to the waiting of corrections. In the quality control laboratory, the data integrity is very important because poor practices can allow impact patient safety, product and process quality effects. The integrity and reliability of the data provides to the regulators a positive opinion of the personnel and the company as a whole.

Data integrity refers to the completeness, consistency, and accuracy of data [2]. Complete, consistent, and accurate data should be attributable, legible, contemporaneously recorded, original or a true copy, and accurate (ALCOA) [2]. Data integrity is an important component of industry's responsibility to ensure the efficacy, safety and quality of drugs. Today, due to the numerous problems found in regulatory agencies inspection, the data integrity is big issue for the regulators around the world. Data integrity is an important component of industry's responsibility to ensure the efficacy, safety and quality of drugs.

With the implementation of Lean Manufacturing approach, organizations can remove all the wasteful processes. Kaizen is one of critical concept in Lean Manufacturing [3]. Kaizen is based in small incremental improvements, being a cost-effective strategy. For the effective implementation of Kaizen is very important the participation of all employees in solving real problems that once solved improve the business [3]. At the graduate business school of the Instituto Tecnológico y de Estudios Superiores de Monterrey (ITESM) Mexico, a research was conducted with the systematic application of Kaizen in an Operations Management course of the Master in Business Administration (MBA) of this institution. Their purpose was to provide empirical evidence of how Kaizen's continuous improvement cycle (PDCA) enables better results in students who have taken the subject of Operations Management course in a business school [4]. Some research benefits at the end of the project were: the course was standardized in sequence, execution and evaluation allows to have a homogeneous improvement platform in each quarter and, the professor had the opportunity to plan his course focusing on his "client", the student, and thus in his learning [4].

One case study was conducted in an automobile industry. One of the problems that the company was experiencing with high frequency was breakdowns of machines. The researches were used the Total Productive Maintenance (TPM) and the Kaizen approach. The TPM is related to business excellence strategies such as Kaizen, Just-In-Time (JIT), and Total Quality Management (TQM) [5]. Kaizen implies continuous improvement and has a direct link to the TPM strategy of focused improvement, also TPM provides a foundation for JIT to be successful [5]. In Kaizen, elimination of waste is a major step [5]. Wastes are defined as human activities which absorb resources but create no values for an organization and reduce the productivity and profits of it. Non-value adding activities are activities that do not add value to the final product, for example: activities that take time, resources and / or space. Waste elimination is the

most cost-effective way to improve productivity [5]. After TPM and Kaizen, the breakdown status of machine got drastically reduced [5]. Reduction in breakdowns hours from 20 hours in the month of June to 2 hours in the month of April shows very good improvement [5]. TPM and Kaizen not only help to reduce the breakdown hours, they also improve the availability, performance efficiency and quality. When the implementation of these approaches is successful, dramatical improvements in productivity and quality can be accomplish.

The intent of Kaizen is to make employees jobs easier by studying them and making little improvements [6]. It is make jobs safer and more efficient by improving the working environment and the focus is immediate action rather than longer-term alternatives to change [6]. Changes created through the Kaizen approach are very sustainable [6]. One of the key concepts of a Kaizen is that "If there is No Action, there can be No Success" [6].

METHODOLOGY

The method used to accomplish the objectives of this research was Kaizen method. The term Kaizen is derived from two Japanese words: KAI – change and ZEN – continuous improvement. Kaizen means continuous improvement involving everyone in the organization from top management, to managers then to supervisor, and to workers [7]. Kaizen is not only an approach to manufacturing competitiveness but also everybody's business [7]. Kaizen generates process-oriented thinking, is people-oriented, and is directed at people's efforts [7]. Kaizen uses small incremental changes introduced gradually over a prolonged period to eliminate waste and to improve efficiency. Kaizen help to improve all parts of a company through the standardization of production processes.

The strategy used in this research for executing and support Kaizen method was the PDCA (or PDSA) Cycle, which is the Lean working structure. One of the main goals of Kaizen method is to eliminate waste. Kaizen approach is based on the premise that there is no perfection in a process, because no structure, product, or system ever achieves the ideal stage and where it can be improved by further reducing waste [7]. Standards are set by management, but they must be able to change when the environment change [7]. Great practices to achieve dramatic improvement in processes are: review the standards constantly, collect and analyze data on defects, and encourage teams to conduct problem-solving activities [7]. Once standards are in place, then are being followed by employees. If there are deviations, employees will review standards and either correct the deviation or advise management on changing and improving the standard [7]. Using Kaizen method supported by the PDCA cycle is an effective way to evaluate documents, improve them and avoid process errors.

PDCA (Plan-Do-Check-Act) is an iterative, four-stage approach for continually improving processes, products or services, and for resolving problems [8]. It promotes testing improvements on a small scale before updating company-wide procedures and work methods [8]. The PDCA process supports both the principles and practice of continuous improvement and Kaizen [8]. Kaizen focuses on applying small, daily changes that result in major improvements over time [8]. The PDCA Cycle provides a framework and structure for identifying improvement opportunities and evaluating them objectively [8]. Using PDCA, an organization undergoing continuous improvement can create a culture of problem solvers and critical thinkers [8]. Improvement ideas can be rigorously tested on a small scale [8]. It provides a structure for identifying improvement opportunities and evaluating them objectively [8]. The iterative process of the PDCA cycle enables ideas to be continuously tested and promotes a continuous improvement and continuous learning culture [8]. After an idea has been shown to be effective, it can be standardized and implemented companywide [8]. On the following table 1 are presented the PDCA cycle and the cycle terms definitions:

Table 1
The PDCA Cycle

PDCA cycle	Description
Plan	Identify the problem, collect relevant data, and understand the problem's root cause, develop hypotheses about what the issues may be, and decide which one to test [6].
Do	Develop and implement a solution; decide upon a measurement to gauge its effectiveness, test the potential solution, and measure the results [6].
Check	Confirm the results through before-and-after data comparison. Study the result, measure effectiveness, and decide whether the hypothesis is supported or not [6].
Act	Document the results, inform others about process changes, and make recommendations for the future PDCA cycles. If the solution was successful, implement it. If not, tackle the next problem and repeat the PDCA cycle again [6].

RESULTS AND DISCUSSION

The strategy used in this research for executing and support Kaizen method was the PDCA Cycle to standardize a process for the water analysis documentation to monitor and prevent data errors in the Raw Material Laboratory. The PDCA cycle for the research was the following:

Table 2
PDCA Cycle Details

Table 2: PDCA cycle details	
Plan	Identify the problem, collect relevant data, and understand the problem's root cause.
Do	Implement the solution.
Check	Monitor the results.
Act	Standardize the new process.

Plan

A meeting was performed with people that know the water analysis in the Raw Material Laboratory, people included were: one analyst, two reviewers, supervisor and documentation specialist. The problem was identified, and it was the following: During the reviewing data of water analysis in the Raw Material Laboratory, the reviewers founded many documentation discrepancies between laboratory analysts, making this task difficult and affecting the cycle time due to the waiting of corrections. In the Raw Material Laboratory, did not exist a standardized process for the water analysis documentation to monitor and prevent data errors. After many observations, it was found the following root causes in the Water Analysis Area:

- Did not exist a standardized process for the water analysis documentation to monitor and prevent data errors.
- Analysts must make too many testings with different pharmacopeias: USP (United States Pharmacopeia), EP (European Pharmacopeia), and ChP (Chinese Pharmacopeia), making more difficult to perform the documentation.

Do

To get a solution for the documentation errors in the Water Analysis of the Raw Material Laboratory, a meeting was held where the following correction was proposed:

- A standardized process for water analysis documentation. In the Raw Material Laboratory, there is a reconciliation sheet where the analysts write all the information related with the water points and testing done during this day. This reconciliation sheet was modified adding an analyst checklist of the important tasks where analysts must complete the Water Analysis in one day. It is important that analysts complete all the tasks in one day, because the expiration day of the water points sampled is 24 hours. For this reason, the

completion of the water documentation is very important.

In the old reconciliation sheet, the analysts had to make:

- Too many obliterations with Not Applied.
- The sheet had water points that are eliminated in the company.
- Analysts did not have space for the Lot number.
- Did not have an Analyst Checklist, to help him/her to be aware of what tasks have completed or need to be completed in the water analysis.

After checked the old reconciliation sheet in the meeting, the decision was to modify it and a new reconciliation sheet was proposed. After compare both reconciliation sheets, all came to an agreement to fix the documentation process. The following figures present the old and the new reconciliation sheet, to demonstrate the changes made to both sheets:

WATER LOTS RECONCILIATION & DATA REVIEWING CHECK LIST

PRODUCT: PURIFIED WATER, CODE: 19670 / FEED WATER, CODE: 60187

For Water Chemical Solution used, refer to Logbook _____, page: _____. (PSGA-DOC-1730)

Area	Water Chemical Analysis Logbook: _____						Analyst By / Date	* Verified By / Date
	Point ID	Page	Point ID	Page	Point ID	Page		
Pharma Purified Water	☐ USPP-18		☐ USPP-19		☐ USPP-22			
	☐ USPP-22A		☐ USPP-23		☐ USPP-24			
	☐USPP-25		☐USPP-26		☐USPP-27			
	☐USPP-28		☐USPP-29		☐USPP-30			
	☐USPP-31		☐USPP-32		☐USPP-33			
MEX Purified Water	☐ HPL-34		☐ HPL-35		☐ HPL-36			
	☐ USPM-37		☐ USPM-38		☐ USPM-39			
	☐ USPM-40		☐ USPM-41		☐ USPM-42			
	☐ USPM-43		☐ USPM-45		☐ USPM-46			
	☐ USPM-47		☐ USPM-48		☐ USPM-49			
	☐ USPM-50		☐ USPM-51		☐ USPM-52			
	☐ USPM-53		☐ USPM-54					
JII Purified Water	☐ USP-18		☐ USP-19		☐ USP-20			
	☐USP-21		☐USP-22		☐USP-23			
	☐USP-22A		☐USP-22B		☐USP-22C			
OROS Purified Water	☐ USP0-55		☐ USP0-56		☐ USP0-57			
	☐ USP0-58		☐ USP0-59		☐ USP0-60			
	☐ USP0-61		☐ USP0-62		☐ USP0-63			
	☐ USP0-64		☐ USP0-65		☐ USP0-66			
	☐ USP0-67		☐ USP0-68		☐ USP0-69			
	☐ USP0-70		☐ USPT-71					
Clean Steam	☐CS-04		☐CS-06		☐CS-07			
	☐CS-08		☐CS-09		☐CS-10			
DI-Water	☐DIQ-01		☐DIQ-12					
	☐DIQ-10							
RO Water	☐S-RS1							
CDI Water	☐S-CD5		☐S-CD2-1		☐ S-CD6			

*Peer Reviewer signatures indicate that the testing information below has been verified, and the logbooks reconciliation have been performed.

FINAL APPROVAL SIGNATURE

SUPERVISOR or DESIGNEE: _____ DATE: _____

Figure 1
Old Reconciliation Sheet 1

WATER LOTS RECONCILIATION & DATA REVIEWING CHECK LIST

PRODUCT: PURIFIED WATER, CODE: 19670 / FEED WATER, CODE: 60187

Area	Water Chemical Analysis Logbook: _____						Analyst By / Date	* Verified By / Date
	Point ID	Page	Point ID	Page	Point ID	Page		
Potable / In-process	☐ FW-01		☐ DIA-07		☐ DIA-O8			
	☐ DIB-09		☐ DIB-10		☐ DIC-11			
	☐ DIC-12		☐CP-13		☐CP-14			
	☐ UF-15		☐UF-16		☐UF-17			
	☐UF-18							
Area	Water Chemical Analysis Logbook: _____						Analyst By / Date	* Verified By / Date
	Point ID	Page	Point ID	Page	Point ID	Page		
Other points Analyzed								

*Peer Reviewer signatures indicate that the testing information below has been verified, and the logbooks reconciliation have been performed.

Peer Reviewer Checklist		Applicable
Correct sample and specification was used.		☐
The standards have the correct purity % as per the current certificates of analysis.		☐
Chromatographic Data (information applicable to one or more analytical tests within the lot raw data)**		
☐ n/a	Printouts of the Active, Alter, Results and Sample Sets Tablets	☐
	Printouts of the instrument and Processing Method Reports	☐
	Chromatographic Reports and Chromatograms appropriately completed/labeled	☐
**If applicable is checked, itemize the test(s)		
All data are in compliance with cGMPs and applicable SOPs.		
Data and documentation is neat and completed.		☐
Initials and date with proper corrections.		☐
Numbers are rounded for correct reporting.		☐
All raw data is appropriately labeled with relevant information.		☐
Deviation (SMA)/Investigation #s, if any:		Approver
Laboratory Deviations/Investigations are approved (if applicable), and the original reports are included in the data package.		☐ ☐ n/a

FINAL APPROVAL SIGNATURE

SUPERVISOR or DESIGNEE: _____ DATE: _____

Figure 2
Old Reconciliation Sheet 2

WATER LOTS RECONCILIATION & ANALYST AND DATA REVIEWING CHECKLIST FORM OF PURIFIED WATER FOR ANALYTICAL TESTING

PRODUCT: PURIFIED WATER, CODE: 19670 / FEED WATER, CODE: 60187

SPECIFICATION NUMBER: DS-SPE-23183

For Water Chemical Solutions used, refer to Logbook: _____, page: _____ Lot: _____

For Water Test Report used, refer to Logbook: _____, page: _____

Area	Water Chemical Analysis Logbook: _____						*Analyzed By /Date	Verified By/Date
	Point ID	Page	Point ID	Page	Point ID	Page		
Pharma Purified Water (USPP-)								
MEX Purified Water (USPM-)								
OROS Purified Water (USPO-)								
JII Purified Water								
Clean Steam (CS-)								
DI Water (DIQ-)								

Figure 3
New Reconciliation Sheet 1

WATER LOTS RECONCILIATION & ANALYST AND DATA REVIEWING CHECKLIST FORM OF PURIFIED WATER FOR ANALYTICAL TESTING
PRODUCT: PURIFIED WATER, CODE: 19670 / FEED WATER, CODE: 60187
SPECIFICATION NUMBER: DS-SPE-23183

CDI Water (CDI- and S-CD)								
Other Points Analyzed								

*Analyst signature indicates that all water analysis was performed and the documentation on logbooks was performed following CGMP.

*Peer Reviewer signatures indicate that the testing information below has been verified, and the logbooks reconciliation have been performed.

Analyst Checklist	Applicable
Water Chemical Checklist was checked and signed.	☐
TOC logbook was documented, signed and verified.	☐
Water Chemical Solutions logbook was documented, signed and verified.	☐
Water Chemical Analysis logbook was documented and signed.	☐
All TOC print outs were signed and copied.	☐
All solutions for Purified Water tests were documented and they are current.	☐
All tests were performed using the current corresponded pharmacopeia and documented.	☐
This reconciliation sheet was signed by authorized personnel.	☐
All the Purified Water points corresponding at this day were collected, analyzed and documented.	☐

Figure 4
New Reconciliation Sheet 2

WATER LOTS RECONCILIATION & ANALYST AND DATA REVIEWING CHECKLIST FORM OF PURIFIED WATER FOR ANALYTICAL TESTING

PRODUCT: PURIFIED WATER, CODE: 19670 / FEED WATER, CODE: 60187

SPECIFICATION NUMBER: DS-SPE-23183

Peer Reviewer Checklist		Applicable
Correct sample and specification was used.		☐
The standards have the correct purity % as per the current certificates of analysis.		☐
All data are in compliance with cGMPs and applicable SOPs.		
Data and documentation is neat and completed.		☐
Initial and date with proper corrections.		☐
Numbers are rounded for correct reporting.		☐
All raw data is appropriately labeled with relevant information.		☐
Deviation / Investigation #s, if any:		Approver
Laboratory Deviation/Investigation are approved (if applicable), and the original reports are included in the data package.	☐	N/A ☐

Analyst: _____ Date: _____

Reviewer: _____ Date: _____

Approver: _____ Date: _____

Error Codes: E1 = Transcription Error, E2 = Significant figures Error, E3 = Calculation Error, E4 = Reference Correction, E5 = Date Correction, E6 = Grammatical or Lexical Error, E7 = Other (Explain)

Figure 5
New Reconciliation Sheet 3

After all the recommendations in the meeting, the supervisor review the new changes suggested for the reconciliation sheet and, then they were send to the documentation specialist. The new reconciliation sheet for the water analysis was presented to the documentation specialist, to upload it in the system and to make it official for the benefit of analysts and reviewers.

Check

The documentation specialist made official the new reconciliation sheet in the system. It was proceeded to present the new reconciliation to all the persons that work in the water analysis, to explain the modifications and changes made to new reconciliation sheet. After a week of the implementation of the new reconciliation sheet, the following questions were asked to the analysts and reviewers: What they think about the new reconciliation sheet? Is it easier to do the documentation in the new or old reconciliation sheet? A positive feedback was received from analysts and reviewers. They feel more comfortable with the new changes. For analysts the documentation is simpler, and reviewers observed less documentation errors from the analysts.

Act

As a result of all these changes made to the new reconciliation sheet, a standardized process

was created for the water analysis documentation to monitor and prevent data errors. The results of this project contribute to improve the data integrity, to eliminate wastes and, to create a standardized process to maintain in control the water analysis documentation errors. But, it is important to remember that PDCA is a cycle, not a process with a beginning and an end. This means that the improved documentation process becomes the new baseline, and analysts or reviewers can continue to look for ways to make it even better for the Raw Material Laboratory.

CONCLUSION

The new reconciliation sheet for the water analysis in the Raw Material Laboratory was a great advantage for the area. This modification helps the reviewers to finds less documentation discrepancies between laboratory analysts; making easy the data review and reducing the chance of affect the cycle time due to the waiting of corrections. Now, in the Raw Material Laboratory exists a standardized process for the water analysis documentation to monitor and prevent data errors. Moreover, with this new documentation procedure, data integrity failure can be prevented.

This research project supports the Company's goal of Data Integrity, to prevent Federal Drug Administration (FDA) observations related to Current Good Manufacturing Practice (CGMP) issues. The standardized process for the water analysis documentation in the Raw Material Laboratory can ensures data integrity, which is an important component of industry's responsibility to ensure the efficacy, safety and quality of drugs. The results of this project contribute to improve the data integrity, to eliminate wastes and, to create a standardized process to maintain in control the water analysis documentation errors.

For future research, the benefit of this standardized process for the water analysis documentation in the Raw Material Laboratory can be quantified. It can be done observing the cycle time of the water analysis documentation. Also, the water analysis area needs a better organization. The 5's concept can be use; it is an important visual tool in any organization. It can help to increase the productivity in the following manner: identification and arrangement easier for benefits of the employees to find the things necessary for the process, easier to catch any problem during the process and working with standardize process.

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