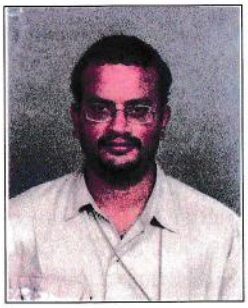
Application of Lean Concepts in a Process Industry — Case Study of Performance Improvement through Lean in Bulk Drug Manufacturing

Lean Manufacturing philosophy, with its origins in the Toyota Production System (TPS), has been well established world wide as a way to improve operational performance in the automotive and other discrete manufacturing sectors. However, there is a lot of scepticism in implementing lean in process industries where manual intervention is a bare minimum.

This paper seeks to dispel such doubts through practical case examples of lean based process improvement undertaken in bulk drug manufacturing. It touches upon how the lean paradigm can be used in such process industries to understand the current state and identify potential areas for improvement. It also details actual improvement projects to explain the application of the core Lean concept of waste elimination. In Lean, waste is defined through the 3Ms – Muda (non value adding activities), Muri (Physical strain or stress) and Mura (inconsistency).

This experience of practical implementation is used to share some of the differences in how lean is applied in process industry as compared to discrete manufacturing. However, it would be premature to draw specific conclusions from this paper as it is based on a small sample of bulk drug manufacturing units. The findings would need to be validated through a much more comprehensive study of lean implementation in various sectors of process manufacturing.

This paper is however useful in throwing some light on applicability and benefits of implementing Lean in sectors which have traditionally not been exposed to this widely proven management philosophy.



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1. Introduction

The Indian pharmaceutical industry has grown rapidly over the past decade with the opening up of the global market. This has in turn driven the expansion of the supply chain as pharmaceutical majors developed vendors to supply the various intermediates required by them. These manufacturers of bulk drugs and intermediates are mostly MSMEs and as their volumes rise, they often struggle to meet the customer expectations of on time delivery. The main constraints are the need to invest in expanding facilities including Effluent Treatment Plants and the lack of skilled workforce to operate and maintain the same. In addition, aspects like safety, environment and working conditions in their plants are often neglected and this has a negative impact on the people working in the unit as well as those who live or work in nearby areas.

The bulk drug industry follows a process manufacturing method. The typical process involves material synthesis in reactors, separation of the liquid phase in centrifuges and drying of the wet product mass in dryers before the final dry product is packed. In certain cases, milling and grinding of dry product may be done and the fine powder is packed and dispatched to the customer. The liquid by products from the centrifuges / filters may undergo distillation process during which solvent recovery happens. The unwanted part is finally sent to effluent treatment plants and may be either completely treated and discharged from the factory itself or may be partially treated and sent to common treatment facilities.

Since manual intervention is highly limited, there are very few documented cases of implementation of well established process improvement methodologies like Lean in this industry. One such case is that of pharmaceutical giant Dr. Reddy's (DRL) implementing Theory of Constraints (TOC) to improve supply chain performance [(1)]. However, even the vendors of DRL, mainly of the Small and Medium Enterprise (SME) category, were highly sceptical about its potential to improve their own processes. Lean with its origins in the Toyota Production System has been widely applied across discrete manufacturing sectors and these have been well documented. There is however a question mark on whether it has relevance and is useful as an improvement philosophy in process industries. This article seeks to dispel any such doubts about the applicability of Lean in process / continuous plants and its ability to deliver significant benefits to them. The article is based on the practical implementation of Lean in a cluster of bulk drug units and highlights how some well known lean tools and techniques are applied for operations improvement in this type of manufacturing process.

The Lean Manufacturing Paradigm

Lean manufacturing is a philosophy born out of the Toyota Production System (TPS) [(2)]. The core concept of Lean is to ensure flow of material through the supply chain thereby increasing the throughput while reducing the lead time from order to cash. This is achieved by observing the process, identifying and eliminating the hindrances to flow which are commonly referred to as Waste in the Lean context. This waste is categorised under the 3 Ms – *Muda* (non value add or waste), *Muri* (overburden or physical strain) and *Mura* (inconsistency or variation in process / product).

Table 1 — Key Differences between Discrete and Process Manufacturing

Parameter	Discrete Manufacturing	Process Manufacturing
Product	Unique, easily identifiable, measured in numbers	Undifferentiated, measured in terms of weight or volume
Operations	Not continuous, each can operate independently at its own rate	Continuous, all the steps are generally linked
Key components	Assembly of parts, Bill of Materials	Mixing of ingredients, recipes / formulations
Outcome	Reversible, parts can be reused as mainly physical change only	Irreversible, often chemical change

The automotive and engineering industries are discrete in nature as opposed to the process manufacturing of bulk drugs. Some of the key differences in the nature of these two major types of manufacturing are highlighted in Table 1 and are likely to impact how Lean is applied to each of them.

With its origins in TPS, most of the Lean tools and techniques like SMED, workstation design, line balancing and error proofing were initially developed to improve flow of material in the machining centres, press shops and assembly lines [(3)].

However, in a process industry such as chemical, oil or pharmaceutical, material flow is already an integral part of the manufacturing by design. All the steps are already linked and the process can be called Lean by nature. So is there any scope for the existing lean tools and techniques to be implemented here for significant gains? Let us now understand this through a few case examples from the bulk drug manufacturing units that illustrate the lean journey from current state

assessment to improvement and standardization. This Lean implementation was done in a mini cluster of three bulk drug units and this article includes examples from each of the units.

Current State Assessment & Framing Improvement Roadmap

The first step in any Lean implementation is to assess the current state with respect to the business goals and targets and identify the constraints. An improvement roadmap of projects is then framed for eliminating these constraints.

To understand the nuances of current state assessment for bulk drug manufacturing, we will take the case of Manufacturing Unit 1 which was producing about 28 TPM (Tons per month) of Product AA for a European customer. In the coming year, the customer indicated willingness to take up to 40 TPM. In a bid to increase output quickly without having to invest in new infrastructure, Unit 1 decided to improve existing processes in order to meet customer demand. A Value Stream Map (VSM)[4] was developed to assess the current state for product AA which is manufactured through a series of processes.

In a discrete environment, VSM is made using data from practical observation; cycle times and changeover times are recorded by observing the process when it is on. Most of the cycle times are in seconds or minutes and this is practically feasible.

In the pharmaceutical industry, the reaction cycle times are often of the order of several hours and the process is not visible. However, it is mandatory to maintain a detailed batch record and in this case the process data from the records of recently completed batches was compiled to prepare the VSM. The steps for making current state VSM are described below.

Step 1: Identify the average market requirement for the next one year; this is taken as the target for the Value Stream. In this case, the projected customer requirement was 40 TPM of finished product AA.

Step 2: Compute batch equivalent so as to have a common output measure for all the processes. This is again a unique feature of the chemical industry. The output to input ratio is not necessarily 1 as is the case with discreet manufacturing as here each process can have a different ratio based on the chemical reaction taking place. In this case, batch size was 500 kgs but batch equivalent varied for each process.

Step 3: Convert target to *takt* time. Calculation for product AA is shown below.

Available time: 30 days x 24 hrs = 720 hours per month

Customer demand: 40 TPM ÷ 500 kgs per batch = 80 batches per month

Takt time = Available time ÷ customer demand = 720 ÷ 80 = 9 hours

Hence, the plant is expected to deliver **one batch of finished product every 9 hours** and every process in the value stream has to produce at this or faster rate.

Step 4: Compile process wise data from the batch records and put the same into VSM format. Identify constraint or bottleneck(s) processes which need to be improved. The VSM, which also depicts the manufacturing process for Product AA, was made by following these 4 steps and is shown in *Table 2*. The bottleneck processes have been highlighted and it can be seen that there is high batch to batch variation in these processes. A similar VSM made for manufacturing unit 2 for its main product PV is depicted in standard pictorial form in ***Diagram 1*** wherein the current constraints shown as clouds.

Step 5: A walk through of the shop floor to identify specific improvement opportunities with respect to the working conditions, safety and environment as well as upkeep of the plant and machinery.

Table 2 — Part of the Value Stream Map (VSM) for Product AA

Process cycle times > *takt* time and those with high variation are highlighted in the table

Process	Available equipment			Cycle time	Value Add Time	Change-over time	Hours per batch	VA ratio
	Nos	Batch equivalent		(hours)	(hours)	(hours)		
Reaction	**5**	**5**	Average	67	57	4	**13.4**	85%
			Min.	57	46	0		
			Max.	87	73	10		
Neutch Filter	**1**	**1**	Average	11	4		10.6	33%
			Min.	6	1	0		
			Max.	18	6	0		
Dissolution	**1**	**1**	Average	6	2		5.8	33%
			Min.	4	1	0		
			Max.	12	3	0		
Carbon	**3**	**1.5**	Average	18	12		**11.7**	69%
			Min.	12	8	0		
			Max.	27	20	0		
Acidification	**3**	**3**	Average	16	6		5.3	37%
			Min.	10	4	0		
			Max.	26	11	0		
Drying (Part-II)	**4**	**2**	Average	20	8		**10.0**	**39%**
(350 kgs per drier)			Min.	16	4	0		
			Max.	41	21	0		
Methanol Purification	**1**	**1**	Average	11.8	3.8		12	32%
			Min.	7.5	3	0		
			Max.	34.75	6	0		
Filtration	**3**	**3**	Average	21	12		7.0	55%
			Min.	11	4	0		
			Max.	34	21	0		
Drying Part - III	**1.5**	**1.035**	Average	21.4	8.44		**20.7**	**39%**
(350 kgs per drier)			Min.	10.5	2	0		
			Max,	30	9	0		

A lean roadmap was then made listing out the performance goals and the improvement projects to be taken up for achieving these. About 7-10 projects were identified in each of the three units, focusing on the core concept of lean of elimination of waste or the 3 M – *Muda, Muri* and *Mura*. The rest of this paper is devoted to explaining how each of these three wastes are observed, understood and reduced in the context of bulk drug manufacturing. This is done through detailing of one example each of an improvement project done for reducing these three wastes.

Improvement Projects using Lean Tools and Techniques

1. Reducing *Muda* – Minimizing batch wait time

Problem Definition

To understand the concept of *Muda* as it applies to a process plant we shall take the case of Product PV from manufacturing unit 2. The VSM shows a constraint of high cycle time in the distillation stage of the process; the cycle time is 540 minutes per batch as against *takt* time of 450 minutes per batch. A cross functional team was therefore formed to work on reducing the cycle time to below 450 minutes.

Observation & Analysis

The product is processed through 3 successive stages, each stage being carried out successively in Reactor No's 114, 115 and 116 with the key distillation process taking place in stage 2. The existing process details are shown in ***Diagram 2***. Reaction takes place in Stage I under brine based cooling condition while distillation in stage 2 needs high temperatures. After reaction, the separated organic layer is first transferred to Reactor 115. The aqueous layer is then extracted with solvent and transferred next. After this, distillation process begins in Reactor 115. There is a waiting period between the two transfers.

Diagram 1: Current State VSM for Product PV

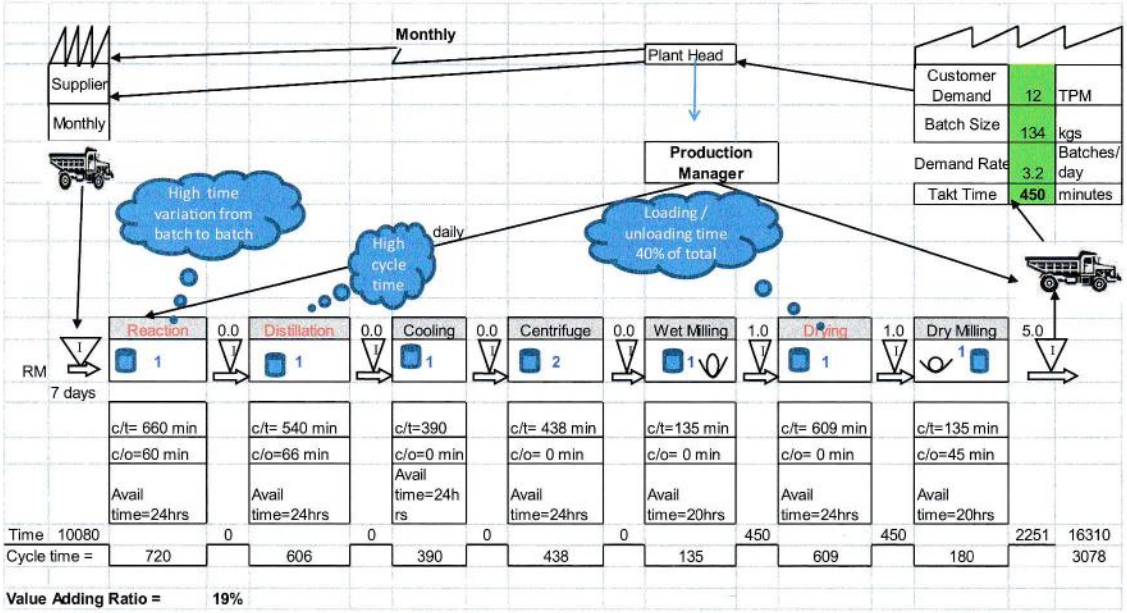
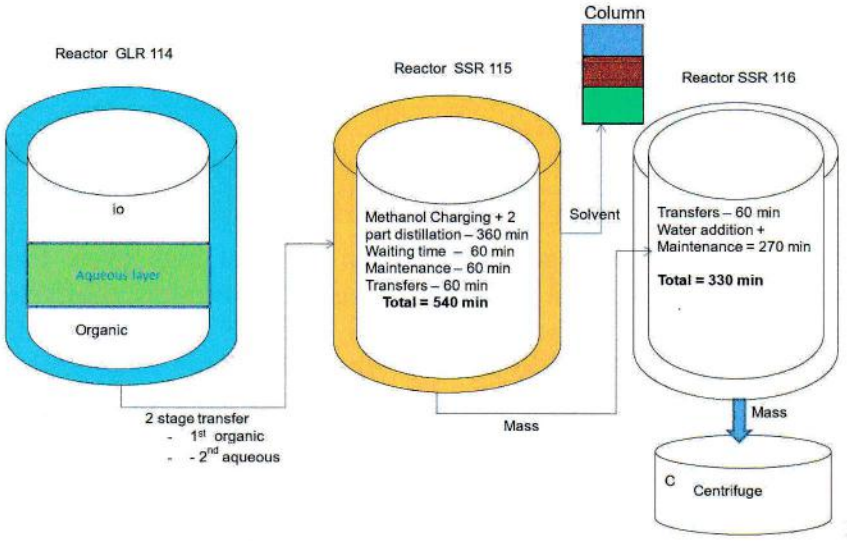


Diagram 2: Existing 3 stage process for Product PV



Detailed process observation was carried out for the distillation process wherein four consecutive batches data was taken over two days. For each batch, hourly distillation quantities were monitored along with the relevant process parameters (*refer* ***Table 3***). The data points where the actual figures significantly deviated from target were highlighted and analysed in further detail. This analysis of data threw up the following key process variations.

- Excess water found in organic layer transferred from previous stage
- Steam pressure fluctuation leading to variation in temperature being maintained and slower distillation rate in one batch
- The cycle time of next process in Reactor 116 was only 330 minutes.

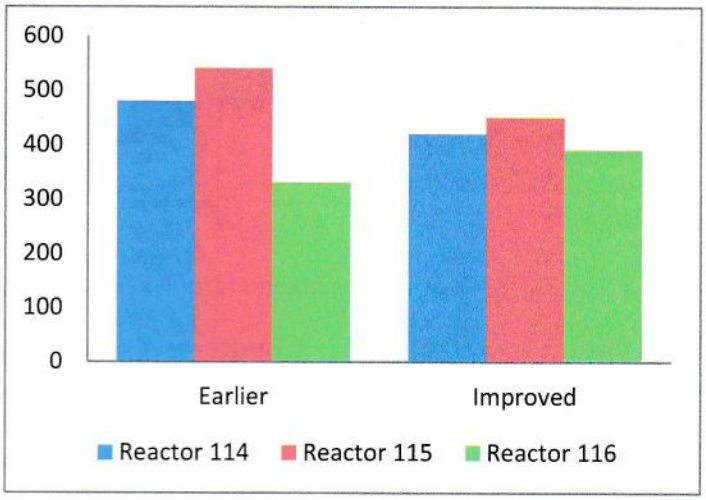
Countermeasures Implemented

Eliminate, Combine, Simplify and Rearrange (ECSR) principles were used to improve the process. The key solutions implemented were:

Table 3 — Distillation Monitoring

Distillation Monitoring Board								
Batch No.	1st hour	2nd hour	3rd hour	4th hour	5th hour	6th hour	Total time (minutes)	Total quantity (litres)
Target	350	225	225	150	100	0	300	1050
1	480	220	225	127	93		315	1145
2	345	235	234	122	90	21	310	1047
3	345	215	200	135	80	90	410	1065
4	340	221	225	150	120	153	400	**1209**

Chart 1 – Reactor Line Balancing



Cycle time in miutes

- The reactor level indicator was made more visible to the operator and water flow c ontrol valve shifted next to it to **simplify** and enable filling of correct quantity of water in Stage 1
- The waiting time between transfer of organic and aqueous layers was **eliminated** by starting the distillation immediately after getting first Layer from previous stage
- A ***Kaizen*** was done to reduce distillation time by preheating of R 115 by hot water . Hot water already available from another process was routed to an existing overhead tank. A pipe was fitted and connected to Reactor 115 which was then preheated before each transfer. This small modification using existing resources was implemented within 2 days and resulted in significant reduction and consistency in distillation time.
- The last step in Reactor 115 was maintaining the mass without stirring for 60 minutes post distillation. Since the next stage in reactor 116 had a lower cycle time, this step was **rearranged** to be done there by transferring the mass immediately after distillation.

Result

The line was balanced as can be seen from ***Chart 1*** – now the highest cycle time is 450 minutes as against 540 minutes and there is only marginal difference between the three stages. As a result, an average of 3.3 batches could be produced per day which is 30% higher than earlier as well as more than adequate to meet customer requirements.

2. Reducing *Muri* – Eliminating dust in the Milling Room

Problem Definition

The time taken for dry milling of Product PV is well within the takt time. However, during the shop floor walkthrough at the time of current state

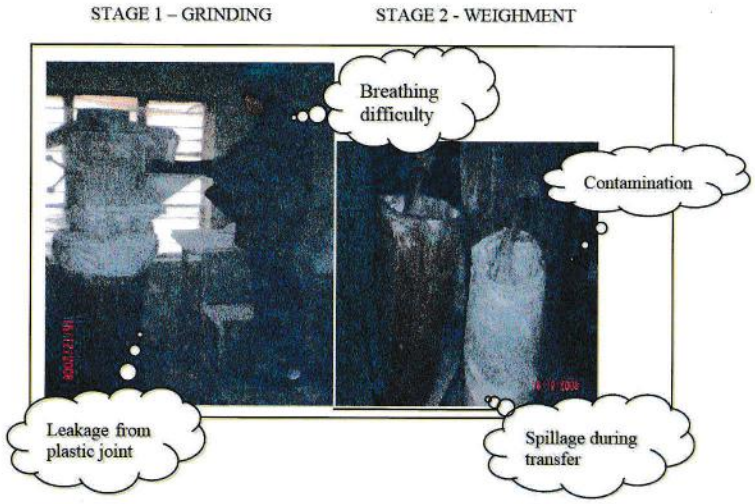


Fig. 1: Observed Conditions in Dry Milling

assessment, it was observed that the operation was resulting in generation of a lot of fine dust and powder. This in turn was not only leading to material loss at the final stage of processing but also affecting the working environment and health of the operators in the room. An improvement project was therefore taken up with a goal to ensure Zero Powder loss by eliminating all leaks and spills of material at this stage.

Observation & Analysis

The operation was observed in detail (*see Figure 1*) and Why-why analysis done to identify root causes of spillage and leakage. Key observations included:

- Material spillage observed while feeding the miller, leakage of fine dust during operation from sides of the dome, and while collecting the material into the bags.
- Weighing and packing was done manually in the next step and involved manual transfer of finished product from one bag to another. Material spillage as well as generation of fine dust observed during the transfer.
- Physical strain of the operators and helpers while lifting the bags weighing 25 kgs each on filling.

Countermeasures Implemented (*see Figure 2*)

1) To reduce the strain and make the feeding hopper easily accessible the milling stand height was increased.
2) By providing the weighing scale directly underneath the miller, manual weighing activity and transfer of fine powder from one bag to another was eliminated.
3) All valve leakages and generation of fine dust during milling was eliminated by sealing the miller and providing venting arrangement for releasing trapped air.

Result

Zero Dust working environment created where the operator could work comfortably without even feeling the need to wear a protective mask. Product loss due to spillage and leakage was eliminated.

3. Reducing *Mura* - Smoothening inconsistency in reaction time

Problem Definition

The VSM for Product AA shows the first operation of reaction to be the bottleneck process and constraining the manufacturing unit's capability to meet customer demand. Five reactors

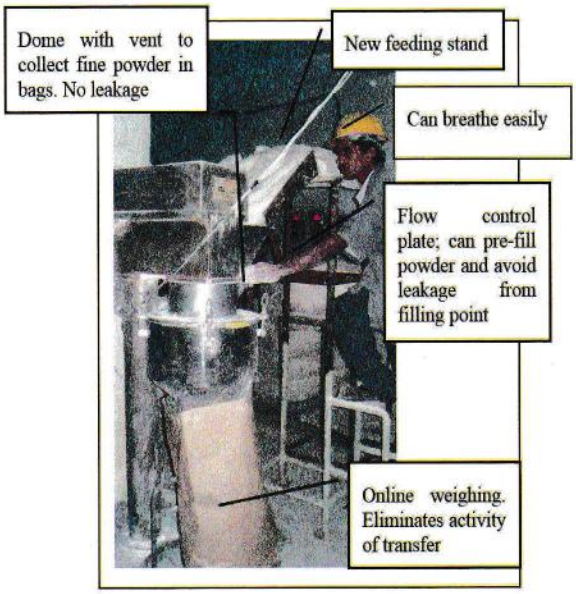


Fig. 2: Improved Condition in Dry Milling

were available for carrying out the single stage reaction process for Product AA and all of them were utilized fully to try and meet the required output. Analysis of batch data during the VSM stage showed that the average cycle time was 57 hours which translated to an effective cycle time of 13.4 hours per batch with 5 reactors being used. However, this was well above the *takt* time of 9 hours per batch. A cross function team was formed to work on this problem and bring down the reaction time to below 45 hours per batch which would effectively meet the takt time.

Observation & Analysis

Data showed wide fluctuation in cycle times from batch to batch with the actual value adding (reaction) time ranging from 46 hours to 73 hours. Since 5 reactors were used for carrying out the same reaction, the ***Differential Diagnosis*** [5] technique was used to analyse the problem and arrive at the root cause(s) of this variation.

Differential Diagnosis is a backward or deductive approach for solving chronic problems. A combination of direct process observations and data collection is used to answer a series of questions under the following categories:

1. What is the problem is (WHAT),
2. Where or in Which Place Does it Occur
3. When Does it Occur
4. How Much (quantity or frequency).

In each question both the Presence and Absence of the condition is noted. Through this the problem is narrowed down and what remains at the end will yield the root cause through a Why-Why examination.

In this case, the data showed that all 5 reactors exhibited significant variation in reaction times which meant that there was a common cause for the inconsistency. Each reactor had in some batches, been able to complete the reaction in a low time of below 50 hours. By comparing these low times to the higher times, the root cause could be identified. Whenever the reaction temperature of 145 -147 deg C was consistently maintained, cycle time was between 46 – 50 hours irrespective of which reactor was doing the process. In other cases cycle time fluctuated to much higher levels. It was observed that whenever the temperature dropped, it took at least 2 hours to come back to the required range in which the reaction occurs. This drop was traced back to fluctuation in steam used for heating and the root cause was finally identified as the manual steam valve control operation.

Countermeasures Implemented

An improved method of steam control was put in place which included valve marking and positioning and an alert mechanism for pressure deviation. A process chart was prepared and visual management system for monitoring of parameters put in place. To ensure that there was no other possibility of variation, recalibration of all temperature sensors and display units and cleaning of thermo-wells was carried out.

Result

Variation in time fell by 50% across all the reactors (*refer* ***Chart 2***) and average reaction time

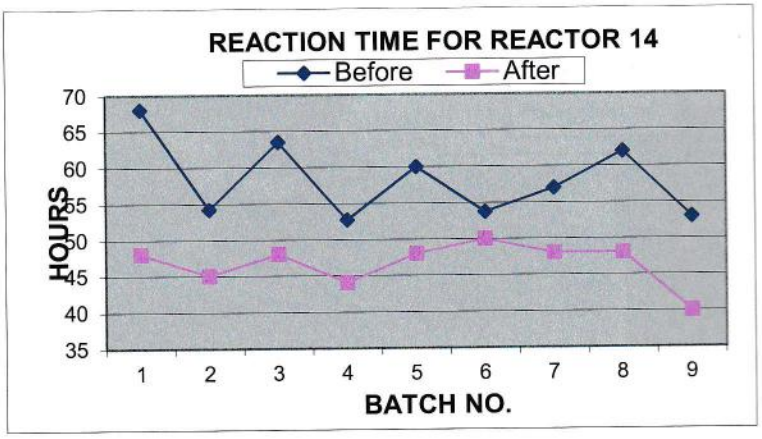


Chart 2: Reactor Time Variation

came down to 44 hours from earlier level of 57 hours. As a result output of the product shot up from 28 TPM to 33 TPM while lead time came down from 10 days to 4.5 days.

Conclusion

The above case examples clearly show that the **core lean concepts of Flow and Waste Elimination** are equally applicable in process plants as in the regular discrete manufacturing setup.

Lean tools and techniques like VSM, ECSR, problem solving and visual management have been applied with significant impact on the performance of these units. The gains have been on the standard PQDCSM parameters such as:

- ✓ Throughput and productivity increase by debottlenecking
- ✓ Lead time reduction and delivery performance improvement
- ✓ Cost reduction through minimizing waste of resources and productivity
- ✓ Safe and better working conditions for the operators
- ✓ Improvement in morale as the employees were part of the cross functional teams and were given responsibility for improving their respective work areas

This experience with bulk drug manufacturing also threw up some subtle differences between how lean is to be applied in a process industry as compared to a discrete manufacturing unit.

- *Muda* is observed by understanding the change that has happened to the material during processing through its chemistry as this change is often not visible or obvious visually. In a discrete set up, direct physical observation of the seven wastes can be easily carried out.
- Reducing *Mura* leads to significant benefits in these industries as the processes are reaction based and depend on multiple process parameters and raw material variations. For this, the collection of accurate data is very important. In discrete manufacturing, working on *Muda* itself has a significant impact as process variations are limited to manual operations. Even these variations can be observed visually and acted upon.
- In process manufacturing, effective value addition depends on utilities like boilers, chillers and compressors being able to help maintain the required conditions. The focus is therefore on ensuring these utilities perform to their optimum. In discrete manufacturing, the focus is operator's work methods in conjunction with production

A much more comprehensive study and analysis would need to be done to truly understand these and more differences in application of Lean in the process industry. This should include data and findings from

implementations done in continuous process industries such as food processing, chemical, primary metal production and pharmaceutical amongst others. Comparing this with the well researched and documented findings from discrete manufacturing will help in providing definite conclusions on the differences in successful application of Lean concepts in both these main types of manufacturing.

In conclusion, it may be said that the core philosophy and paradigm of Lean remains equally relevant to a process industry as it is to the discrete manufacturing sectors. The concepts need to be applied keeping in mind the inherent nature of process manufacturing by slightly tweaking the methods of observation and focus on data collection. The benefits of implementing lean are equally significant as could be seen from the case examples cited in this article.

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