IOSR Journal of Engineering (IOSR JEN) **www.iosrjen.org**
ISSN (e): 2250-3021, ISSN (p): 2278-8719
PP 42-50

Process Improvement in a Pharmaceutical Company using DMAIC Approach

M. Prabhakaran[1], Prasanna Kattimani[1], Amol NayakappaPatil[1], Karan Mehrotra[2]

[1]*Assistant Professor, Department of Mechanical Engineering, Agnel Institute of Technology and Design, Goa, India*

[2] *Final year Student, Department of Mechanical Engineering, Agnel Institute of Technology and Design, Goa, India*

Abstract: *Lean six sigma is the name designated to the processes which are meant for reducing the material loss in an industry. The DMAIC method is a fool proof approach for successful implementation of six sigma methodology in any industry. This research endeavors to improve the tablet production of a pharmaceutical company by reducing the amount of material lost in one of the stages of the production. In define phase, the exact problem encountered in the process is briefed with supporting data. In measure phase, the amount of material lost in the important processes such as compression, Fluid Bed Dryer, Rapid Mix Granulator and Double Cone Blender are measured and focus is made on the process which accounts for majority of the material loss. In analyze phase, an experimental design using Taguchi's L9 orthogonal array is adopted. From the data obtained through main effect plot for means the optimal set of parameters are captured in the improve phase. In addition, a wind deflector is designed and installed to reduce the amount of material loss further. A cost benefit analysis is also made to show the amount of cost saved by the company due to reduction in material loss. Finally, in the control phase, a process control check list has been made to monitor and document the process.*

Keywords: *Cost benefit analysis, DMAIC, Lean Six Sigma, Material Loss, Taguchi*

I. Introduction

Six Sigma is a problem-solving model to build robust processes at various stages in all areas of operation including marketing and sales, accounts, purchase, manufacturing, service and others to achieve 3.4 Defects Per Million Opportunities (DPMO). It is a structured, project based approach to achieve significant impact for any company using statistical methods.Six Sigma has both technical and management components. On the technical side, the focus is for improving the performance of the system using the data obtained from the process and various statistical tools and techniques. On the management side, it focuses on getting the right process metrics and goals, a right project with right people working on it and use of management systems to complete the project successfully and sustain the gains over a period of time.

Problem Description

Pharmaceutical companies in general have a wide scope for the implementation of six sigma in their industry. Reason being that this industry has a lot of processes underlying, to get the final product andthe final product could become defective due to improper processing at any one of the stages. This research focuses on a pharmaceutical company located at Goa, India, which produces medicines for common cold. Of the various medicines manufactured in the plant, this research endeavors to reduce the amount of material loss in one of the tablet production lines.

II. Literature Review

Sri Indrawati and Muhammad Ridwansyah (2015), conducted research using lean six sigma method to improve the manufacturing process capability of the iron ore industry. They focused on the waste analysis and the amount of non-value-added activities that occurs during the production process using Failure Mode Effect Analysis tool. G. V. S. S. Sharma and P. Srinivasa Rao (2014), elaborated the DMAIC approach of six sigma for reducing the process variation of the hole boring operation in the manufacture of the crank shaft.By effective implementation of the DMAIC method the process potential capability index values were increased considerably. A. Kumaravadiveland U. Natarajan (2013), made a study using six sigma methodology to measure the performancecriteria of the process through investigating the effectof working parameters, namely, moisture content, greenstrength, permeability, and loss on ignition on sand preparation.The researchers modeled the obtained results through response surface methodology. E. V. Gijo and JohnyScaria (2014), investigated the reasons for the rejection and rework of the plunger in automobiles using DMAIC process.Joseph C et al conducted a Taguchi based six sigma research to optimize the roundness of the holes made using plasma cutting process.

DMAICPROCESS

Six Sigma offers a structured problem-solving methodology to achieve break-through improvements by systematically identifying root causes and eliminating them using an integrated set of statistical tools, problem-solving techniques, data, and disciplines.

The Six Sigma DMAIC methodology can be thought of as a roadmap for problem solving and product/process improvement. Most companies begin implementing Six Sigma using the DMAIC methodology, and later add the DFSS (Design for Six Sigma) methodologies when the organizational culture and experience level permits. DMAIC methodology consists of the following five steps, **D**efine, **M**easure, **A**nalyse, **I**mprove and **C**ontrol. This research intends to reduce the amount of material loss in the tablet manufacturing process through the exertion of DMAIC process.

Define

The define phase is the initial phase of the six-sigma implementation. It sets forth the problem to be addressed and elucidates the necessary information required for carrying out the project. Moreover, it clearly states the scope of the project, resources which are available at disposal for the completion of the project, project team involved, cost and the stake holders' details. Tools such as SIPOC diagram, Pareto Chart and brainstorming are employed in this phase to get the abstract of the project to be carried out. The SIPOC diagram shown in Table 1 gives all the vital information necessary for the process to be carried out.

Table 1: SIPOC Diagram

PROCESS: Tablet Manufacturing **START: Raw Material** **END: Packaged Tablets, Ready for Shipment**				
SUPPLIERS	**INPUTS**	**PROCESS**	**OUTPUTS**	**CUSTOMERS**
Paracetamol - FarmsonPharmaceuticals ChlorpheniramineMaleate IP - Supriya Lifescience Phenylephrine HydrochlorideMalladi Drugs & Pharmaceuticals Microcrystalline Cellulose - Chemfield Cellulose	Raw Material for the tablet Starch Polyvinyl Pyrrolidine Paracetamol ColloidalAnhydrous Silica Pregelatinized Starch Magnesium Stearate Crospovidone	Dispensing Sieving Dry Mixing Granulation Drying Milling Lubrication Blending Compression Testing Inspection Packaging Dispatch Shipping	Finished Tablets, which conform to the medical requirements Packaged Tablets	Primarily for consumers suffering from the common cold Pharmacies in and around the state of Goa

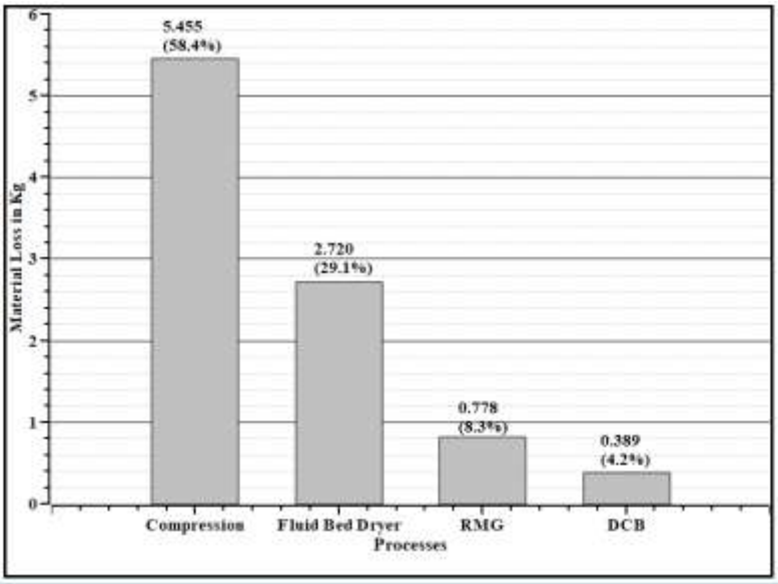

Fig 1: Material Loss at Various Processes

The amount of material loss in the various stages had been collected for 40 batches. From the pareto chart shown in fig. 1, it can be inferred that the compression stage accounts to 58.4% and Fluid Bed Dryer (FBD) stage accounts to 29.1% of the overall material loss. Thus around 88% of the total material loss occurs at these two stages only. Though it is identified that the material loss occurs at these two stages, priority is given to the compression stage and this research focuses towards minimizing losses occurring at compression stage only.

Measure

Measure is about documenting the current process, validating how it is measured, and assessing baseline performance. Often, the Measure phase provides early clues that will direct team toward top problem areas and solutions. The purpose of this step is to establish current process performance baselines as the basis for improvement. The performance metric baselines from the Measure phase will be compared to the performance metric at the conclusion of the project to determine objectively whether significant improvement has been made. The tablet production process is illustrated in Fig. 2 which gives a clear picture of the various process the raw material undergoes before being converted into tablet.

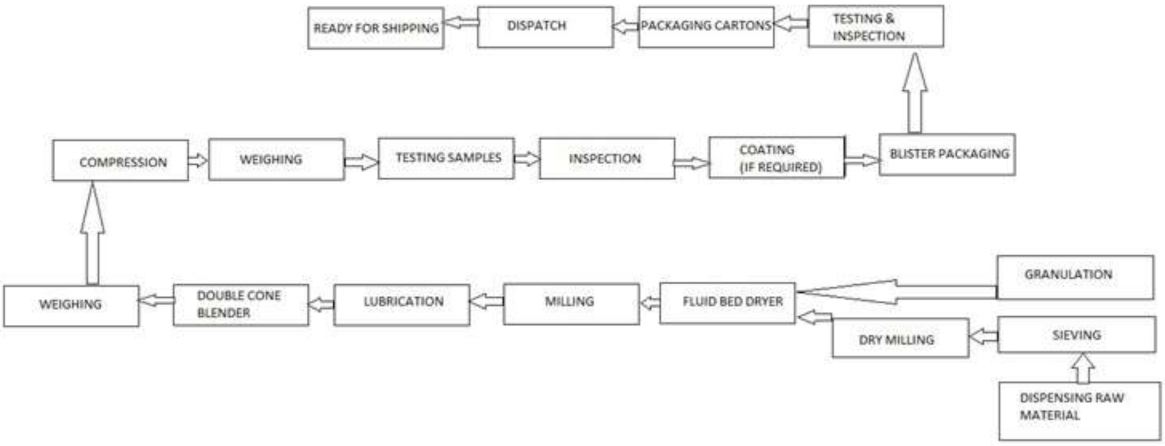

Fig 2: Process Map of Tablet Production

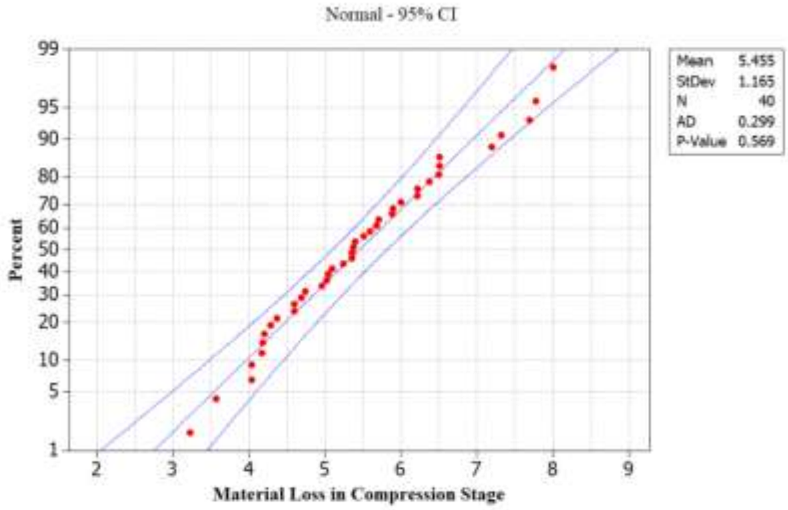

Fig 3: Distribution Plot for Compression Stage Data

From the Fig. 3, it is evident that the amount of material loss in the compression stagefollows a normal distribution and its corresponding descriptive statistics is shown within the box. It can be observed that the AD value obtained is 0.299, which is very less and shows that the data falls very much within the normal distribution.

Analyze

Analyze phase details the root causes for the loss of material in tablet production process. Identifying the base six sigma value of the existing process becomes necessary, since it will give the basis of comparison of the process before and after improvement. The sigma values for the given DPMO are shown in the Table 2.

Table 2: Sigma Table with corresponding DPMO

σ	DPMO	σ	DPMO	σ	DPMO	σ	DPMO	σ	DPMO
1	697672	2	308770	3	66811	4	6210	5	233
1.1	660083	2.1	274412	3.1	54801	4.1	4661	5.1	159
1.2	621378	2.2	242071	3.2	44567	4.2	3467	5.2	108
1.3	581815	2.3	211928	3.3	35931	4.3	2555	5.3	72
1.4	541694	2.4	184108	3.4	28717	4.4	1866	5.4	48
1.5	501350	2.5	158687	3.5	22750	4.5	1350	5.5	32
1.6	461140	2.6	135687	3.6	17865	4.6	968	5.6	21
1.7	421428	2.7	115083	3.7	13903	4.7	687	5.7	13
1.8	382572	2.8	96809	3.8	10724	4.8	483	5.8	9
1.9	344915	2.9	80762	3.9	8198	4.9	337	5.9	5
								6	3.4

A large number of potential root causes of the research problem are identified via root cause analysis. The prominent root causes, which causes material loss in compression stage alone are selected using multi-voting technique.The Fig. 4 shows the root cause and effect diagram for the material loss in compression stage.

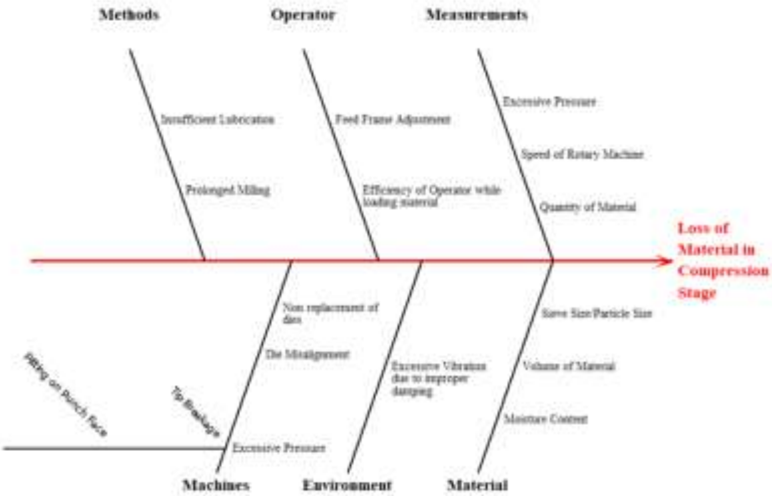

Fig 4: Cause and Effect Diagram for Material Loss in Compression Stage

Multi voting is carried out among the professionals involved in the production process, by grading the various factors leading to loss of material. The Table 3 shows the various grades given to the different factors.

Table 3: Multi Voting Table

Factors	Engineer	Supervisor 1	Supervisor 2	Operator 1	Operator 2	Operator 3	Operator 4
Moisture Content	5	4	5	5	4	4	5
Volume of raw material	1	2	1	3	1	2	2
Speed of Machine	3	3	2	2	2	3	2
Particle Size	5	4	5	4	3	4	5
Amount of Binding Material	4	3	4	5	4	4	4
Machine Vibrations	2	1	2	2	2	1	1

As it can be seen from Table 3, Moisture content of the raw material, Particle size and the amount of binding material used, carry more grades among the six factors. Hence these parameters have to be fiddled with for controlling the amount of material lost in compression stage. An experimental design was proposed to carry out experiments for collecting data by varying the values of the above three factors. Table 4 shows the three levels of the three factors chosen for conducting the experiments. The three levels for each of the factor was determined through expertise consultation from the supervisors and operators.

Table 4: Factors and Levels

FACTORS	LEVELS		
	Low Level	Mid-Level	High Level
Moisture Content (A)	1.25%	1.50%	1.75%
Binder Quantity (B)	143 kg	145 kg	147 kg
Sieve Size(C)	40 US Mesh	50 US Mesh	60 US Mesh

Three factors with 3 levels each are chosen for conducting the experiments. Hence, Taguchi's L9 Fractional Factorial design was chosen to carry out the experimentation. According to L9 orthogonal array, a total of 9 trials is required to complete the study. Table 5 shows the L9 orthogonal array used in the project DOE.

Analysis of Variance

Analysis of Variance (ANOVA) is conducted on the obtained data to know the significance of each factor on the amount of material loss. The ANOVA results depicted in Table 7 shows that the F Value attained by the factors moisture content and binder quantity are more than the F critical value. This enables to justify that the factors A and B are significant in causing material loss in compression stage.

Table 5: L9Orthogonal Array

Trial Number	Factor Levels		
	A	B	C
1	1	1	1
2	1	2	2
3	1	3	3
4	2	1	2
5	2	2	3
6	2	3	1
7	3	1	3
8	3	2	1
9	3	3	2

Based on the design of the L^9 orthogonal array, the experiments were performed and the data obtained is shown in Table 6.

Table 6: Response Table

TRIALS	FACTORS			Material Loss (Kg)		
	A	B	C	Rep. 1	Rep. 2	Average
1	1.25%	143	40	5.90	5.96	5.93
2	1.25%	145	50	4.33	4.41	4.37
3	1.25%	147	60	7.98	8.10	8.04
4	1.50%	143	50	6.46	6.54	6.50
5	1.50%	145	60	5.28	5.52	5.40
6	1.50%	147	40	4.84	5.08	4.96
7	1.75%	143	60	4.49	4.67	4.58
8	1.75%	145	40	1.92	2.20	2.06
9	1.75%	147	50	5.40	5.66	5.53

Table 7: Analysis of Variance for Material Loss in Compression Stage

Source of Variation	DOF	SS	MSS	F Value	F Table Value
Moisture Content	2	6.9173	3.4586	3.89	3.11*
Binder Quantity	2	8.2259	4.1129	4.63	
Sieve Size	2	4.4702	2.2351	2.51	
Error	2	1.7785	0.8892		
Total	8	21.3918			

* - F Table value obtained for $dof_1 = 2$, $dof_2 = 8$, $\alpha = 0.1$

Improve

This phase involves improving process performance characteristics by addressing and eliminating the root causes/defects for achieving desired results and goals. This phase involves application of scientific tools and techniques for making tangible improvements in profitability and customer satisfaction.Having identified the factors leading to the loss of material, steps were taken to single out the exact levels of these factors which would fetch minimal material loss. This is done by plotting graphs for means and SN ratios.

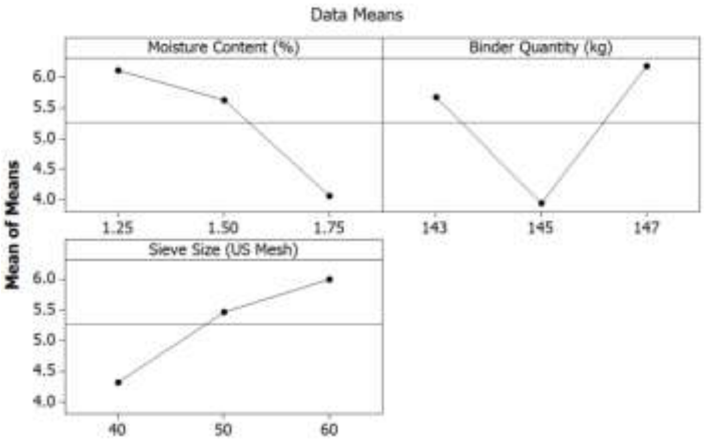

Fig 5: Main Effect Plot for Material Loss

From the main effect plot for means shown in Fig.5 it can be seen that moisture content of 1.75%, binder quantity of 145 kg and sieve size of 40 US Mesh gives the lowest amount of material loss. The same results can be confirmed by looking at the main effects plot for SN ratios shown in Fig. 6 wherein the same levels of the factors are above the SN ratio line.

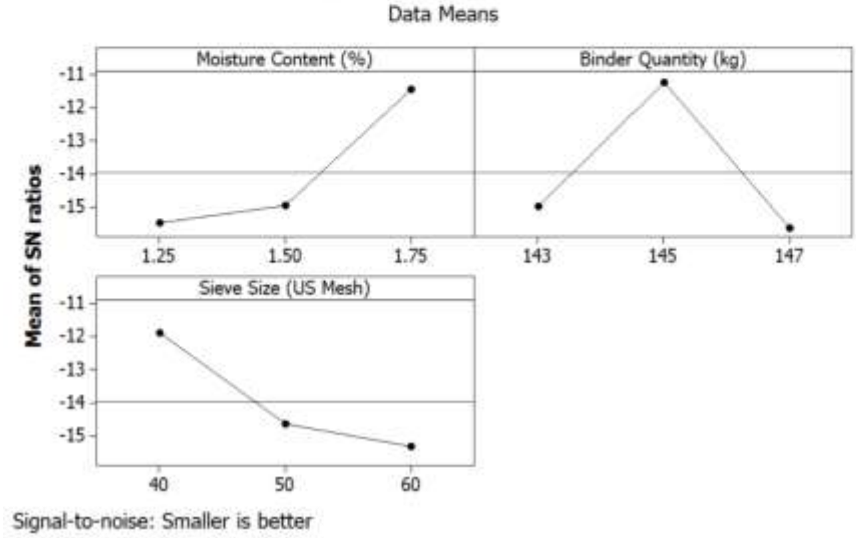

Fig 6: Main Effect Plot for SN Ratios

In order to improve the process better another improvement is suggested in the compression process. While the material is fed in the hopper during the compression process some of the material is carried away by the air blown through the air conditioner duct, which is placed just opposite to the hopper. Hence it is planned to install an air deflector, as shown in Fig. 7 such that the direction of the air flow does not meet the hopper.

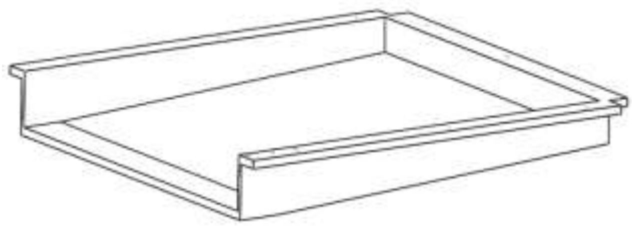

Fig 7: Air Deflector

Now the compression stage is upgraded with two improvements, the first one being the new set of optimal parameters obtained through the main effect plots of means and main effects plot for SN ratios and the latter one is the diversion of the wind direction through an air deflector. In order to compare the amount of material loss in compression stage before and after improvement in process, new set of data is collected by running the process using the new optimal set of parameters. Table 7 shows the amount of material loss in compression collected for 10 batches of production, where each batch consists of 1 million tablets.

Table 8: Material Loss in Compression Stage after Improvement

Batch	1	2	3	4	5	6	7	8	9	10
Material Lost (kg)	0.70	0.64	0.64	0.66	0.67	0.62	0.70	0.66	0.62	0.67

Table 2 shows the sigma levels for the corresponding DPMO.Now comparing the amount of material loss in the compression stage after improvement with that of before improvement it can be inferred that the sigma level has improved from 3.68 to 4.07. Hence a considerable improvement has been made in the process thus leading to the reduction in the amount of material loss.

Cost - Benefit Analysis
The cost benefit analysis is carried out to estimate the net savings that will be obtained once the improvement methods have been put into place.

Hence, For the Compression process, the mean value for material saved is expected to be 4.795 kg [3.395 kg as per DOE suggestions and 1.4 kg by using a wind deflector].

No. of Tablets manufactured per batch	=	1,000,000 tablets.
No. of Tablets that can be manufactured using saved material	=	7,376 tablets
Now of tabletsin each strip	=	10 tablets.
No. of Strips of saved material per batch	=	737 strips.
Cost price per strip	=	Rs. 13.5/-
Cost saved per batch	=	Rs. 9,950/-
No. of batches of production every month	=	15 batches
No. of batches of production every year	=	180 batches
Cost saved per year	=	**Rs. 17,91, 000/-**

Control

The purpose of this step is to standardize the improved process and deploy process controls. This phase requires the process conditions to be properly documented and monitored through statistical process control methods. Depending upon the results of such a follow-up analysis, it may be sometimes necessary to revisit one or more of the preceding phases.Control phase is about sustaining the changes made in the Improve phase. Monitor the improvements to ensure continued and sustainable success. Create a control plan which encompasses process settings, setup procedures, etc., requiring that employees follow specific requirements in daily operations – these items are typically documented in a control plan.
For the purpose of the project, a simple checklist as shown in Table 9was formulated in order that the operators working on the floor can follow the checklist and obtain desired results with regard to yield of production.

Table 9: Control Checklist

S.No.	Particulars	Checking to be done
Dispatch Checklist		
1.	Material Sent Out	As per the constituents of the table
Sieving Checklist		
2.	Sieve size used	40 US Mesh
3.	Sieve condition	Visual inspection for any damage or wear
Fluid Bed Dryer Checklist		
4.	Pressure	To be maintained at 14 bar
5.	Drying Time	To be dried for 24 minutes and moisture level to be maintained at 1.75%
6.	Drying Temperature	Maintain 68°c
Lubrication Checklist		
7.	Amount of binder material used	145 kg
Before Compression Checklist		
8.	Pressure	As set by the manufacturer
9.	Machine rpm	As per the manufacturer instructions
10.	Feed frame adjustment	Adjust for perfect alignment with cavity
11.	Die check	Check alignment Check for signs of wear
12.	Vibration	To be kept minimal

III. Conclusion

This research focused on reducing the amount of material loss in the tablet production process and thereby increasing the sigma level using DMAIC approach. The vital factors causing material loss were identified and an DOE was conducted to get the optimal set of parameters. In addition to that, a wind deflector is also designed and installed to divert the air flow direction which added up in the amount of material saved. In total, the average amount of material saved in the compression process was reduced to 0.66 kg from 5.455kg. This increased the sigma level from 3.68 to 4.07. Finally, in order to have a control on the process, a process control check list is made. This sigma level can be further improved by doing focusing on other stages of the table production process.

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