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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:

Create a standardized step-by-step agenda on the execution process with set production cycle times.

Establish the number of operators needed to manufacture the product.

Analyze how many production shifts are required to manufacture the batch lot.

Analyze how many quantities of blending production batches can be made per year.

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]

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:

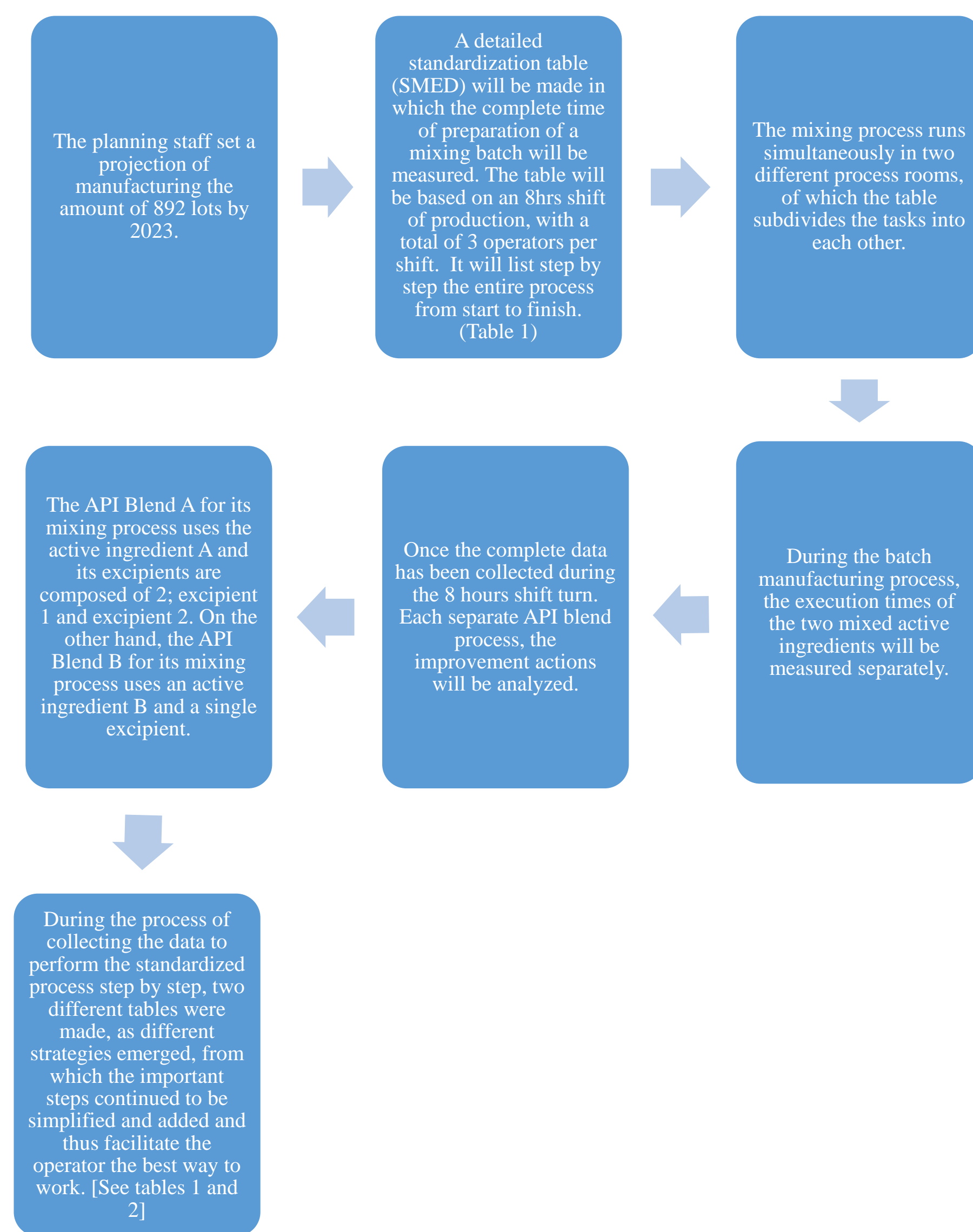


Table 1. First SMED standardized table with step-by-step times of the complete mixing process

Element	Start	End	Time (min)
1	08:00	08:15	15
2	08:15	08:30	15
3	08:30	08:45	15
4	08:45	09:00	15
5	09:00	09:15	15
6	09:15	09:30	15
7	09:30	09:45	15
8	09:45	10:00	15
9	10:00	10:15	15
10	10:15	10:30	15
11	10:30	10:45	15
12	10:45	11:00	15
13	11:00	11:15	15
14	11:15	11:30	15
15	11:30	11:45	15
16	11:45	12:00	15
17	12:00	12:15	15
18	12:15	12:30	15
19	12:30	12:45	15
20	12:45	13:00	15
21	13:00	13:15	15
22	13:15	13:30	15
23	13:30	13:45	15
24	13:45	14:00	15
25	14:00	14:15	15
26	14:15	14:30	15
27	14:30	14:45	15
28	14:45	15:00	15
29	15:00	15:15	15
30	15:15	15:30	15
31	15:30	15:45	15
32	15:45	16:00	15
33	16:00	16:15	15
34	16:15	16:30	15
35	16:30	16:45	15
36	16:45	17:00	15
37	17:00	17:15	15
38	17:15	17:30	15
39	17:30	17:45	15
40	17:45	18:00	15
41	18:00	18:15	15
42	18:15	18:30	15
43	18:30	18:45	15
44	18:45	19:00	15
45	19:00	19:15	15
46	19:15	19:30	15
47	19:30	19:45	15
48	19:45	20:00	15
49	20:00	20:15	15
50	20:15	20:30	15
51	20:30	20:45	15
52	20:45	21:00	15
53	21:00	21:15	15
54	21:15	21:30	15
55	21:30	21:45	15
56	21:45	22:00	15
57	22:00	22:15	15
58	22:15	22:30	15
59	22:30	22:45	15
60	22:45	23:00	15
61	23:00	23:15	15
62	23:15	23:30	15
63	23:30	23:45	15
64	23:45	24:00	15
65	24:00	24:15	15
66	24:15	24:30	15
67	24:30	24:45	15
68	24:45	25:00	15
69	25:00	25:15	15
70	25:15	25:30	15
71	25:30	25:45	15
72	25:45	26:00	15
73	26:00	26:15	15
74	26:15	26:30	15
75	26:30	26:45	15
76	26:45	27:00	15
77	27:00	27:15	15
78	27:15	27:30	15
79	27:30	27:45	15
80	27:45	28:00	15
81	28:00	28:15	15
82	28:15	28:30	15
83	28:30	28:45	15
84	28:45	29:00	15
85	29:00	29:15	15
86	29:15	29:30	15
87	29:30	29:45	15
88	29:45	30:00	15
89	30:00	30:15	15
90	30:15	30:30	15
91	30:30	30:45	15
92	30:45	31:00	15
93	31:00	31:15	15
94	31:15	31:30	15
95	31:30	31:45	15
96	31:45	32:00	15
97	32:00	32:15	15
98	32:15	32:30	15
99	32:30	32:45	15
100	32:45	33:00	15

Table 2. Second SMED table with more specific and standardized details for better understanding and visual aid for operators.

Element	Start	End	Time (min)
1	08:00	08:15	15
2	08:15	08:30	15
3	08:30	08:45	15
4	08:45	09:00	15
5	09:00	09:15	15
6	09:15	09:30	15
7	09:30	09:45	15
8	09:45	10:00	15
9	10:00	10:15	15
10	10:15	10:30	15
11	10:30	10:45	15
12	10:45	11:00	15
13	11:00	11:15	15
14	11:15	11:30	15
15	11:30	11:45	15
16	11:45	12:00	15
17	12:00	12:15	15
18	12:15	12:30	15
19	12:30	12:45	15
20	12:45	13:00	15
21	13:00	13:15	15
22	13:15	13:30	15
23	13:30	13:45	15
24	13:45	14:00	15
25	14:00	14:15	15
26	14:15	14:30	15
27	14:30	14:45	15
28	14:45	15:00	15
29	15:00	15:15	15
30	15:15	15:30	15
31	15:30	15:45	15
32	15:45	16:00	15
33	16:00	16:15	15
34	16:15	16:30	15
35	16:30	16:45	15
36	16:45	17:00	15
37	17:00	17:15	15
38	17:15	17:30	15
39	17:30	17:45	15
40	17:45	18:00	15
41	18:00	18:15	15
42	18:15	18:30	15
43	18:30	18:45	15
44	18:45	19:00	15
45	19:00	19:15	15
46	19:15	19:30	15
47	19:30	19:45	15
48	19:45	20:00	15
49	20:00	20:15	15
50	20:15	20:30	15
51	20:30	20:45	15
52	20:45	21:00	15
53	21:00	21:15	15
54	21:15	21:30	15
55	21:30	21:45	15
56	21:45	22:00	15
57	22:00	22:15	15
58	22:15	22:30	15
59	22:30	22:45	15
60	22:45	23:00	15
61	23:00	23:15	15
62	23:15	23:30	15
63	23:30	23:45	15
64	23:45	24:00	15
65	24:00	24:15	15
66	24:15	24:30	15
67	24:30	24:45	15
68	24:45	25:00	15
69	25:00	25:15	15
70	25:15	25:30	15
71	25:30	25:45	15
72	25:45	26:00	15
73	26:00	26:15	15
74	26:15	26:30	15
75	26:30	26:45	15
76	26:45	27:00	15
77	27:00	27:15	15
78	27:15	27:30	15
79	27:30	27:45	15
80	27:45	28:00	15
81	28:00	28:15	15
82	28:15	28:30	15
83	28:30	28:45	15
84	28:45	29:00	15
85	29:00	29:15	15
86	29:15	29:30	15
87	29:30	29:45	15
88	29:45	30:00	15
89	30:00	30:15	15
90	30:15	30:30	15
91	30:30	30:45	15
92	30:45	31:00	15
93	31:00	31:15	15
94	31:15	31:30	15
95	31:30	31:45	15
96	31:45	32:00	15
97	32:00	32:15	15
98	32:15	32:30	15
99	32:30	32:45	15
100	32:45	33:00	15

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 3.

API Blend A STD Hours	6.0
API Blend B STD Hours	5.0
Sampling	0.0
Minor Clean/Movements	0.5
CYCLE TIME AVERAGE	6.1

Table 5.

Lot	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	TOTAL
Lot/Week	21.5	21.0	21.2	20.3	20.2	20.7	20.6	20.7	20.6	20.7	20.6	20.6	20.7	20.6	20.7	20.6	20.7	20.6	20.7	20.6	20.7	20.6	20.7	20.6	20.7	250
Takt Time (Lot/Day)	3.1	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.6

Table 6.

Plant	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100
Plant	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41																																																											