Optimization of Setup in the compression phase and Validation of cleaning process

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Abstract: Nowadays, industrial fast pace development leads companies to search for strategies and methodologies that would help to reduce costs and improve the product quality, gaining in that way a big competitive advantage. In the XXth century Kaizen philosophy and Lean Manufacturing methodology began the development to meet the company's needs, so the fundamental concepts such as 5S, SMED, poka yoke, Just-In-Time (JIT), Total Productive Maintenance (TPM), among others, were developed. Empresa X is the market leader in the production of generic tablets in Portugal, which in partnership with the Kaizen Institute has implemented the Lean methodology throughout its organization. Due to the need for normalization and continuous improvement of processes, namely in the phase of setup in the compression that presents five compressors in itself, the theme of this Master's Dissertation appeared. An exhaustive analysis of causes responsible for the long setup times was carried out and Kaizen-Lean tools, such as SMED and PDCA and 5S cycle, were applied in order to reduce the times recorded. After the implemented implementations, it was possible to record improvement in the dynamics of the setup and decrease of the operations times in 27% on Machine 1 and 19 % on Machine 2, as was pretended. Finally, a consolidation of the cleaning validation procedure was performed, evidencing an advantageous critical point.

Key words: *lean manufacturing*, Kaizen, SMED, compressors

1. Introduction

1.1. Contextualization of the problem

The global economic and business environment has fundamentally changed in the last two decades. Companies are more and more suffer from pressure to look for opportunities in the marketplace. Intense global competition has forced many companies to rethink their core business processes and devise plans capable of responding to a constantly growing competitive market. Large pharmaceutical companies, not being an exception, have witnessed a significant change in the operational model in the last decades. Several studies have shown that the challenges of declining industry productivity, the transition from commercial models and the rapid growth of new markets are the main factors contributing to the sector's economic performance (Gautam & Pan, 2016). In the succession of this dynamic, for industry and science, the lean concept has become a promising opportunity to develop a continuous improvement of quality and efficiency (Rybski & Jochem, 2016). The pharmaceutical industry is increasingly encouraged to implement *Kaizen-Lean* approaches, training its employees and relying on topics such as 5S, standardization, types of waste, among others. It was in this context of a strong spirit of optimization and tendency for the competitiveness of markets that the opportunity arose for the elaboration of this Master's Dissertation.

1.2. Methods

Initially the company's exposure and the characterization of the productive process are made, as well as the study focus for this dissertation.

Next, an exhaustive bibliographic review is done on the Kaizen and *Lean Manufacturing* issues, addressing the most relevant tools that compose them. Still, illustrative examples are shown in the scope of continuous improvement, which have been found beneficial in their application in the mentioned industries.

Subsequently, the in-depth analysis of the initial situation is carried out and the causes responsible for less efficient processes are identified. In the succession of this evaluation, a proposal of solutions and the respective economic evaluation of the potential gains is realized, whose objective is the reduction of the time spent in the operations.

Next, there is a validation of solutions, previously proposed, and the evaluation of the gains recorded in practice. This phase is divided into two strands, such as the implementation of small solutions that aim at the operator's day-to-day efficiency and global implementations that modify the operative mode of the machines in order to make the setup more agile. In this last one, in order to reinforce the validity of the implementations, an exploration and comparison of parameters of effectiveness of the machines is realized. Finally, future implementations are explored and suggested for continuous improvement.

Finally, the method of cleaning validation is explored and the importance of the operative mode in which it is performed is evidenced.

2. Problem Description

Company X is a Portuguese Pharmaceutical Laboratory market leader, with the largest portfolio of products in Portugal and with a production capacity of 30 million packages, equivalent to 1,170 million units. In 1982 Farma-APS, precursor of Company X began its operations as a distributor of hospital products. Subsequently, in 2002, the brand Company X was created, quickly occupying the leadership in Portugal in terms of spontaneous notoriety. The facilities of Venda Nova were inaugurated in 2006, with a state-of-the-art research and development (R & D) center, reflecting an investment of 35 million euros. Thanks to the intense work of the R & D department, it was possible to create a portfolio of some 310 molecules registered and approved by INFARMED.

In 2011, the leadership in the Portuguese market was reached, and in 2013 a close collaboration with the Kaizen® Institute began, working together to implement new processes, optimizing and maximizing industrial operations, thereby increasing the level of satisfaction of its customers.

In 2014 the absolute leadership of the Portuguese pharmaceutical market was reached, presenting itself as the company with more units sold. In 2017, Company X is acquired by the International Group, which has allowed it

to broaden its horizons to the European market, where it has a strong position.

In the past, Company X has four business areas, namely, Ambulatory, Hospital, Licensing Out and Contract Manufacturing (RH, D., 2015).

The fields of action of the products vary from the areas of oncology, anti-infectious, hormones, central nervous system to general consumption.

2.1. Production Cycle

Company X presents an elaborate drug manufacturing process, which comprises several fundamental steps in itself.

Production begins with weighing of selected raw materials according to the information from AIM dossier, these consist of the main raw material and secondary raw material, the excipients, being added components with a view to assign technological efficiency to the medicine.

Wet granulation, as the next step, ensures that the material mixture becomes a wet mass by addition of a liquid with or without binder. Once the wet mass is obtained, it is sent to the drying stage to form a mixture of agglomerates of different dimensions and characteristics, which need to be calibrated.

Subsequently, in order to obtain a homogeneous, granulate and with properties that allow the entry into the compression phase, proceed to the mixing phase. At this stage other excipients with various functions are added.

Finally, the granulate is subjected to the compression phase, being possible to be sent to the packaging and distribution phase. However, in some cases the final stage of the production process consists in the application of coating to the tablets, herein called, cores, with various functions such as camouflaging the taste and / or odor, changing the release profile of the active substance, preventing the release of particles, protect API's sensitive to humidity, light.

Company X also has a production phase for the filling of capsules, where they are filled into hard gelatin capsules, powders, granules or tablets, as described in AIM dossier.

2.2 Compression phase

The compression stage consists of five compression machines of different types, namely Machine 4, Machine 5, Machine 3, Machine 2 and Machine 1.

The compression process, shown in Figure 1, is characterized by the action of the upper and lower punches, which rest on respective matrices.

The process starts with the descent of the lower puncture, which allows the creation of a cavity in the matrix for which by gravity and suction action the mixture is fed. The depth of the lower punch is carefully controlled so as to regulate the amount of product filling the die cavity, the excess is leveled by a weight adjusting mechanism. Thereafter, the upper punch comes into contact with the blend in the pre-compression phase, causing the pressures exerted by these rollers to expel air between the particles of the material. The greater compression force from the main rollers ensures that the granular material melts and results in a solid tablet. After this process, the lower puncture is lifted with the intention of expelling the medicine through a ramp of its own. (Schwartz, Lachman, & Lieberman, 1990).

The multi-station compression machines can be classified according to the punch and die set that they can use, these can be type B or D.

The Type B configuration usually shows punches with a diameter of 19 mm. This can be used with two types of matrices: diameter matrix 30.16mm - matrix B and a smaller matrix - BB, which has a diameter of 24mm, being suitable for tablets of diameter between 9-11mm. Type D shows punch diameter 25.4mm and diameter matrix 38.10mm.

The compressive force that is obtained in a machine depends on the type of instruments that are used. In type B compression machines, the maximum force is about 6.5 ton, while type D is about 10 ton. (Cole & Bennett, 2003)

Company X presents in its compression stage the multi-station machines type B, such as Machine 5 and Machine 3 and type D, are Machine 4, Machine 1 and Machine 2.

Despite the differences in size, all compression machines have similar components such as the hopper, powder

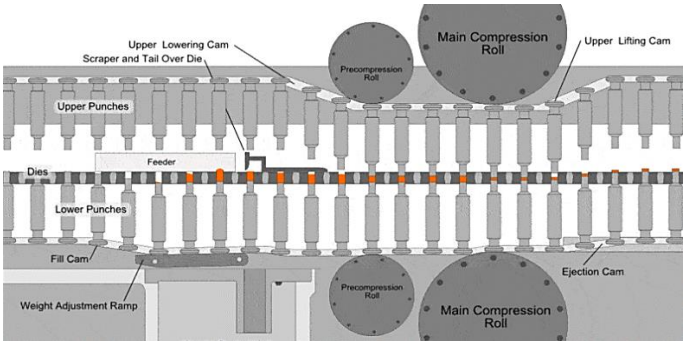

Figure 1 – Compression mechanism scheme.

distributor, filler ramps, scraper, rejection ramp, tablet removal blade, dies powder leveler, rollers pre-compression and main compression rollers. In addition to the fundamental parts, there is a deduster and a metal detector associated with each machine.

These two elements serve to remove the powder that the machine releases in the compression of each tablet, facilitating the subsequent stage of packaging and evaluate the presence of metal particles in the product from the eventual degradation of the equipment through which it passes throughout its entire manufacturing process.

In Company X there are three types of cleaning: the minor – type A setup, the line clearance – type B setup and the major – type C setup.

Type A setup is performed at the end of each day when there is no change of product or between batch changes of the same product; type B cleaning is performed when dosage changes of the same product occur and finally major cleaning – type C, occurs whenever a product change is effected, ie, change of API.

This cleaning is done immediately after completion of the manufacturing phase by the machine. This dissertation will focus only on the type C setup

To do this, it is important to know the setup steps, namely: end of the batch, disassembling the machine, cleaning the machine, cleaning the parts, cleaning the room, the assembly, the preparation of the next batch and finally the adjustment of the machine.

3. State of Art

3.1. Kaizen Methodology

Many business leaders today face the challenge of making decisions about improving operational efficiency. However, with regard to the implementation of a major change, the process is much simpler, since it presents only two options: to operate in the current state and maintain the status quo or to opt for change (Line, 2007).

Since the mid-1980s, when Masaaki Imai introduced the term kaizen, it has been freely used in conjunction with Japanese companies. In fact, the concept has gained so much success that kaizen is considered the key to the competitiveness of Japanese companies in the last three decades (Imai, 1997, Suárez-Barraza, Ramis-Pujol, & Kerbache, 2011). Over the past twenty years some companies have applied the concept as a "magic formula" by engaging employees in drawing up suggestions for improvement, while others have viewed their workers exclusively as a group of technicians.

The kaizen philosophy is based on the understanding that everyday life requires constant improvement. Thus, the best way to respond to the increasing global competitiveness of enterprises is to carry out continuous improvement activities to reduce waste (Maarof & Mahmud, 2016).

Kaizen has as the main focus of improvement - the process, manages to generate a people-oriented thinking and their efforts, instead of identifying them as the problem. The philosophy holds that employees are able to generate ideas for process improvements better than anyone because they are the ones who understand the most.

The implementation begins with a definition of a perfect process state, which will never be reached, however, in the direction of which small improvements will be made. Next, it is necessary to evaluate the current value chain of the process and identify opportunities for improvement. These opportunities are usually of *Muda* (Japanese word for waste), especially *Muda* - Type 2, that is, waste that adds no value and is unnecessary to the process (Rahman, Sharif, & Esa, 2013). Subsequently, a plan of action should be established to change the aspects that need to be improved. In the succession of this work, it is proposed to move to the place (Gemba) and to the effective implementation of the improvement. Finally, the results of process improvement must be observed and recorded, and what has been learned must be determined (Thessaloniki, 2006).

3.1.1 PDCA

One of the first steps in implementing kaizen is to analyze the value chain, mapping it, and identifying opportunities for improvement. For this it is necessary to establish the PDCA (Plan) - Do (Check) - Act cycle, also known as the Deming cycle or Shewhart cycle. This tool guarantees the constant kaizen process in all the analyzed areas (Thessaloniki, 2006) (Rahani & al-Ashraf, 2012).

Each step of the cycle makes an important contribution to the process of analysis for the construction of the value chain:

o - Planning - consists of evaluating the process and identifying the object of improvement;

o - Do (Do) - at this stage the measures from the evaluation of the process are established;

o - Verify - involves moving to the terrain (Gemba) and recording the changes triggered by the improvement;

o - Act - implementation and standardization of new procedures in order to avoid initial problems or establish new goals for improvement.

The PDCA cycle is iterative and repeats itself constantly in search of new improvement. However, before starting the cycle, any process under analysis has to stabilize, in this way, the cycle (SDCA).

The difference between these two cycles is the purpose of each cycle, while that in the SDCA cycle process normalization occurs, during the PDCA cycle the improvement of these same processes occurs (Imai, 1997). However, these two cycles are most responsible for the construction and analysis of the value chain.

3.2. Lean Methodology

For decades, producers have tried to optimize operations, management chains and the distribution of monetary goods. Lean production methodology, when compared to mass production, typically uses only half the human effort in manufacturing, half the production space, and half the investment in instruments and engineering hours to develop a new product (Wahab, Mukhtar, & Sulaiman, 2013).

According to the study by Bayou and Korvin, lean production is a strategy that aims to use less resources of the organization (that is, reduce "waste" waste) and reach higher quality and quantity of products sold (Bayou & de Korvin, 2008). Essentially, the key idea of lean manufacturing is to maximize value for the consumer while minimizing waste.

The main goal of its implementation in production is to increase productivity, visibly improving quality, reducing waiting times and reducing costs. These factors turn out to be the performance indicators of the lean production system.

With the development of information technologies, the pursuit of optimization has intensified the speed of demand, flexibility, waste elimination, process control and global demand, which have allowed companies to gain a competitive edge.

3.2.1 Lean tools

All the companies present diverse resources, as people, machines, processes and materials, to which inevitably related wastes of different natures are. Activities that do not add value give the name "*Muda*", i.e. to the excesses that the client is not willing to pay, which should be eliminated. (Pinto, 2009) "*Mura*" refers to the irregularities that arise in the production process and that must be solved implemented the just-in-time (JIT) system and pull

strategy, performing only what is necessary when the request for the product is made (Melton, 2005). The type of waste "*Muri*" is related to the imbalances in the workloads, through excesses or insufficiencies, this must be filled with standardization of the activities.

Lean system has as its main objective to reduce waste, waiting times and improve quality, relying on its main techniques like Jidoka (improving processes, eliminating waste), JIT, standardization, pull strategy. In order to achieve the imposed objectives, several instruments such as Kanban, 5S's, visual control, poka yoke, SMED (single minute exchange of die) and TPM (total productive maintenance) are used (Melton, 2005) (Wahab et al. 2013).

In the present case study, the most relevant tools for optimizing the operation of compression machines will be 5S's, SMED and TPM, explored in more detail below.

However, it is important to note that although lean thinking shows many benefits, illustrated in figure 20, there is always inherent natural resistance to innovation within each company, such as employee skepticism, lack of availability, and others (Melton, T., 2005).

3.2.1.1. 5S

In Japan the 5's represent Seiri, Seiton, Seiso, Seiketsu, and Shitsuke, which in turn mean Choose, Organize, Clean, Standardize and Maintain, respectively. The main idea of his methodology is to guarantee in a systematic way the cleaning, cleaning and security of people, equipment and materials (Castro, 2012).

The concept of 5S is widely recognized as the key step towards continuous improvement. It is a practical way to introduce employees to the concepts of waste and productivity, promoting a cleaner, more efficiently organized work space while giving employees the opportunity to improve their work environment.

The 5S methodology can identify and remove unnecessary products, instruments and activities, which drives the development of better organization methods, storage systems, etc. (Borris, 2006).

By contributing to the physical cleanliness of the work area, 5S allows the sources of contamination to be more easily identified and removed, thereby improving the quality of the product.

A study was carried out on a small producer and distributor of pharmaceutical and non-pharmaceutical products, whose facilities consisted of about 1000 m2, 12 workers and four production lines.

The first problem of the company was an inefficient use of the already reduced space of the factory, as raw materials and unmanufactured products were being stored in a disorganized way. The second problem was the inability to deliver products to several markets on time, which was a result of customer dissatisfaction and a huge loss of sales.

In order to solve the identified problems, a value chain mapping was carried out, identifying its causes and as a more effective measure the principles of 5S were applied to various operations of the factory. The processes like labeling, encapsulation, filling and coding were subject to the methodology in question, allowing a greater organization and cleaning of the space.

Thus, thanks to the mapping of the value chain that returned the causes of the identified problems and the application of the 5S methodology to various production processes and manufacturing space, it was possible to reduce waiting times, production cycle time and the inventory of products in the process of manufacture. In addition, the warehouse area was reduced by about 38%, as well as the number of employees decreased by 50% (Chowdary & George, 2011).

3.2.1.2. SMED

The Single Minute Exchange of Die (SMED) methodology was developed by Taiichi Ohno at Toyota in the mid-twentieth century when he decided to take the consumer's point of view with the aim of eliminating processes that did not bring any added value to the product ie " *Muda* ".

It is a method that efficiently allows you to move from the production process of one product to the next. Rapid exchange is the key to reducing product batches, thereby improving production flow.

Increasingly, the need to use SMED is greater because of the steady increase in demand variability, reduced product life cycles, and reduced inventories (Yash Dave & Nagendra Sohani, 2012) (Borris, 2006).

The basic idea of SMED is the reduction of setup time, of the machine, this is only possible from a structured analysis associated with the tool change.

The SMED implementation process begins by recording the process with all non-discriminated activities, from start to finish, through video, time notes, interviews, among others. (Preliminary stage). Then, it is necessary to carry out the analysis of the operative mode and the identification of activities (Step 1).

There are two types of activities: internal and external. Internal activities are those that can be performed only when the machine is stopped, while the external activities can be done while the machine is running. In step 2 the main focus is the transition from the maximum of internal to external activities, since it reduces the downtime of the machine.

Subsequently, improvements are made to internal tasks in order to shorten their time, and external, through the implementation of parallel operations, elimination of adjustments, etc. (Step 3).

At the end of this methodology, the new procedure must be registered and the employees must be trained in a continuous and continuous way, in order to encourage the continuous improvement of the process.

An example of success in implementing SMED and improving equipment efficiency (OEE) comes from an Italian pharmaceutical industry, which produced about 96.2 million units in 2011 (Bevilacqua, Ciarapica, De Sanctis, Mazzuto, & Paciarotti, 2015) The company aimed to reduce tool change time by 20% and increase efficiency by 25%. Meeting these goals, the drugmaker would be able to compete more effectively against the biggest competitors in its industry.

3.2.1.3. Total Productive Maintenance (TPM)

The modern maintenance system began with preventive maintenance in the United States, known as PM (Productive Maintenance). However, Total Productive Maintenance (TPM) consists of a set of tools that ensure constant monitoring of processes.

Developed in Japan, it is a technique that involves all levels and functions of the organization, from top management to factory employees (Castro, 2012).

The major goals imposed for the implementation of the TPM methodology were the reduction of production costs and delivery times, as well as the production of a high quality product. After the first failed implementation attempt in the early 1990s, the strategy for implementation was rethought in the 2000s, by investing in a much better structured plan, training of all staff and support from top management. In this way, it was gradually possible to observe the benefits of the implemented strategy.

There was an increase in equipment productivity by about 83% and equipment downtime was reduced from 517 to 89 times, these improvements were reflected not only in machine efficiency but also in product quality. In addition, the continuous training and constant support by the supervision, promoted the development of more organized work habits, new technical skills and also the creation of a multifunctional team motivated to improve the company.

TPM can be defined through overall equipment effectiveness (OEE), which encompasses the combination of three characteristics: the availability of the equipment to produce, the efficiency of the equipment and the quality of the product (Castro, 2012). Its purpose is to maximize the effectiveness of the equipment and consequently, OEE is the instrument for measuring its effectiveness.

According to (Nikajima, 1988), OEE measurement is an efficient method of analyzing the efficiency of a single equipment or an integrated system of machines. It is a function of availability, rate of performance and quality, which in turn are parameters for evaluation of losses in an equipment. According to the Nikajima there are losses of breakage / failure, setup and recalibrations, small stops, reduced speed, defect / rework and initialization (Chan et al., 2005).

4. Process characterization

In order to take advantage of the *Kaizen-Lean* tools, PDCA cycle thinking was combined with the SMED methodology, applied to the compression phase.

Therefore, the preliminary stage and stage 1 of the SMED methodology, where the initial diagnosis of the situation and the classification of the tasks in internal and external phases, were associated with the Plan phase; Step 2 and 3, which focus on the implementation of the improvements and their respective visualization, are associated with the Do and Check phases.

Finally, as the final stage, improvements and consolidation were recorded in the Act phase.

In this way it was certified the phased implementation of each step and the final documentation of the proposed and implemented changes, with a view to perpetuating the same

The study of the case began with the initial phase of analysis of the state of the machine, which had the objective of identifying the main activities and recording the corresponding times. Still as a second phase of the analysis, was performed the classification of activities in internal and external.

After completing these steps, it was possible to construct the detailed model of the initial state of the compression machine.

It was also concluded that because of the extreme similarity of the two machines, namely Machine 1 and Machine 2, it would be more advantageous to perform an exhaustive analysis on only one compression machine, Machine 1, since both the operating mode and the suggestions will be cross-sectional, as well as relatively similar gains.

The setup that includes waiting time, reflects the actual situation where interruptions occur due to waiting for the cleaning team to clean the room, which is also monitored by the OEE platform.

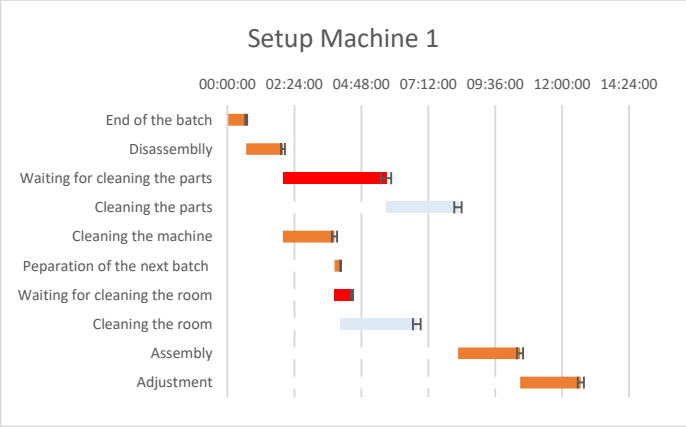

Figure 2 – Time registered for each fase of setup (in hh:mm:ss) for the Machine 1.

As is shown on figure 2, it was registered 12h and 40 min for this setup.

5. Study of improvement opportunities

In order to reduce the changeover time, an exhaustive analysis of all the tasks in each setup phase was carried out, which had scope for the implementation of improvements.

Were evaluated the series of internal tasks that took place during the setup, which could eventually be carried out while the machine was still in operation, turning these in external tasks.

Subsequently, it was necessary to carry out an in-depth analysis of the tasks of each phase, in order to identify the most critical ones, so as to focus especially on those who are responsible for the longer time spent. In this way, the actions taken in the optimization of these tasks will have greater impact in reducing the total time of each phase.

5.1. External tasks

Firstly, it was opted to analyze the temporal and monetary impact of the tasks that could be transferred to external tasks, that belong to the disassembly fase, namely, the

logbook registrations and the picking of the cart for parts of equipment.

Based on the observations made, the combined time of the two tasks selected to be external is 11 minutes for each setup performed, which can reduce approximately 14.1h/year/machine and 87.6 h/year/all machines.

5.2. Internal tasks

In order to decrease the setup time, as next step, was decided to analyze internal tasks of each fase and optimize them.

For the phases end of batch and disassembly were identified through Pareto graphs and Ishikawa diagrams, tasks that had major durability and were analyzed the causes. Thus, it was possible to conclude, that the main problem was lack of the workforce and the proposal was to allocate one shift helper to these few tasks.

Also, it was identified a problem of lack of material, as cleaning carts, that showed 9.2 min for preparation, that annually result in 73,3h of time loss. Therefore, as proposal for improvement was economically analyzed the purchasing of 2 more carts, that will be enough for daily setup needs.

Through estimated reduction of 4,5 min in this task, were made calculations of Return on Investment (ROI) and were obtained 185%. Thus, it is safe to affirm that this purchase should bring profit to the company.

Finally, for the assembly, the main causes responsible for long times of tasks weren't able to be solved by increasing the workforce, so it was proposed a different approach, namely, performance of assembly of some parts, that can be assembled out of the machine, simultaneously, while the cleaning team are working at the main room.

5.3. Global analysis of potential gains

In order to evaluate the total impact of all previously proposed solutions, the measures were aggregated in a new proposed operating mode.

This includes, as shown in, shift helper allocation in the phase of end of the batch and disassembly tasks, as well as simultaneous tasks together with the work of the cleaning team in the following steps.

After accounting for the total time with the proposed implementations, it became necessary to visualize temporal gains with the actual initial state, namely the total setup with waiting time, and it was expected reduction of 30.7% of setup time and 299,5h/year on Machine 1

6. Results

After the studies to optimize and improve the operating mode of the compression machines, it became necessary to carry out practical tests of validation of proposed solutions.

6.1. Limitations

Throughout the study it was necessary to take into account a series of limitations inherent in a constantly evolving industrial environment.

Therefore, it was not possible to carry out the number of ideal implementation tests required under the desired conditions.

However, the results that were obtained were quite illustrative and sufficient to be indicators for a positive implementation.

6.2. Minor improvements

As this work was proceeding, it was felt the need to apply the 5S method to the carts of pieces, allocating these to each room of compression.

This measure not only required the operator not to waste time looking for a cart for his parts, but also made sure that he was always at his disposal in the machine room.

Implementation was also carried out in the passage from manual wrench to the dies, to the electric screwdriver with the appropriate tip. To this extent, in addition to small temporal improvement, an increase in efficiency was noticed for the operator.

Finally, due to the economic analysis carried out, it was possible to carry out the acquisition during the internship period plus two cleaning trolleys.

These small measures, in spite of increasing small time savings, are the actions of the *Lean* methodology that contribute to the efficiency of the operator's work.

6.3. Major improvements

5.3.1 Machine 1

In the succession of studies performed, a test was carried out that aimed at the implementation of all improvement measures previously described.

By performing this experiment, it was not possible due to the lack of availability of shift helper, its allocation to end-of-lot tasks. However, the result of this test was recorded in Table 1, it can demonstrate that it was possible to save about 3 hours and 22 minutes, equivalent to a reduction of approximately 27%.

Table 1 – Results for setup before and after improvements for Machine 1.

	Total (hh:mm:ss)
Setup w/waiting times	12:40:24
Setup after improvements	09:18:00

5.3.2. Machine 2

With the objective of studying the impact of the work of two operators throughout the setup, the Machine 2 was chosen because this is the largest machine in terms of dimensions, which allows the logistics of disassembling, cleaning and assembling the same simultaneously two operators.

Thus, a comparison test was performed between the work of one operator and two.

The respective results can be verified in table 2, where it can be understood that when having two operators to make a line change, without changing the existing operating mode, the reduction of setup time is 2 hours and 30 minutes, corresponding to the reduction of 19%.

Table 2 - Results for setup with one and two operators for Machine 2.

	Total (hh:mm:ss)
Setup w/waiting times	13:00:00
Setup after improvements	10:30:00

7. Discussion

The results of implementations on the Machine 1, evidenced a great time reduction.

However, it is advantageous to perform an analysis and comparison of OEE values corresponding to the same product on the day of regular operation and on the day the implementations were performed.

Table 3 shows the two-day results of the same product X. In order to interpret the values it was necessary to thoroughly explore and understand the parameters that influence them.

Table 3 - OEE platform data for product X on the day of regular operation and on the day of implementation, respectively

OEE	**58,8%**	**68,6%**
Avaliability (A)	54,9%	59,5%
Efficiency (E)	111,7%	117,7%
Quality (Q)	95,9%	97,9%

The equipment efficiency parameter (E) was initially approached, which was calculated by the quotient between the actual speed and the predicted speed. Given that this factor showed in the two days, values above 100%, it was concluded that the expected speed, namely of 80000 units / hour is a very low value, which should be adjusted for this type of product and machine. Because it results in values above 100%, this factor influences the OEE in its entirety, and if it is interpreted only, without analyzing each parameter that compose it, the OEE value makes it difficult to identify the causes of losses (OEE standard, 2018).

Next, the quality rate (Q), which is summarized as a ratio between the volume produced according to the volume to be produced, was evaluated. As can be seen, this was a parameter that showed values over 95% over two days. The higher value on the implementation day was due to a larger volume produced, which resulted from a higher actual speed, which directly reflects the equipment efficiency parameter.

Finally, the availability of equipment (A) was interpreted, which is directly influenced by the available equipment time.

In the case of the day of regular operation, there was an availability of equipment of 54.8%. This value was due to the high values of the availability losses which include setup time, BIN filling and machine lubrication.

Compared with the implementation day, the parameter value was 59.5%, which although not much higher than expected, showed an increase of 4.7%.

Thus, the reason why it was possible to verify an increase of this factor, is the clear decrease of availability losses due to the reduction of the setup time. Moreover, on this day, in addition to the setup time, in the availability losses were also waiting for the materials (to start production), which corresponded to 3h and 41 minutes. Nevertheless, by making a pure comparison of only the loss of availability between the two days, there is still a 20%of time reduction.

Continuing to evaluate results, now on the Machine 2, an economic analysis, namely the return on investment, was first performed on the second operator's working hours if this is allocated whenever a line change occurs on this machine.

Once the investment value was determined, the return on investment (ROI), was computed, which compares, once again, the estimated gains and the investment needed, showing if in the long run when allocating these resources, the company will suffer or you can make a profit.

Therefore, the value of ROI was positive and equal to 54.8%, from which it can be concluded that in making this investment the company will obtain € 0.54 more for each euro it invested (Investopedia, 2018). Thus, it is an implementation that will bring profit and that should be considered.

Finally, a similar analysis of OEE was carried out in Machine 2, table 4, which was carried out in the Machine 1 machine, with a view to evidencing the impact of reducing setup time.

Table 4 - OEE values on day with 1 operator and day with 2 operators on Machine 2, respectively

OEE	**47,3%**	**65,4%**
Avaliability (A)	42,7%	62.0%
Efficiency (E)	114,4%	109,3%
Quality (Q)	96,9%	96,6%

The efficiency of the equipment in this machine has the similar problem of Machine 1, because, as the values of these factors are greater than 100%, it is concluded that the standard speed is below what it should, which ends up camouflaging the causes of possible losses efficiency.

However, in the day with only 1 operator, the actual speed was higher, namely 95302 units / hour whereas in the day with 2 operators it was only 91113 units / hour, which influences the volume produced each day, as well as the rate itself of quality.

Also, it is important to note that the theoretical quantity in the day with 1 operator is lower than the day with 2 operators. The value below 1500 000 units, which is common to this type of product, is conditioned by the previous stage, namely granulation. Thus, during the previous phase there were more losses than expected,

which conditioned a smaller amount of material to be transferred to the compression phase. In this situation, it is necessary to adjust the theoretical quantity in the OEE platform. Thus, due to this constraint, we chose not to compare these two parameters with each other.

Arriving the availability of equipment, it becomes evident its increase from 42.7% to 62.0%, that is, 19.3%. This was due not only to the greater available time in the day with 2 operators, but also to a clear temporal decrease of about 51.9% of the availability losses, where setup time has a direct influence.

Therefore, it has been shown that the improvement proposals in the machines studied are economically advantageous and increase the efficiency of the equipment.

8. Recommendations

As a focus for future projects, it makes sense to pay attention to the task in the assembly phase, namely the valve change. Data analysis was performed in order to visualize the time loss in the three machines affected by this problem, that is shown at the table 5.

Table 5 - Resources lost with the valve replacement task, annually.

	Machine 3	Machine 2	Machine 1
Hours/year	3,00	13,50	10,43
Total /year	28		

Since the solution for acquiring a greater number of valves is not a viable solution, the recommended idea is, in partnership with the maintenance department, to develop a different mechanism that is capable of adapting older valves in larger numbers to the existing feed system. For although it does not have an extremely remarkable impact, in operative terms it is a rather uncomfortable and inefficient operation.

9. Cleaning process validation

The establishment of proper cleaning procedures is essential in limiting the contamination to acceptable levels of a product during its processing. Cleaning Validation activities document the evidence that the cleaning procedures implemented are adequate and meet the requirements to be used in the processing of a pharmaceutical product (PIC / S, 2007).

Cleaning Validation of a production sector takes into account not only the cross-contamination of products, but also the presence of detergent residues and the control of microbiological contamination.

It was decided that it would be interesting, in partnership with the Quality Assurance Department to carry out the cleaning validation of a compression machine in the succession of adjustments of the operative mode in the Machine 1 and to make the suggestion an additional critical point, taking advantage of knowledge of the equipment, due to the previous work done.

The list of critical points used was analyzed and it became pertinent to add one more critical point, namely the "Metal detector output ramp". Because it is an area where many tablets pass and is susceptible to accumulation of dust, it is still a part that is directly accessible to the contact of the operator.

By evaluating the pre-defined critical points as well as the suggested new hot-spot, it is verified that the results of the chemical inspection by the HPLC method were shown to be below the maximum allowed value, which is concluded that they are within the conformities.

As in the microbiological analysis, all the critical points, including what was proposed, were in agreement.

From this it can be concluded that the addition of an extra critical point and the evaluation of the existing ones confirms that the adjustment of the operating mode of the machine did not jeopardize the respective cleaning process.

10. Conclusions

The present dissertation consisted in the development of a continuous improvement project applied to the compression phase in the productive cycle of Company X. To that end, Kaizen-Lean methodologies were studied and applied, together with the most pertinent and advantageous tools for the case study.

Initially a detailed survey of the initial state of the proposed machines was carried out and it was concluded that the proposed solutions would be transversal to the five machines, so it was decided to focus and test the improvements only on the two machines.

In this way analyzes of causes of long setup times were carried out, phase by phase and proposals were proposed for the reduction of existing times.

The implementation of improvements had two aspects, the small scale changes, such as the application of 5S methodology and automation of small tasks that despite not having demonstrated substantial time gains, fostered organization and efficiency.

The second aim was to adjust the operative mode aiming at decreasing the overall setup time. In this study, on the one hand there was the exploration of the method that encourages the accomplishment of tasks simultaneously with the hygiene team and the occasional allocation of shift assist, on the other, the allocation of an extra operator during the whole setup process.

Tests carried out on the implementations described clearly showed positive and economically viable gains, namely a reduction of about 3 hours and 22 minutes per line change, corresponding to a reduction of approximately 27% for the Machine 1, in terms increase in the availability of equipment as a parameter of the OEE, where setup time has a direct influence, an increase of 4.7% was observed.

For the Machine 2 test, where 2 operators were allocated throughout the whole setup, there was a decrease of 2h and 30 minutes, equivalent to 19% of the initial time recorded, in terms of parameter increase of availability of OEE equipment, this was 19%.

It can be concluded that there are at least two proven solutions that can be applied to compression machines that adapt to a variety of situations, such as the most efficient coordination between the operator and the hygiene team

or in case of loss of time due to waiting by the inevitable hygiene, the reduction of the setup phases through the presence of 2 operators.

Finally, an analysis of the validation method of cleaning the machine was carried out in partnership with the Quality Assurance Department, and it was possible to demonstrate the importance of the most assertive mode of cleaning validation.

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