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Applications of Six-Sigma in Pharmaceutical Industries

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Abstract
Six Sigma is one of the most evolutionary methods used by present manufacturing organizations. Motorola Company first implemented it. Toyota Motor Company used Toyota Production System which resulted in highly improvised quality products and waste minimization. Thus, it achieved one-in-one million defects. In Pharmaceutical Industries slightest error can have a disastrous and hazardous impact on human health. Hence Six Sigma methodology plays an important role in Pharmaceutical Industries as it results in 99.9997 % accuracy rate. We have applied Six Sigma & process capability into pharmaceutical process i.e. metals in tablets during coating operation. We have used DMAIC as a Six Sigma methodology. Some of the preventive measures are taken. This Paper depicts the applications of Six Sigma in Pharmaceutical industries.

Keywords
Six Sigma, Process Capability, DMAIC, Pharmaceutical process

I. Introduction

A process is a combination of man, machine, materials and methods for producing a desirable & measurable output. Processes are evaluated by statistical methods and must have inherent statistical variability. Six-sigma is a highly disciplined process that enables organizations to deliver nearly perfect products & services. It's a quality philosophy & the way of improving performance by knowing where you are & where you could be. It is considered as a philosophy & a goal, as perfect as practically possible, to improve the performance. At six sigma level, there are 3.4 defects occurred per million opportunities. Six sigma is implemented by six sigma project initiation & six sigma infrastructure creations in process. The paper will be a guideline for decision maker of pharmaceutical industries.

II. Literature Review

Table 1:

AUTHORS	FOCUS
1. Sharma O.P, Gupta V.,Rathore G.S., Saini N.K.,Sachdeva K. (2011)	Six sigma in Pharmaceutical industry & Regulatory Affairs : A Review
2. Mohammed Raihan Chowdhury (2013)	Process capability Analysis in Pharmaceutical production
3. Asmita S. Joshi(2012)	Six sigma implementation using DMAIC approach
4. Dreachslin, Janice L;Lee,Pegg D. (2007)	Applying Six sigma & DMAIC to diversity Initiatives
5. Rahem M.Haleem, Maissa Y.Salem, Fateh A. Fatahallah, Laila E. Abdelfattah (2014)	Quality in tha pharmaceutical industry- A literature review
6. Promote Cholayudth (2013)	C_{pk} Distribution : The fact Underlying process capability Indices

III. Applications of Six-Sigma in Pharmaceutical Process

The application of six sigma in pharmaceutical process are reduction of waste, effective change in manufacturing process to increase the operational efficiency; which further increase the quality products & improve customer service. The desired specification and requirement of a product or service met by the process is called process capability. Process capability index is the ability of the process to produce measurable output within specification constraints. It is denoted by C_{pk}. The natural variation experienced by a process with respect to its specification limits are measured by process capability index. Process capability indices are formed to express highly desirable capability with an ascending higher value. The values present near or below zero highlights that process is operating at higher variation. Toyota implemented Process capability index by Just-In-Time (JIT) philosophy which is one of the concept of Toyota Production System (TPS). TPS is also known as Thinking People System. This methodology allows an organization to improve competitiveness in business via improved product quality, reliability of delivery and reduced product costs.

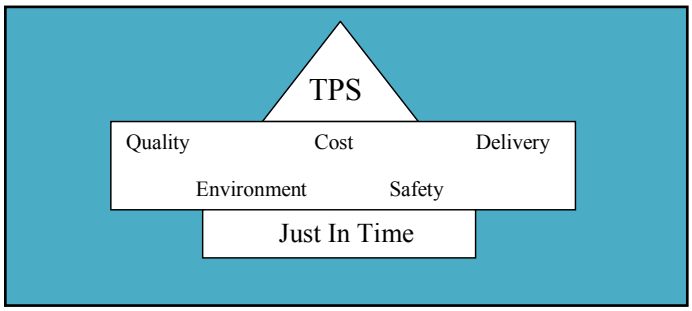

Fig. 1: Toyota Production System

A tablet is a pharmaceutical dosage form which consists of a mixture of active as well as natural or synthetic substances in a powdered form, pressed or compacted form from a powder into a solid dose. The coating in tablets consists of one or multi layer of mixture of various substances like natural or synthetic resins, inactive and insoluble filler, gum, sugar, plasticizer, polyhydric materials, alcoholic contents, waxes, authorized coloring material & sometimes flavored material & may also some active ingredients. Sugar coating or film coating are generally two types of tablet coating. Sugar coating was mostly used in past & film coating is being used in present years.

Generally these tablet coatings are done to:

- Protect the tablet from stomach acids
- For maintain the shape of the tablet
- Protect stomach lining from aggressive drugs
- Delays the release of the medication

To improve the longevity of the handling of the tablet, the tablet must be strong and stable. Tablets must not stick together during the coating process, and should follow the fine contours of logos on tablets. Coatings are done in tablets to eliminate unpleasant taste, and for smoother finishing which makes large tablets easier to swallow. Brand recognition can be improved by special

coating.
The coatings can be specially formulated to regulate how fast the tablet dissolves & where the active drugs are to be absorbed into the body after ingestion.
Tablet coating processes are takes place in a controlled atmosphere inside a perforated rotating drum & usually performed by a batch driven tasks consisting of the following phases:

- Batch identification and recipe selection (sugar/film coating)
- Dispensing i.e. accurate dosage of required raw materials
- Warming
- Spraying

IV. DMAIC

DMAIC is a data driven quality improvement strategy to enhance the efficiency and effectiveness of process (es). It reduces the cost as well as time variation & improve defect free performance about a target to drive a project in a short run (three-nine months) i.e. it addresses PFQT [P=Productivity (how many), F=Financial (how much money), Q=Quality (how well) & T=Time (how fast)]. This tool is encouraged & promoted by Juran to optimize, stabilize & improve the processes. It's one of the six sigma methodologies followed by Deming's PDCA (Plan-Do-Check-Act) cycle.

DMAIC generally includes the following 5 phases (fig.1):

Fig. 2: Phases of DMAIC

A. Define Phase

In Define Phase We are going to Define the Problem namely

1. What is Metal in Tablets?

The residues of Metals that can be present in the original form of the metal or in the form of Metallic element in the tablets is known as Metal in Tablets.

2. How Metal enters in the Tablets?

A metal enters the tablets by various causes. They are:

- Wear Particles generated from Processing Machinery
- Inputs from raw materials
- Inefficient handling by the workforce.
- Absence of modern technologies in detecting metals

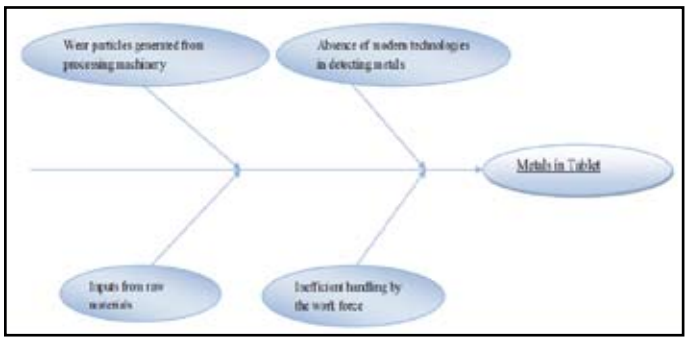

Fig. 3: Fish-Bone Analysis of Metals in Tablet

3. How are Metals Classified as Per Their Toxic Level?

Metals are classified into 3 categories based on their severity of impact on the human health.
Class 1 Metals: Metals with significant safety concern.
Class 2 metals: Metals with low safety concern .Metals with lower toxic level. They are generally well tolerated up to exposure. They may be found as trace metals. Class 3 metals: Metals with minimal safety concern. Metals with no significant toxicity.

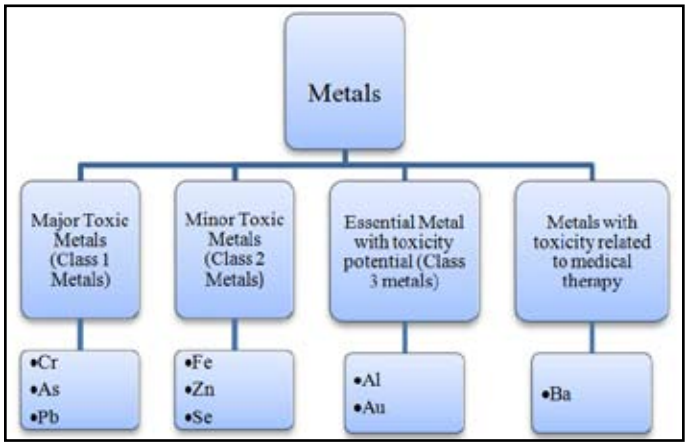

Fig. 4: Types of Metals as Per the Toxic Levels it Contained

B. Measure Phase

In this phase we are going to perform various operations:

- Estimating the weight of the tablet which is found to be 300 mg (Theoretical value)
- Raw material checking
- Coating Material Analysis
- In-Process Test

1. Processes to Find Metals in Tablets

(i). Assay

It is an analytical process in Pharmaceutical Industries for qualitative or quantitative assessment and measurement of the presence of the analyte. The analyte can be a drug or biochemical substance. The measured entity is generally called the analyte. The intensive property of the analyte is measured by the Assay like molarity, density etc.
General steps of any assay
An assay is a process and consisting of pre- and post analytic procedures. The pre analytic procedures consist of a request to perform an assay and further information processing or specimen handling (e.g. collection transport and processing).Preanalytic steps consist of step by step documentation, verification of results.
Assays can be very diverse, but generally involve the following general steps:

- **Sample processing/manipulation:** In order to selectively present that target in a discernible/measurable form to a discrimination/identification/detection system. It might involve a simple centrifugal separation or washing or filtration or capture by some form l
- **Target specific DISCRIMINATION/IDENTIFICATION principle:** To discriminate from background (noise) of similar components and specifically identify a particular target component ("analyte") in a biological material by its specific attributes.
- **Signal (or target) AMPLIFICATION System:** The presence and quantity of that analyte is converted into a detectable signal generally involving some method of signal amplification, so that it can be easily discriminated from noise and measured.
- **Signal DETECTION (and interpretation) system:** A system of deciphering the amplified signal into an interpretable output that can be quantitative or qualitative. It can be visual or manual very crude methods or can be very sophisticated electronic digital or analog detectors.
- **Signal enhancement and noise filtering:** It may be done at any/all of the steps above. Since the more downstream a step/ process during an assay, the higher the chance of carrying over noise from the previous process and amplifying it, multiple steps in a sophisticated assay might involve various means of signal-specific sharpening/enhancement arrangements and noise reduction or filtering arrangements.

(ii). Heavy Metal Testing

Metal ions can affect the stability of the formulation, catalyze the degradation of the active pharmaceutical ingredient (API) and cause unqualified degradates to form, or pose a toxicity threat on their own.

Methods used for Heavy Metal Testing:
USP<231> is a traditional Metals Test in Pharmaceutical industries. It is a limit test for heavy metals in samples. It is a qualitative (at best semi-quantitative) test that indicates the content of metallic impurities by colored sulfide precipitate.
Elements for which the method can be used are silver, arsenic, bismuth, cadmium, copper, mercury, molybdenum, lead, antimony, and tin. It is over 100 years old (circa 1905).It uses Colorimetric method.

USP<231> Sample Preparation Three different sample preparation techniques can be utilized for USP<231>, depending on the sample type

- Method I
It is used for samples that are clear colourless solutions. After the addition of a sulphide reagent, the colour is compared to both a standard as well as a sample spiked at the limit.

– Method II
Solid organic samples are heated with sulphuric acid and residual carbon is burned in a muffle furnace. Metals are then extracted from the residue. Analysis is free from any organic interference.

– Method III
Solids are first digested with a mixture of sulphuric and nitric acid. Then treated with hydrogen peroxide to ensure complete oxidation.
(Methods II and III are very aggressive and lead to loss of target analytes.)
(Source: Agilent Technologies USP Webinar Dec 8, 2010)
(iii). Varian Atomic Absorption (AA) and Inductively Coupled Plasma Optical Emission Spectrometry (ICP-OES) along with Agilent's ICP-MS products provides a complete portfolio for routine and research analysis in Pharmacy sector.
(iv). CU: CU stands for Contents of Uniformity, is a pharmaceutical analysis technique for the quality control of tablets. Here multiple tablets are selected at random and a suitable analytical method is applied to assay the individual content of active ingredient in each tablet.
(v). Using Scanning Electron Microscopy (SEM)/ Energy Dispersive X-Ray Spectrometer (EDS)To Positively Identify the Contaminant
Electrons are used to form an image in SEM. Electrons are bombarded into the sample, and atoms in the sample interact with the electrons to produce secondary electrons and backscattered electrons. Detectors are used to collect the electrons which produce a high-quality morphological image showing the physical features of a sample. Backscattered electron signal are used to distinguish metal material and organic materials.
X-Rays from the sample are generated from the electron beam of the SEM. An unique x-ray pattern is found, The x-rays are collected from the EDS Detector and their energies are analyzed.

C. Analyze Phase

Metals are generated from equipment. The clearance between the baffles and coating pan is very less. So there is an attrication between both of them. So, the metal particles are generated and they are incorporated into the tablets. Henceforth they are coated away along with the coating materials.

D. Implementation Phase

We have to increase the clearance between the baffles and coating pan so that the metal generation from the equipment can be controlled.

E. Control Phase

We have to go for process capability index at the start of every process. Samplings of 75 tablets are taken for every 30 minute during the coating process and in-process QC parameters are checked.
The distance between the baffle & the coating pan was increased to a distance of 0.5mm & the process verification was carried out. The data are as follows:

PRESS QUALIFICATION STUDY

Product Name	Misoprostol Tablets USP 300 mg				
Product #	3	Rev.		Lot #	
Scientists	Sujit Kumar Acharya	&	Archita Laha		

Press #		Pre-comp		Pnch Pen	
Date	20.09.2014	Pad spd		Tooling Rating	

	Weight	Thick	Hard
Target	300	2.5	10
Low Limit	285.000	2.2	5
Up. Limit	315.000	2.8	15

Note: default weight limits are +/- 5% for individuals

Press Speeds (RPM)	
LOW	2
HIGH	5

55 station Manesty Mark IV

LEFT

	WEIGHT		HARDNESS		THICKNESS	
	LOW	HIGH	LOW	HIGH	LOW	HIGH
AVG	311.680	311.800	11.1	11.1	2.500	2.500
STD	6.579	6.386	0.7	0.7	0.064	0.064
Cpk	0.17	0.17	1.84	1.84	1.57	1.57
Adj. Cpk			3.35	3.35		
Cpl	1.35	1.40	2.88	2.88	1.57	1.57
Cpu	0.17	0.17	1.84	1.84	1.57	1.57
Cp	0.76	0.78	2.36	2.36	1.57	1.57
Adj. Cp			4.29	4.29		
R-bar	19.0000	19.0000	2.00	3.68	0.2000	0.2000

RIGHT

	WEIGHT		HARDNESS		THICKNESS	
	LOW	HIGH	LOW	HIGH	LOW	HIGH
AVG	311.800	331.900	11.1	11.1	2.500	2.630
STD	6.386	32.924	0.7	0.7	0.064	0.192
Cpk	0.17	-0.17	1.84	1.84	1.57	0.30
Adj. Cpk			3.35	3.35		
Cpl	1.40	0.47	2.88	2.88	1.57	0.75
Cpu	0.17	-0.17	1.84	1.84	1.57	0.30
Cp	0.78	0.15	2.36	2.36	1.57	0.52
Adj. Cp			4.29	4.29		
R-bar	19.0000	118.0000	2.00	2.00	0.2000	0.6000

SPC Limits

	upper	lower	upper	lower
Adjust limits	313.475	286.525	11.40	8.60
Retest limits	306.001	293.999	15.1	4.9
Range limit	77.744		3.9	

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2.0 RPM
LEFT SIDE

Product Name	Misoprostol Tablets USP 300 mg					
Product #	001	Rev.	0	Lot #	1	
Scientists	Sujit Kumar Acharya			&	Archita Laha	
Press #	12			Pre-comp	0	
				Pad spd		
				Pnch Pen	0	
				Tool Rate	0	

	Weight	Thick	Hard
Target	300	2.5	10
Low Limit	285.000	2.2	5
Up. Limit	315.000	2.8	15

0 minute

	Weight	Hardness	Thickness
1	300.000	10.0	2.5
2	309.000	11.0	2.4
3	310.000	12.0	2.4
4	302.000	11.0	2.5
5	312.000	11.0	2.5
6	314.000	12.0	2.5
7	316.000	11.0	2.6
8	317.000	12.0	2.6
9	319.000	11.0	2.5
10	319.000	10.0	2.5
Avg.	311.800	11.1	2.500
Range	19.000	2.0	0.200

5 minute

	Weight	Hardness	Thickness
1	300.000	10.0	2.5
2	300.000	11.0	2.4
3	310.000	12.0	2.4
4	302.000	11.0	2.5
5	312.000	11.0	2.5
6	314.000	12.0	2.5
7	316.000	11.0	2.6
8	317.000	12.0	2.6
9	319.000	11.0	2.5
10	319.000	10.0	2.5
Avg.	310.900	11.1	2.500
Range	19.000	2.0	0.200

10 minute

	Weight	Hardness	Thickness
1	300.000	10.0	2.5
2	312.000	11.0	2.4
3	310.000	12.0	2.4
4	302.000	11.0	2.5
5	312.000	11.0	2.5
6	314.000	12.0	2.5
7	316.000	11.0	2.6
8	317.000	12.0	2.6
9	319.000	11.0	2.5
10	319.000	10.0	2.5
Avg.	312.100	11.1	2.500
Range	19.000	2.0	0.200

15 minute

	Weight	Hardness	Thickness
1	300.000	10.0	2.5
2	309.000	11.0	2.4
3	310.000	12.0	2.4
4	302.000	11.0	2.5
5	312.000	11.0	2.5
6	314.000	12.0	2.5
7	316.000	11.0	2.6
8	317.000	12.0	2.6
9	319.000	11.0	2.5
10	319.000	10.0	2.5
Avg.	311.800	11.1	2.500
Range	19.000	2.0	0.200

20 minute

	Weight	Hardness	Thickness
1	300.000	10.0	2.5
2	309.000	11.0	2.4
3	310.000	12.0	2.4
4	302.000	11.0	2.5
5	312.000	11.0	2.5
6	314.000	12.0	2.5
7	316.000	11.0	2.6
8	317.000	12.0	2.6
9	319.000	11.0	2.5
10	319.000	10.0	2.5
Avg.	311.800	11.1	2.500
Range	19.000	2.0	0.200

2 RPM
RIGHT SIDE

Product Name	Misoprostol Tablets USP 300 mg					
Product #	003	Rev.		Lot #		
Scientists	Sujit Kumar Acharya			&	Archita Laha	
Press #				Pre-comp		
				Pad spd		
				Pnch Pen	0	
				Tool Rate	0	

	Weight	Thick	Hard
Target	300	2.5	10
Low Limit	285.000	2.2	5
Up. Limit	315.000	2.8	15

0 minute

	Weight	Hardness	Thickness
1	300.000	10.0	2.5
2	309.000	11.0	2.4
3	310.000	12.0	2.4
4	302.000	11.0	2.5
5	312.000	11.0	2.5
6	314.000	12.0	2.5
7	316.000	11.0	2.6
8	317.000	12.0	2.6
9	319.000	11.0	2.5
10	319.000	10.0	2.5
Avg.	311.800	11.1	2.500
Range	19.000	2.0	0.200

5 minute

	Weight	Hardness	Thickness
1	300.000	10.0	2.5
2	309.000	11.0	2.4
3	310.000	12.0	2.4
4	302.000	11.0	2.5
5	312.000	11.0	2.5
6	314.000	12.0	2.5
7	316.000	11.0	2.6
8	317.000	12.0	2.6
9	319.000	11.0	2.5
10	319.000	10.0	2.5
Avg.	311.800	11.1	2.500
Range	19.000	2.0	0.200

10 minute

	Weight	Hardness	Thickness
1	300.000	10.0	2.5
2	309.000	11.0	2.4
3	310.000	12.0	2.4
4	302.000	11.0	2.5
5	312.000	11.0	2.5
6	314.000	12.0	2.5
7	316.000	11.0	2.6
8	317.000	12.0	2.6
9	319.000	11.0	2.5
10	319.000	10.0	2.5
Avg.	311.800	11.1	2.500
Range	19.000	2.0	0.200

15 minute

	Weight	Hardness	Thickness
1	300.000	10.0	2.5
2	309.000	11.0	2.4
3	310.000	12.0	2.4
4	302.000	11.0	2.5
5	312.000	11.0	2.5
6	314.000	12.0	2.5
7	316.000	11.0	2.6
8	317.000	12.0	2.6
9	319.000	11.0	2.5
10	319.000	10.0	2.5
Avg.	311.800	11.1	2.500
Range	19.000	2.0	0.200

20 minute

	Weight	Hardness	Thickness
1	300.000	10.0	2.5
2	309.000	11.0	2.4
3	310.000	12.0	2.4
4	302.000	11.0	2.5
5	312.000	11.0	2.5
6	314.000	12.0	2.5
7	316.000	11.0	2.6
8	317.000	12.0	2.6
9	319.000	11.0	2.5
10	319.000	10.0	2.5
Avg.	311.800	11.1	2.500
Range	19.000	2.0	0.200

5 RPM
LEFT SIDE

Product Name	Misoprostol Tablets USP					Weight	Thick	Hard
Product #	003	Rev.	Lot #	3	Target	300	2.5	20
Scientists	Sujit Kumar Acharya		&	Archita Laha	Low Limit	285.000	2.2	5
				Pre-comp	Up. Limit	315.000	2.8	15
Press #				Pad spd				
				Pnch Pen	0			
				Tool Rate	0			

	0 minute			5 minute			10 minute		
	Weight	Hardness	Thickness	Weight	Hardness	Thickness	Weight	Hardness	Thickness
1	300.000	10.0	2.5	300.000	10.0	2.5	300.000	10.0	2.5
2	309.000	11.0	2.4	309.000	11.0	2.4	309.000	11.0	2.4
3	310.000	12.0	2.4	310.000	12.0	2.4	310.000	12.0	2.4
4	302.000	11.0	2.5	302.000	11.0	2.5	302.000	11.0	2.5
5	312.000	11.0	2.5	312.000	11.0	2.5	312.000	11.0	2.5
6	314.000	12.0	2.5	314.000	12.0	2.5	314.000	12.0	2.5
7	316.000	11.0	2.6	316.000	11.0	2.6	316.000	11.0	2.6
8	317.000	12.0	2.6	317.000	12.0	2.6	317.000	12.0	2.6
9	319.000	11.0	2.5	319.000	11.0	2.5	319.000	11.0	2.5
10	319.000	10.0	2.5	319.000	10.0	2.5	319.000	10.0	2.5
Avg.	311.800	11.1	2.500	311.800	11.1	2.500	311.800	9.5	2.500
Range	19.000	2.0	0.200	19.000	2.0	0.200	19.000	10.4	0.200

SREL% Ma: 11.6

	15 minute			20 minute		
	Weight	Hardness	Thickness	Weight	Hardness	Thickness
1	300.000	10.0	2.5	300.000	10.0	2.5
2	309.000	11.0	2.4	309.000	11.0	2.4
3	310.000	12.0	2.4	310.000	12.0	2.4
4	302.000	11.0	2.5	302.000	11.0	2.5
5	312.000	11.0	2.5	312.000	11.0	2.5
6	314.000	12.0	2.5	314.000	12.0	2.5
7	316.000	11.0	2.6	316.000	11.0	2.6
8	317.000	12.0	2.6	317.000	12.0	2.6
9	319.000	11.0	2.5	319.000	11.0	2.5
10	319.000	10.0	2.5	319.000	10.0	2.5
Avg.	311.800	11.1	2.500	311.800	11.1	2.500
Range	19.000	2.0	0.200	19.000	2.0	0.200

5 RPM
RIGHT SIDE

Product Name	Misoprostol Tablets USP 300 mg					Weight	Thick	Hard
Product #	003	Rev.	Lot #		Target	300	2.5	10
Scientists	Sujit Kumar Acharya		&	Archita Laha	Low Limit	285.000	2.2	5
				Pre-comp	Up. Limit	315.000	2.8	15
Press #				Pad spd				
				Pnch Pen	0			
				Tool Rate	0			

	0 minute			5 minute			10 minute		
	Weight	Hardness	Thickness	Weight	Hardness	Thickness	Weight	Hardness	Thickness
1	322.000	10.0	3.0	322.000	10.0	3.0	322.000	10.0	3.0
2	321.000	11.0	2.9	321.000	11.0	2.9	321.000	11.0	2.9
3	343.000	12.0	2.4	343.000	12.0	2.4	343.000	12.0	2.4
4	312.000	11.0	2.8	312.000	11.0	2.8	312.000	11.0	2.8
5	309.000	11.0	2.5	309.000	11.0	2.5	309.000	11.0	2.5
6	301.000	12.0	2.5	301.000	12.0	2.5	301.000	12.0	2.5
7	354.000	11.0	2.6	354.000	11.0	2.6	354.000	11.0	2.6
8	419.000	12.0	2.6	419.000	12.0	2.6	419.000	12.0	2.6
9	319.000	11.0	2.5	319.000	11.0	2.5	319.000	11.0	2.5
10	319.000	10.0	2.5	319.000	10.0	2.5	319.000	10.0	2.5
Avg.	331.900	11.1	2.630	331.900	11.1	2.630	331.900	11.1	2.630
Range	118.000	2.0	0.600	118.000	2.0	0.600	118.000	2.0	0.600

SREL% Ma: 9

	15 minute			20 minute		
	Weight	Hardness	Thickness	Weight	Hardness	Thickness
1	322.000	10.0	3.0	322.000	10.0	3.0
2	321.000	11.0	2.9	321.000	11.0	2.9
3	343.000	12.0	2.4	343.000	12.0	2.4
4	312.000	11.0	2.8	312.000	11.0	2.8
5	309.000	11.0	2.5	309.000	11.0	2.5
6	301.000	12.0	2.5	301.000	12.0	2.5
7	354.000	11.0	2.6	354.000	11.0	2.6
8	419.000	12.0	2.6	419.000	12.0	2.6
9	319.000	11.0	2.5	319.000	11.0	2.5
10	319.000	10.0	2.5	319.000	10.0	2.5
Avg.	331.900	11.1	2.630	331.900	11.1	2.630
Range	118.000	2.0	0.600	118.000	2.0	0.600

QUALIFICATION RESULTS:

Qualified Weight Range	285.000	-	315.000	Gms
Qualified Thickness Range	2.200	-	2.800	Inches
Qualified Hardness Range	5.0	-	15.0	SCU
Qualified Speed Range	2	-	5	RPM

From the process verification phase, the values are found to be $C_p <$ 2 & $C_{pk} \leq 1.33$. This shows the process is out of control limits. So, some additional measures are to be taken to control the process. They are:

1. Maintain the differential pressure between the coating pan and external environment.
2. Increase in the exhaust fan speed so as to pull up the metal particle from the coating pan.
3. Optimizing the coating pan speed.
4. Providing an additional layer coating of Poly vinyl spirolidum (K-30) in the coating pan.

By incorporating the above measure, coating level of the process is found to be within the control & the C_p, C_{pk} limits were found to be >1.33 ,which shows the process is within the control limits.

V. Conclusion

Metals in tablets are very much injurious to health. It causes Heavy metal poisoning which is related to all the diseases related to nerves and brain (E.g. Head ache, weakness, muscle and joint pain, constipation, etc.). Even these metals are enters into the food chain and affect the offspring's. To manage this problem, this paper emphasizes on six sigma methodology to decrease the metal coating thickness upto certain QC limits. Also the C_p & C_{pk} values are evaluated. In our data, these process capabilities & its indices are out of control. Therefore, we have suggested some additional measures by following which the process can be controlled in this paper.

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