Improving the SOP of managing controlled CII substances in the laboratory from receiving to discarding

Author: Zahíra D. Rodríguez Cartagena
Advisor: Rafael Nieves Castro
Industrial Engineering Department

Abstract

As a contract manufacturing operation, the needs of our clients are our priorities. The inclusion of controlled substance schedule II to our list of products has been a challenge that we are still trying to overcome. Regulations and requirements for the management of controlled substances schedule II are very rigorous. They must be monitored from the time they arrive to the time they are disposed. A standard operating procedure (SOP) is established in order to meet regulations and have a clear and consistent procedure to manage CII substances as required. Nevertheless, flaws and gaps are found in the current SOP and it is mandatory to improve the procedure to meet regulations. The DMAIC tool was used to identify the deficiencies in the process. An improved process was suggested after analysis phase. The SOP was revised, and the improved process was placed as a new revision after giving training to the corresponding personnel.

Background

Controlled substances are regulated by the Drug Enforcement Administration (DEA) and the Puerto Rico Health Department (law #4 Jun3 23, 1971) because of its potential for abuse and addiction. Following the Code of Federal Regulations (CFR 21 Part 1308), they are placed in different schedules (I to V) based on its medical use, potential of abuse, addiction and safety; being schedule I the more addictive. Controlled substances schedule II has a high potential for abuse but unless schedule I, they have medical uses. One big problem of controlled substances is that even if they have medical uses, the abuse may lead to psychological or physical dependence. Schedule II includes stimulants, narcotics, barbiturates, opiates, depressants, hallucinogenic substances and immediate precursors. In addition, it includes the salts, isomers, isomer salts, esters and ethers if they are chemically possible to exist.

Problem

The pharmaceutical industry must be aligned to the controlled substances' regulations. An operating standard procedure (SOP) is established to delineate such process. It has been a concern that gaps, and flaws are found in our processes (SOP). It is important to fill the gaps and identify the flaws to improve them and meet regulations and clients' needs. The project pretends to delineate the flow of the Controlled II substances from the time they arrive to the laboratory to the time they leave the laboratory for disposition, to improve the SOP M700-160.

Methodology

Six Sigma Tool: DMAIC
Define phase: The problem is identified and well defined. Measure phase: The performance/output of the problem is measured, and the current state is well identified and presented. Analyze phase: The cause of the problem is identified. Improve phase: A solution to the problem is found and put to test. Control phase: The proposed solution is being monitored to assure that the problem is solved.

Define Phase

To define the problem, two meetings were held to discuss the problem statement. In the meetings, a SACAPA (Stand Alone Corrective Action Preventive Action) was discussed to include those corrective action in the SOP revision. The SACAPA points out some deficiencies of the SOP. Such deficiencies were:

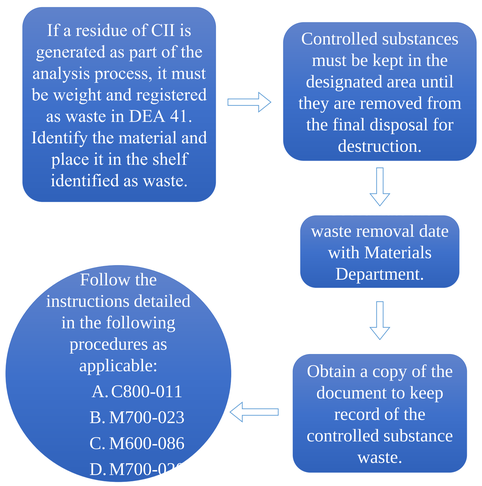
1. Reconciliation for the sample when received between sample label and quantity received (first weight).
2. Include in SOP how to handle samples spill, how to discard and how to reconcile the spilled sample.
3. Correct section I step 12, it refers to a section and step that is not in the SOP.

Other deficiencies were discuss giving emphasis to the lack of information in the discarding process and the flow of the CII substance through the laboratory. All discussed deficiencies were attended, and it is expected to find more during the Analyze

Measure Phase

In this phase, the current version of the SOP was read and the main steps were identified: receiving, use and discarding. All steps were measured. The process which has more impact or change (discarding process) was selected and a flow diagram was created to compare the current written process with the improved one.

Figure 1: Discarding Process as per SOP



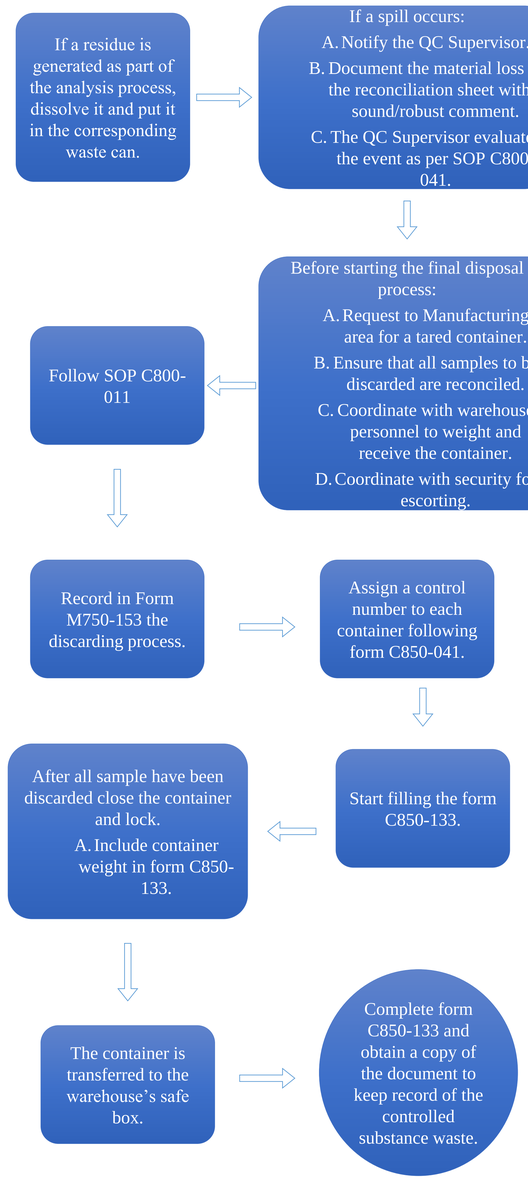
Analyze Phase

The current SOP has several deficiencies. It has misguided, incorrect and missing information in most of its parts. There is discrepancy between the SOP and current practices. It is expected that a process is performed as stated on the SOP. If that is not the case, a revision to the SOP must be performed in order to improve it and align it to the correct process and current practices. All steps were analyzed and improved but this project focus on the three main steps: receiving, use and discarding.

Improve Phase

In this phase, an improved version of the whole process was presented focusing on the mentioned three main steps. Given that the discarding step was the more impacted, a flow diagram was created to compare before and after.

Figure 2: Improved Discarding Process



Control Phase

The SOP M700-160 R.2 was revised for improvement. The Improvement phase has the receiving, use and discarding process but the SOP was improved in other areas as well. Sections of the SOP were eliminated because they were not relevant to controlled II substances or were redundant. Section were consolidated because they state the same process. Steps were re-arranged and necessary information was added to improve SOP and comply with regulations.

To make the SOP friendlier, paragraphs were changed to bullet points (in this case letters) or divided into steps. It is easier to read and understand instructions if they are redacted in bullets and multiple steps rather than paragraphs. People tend to avoid reading long boring paragraphs and the objective of the SOP is to be read by the person executing the task.

Training was given to the scientists. Important changes of the SOP were highlighted for their convenience. A quiz was given to all of the corresponding personnel previous to the implementation of the new revision. After obtaining more than 80% of personnel trained, the SOP was implemented on 06Sep2019.

Conclusions

The objective of the project was met given that the SOP was considerably improved. The process of substances CII from arriving to leaving the laboratory was well defined and explained. Key instructions and steps were added to indicate how to manage the samples and forms all the way.

The DMAIC tool helped the process of improving the SOP. The Analyze phase was the key to compare the current state of the process (current practices) with the current SOP and identify the gaps in it. There were steps that were being performed but were not included in the SOP so they were included in the new revision because they were part of the process.

Additional recommendations were included in order to attend a problem regarding samples' reconciliation. Given that this revision were implemented with a SA CAPA due date, there was a time limitation. For that reason, those recommendations will be evaluated for future revision given that some of them require change controls or more time to discuss it with the corresponding personnel.

References

- Bennett, Jason. *LEAN: Ultimate Collection - Lean Startup, Lean Analytics, Lean Enterprise, Kaizen, Six Sigma, Agile Project Management, Kanban, Scrum (Lean Thinking, Lean Manufacturing, Management, Running Lean)* (p. 242). Kindle Edition.
- Barbé B., et al. (2016) *The art of writing and implementing standard operating procedures (SOPs) for Laboratories in Low-Resource Settings: Review of Guidelines and Best Practices*
- United States Drug Enforcement Administration, U.S. Department of Justice, The Controlled Substances Act. Available: https://www.dea.gov/controlled-substances-act
- Drug Enforcement Administration, U.S. Department of Justice, Controlled Substances Schedules. Available: https://www.deadiversion.usdoj.gov/ schedules/
- Departamento de Salud de Puerto Rico (August 1, 2002), Ley de sustancias controladas de Puerto Rico. Available: http://www.lexjuris.com/LEXLEX/lexotras/lexdroga.htm