

Standardization Times in a Blending (Flex 2 Unit Operation) Manufacturing Process

Abstract

The continuous evolution in standardization, digitalization, and constant changes in the ways of working in manufacturing processes in the pharmaceutical industry and the increase in production for product X by 2023, has made it necessary to study the work process and standardize the Blending production unit of the Flex 2 production area. The Flex 2 area is dedicated to a single product only. For the preparation of the drug the area of Flex 2, performs 2 different types of API mixing since the drug in its final stage of compression is a Bi-layer tablet; this means that it is a tablet divided into two active ingredients layers. The blending process requires standardizing the number of operators needed to execute the batches and standardizing the number of batches that can be manufactured in the Flex 2 Blending unit. In 2022 a total of 610 batches were processed and the average batch cycle time was 7.0hrs.

Introduction

The production expectation for the year 2023 is to manufacture a total of 892 batches of blending for product X. The objectives we want to develop and analyze are.

velo	op and analyze are:	
	Create a standardized step-by-step agenda on the execution process with set production cycle times.	Establish the num of operators neede manufacture th product.
	Analyze how many production shifts are required to manufacture the batch	Analyze how ma quantities of blen production batche be made per ye

Background

The business of the pharmaceutical industry configures many dynamic factors, of which it represents the social, economic, and scientific areas, contributing to the export markets are multinational and global. The activities carried out in the pharmaceutical environment are based on regulations subject to laws and policies applicable to the approval, manufacture, quality, and sales of medicines. These terms establish good manufacturing practices (GMP's), guaranteeing the integrity of industrial operations, their safety and efficacy in the product. [1] The mixing process in the pharmaceutical industry is one that is highly used, since it is an efficient unitary operation for the manufacture of a product. This process involves the active ingredient of the product and the excipients, achieving a uniform mixing with the exact quantities for the process. [2] The concept of Lean means producing only what the customer needs, when they need it, in quantities ordered by the customer, and with only minimal resources. Specifically, to manufacture products in a way that minimizes the time required to deliver finished products, to a required amount of labor and required storage space, meeting quality standards, generally at the lowest cost by eliminating waste. [3] To execute the SMED technique well, it is important to identify the area where an opportunity for improvement is required. Then the important elements to make the changes are identified. It is a good option to identify the specific points that are immersed in the process of change. It is necessary to establish a dynamic of observation of whether the process to be analyzed is a process that is mostly executed by a human or by a machine.[4]

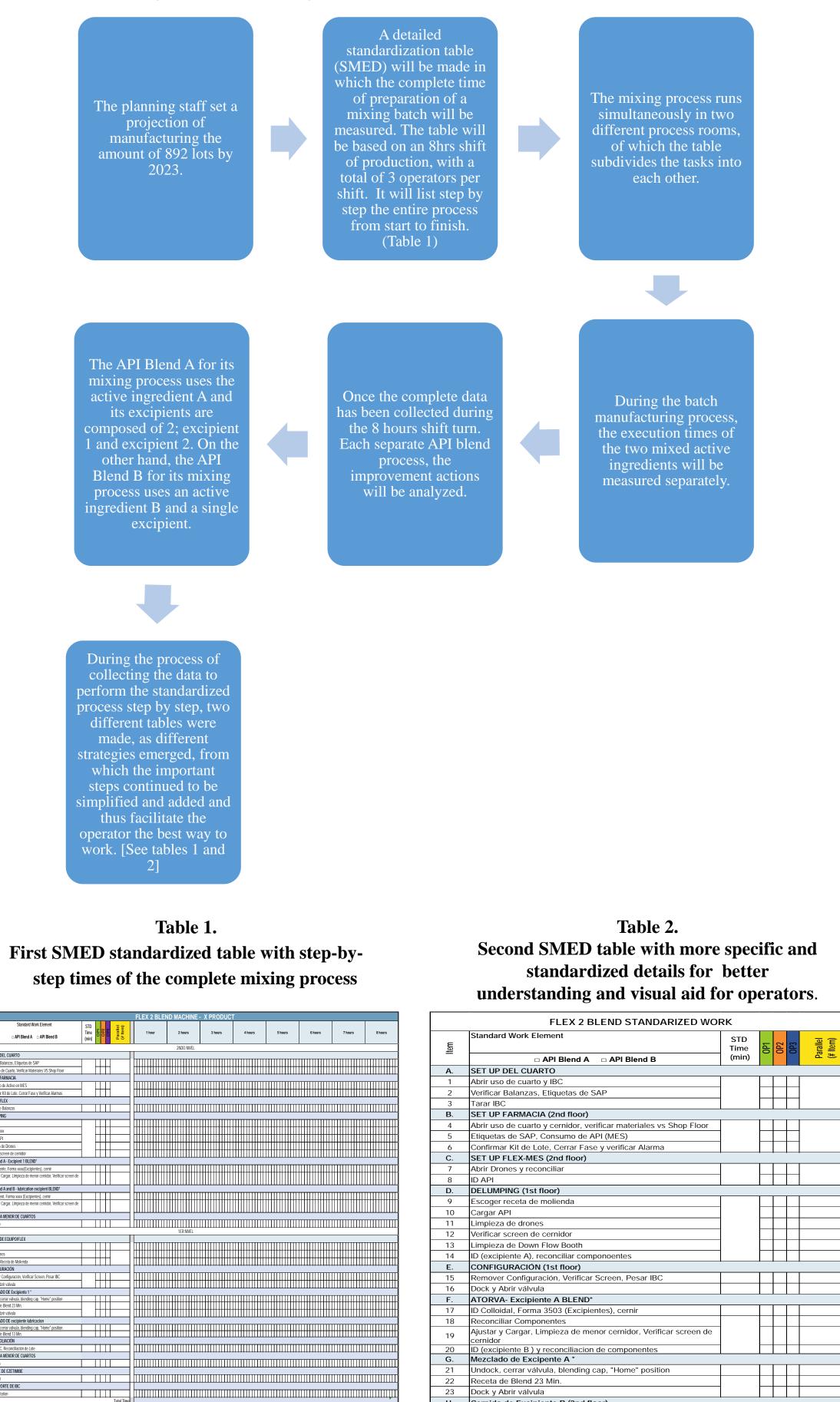
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Problem

The research will concentrate on studying and analyzing the complete (END to END) production process of the unit operation that is performed in Flex 2 and analyzing the production times step by step and analyzing the production capacity, due to the increase in production. By the year 2023 the planning staff set a challenge to manufacture a quantity of 892 batches of blending.

Methodology

To meet the customer's need to analyze the times needed for the standardization of a blend batch in the production area of Flex 2, the following data is being collected:



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Reconciliacion 1er piso

TRANSPORTE DE IBC

Pedir 2 lotes adicionales

Limpieza Menor de cuartos

esar IBC, Reconciliacion del lo

impieza de cuarto, downflow boot

Buscar materiales proximo lote en el airlock

Indock, cerrar válvula, blending cap, "Home" posit

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Lot End Date/End Time

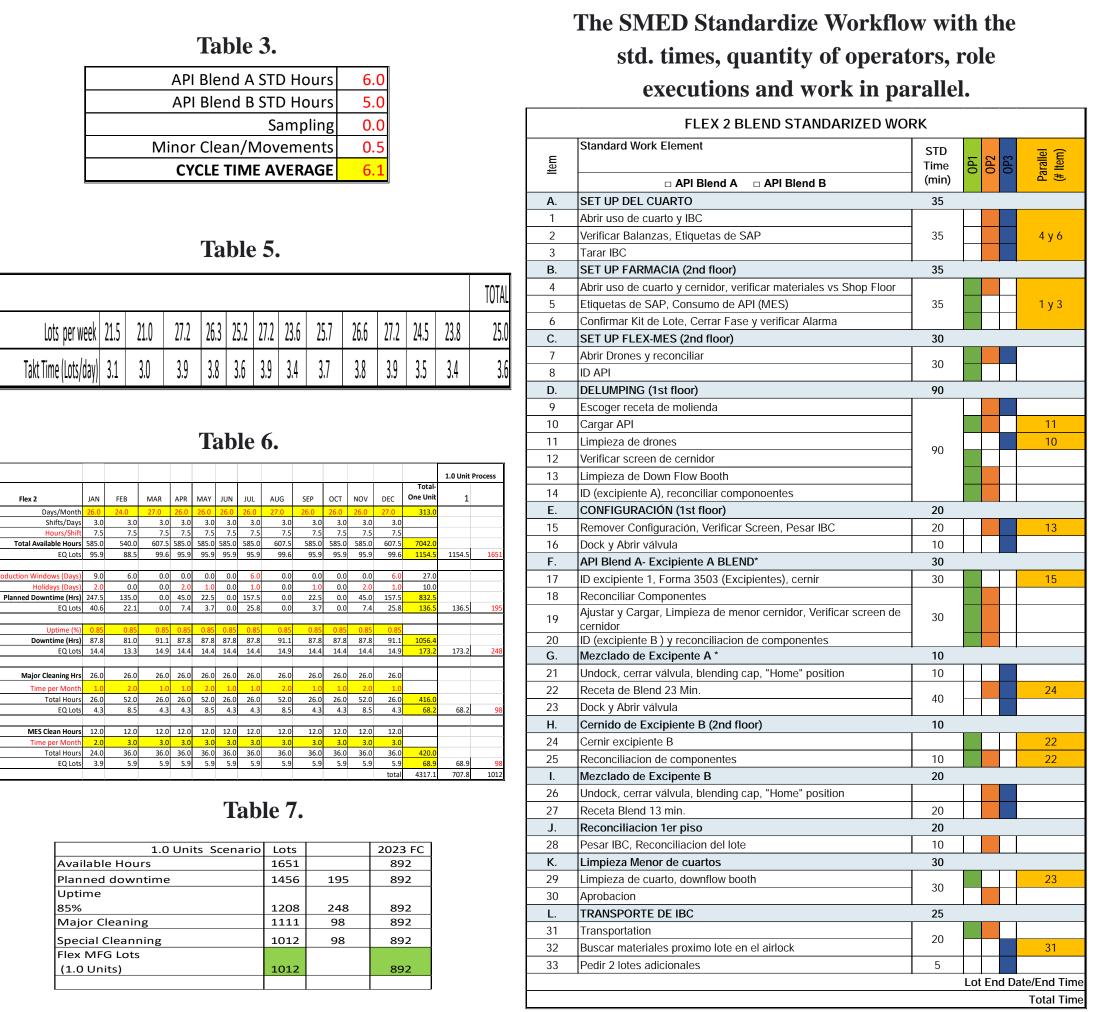
Results and Discussion

• Batch lot preparation in the Flex 2 production unit for the API Blend A is **5.5** hrs. average, and **4.5** hrs. for the API Blend 2. • According to the standardized schedule to support the manufacturing times of each batch, a total of 3 operators per shift is required to support production.

• Define the specific tasks that operator 1, operator 2, and operator 3 perform individually.

• The tasks that are performed jointly between the 3 operators are defined.

• The additional step that corresponds to the API Blend A is established in the standardized table, since this process includes the operation of sifting an additional excipient. (Steps G and H) • Times were established using an Electronic Bath Record (EBR) process. Table 4.



• A margin of error of 0.5hrs is being given to the mixing batches and the cleaning time between batches of 0.5hrs. is given to obtain a more realistic view of production process.

The cycle time average for the study for both standardize blends (A and B) is 6.1hrs. (See table #3).

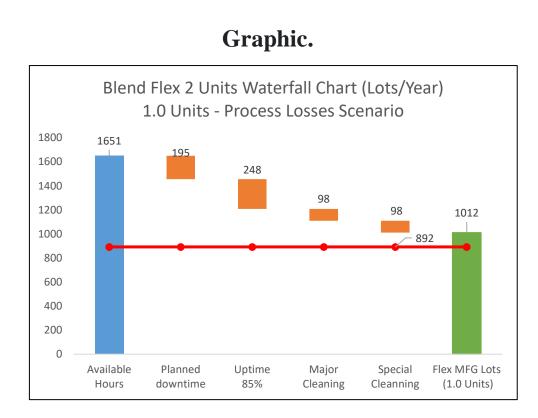
• The table #5 lists the total of 25.0 lots per week considering the 7 days that can be produced.

• The takt time of 3.6 lots manufactured per day is the result of the Total Available Hours EQ lots.

• The table #6 are subdivided in the number of days per month, the number of shifts per day, the number of hours per shift, to obtain the available number of total hours and the total number of batches per hour.

• The total of 1012 lot per year can be produced in the flex 2 Unit Operation. The value of 4317.1 hours per year, is the result of the total available hours subtracting the 4 other different scenarios.

The total of 707.8 lots per year refers to the number of lots with the standardized cycle time value of 6.1 hours. To get a more a concrete idea of the goal; with the actual standardization target of 5.5hrs. and 4.5hrs. it takes to produce a blend in Flex 2, we calculate with a more realistic 1.0 Unit Scenario process and the number of batches can be produced increase to 1012 batches per year. (See table 6)



The cycle time (Miu A) of 7.0 hrs. of duration of the blend process without standardization vs. the new standardized process with a cycle (Miu B) of 5.0 hrs. and measuring a production capacity of 610 batches vs 1012. In relation to the hypothesis, that with 95% reliability it is validated that the Cycle time (Miu A vs Miu B) is greater than the new after the implementation of the project. (Refer to table #8)

Any operation that requires a standardization of its processes, requires time for planning and development to obtain results. The manufacturing process in the pharmaceutical industry is a challenging one, due to the large number of regulations and constant organizational changes to increase its production. By obtaining the results of the Flex 2 production unit and being able to analyze the number of batches that can be made vs. the quantity that they grant management, it has been a success, since a process could be standardized through lean manufacturing techniques and there was a great commitment to help among operators to maximize the areas of operations within manufacturing.

An opportunity for improvements in the process, it is possible to better define the times to reduce downtimes by 5% more in the process, the holidays and shutdowns days, the break relief of 30 minutes, the lack of personnel due to absenteeism can be add a 1hr/lot to the process, standardization in the times of major and minor special cleanings, the challenges of a significant increase in production and support standardized times so that the production time between batches does not increase.

support.

6, 2012





Table 8.					
Hypothesis					
Ho: μCT Before	EQUALS TO	μ CT After			
Select one	MORE THAN	LESS THAN	NOT EQUAL		
1 = YES	1				
H1: μCT Before	MORE THAN	μ CT After			
Test with Unknown Variance (Student T Distribution)					
Hypotheis Test Results					
Miu	7.00	5.00			
Std. Dev.	0.5	0.5			
X Bar	7.0	5.00			
N	610	1012			
Т ехр	78.04				
v	1284.0				
Pvalue	0.0000				
Alpha	0.05				
Miu A is more than Miu B					

Conclusions

Future Work

Acknowledgements

Thanks to the people that helped me conduct my research (Dr. Jose Morales, Daimarik Torres, Dra. Dennise M. Cobian, Company employers and for my parents that give me the total

References

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