Chapter 20
Analyzing the Impact of Lean Approach in Pharmaceutical Supply Chain

Alberto Portioli Staudacher and Alice Bush

Abstract Pharmaceutical industry is experiencing a time of change because of several reasons. This time of change has generated new needs as efficiency and effectiveness. Pharmaceutical Supply Chains need to compete in their industry and the attention paid to those issues is continuously increasing. Some studies have been conducted for this research line, but many of them are non-mathematical and non-numerical studies. The aim of this paper is to present a modeled Supply Chain to understand how Lean Approach can impact on the Pharmaceutical Supply Chain. In fact we implemented some Lean practice along the Supply Chain and we measured the obtained performances.

20.1 Introduction

The Pharmaceutical industry has been defined as the complex of processes, operations and organizations involved in the discovery, development and manufacture of drugs and medications [1].

Pharmaceutical Industry today is experiencing a time of change because of several reasons: reduction of healthcare drug budgets, increased costs to put new medicines on the market, harder global competition and increased cost along the Supply Chain [2]. Thus the Pharmaceutical industry is under tremendous pressure to improve all the related business.

This research field is becoming more and more relevant for all the players involved in this industry, because the whole Chain needs to be efficient to stay competitive in the Pharmaceutical industry.

A.P. Staudacher (✉) • A. Bush
Department of Management, Economics and Industrial Engineering,
Politecnico di Milano, Milano, Italy
e-mail: alberto.portioli@polimi.it; alice.bush@mail.polimi.it

A. Matta et al. (eds.), *Proceedings of the International Conference on Health Care Systems Engineering*, Springer Proceedings in Mathematics & Statistics 61,
DOI 10.1007/978-3-319-01848-5_20,

On the other hand, today to improve performances in terms of effectiveness and efficiency in a specific Company, working on its internal operations is not enough. An open issue is to improve performance along all the stages of the Supply Chain.

As a contribution of the new challenges of Pharmaceutical Industry, in this paper we will present a modeled Pharmaceutical Supply Chain and we will propose the Lean Approach to answer to the new Industry's needs.

20.2 Literature Review

In 2012 Narayana, Pati and Vrat published a literature review of Pharmaceutical Industry showing the major issues of this contest. The authors collected articles published from 1999 to 2009 and they genereted a classification of these studies in two general categories : non-behavioural studies (64% of the collected literature, 304 studies) and behavioural studies (36%, of the collected literature, 304 studies). Considering only the non-behavioural studies, Narayana, Pati and Vrat highlight that the most addressed issue are The Pricing & Medical Expenditures contributing with 21.7%, R&D and Supply Chain Management, with 10.1% and 9.2% respectively.

The number of articles about SCM in Pharmaceutical Industry is 34 and it's interesting to notice that half of them have been published in the last 2 years of the considered period, indicating an increasing interest on this topic.

Narayana, Pati and Vrat also show that the case study is the most frequently used methodology in studying Supply Chain managerial issues in the Pharmaceutical industry. The second one is mathematical modelling and data analysis. The interest in the mathematical methodology is increasing in the last years in this particular sector; this is due to the new need to finding some principles to improve the whole system [3].

In the United States a Securities and Exchange Commission (SEC) intervened in the US Pharmaceutical SCs, catalysing the adoption of Information Sharing Approach along the Chains. This caused a significant inventory reduction along the Supply Chains for Pharmaceutical products [4]. The distributors used investment buying to gain higher margins and then the performances along the whole Supply Chains were un-efficient. The investment buying was replaced with a fee for service model [5] with inventory management agreements. Indeed Pharmaceutical distributors receive fees from manufacturers for the distribution services that the distributors provide.

Other authors investigated the impact of information sharing Approach on Supply Chain performances (see [6, 7]) showing a significant impact on the inventory level reduction.

But information sharing is not always applicable; therefore it is interesting to investigate the impact of alternative approaches.

Lean management represents one of the most effective practices to improve systems, in general, and to reduce inventory, in particular.

A study carried out by Robert E. Spector [8] represents the Lean implementation in the Pharmaceutical industry. The performance index measured has been the inventory turns as it indicates how the company is improving its processes.

Spector concluded that there wasn't a significant overall improvement. Spector claimed that the poor results were due to the fact that Lean was implemented in only one stage of the Supply Chain, rather than at all stages.

In this study we want to deepen the knowledge on the possible impact of adopting Lean Approach in a Pharmaceutical Supply Chain, and to find a possible explanation why Lean is not widely implemented at the Supply Chain level.

In particular, we want to understand the impact of adopting Lean at one stage only, in the Supply Chain, and the impact of adopting Lean at all stages. In order to do so, we built a simulation model of a typical Pharmaceutical Supply Chain, and we simulated the impact of two Lean Practices: reducing order and production batch sizes and focusing on the flow, by adopting a FIFO rule at all stages, rather than a rule focusing on the single stage efficiency, as, for example, minimum setup.

20.3 The Model

20.3.1 The Modeled Supply Chain

A common Pharmaceutical Supply Chain is composed by Primary Manufacturers, Secondary Manufacturers, Distributors, Retailers and/or Hospitals [1].

The Primary Manufacturer is in charged to produce the active ingredient (API or AI). The characterizing processes are chemical synthesis and separation stage. The secondary Manufacturer add to the Primary Manufacturer's output the "excipient", we can summarize the principals processes as granulation, compression, coating, quality control and packaging [1] (Fig. 20.1).

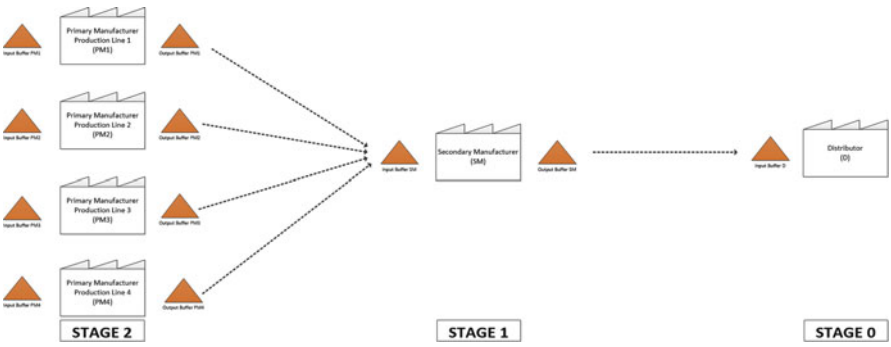

Fig. 20.1 The modeled Supply Chain

We focused on the upstream section of this Supply Chain. There are four different Primary Manufacturers; each one handles a different product line. Every product line is made by six products and differs, from the others, for the input demand.

Each Primary Manufacturer supplies not only this Supply Chain but also others; therefore there is an interaction with other products feeding others Supply Chains. There is no constraint in the availability of raw material. Downstream of the Primary Manufacturers there is a Secondary Manufacturer processing all products and its capacity is fully dedicated to this Supply Chain. Downstream of the Secondary Manufacturer there is a Distributor facing end retailers' and hospitals' demand. Each stage of the Supply Chain is decoupled by an input buffer and an output buffer.

The production stages have set ups to change from a product to another and set ups are shorter if the two products appertain to the same product line, longer if they appertain to different product lines. The orders' processing times are deterministic; they're different for each product and for each stage. When orders are queued to a production stage they're dispatched with a minimum set-up rule, both for the Primaries and the Secondary manufacturers. The value of the processing times is set in order to ensure a saturation index of 89% in stage 1 and 85% in the stage 2.

For the sake of simplicity Production processes have no downtimes due to failures, lack of information or other causes. The deliveries between the different stages are carried out by trucks with limited capacity and the transportation times are deterministic. In the modeled system it's assumed that the trucks cannot move unless a minimum quantity of materials to transport is reached, in order to limit the transportation cost.

As in Chen et al. [9] and Lee et al. [7] we have used the following formula to set the average final customer demand faced by the Distributor:

$$D_t = k + \rho * D_{(t-1)} + \varepsilon * \gamma$$

Where:

k Is a nonnegative constant?
D_t Is the demand in period t (t = 1, 2000);
ρ Is the correlation parameter; in this study $\rho = 0, 7$ (See [7, 9])
$\varepsilon^* \gamma$ Variability factor
ε Parameter normally distributed with mean 0 and variance σ^2.
γ Experiment parameter; in this study $1 \leq \gamma \leq 2$

20.3.2 The Supply Chain Planning Model

The logic that governs each stage is simple: each stage receives an order from the stage downstream and satisfies it from stock. Each stage decides individually when to place an order to the stage upstream and the quantity of each order.

In this model all the stages use an EOQ policy as in Gavirneni et al. [6], Lee et al. [7], Chen et al. [9], to define when to order and how much to order. The logic used considers the delivery times and the production lead times together with the demand faced by the different stages in order to calculate the order batches.

When a customer order arrives to the Distributor, if he has enough availability of stock fulfills completely the incoming order, otherwise the order is backlogged and is fulfilled only when there will be enough stock. If the order is satisfied from stock, a control on the inventory position of this buffer is carried out. If the inventory position is below the order level, the Distributor places an order to the Secondary manufacturer. The order is satisfied from the Secondary Manufacturer output buffer and the inventory position is checked. If it is below the order level, then a production order is generated and queued at the Secondary Manufacturer stage. Next order to produce is selected according to the minimum setup rule (setups are sequence dependent). The production batch size is set equal to 1 week of average demand.

When a production order is manufactured the required material is taken from the input buffer, and the inventory level checked. If the level is below the order level, an order is placed to the stage upstream: the output buffer of the Primary Manufacturer of that product line.

The same mechanism is applied by the upstream stages PM1 (Primary Manufacturer 1), PM2, PM3, and PM4. The production batch size for the Primary Manufacturers is fixed as 2 weeks of average demand. The Primary Manufacturers' input buffers are fed up by a Supplier who has an infinite capacity.

For each buffer the inventory position is calculated as follows:

$$\begin{aligned} &\textit{Inventory Position} = \textit{Stock in the buffer} + \textit{Orders placed to the stage upstream} \\ &\textit{but not yet arrived} - \textit{Order received by the downstream stage, but not delivered} \\ &\textit{yet } (\textit{Backlogged orders}) \end{aligned}$$

20.3.3 Design of Experiment

In this chapter we will present the model's parameters and the design of the experiments set up to analyze the impact of Lean Approach on the Supply Chain. In particular we decided to investigate the impact of set-ups and batch sizes reduction and the impact of reducing the Lead Time variability.

We adopted a discrete-event simulation study because it allows a detailed replication of the behavior of the Supply Chain even under complex configurations and scenarios.

To determine the simulation run length we used the procedure described by Law and Carson [10]. The initial warm-up period was calculated via Welch procedure [11]. The simulation run time as been set to 2,000 days with a warm-up period of 500 days those are not considered during the collection of the statistics. For every tested experiment we made 10 runs with the same parameters but different stochastic numbers, in order to increase the confidence of the results.

Table 20.1 Parameters of simulated model

	PM1	PM2	PM3	PM4	SM
Order processing time (min)	0.662	0.662	0.662	0.662	0.931
Mean set-up time (min)	20.17	20.17	20.17	20.17	25.17
Production capacity dedicated to the Supply Chain	35%	35%	35%	35%	100%
Daily available time for production (hours)	8	8	8	8	8
Transportation time to downstream stage (hours)	16	16	16	16	8
Minimum number of units to start the truck	150	150	150	150	50

To allow an easier comparison of different experiments, we defined a desired service level of 96% and for every experiment we set the order level of each buffer as the minimum quantity in the system to reach this performance target. The most important output of the simulations is the inventory level as in Gavirneni et al. [6] and Lee et al. [10].

The following table present the values of the parameters in the Supply Chain (Table 20.1).

20.3.3.1 Set-Ups and Batch Sizes Reduction

To investigate the impact of making the system more flexible we decreased the set up times and we reduced the production order batch sizes by the same percentage so the overall capacity saturation remains the same, but the system becomes more flexible.

This reduction of set-ups is one of the most important point of the Lean Approach as depicted by Silva et al. [12]. We have tested set-ups reduction ranging between 20% and 45% to both Primary and Secondary Manufacturers.

We tested the impact of reducing set-ups and batch sizes only at the Primary Manufacturers, then only at the Secondary Manufacturer and finally to both stages simultaneously. Finally we investigated the impact of these changes under three different demand variability condition: low, medium and high.

Plan of the first set of the experiments is depicted in the following table (Table 20.2).

20.3.3.2 The Impact of Production Order Sequence Practice: FIFO Versus Minimum Set-Up

The second aspect of Lean Approach we tested is to move the attention from the single stages to the flow. Minimum set-up practice allows an increasing performances to the single stage, while FIFO practice allows minimizing Lead Time variability (see [13, 14]), so the system would be more reliable and more predictable.

We want to highlight that when there are faster and more predictable time reactions, then Safety Stocks decrease and also the Bullwhip effect decreases.

Table 20.2 First set of experiments

	Variability	Percentage of reduction PMs	Percentage of reduction SM
Set-up reduction at PMs only	$\gamma = 1$ $\gamma = 1.5$ $\gamma = 2$	20%/30%/45%	0%
Set-up reduction at SM only	$\gamma = 1$ $\gamma = 1.5$ $\gamma = 2$	0%	20%/30%/45%
Set-up reduction at PMs and SM coordinated	$\gamma = 1$ $\gamma = 1.5$ $\gamma = 2$	20%/30%/45%	20%/30%/45%

Table 20.3 Second set of experiments

	Variability	Percentage of reduction PMs	Percentage of reduction SM	Production order priority rule
Set-up reduction at PMs and SM coordinated	$\gamma = 1$	20%/30%/45%/ 55%/70%/85%	20%/30%/45%/ 55%/70%/85%	MINIMUM SET-UP
Set-up reduction at PMs and SM coordinated	$\gamma = 1$	20%/30%/45%/ 55%/70%/85%	20%/30%/45%/ 55%/70%/85%	FIFO

The minimum setup rule is set as follow: when the production stage completes an order, the queued order that causes the shortest setup is processed next. If a production order has queued for 3 days or more, then it has the priority to be processed, even if the set-up time isn't the shortest one.

The plan of the second set of experiment is depicted in the following table (Table 20.3).

20.4 Results

20.4.1 Set-Ups and Batch Sizes Reduction

First we decreased (−20%/–30%/–45%) the set-ups time and the batch sizes only for the Primary Manufacturers, leaving the Secondary Manufacturer parameters unchanged. Then we returned at the base case for the Primary Manufacturers, and we decreased the set-ups time and batch sizes of Secondary Manufacturer only.

Last we decreased the parameters (set-ups time and batch sizes) simultaneously both for the Primary Manufacturers and Secondary Manufacturer.

The inventories reduction is referred to the base case.

In the figure below we can see the impact of set-ups and batch sizes reduction to Supply Chain inventories in a medium variability contest.

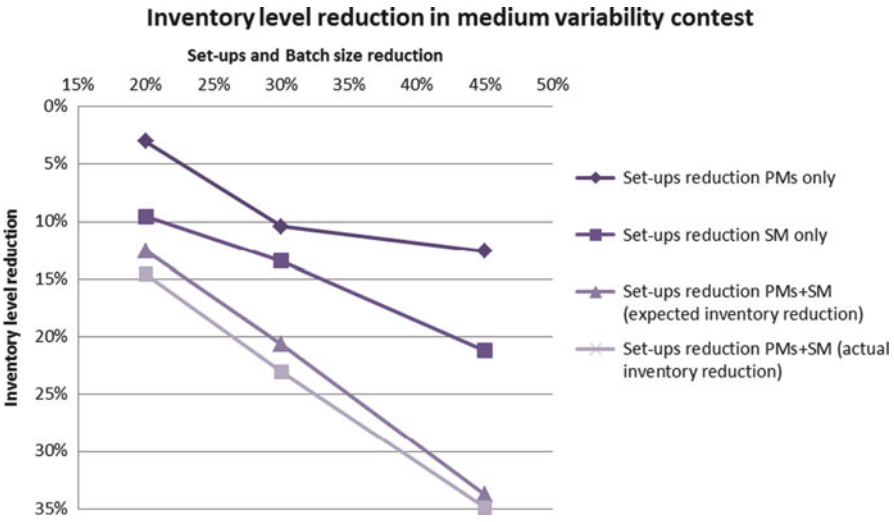

Fig. 20.2 Inventory level reduction in medium variability contest

As we can see in the Fig. 20.2 if we decrease the set-ups time and batch sizes of the Primary Manufacturers, the Supply Chain inventory level can be reduced up to 13% (for set-ups and batch sizes reduction of 45%). On the other hand if we reduce the set-ups time and batch sizes of the Secondary Manufacturer, the Supply Chain inventory level can be reduced until 21% (for set-ups time and batch sizes reduction of 45%).

Reducing only the Secondary Manufacturer gives a greater benefit, in terms of total inventory reduction, because it affects the downstream and upstream stages, while reducing only the Primary Manufacturers influences only the downstream stages (the upstream supplier has an infinite capacity and a fixed lead time).

It is now interesting to add-up the inventory reduction achieved by PMs only and the reduction achieved when reducing SM batch sizes and set-ups time, and compare the result with the actual reduction achieved by reducing set-ups time and batch sizes of both, PMs and SM.

If the actual reduction is the same, it means that it is possible to sum the effects of the two actions, if the actual inventory reduction is larger than the sum of the two single ones, it means that there is a synergetic effect between the two actions.

If the actual result is lower, it means that there is a saturation effect.

The simulation runs show that there is a synergetic effect.

Finally In the figure below we present the impact of the demand variability on the inventory reduction effect:

Figure 20.3 presents the percentage of the difference between the sum of the inventory reduction achieved reducing set-ups time and batch sizes of PMs and SM only, and the inventory reduction achieved by reducing set-ups and batch sizes of PMs and SM simultaneously.

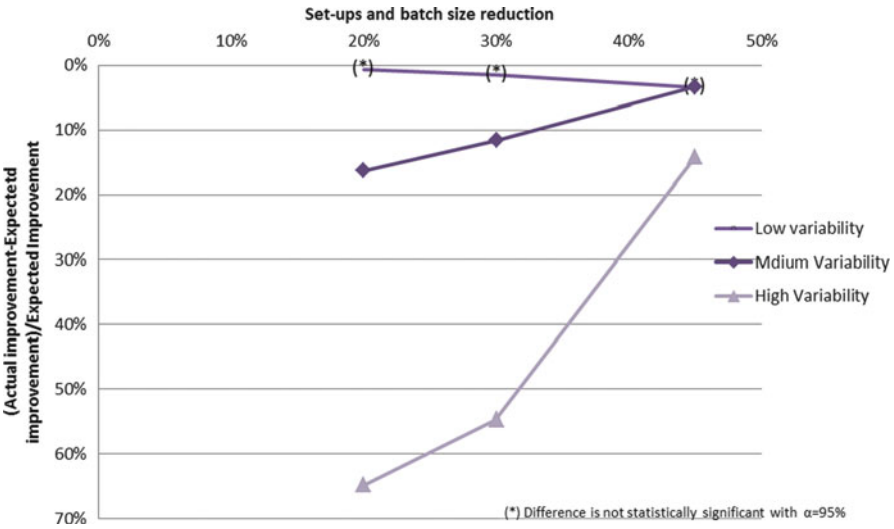

Fig. 20.3 Comparison of expected improvement and actual improvement in three variability contests

Results show that the synergetic effect is higher when demand variability increases, moving from 2% with low variability to 65% with high variability, when set-ups time and batch sizes reduction is set at 20%.

When set-ups time and batch sizes reduction increases, the synergetic effect decreases.

20.4.2 The Impact of Production Order Sequence: FIFO Versus Minimum Set-Up

In the figure below we can see the impact of Production Order sequence practice:

We noticed that for small set-ups time reduction FIFO rule gives to the whole system a disadvantage. In-fact the saturation of the system increases (97%) due to the larger amount of time spent making set-up and the total inventory is higher.

There is a level, decreasing set-ups and batch sizes further, where FIFO is no longer unfavourable. In fact, as we can see in Fig. 20.4, differences of inventory reduction between FIFO and Minimum setup aren't large in the zone between 50% and 70% of set-ups and batches reduction but even inventory level, in FIFO scenario, mainly decrease.

This means that reducing set-ups and batch sizes, not only gives a greater performance to the whole Supply Chain, but it allow to take advantage from the lead times variability reduction.

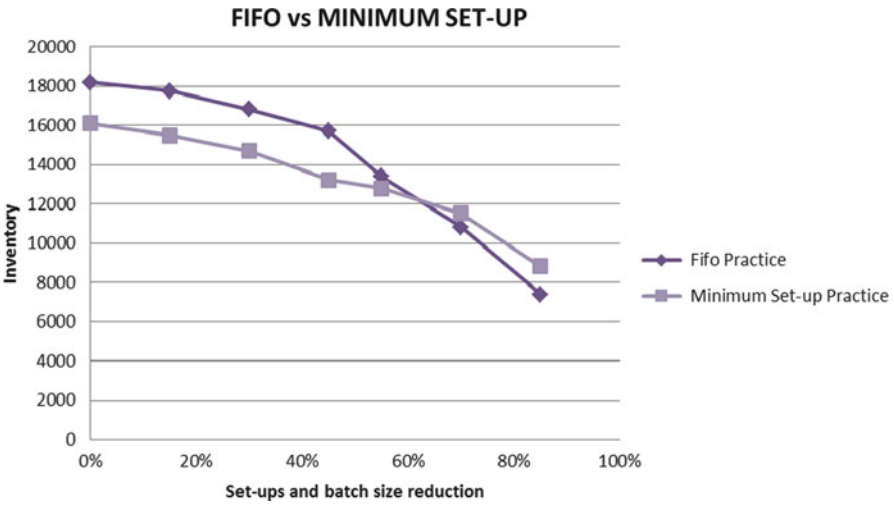

Fig. 20.4 Comparison of two different practice of Production Order sequence practice

20.5 Conclusion

Pharmaceutical Companies are looking for greater efficiency and improving practice along the Supply Chain is a great opportunity to achieve this.

Many authors investigated the impact of adopting an Information Sharing approach (see [4]) and showed that it gives interesting advantages, but other intervenes are possible.

Lean Approach has shown to reduce inventories and lead times, to improve service level, quality, and, in general, the performance of companies, but, there is very little research on quantitative analysis of the impact of adopting Lean Approach, in particular in Supply Chain management, and in Pharmaceutical industry.

The research work presented in this paper, investigates the impact of adopting Lean Approach along a Pharmaceutical Supply Chain, through a simulation model, and a campaign of experiments aimed at measuring and at understanding the impact of adopting typical actions of Lean: reducing set-ups time and batch sizes, and looking at smoothing the flow, by reducing lead time variability.

An important element emerged from the analysis is the synergetic effect of the Lean Approach when it is applied to more than one stage along the Supply Chain.

Reducing set-ups time and batch sizes, not only decreases the inventory level needed to achieve the desired service level, but it also reduces the absolute effect of sequence dependent set-ups time.

This allows to move from set-ups orientated sequencing rules to FIFO rule that gives to the system a strong decrease in lead time variability.

Different players of the Supply Chain have to operate simultaneously and coordinately. They also need to use the same practice and the same strategies. In fact introducing Fifo without bringing set-ups time at the right level make the performances worse as well as reducing batch sizes only in one stage gives to the system a very limited benefit.

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