Increased Efficiency for Compression Setup and Startup Processes

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Abstract — *This research project is focused in the Increased Efficiency for Compression Setup and Startup Processes. The machine compressors are the Table Press 3200i, it is a double sided rotary press used to produce mono and bi-layer tablets. Bilayer is a structure, such as a film or membrane, consisting of two molecular layers. Monolayer a film or layer of one molecule thin [1]. In order to improve the extensive downtime for setup and startup of the compression machine, also increasing capacity for new product demand, the DMAIC methodology was used. This research aims to increase capacity for new product demand and reduce downtimes in setup and startup in the compression process.*

Key Terms – *Bilayer Tablet, DMAIC, Fette Compacting, Granulation, Mono Layer Tablet, Tablet Compressing.*

INTRODUCTION

The company is confronting a problem. Currently they cover customer demand but soon a new product is arriving to the facility and with the process as it is right now there is no capacity to run this new product. In simple words the company needs more capacity to meet the customer demand. Analyzing the current state of the compression process the team acknowledge an extensive downtime in setup and startup. This includes the excessive documentation, parameters and inputs of the machine, mechanics not available, lack of systems and materials, among others.

PROBLEM STATEMENT

The capacity of the Fette compression machines 15 & 16 is expected to be insufficient based on expected product volume for this year 2018 and current process standards for these workstations. Current forecast volume for 2018 is 100% utilization for current and additional products to be compressed. Start-up and setup extensive downtime leads to inefficient capacity use and low yields.

RESEARCH DESCRIPTION

This research is about increasing efficiency for the compression startup and setup processes. Is about how to improve this times, and by doing this the company will be able to absorb new products demand for 2018. There also will be a business impact in expense reduction and machines efficiency and capacity.

RESEARCH OBJECTIVES

The scope of the project is to identify opportunities to make effective use of compression process standard time. Optimize the use of current process resources through better ways of working. Reduce startup and setup lead time by 25%. This represents approximately $80,000 per year. This can be achieved by impacting or looking close to startup and setup of the compression process. Compression run time, in-process testing, reconciliation, minor and major cleaning and assembly.

LITERATURE REVIEW

Pills have been used as a means of delivering a measured dose of a medicine since approximately 1500 BC. There have been used to carry a measured medical dose for over three millennia. It all started with a British artist, inventor and watchmaker called William Brockedon. He produced a compression machine for graphite to produce a better pencil lead. This invention was observed by a keen pharmaceutical company who employed William to retool the instrument to make tablets. It was then that Brockedon received the first ever patent for a device like this in 1843, “Shaping Pills, Lozenges and Black

Lead by Pressure in Dies." This invention allowed the efficient mass production for commercial viable dosage forms, and started the modern pharmaceutical industry. The surprising fact is that for more than 150 years of tablet making, William Brockedon's method hasn't change significantly.

Now drugs in tablet form and pharmaceuticals that make then are by far the most common formulation and over the counter drugs worldwide. Per the FDA, about 46% of approved drugs are manufactured in tablet form, and billions of doses are prescribed and consumed in the U.S yearly.

Many formulations have multiple active pharmaceutical ingredients (APIs), and each of these has their own granulation, wetting, and solubility profiles. But even with a single API, formulations include excipients (non-active ingredients), such as diluents (an inactive filler to achieve a reasonable final pill size), and disintegrating agents to regulate the tablet's dissolution time after administration. Colorants for identification and branding may be added. Serious to many tablet formulations are coatings to comfort swallowing; to cover unpleasant tastes; to protect the ingredients from light, moisture, and air; to control the drug's release site within the gastrointestinal tract; or for aesthetic reasons [2].

Assuring tablet consistency both within and between batches is a complex task. Manufacturers, and the U.S. Food and Drug Administration (FDA) insists, that there is minimal variation in quantity and physical properties of the APIs from pill to pill. This is reached in part by cautiously mixing and granulating the compound to achieve a homogeneous dispersion of the various drugs and excipients throughout the batch before the pills are compressed. Like Brockedon's 1843 invention, the efficiencies gained by deploying such deeply integrated, intelligent automated testing and process control instrumentation could usher in another pharmaceutical manufacturing revolution [3].

General Concepts of DMAIC Methodology

DMAIC is a structured problem-solving methodology widely used in business. The letters are an acronym for the five phases of Six Sigma improvement: Define-Measure-Analyze-Improve-Control. These phases lead a team logically from defining a problem through implementing solutions linked to underlying causes, and establishing best practices to make sure the solutions stay in place. The structure of DMAIC encourages creative thinking within boundaries such as keeping the basic process, product, or service. DMAIC is a valuable tool that helps people find permanent solutions to long-standing or tricky business problems [4].

In Define, the current performance of the production line is determined, the analysis information is collected, and it is focused to identify the problem to be solved. The purpose of this step is to clearly set the business problem, goal, resources, and financial business results.

In Measure, the current baseline is defined; the actual performance of the process is measured and compared with the customer requirements to determine the level of the needed improvement.

In Analyze the analysis of the information is collected to determine the root causes of defects and opportunities for improvement. The objective is to define performance objectives, determine root cause(s), and determine the "vital few, trivial many" relationship

Once the potential causes of the problems have been identified, Improve phase leads the team to identify potential solutions to the problems encountered. Also a financial impact is important to see in money how these solutions benefit the company.

Finally, the Control phase, the lessons learned are driven to be implemented and the tools used will assure that the key variables remain in control. Monitor the improvements will be crucial to ensure continued and sustainable success.

RESULTS AND DISCUSSION

Define – is the first phase for the DMAIC methodology. The purpose of this phase is to state the scope, goals, financial and performance targets for the project. In this phase a SIPOC was used to

identify the basic elements of the process. It captures a high-level view of the operations. See Figure #1.

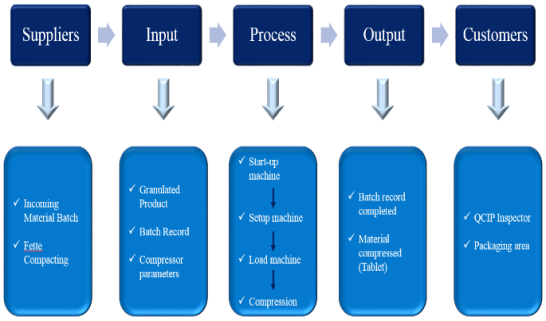

Figure 1
SIPOC

Another tool used in this phase was the CTQ tree Critical to Quality diagram. This is a diagram that aims to convert customer need statements into service or product requirement, used to meet or even exceed customer needs. This diagram makes the transition from general statements to precise functional requirements. The final requirement must be a specific goal or target and that can be measurable. See figure #2.

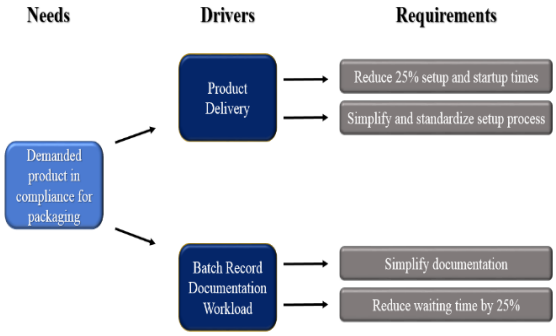

Figure 2
Critical to Quality Diagram

Measure Phase- is the second phase for the DMAIC methodology. The purpose of this phase is to understand the current stat of the process and collect reliable data on process that will use to expose the underlying causes of problems. In this phase a Data collection plan table was used to gather all data regarding the startup times. See figure #3 and #4. The data included time per operator per shift and per product code. In the analyze phase the data will be graphed to appreciate if there is any variation and due to what.

Data Collection Plan			
Cycle time for setup machine times for tablets YY0990			
Shift	Operators	Code	Time (min)
A	1	YY0990	33
A	2	YY0990	28
A	3	YY0990	32
A	4	YY0990	41
B	1	YY0990	24
B	2	YY0990	27
B	3	YY0990	38
B	4	YY0990	20
C	1	YY0990	33
C	2	YY0990	26
C	3	YY0990	31
C	4	YY0990	22

Figure 3
Data Collection Plan for YY0990

Data Collection Plan			
Cycle time for setup machine times for tablets MM5434			
Shift	Operators	Code	Time (min)
A	1	MM5434	40
A	2	MM5434	45
A	3	MM5434	30
A	4	MM5434	51
B	1	MM5434	43
B	2	MM5434	54
B	3	MM5434	49
B	4	MM5434	42
C	1	MM5434	39
C	2	MM5434	55
C	3	MM5434	47
C	4	MM5434	32

Figure 4
Data Collection Plan for MM5434

Another tool used in this phase was the Flowchart or process map chart. See figure #5. This is to have a high-level view of the process in the manufacturing area.

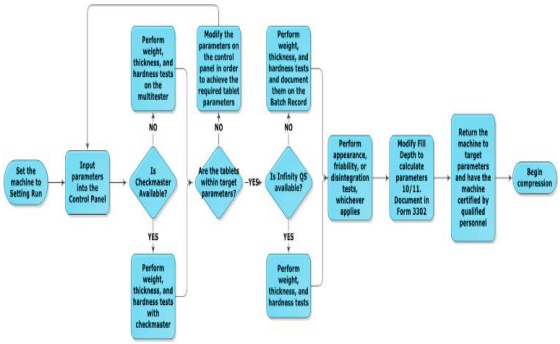

Figure 5
Process Map

Analyze Phase -This is the third phase of the DMAIC methodology. The purpose of this phase is to determine causes affecting the project goals. Also, perform data and process analysis, and determine root cause or causes and prioritizing them. A Cause and effect diagram also known as fishbone or

Ishikawa Diagram was used for this phase. See Figure #6. This tool is used to ensure that all ideas from every category is being analyzed and that all major possible causes are not being overlooked. There are different categories for the cause and effect diagram, the category used for this project was the 6M's: manpower (personnel), machines, materials, methods, measurements and Mother Nature (environment).

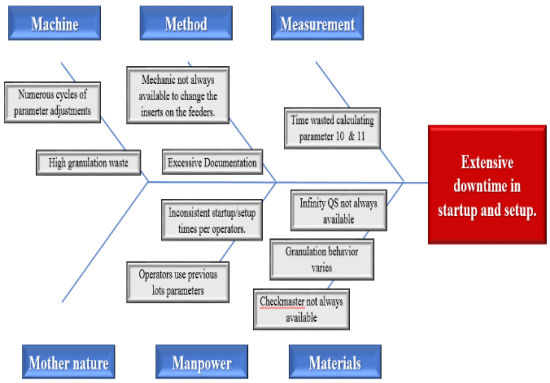

Figure 6
Cause and Effect Diagram

Another tool used in this phase was the Five Whys, this tool is a method to push to think moreover than superficial solutions and keep asking why to reach a solution that will fix it not temporarily but eradicate it. See Figure #7.

Category	Cause	1st Why	2nd Why	3rd Why	4th Why	5th Why	Improvement
People	Inconsistent downtime by startup and setup machine times.	Downtime of startup and setup varies among operators.	Each operator performs setup and startup process differently	There is no an specific or correct way of performing startup and setup to machines.	There is not an standard operating procedure for setup and startup process particularly.	-	Standardize startup and setup process and generate an SOP of this.
Method	Excessive Documentation	There are about 8 logbooks plus 5 forms to be completed for the batch.	The SOP requires it.	Regulatory Compliance audits the processes and data integrity.	To ensure all processes complies with the GMP's	To be approved by FDA agency and other regulatory agencies.	Merge information among logbooks and forms.
Machine	Numerous cycles of parameter adjustments	There are a lot of calculation for parameter 10 & 11 per cycle.	Establish the force limits of the compression machine	Bad tablets might be accepted while good tablets might be rejected	Lack of predetermined acceptable range	Granulation behavior varies	Reduce the number of calculations of parameters 10&11by performing a DOE.

Figure 7
Five Whys

Improve Phase - This is the fourth phase of the DMAIC methodology. The purpose of this phase is to generate potential solutions, apply lean tools, perform risk assessment and execute full-scale implementation. In this phase a brainstorming was performed to generated all potential solutions. See Figure #8.

Implemented Solutions	
Solutions	**Benefits**
Redesigned Logbooks	At least 50% reduction documenting logbooks. Saves time, and eliminates writing same things repeatedly.
Redesigned Forms	Merge forms to have all batch information completed in one. Not repetitiveness in documentation.
Standardize work for startup and setup. SOP step by step with visual aids generated.	Saves time, parallel startup and setup.

Figure 8
Brainstorming Solutions

After applying short term solutions to the process, the new current process was measured to obtain the new cycle times for startup and setup machine downtimes. Refer to figures #9 and #10 for new times after implementation.

Data Collected after implementation			
Setup and start-up downtimes for tablets YY0990			
Shift	**Operators**	**Code**	**Time (min)**
A	1	YY0990	15
A	2	YY0990	12
A	3	YY0990	16
A	4	YY0990	13
B	1	YY0990	11
B	2	YY0990	14
B	3	YY0990	10
B	4	YY0990	12
C	1	YY0990	13
C	2	YY0990	11
C	3	YY0990	13
C	4	YY0990	12

Figure 9
Data for YY0990 after Implementation

Data Collected after implementation			
Setup and start-up downtimes for tablets MM5434			
Shift	**Operators**	**Code**	**Time (min)**
A	1	MM5434	17
A	2	MM5434	13
A	3	MM5434	15
A	4	MM5434	18
B	1	MM5434	16
B	2	MM5434	15
B	3	MM5434	16
B	4	MM5434	19
C	1	MM5434	14
C	2	MM5434	16
C	3	MM5434	17
C	4	MM5434	13

Figure 10
Data for MM5434 after Implementation

Control Phase - This is the last phase for the DMAIC methodology. The purpose of this phase is to complete project work, create process control plans, and hand off improved process and procedures for maintaining gains. In this phase control charts were used to demonstrate the new cycle times for the startup and setup machine downtimes. The control charts are graphed by product code, the reason is product YY0990 takes

less time setting up than MM5434. See Figure #11 and #12. Another tool used was a cost saving calculation to demonstrate financial benefits. This was segregated in two: Capacity Benefit and Cost reduction benefit. See figure #13

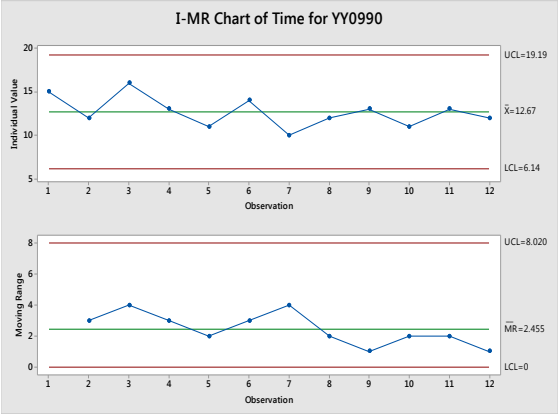

Figure 11
Control Chart for YY0990

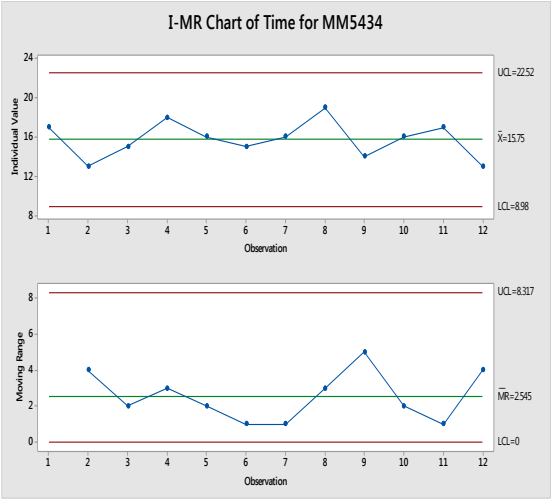

Figure 12
Control Chart for MM5434

Financial Benefits

1. Capacity Benefit: There are 6,000 work hours per year (8hrs shift X 3 shifts X 50 weeks) considering 2 weeks for shutdown. Each lot takes 4 hours to manufacture. With the implementations, there was a 0.37-hour reduction in setup and startup time. This represents a capacity increase of 10%.

   a. Before: $\frac{6{,}000\ \frac{hrs}{yr}}{4\ \frac{hrs}{lot}}$ = 1,500 lots per year

   b. Now: $\frac{6000\ \frac{hrs}{yr}}{3.63\ \frac{hrs}{lot}}$ = 1,652 lots per year

   c. Capacity increase of 10% represents 152 lots more.

2. Potential Cash: Each lot cost approximately $10,000

   a. Before: $1{,}500\ \frac{lots}{yr} \times \$10{,}000\ p.lot$ = $15,000,000 per yr.

   b. Expected: $1{,}652\ \frac{lots}{yr} \times \$10{,}000\ p.lot$ = $16,520,000 per yr.

3. Cost Reduction Benefit: There are four operators working in this area simultaneously. The rate per hour is $60. Before implementation they used to have downtime due to startup and setup tasks of 0.62hr. With implementations, the downtime due to startup and setup reduced to 0.25 hr.

   a. Before: $\$60\ p/hr \times 4\ Operators \times 0.62\ hr = \$148.80$ per lot

   b. Expected: $\$60\ p/hr \times 4\ Operators \times 0.25\ hr = \$60.00$ per lot

   c. Cost Reduction: $88.80 per lot represents $\$88.80\ p.lot \times 1{,}500\ \frac{lots}{yr}$ = $133,200 per yr.

Financial Benefits		
Category	**Before**	**Expected**
Lot Capacity	1,500 lots per year	1,652 lots per year
Operators Cost	$148.80 per lot	$60.00 per lot
Manufacturing time	4 hours each lot	3.63 hours each lot
Cash per lot	15 million per year	16.5 million per year
Setup and Startup time	0.62 hour per lot	0.25 hour per lot

Figure 13
Financial Benefits

CONCLUSION

The "Increased Efficiency for Compression Setup and Startup Processes" has been defined, focusing in the problem and stating the goals that the team wants to achieved. After defining the problem and stating the objectives the setup and startup downtimes current process was measured. With the time collected the project was analyzed in order to

address root causes issues, in this way the real problem would be eradicate if possible if not minimized it. After analyzing the project was improved, potential solutions from brainstorming arise and were implemented within the process. Lastly the project was control, the process was measure again to ensure improvement, not only process capacity and efficiency but also to quantify financial benefits. With this project an improvement of 10% in process capacity was obtain. The downtime process was reduced 0.37 hour this represents 60% downtime reduction. And a financial benefit of more than 1.5 million annually. The goals of this project were achieved. There is still one solution that wasn't implemented, the Design of Experiment in the process for the parameters. This is because of the complexity of the DOE and it was determined as a long-term goal.

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