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Productivity's improvement in packaging lines of a pharmaceutical company

TESI DI LAUREA MAGISTRALE IN
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Abstract

The pharmaceutical industry is subjected to strict regulations and inspections for which production activities require time and compilation of many documents. This also applies to final packaging activities. For this reason, it is necessary to lighten production processes, especially in the case of a company that has recently left the Big Pharma world and is not very automated.

The objective of this study is to optimize packaging flows through Lean Manufacturing techniques. Specifically, reduce packaging times and create a performance monitoring system.

To achieve these objectives, an OEE system is created, followed by the use of the SMED technique, with which the analysis and standardization of activities are carried out to increase the availability factor through the parallelization of the activities of operators and mechanics.

This is sustained by the introduction of improvements regarding the organization of the department, in particular, for the management of operators, mechanics, documentation, and communication between departments.

The results achieved are visible above all thanks to the use of the A3 logic flow and the adoption of Poka Yoke and Kaizen techniques to make the activities simple and free of uncertainties, increasing the availability of the lines and the visibility of information and therefore reducing the possibility of making mistakes.

In conclusion, it can be said that better information management and standardization of activities leads to awareness of the role of the operator on the line and greater attention to the execution of the activities as well as to the reduction of the execution time of the same. In addition, the use of OEE allows understanding of where to intervene and which factor to develop the most.

Key-words: pharmaceutical industry, packaging, OEE, SMED.

Estratto

Il settore farmaceutico è sottoposto a norme e rigide ispezioni per cui le attività di produzione richiedono tempo e compilazione di molti documenti. Questo riguarda anche le attività finali di confezionamento. Per questo motivo è necessario snellire i processi di produzione, soprattutto nel caso di un'azienda da poco uscita dal mondo Big Pharma e poco automatizzata.

L'obiettivo di questo studio è quello di ottimizzare i flussi di confezionamento attraverso le tecniche della Lean Manufacturing. Nello specifico ridurre i tempi di confezionamento e creare un sistema di monitoraggio delle performance.

Per raggiungere questi obiettivi viene creato un sistema OEE, seguita dall'uso della tecnica SMED, con la quale si procede all'analisi e alla standardizzazione delle attività per aumentare il fattore disponibilità attraverso la parallelizzazione delle attività di operatori e meccanici.

Il tutto accompagnato dall'introduzione di migliorie riguardo organizzazione del reparto, in particolare per gestione di operatori, meccanici, documentazione e comunicazione tra reparti.

I risultati raggiunti sono visibili soprattutto grazie all'uso del flusso logico A3 e l'adozione di tecniche Poka Yoke e Kaizen per rendere le attività semplici e prive di incertezze, aumentando la disponibilità delle linee e la visibilità di informazioni e quindi riducendo la possibilità di commettere errori.

In conclusione, si può affermare che una migliore gestione delle informazioni e la standardizzazione di attività porta alla consapevolezza del ruolo dell'operatore sulla linea e una maggiore attenzione sull'esecuzione delle attività nonché alla riduzione del tempo di esecuzione delle stesse. Inoltre, l'uso dell'OEE permette di capire dove intervenire e quale fattore sviluppare maggiormente.

Key-words: settore farmaceutico, confezionamento, OEE, SMED.

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Executive summary

Avara Liscate Pharmaceutical services S.p.A is a contract manufacturing organization that deals with the production and distribution of pharmaceutical products.

The objective of the thesis is the improvement of productivity in packaging lines, providing a monitoring tool and the application of lean techniques including specifically the use of SMED is proposed.

Analysing the different techniques and studying a case like this context then it is used the A3 approach to define the steps to follow. So, starting from the description of packaging department situation is found that, Packaging times are longer than estimated. In particular, focusing on two of the packaging lines, it is asked to monitor performance and verify the reason for these long times. Secondly, it is known that a lot of documentation needed for production is redundant and unnecessary, so it is asked to analyse and find a way to lighten this documentation.

The observation of the operation of the packaging lines started from a Gemba Walk with which the movement of the operators and materials introduced in the department was observed to interpret the activities and look for possible improvements. Initially, an OEE monitoring system is created and subsequently, analysing the two lines, it turned out that the overall availability factor of the OEE is equal to 33% compared to an 8-hour shift. In particular, maintenance times, clearance times, batch preparation times and stand-by times have been recognized as the most widely used times.

For maintenance, a greater frequency of interventions on the cartooning machine of both lines has been noted, for the clearance times the times are prolonged during the counting and cleaning phase, for the preparation of the batch instead, the control of the materials and the control of the line's functionality are those that require more time, finally, the standby (stops greater than 5 minutes), the activities of greatest impact are the waiting for the material, the drying of the vials and the counting of the labels at the end of a pallet, especially in case of problems with incorrect counts.

Therefore, the target is to increase the availability in general of the lines at least by 25%, instead to increase the visibility of the information, observing the

compilation of the documents, it aims to reach at least 65% of completeness by the operators.

The root causes of this low availability are due to the 4M: machine, men, materials and method. For the machines, the problem concerns a critical format for the BA50 line and problems of insertion package leaflets for the MAR line. For men, the critical issues can be classified into: waiting for maintenance and coordinator intervention and presentation of documentation to start production; a limited number of personnel (operators and mechanics), finally, general errors of inattention and forgetfulness. Then Materials are sometimes poor in quality and/or missing on the lines. Finally, for the method, the main cause is a lack of coordination in the department and between the other ones. To overcome the critical issues related to these causes, different countermeasures are proposed and divided by category, the benefits and efforts are calculated using the "Borda Count" method combined with "Weighted Sum" to decide which ones to pursue because "quick win" or "good to do" and which ones are not feasible or achievable in the future. Of these, 32 out of 44 are agreed. Of these 32, 9 have already been applied while the others are "work in progress" but it is estimated to finish them by December, the period of the end of the internship at the company.

However, analysing the results already obtained, on both lines there was a significant improvement on all factors of the OEE, arriving at a first increase in the general availability of 5%. This is thanks to a greater awareness of the operators, the tools provided to them and the targeted interventions of mechanics. Even at the level of visibility of information, operators have reached about 35% of the target.

To achieve greater results must wait till December in which other countermeasures will be applied, in particular the application of standards from SMED, for carrying out activities during clearance and preparation of the lot, estimating a further reduction in waste time of 17% (worst case) and therefore increase in the availability of 9% compared to the current result.

For the future, it is suggested to continue with the future's countermeasures to obtain further improvements both on the availability factor and on productivity. But above all, it is suggested to pursue the idea of electronic documentation to make light and fast its completion and review.

1. Introduction

For the development of this thesis, an internship was carried out at Avara Pharmaceutical Services S.p.A. placed at the Liscate site.

The aim of this is to analyse and monitor the packaging lines' performances and to develop some solutions to overcome inefficiencies.

The most interesting in that case study is the possibility to apply lean techniques in the working world and test their valuable results. Not only focusing on the lines themselves but also touching indirectly other fields that impact mostly on the performances.

With a complete study of the whole context, it is possible to show the weaknesses of a process and how to intervene to avoid delays, overloading of the available capacity and in the end, produce without wastes.

So, entering in the details, the thesis is structured in chapters linked to the steps of the A3 thinking.

The project starts with a brief introduction of the company represented in chapter 2, then, some lean techniques used during the project are described in chapter 3. Therefore, as an example of the application of those tools, a case study was presented in chapter 4.

Afterwards, chapter 5 starts with the description of the problem for which the company asks to find solutions. In chapter 6, instead, it is analysed the AS-IS situation, considering the entire process flow of the packaging lines, the personnel involved in lines' functioning and finally the monitoring system implemented to collect data. All those to better understand the level of performance of the current situation and highlight other possible inefficiencies.

With chapter 7, having defined the problem, consequently, a target is set, it will represent the key indicators to take into consideration for the following steps.

So, having all the factors clear, it is necessary the root cause analysis indicated in chapter 8. After that, in chapter 9 are developed some countermeasures that with the company will be evaluated and only the most impactful and fast to apply will be considered.

Consequently, in chapter 10, the countermeasures are evaluated and selected to be implemented. Each of them is divided into phases to make evident the progress in their completion.

Afterwards, with chapter 11 the results are shown, and the first inefficiencies are overcome. Hence, in chapter 12 the logic flow of the A3 concludes with the suggestion of further implementation to do when the company has the resources.

Finally, chapter 13 summarises all the contents and the achieved knowledge thanks to the development of this project.

2. Company Overview

Avara Pharmaceutical Services S.p.A.[1] was founded as a multinational in 2016 with headquarters in Norman, Oklahoma. The Liscate site, in particular, has undergone several acquisitions over the years by several multinational companies. The last passing of the baton was made by the Pfizer group. It is important to note how the different management changes have led to variations within the organizational system, product portfolio finally funds management.

However, today Avara is a contract manufacturing organization that works globally offering different services to its clients. In particular, Avara operates as a manufacturer of liquid and lyophilized fill-finish sterile substances and finally takes deals with the packaging of these products, making accurate compliance tests. Therefore, it takes care of the whole cycle of the drug supply chain focusing on the needs of the customers.

The products made are mostly for hospital use and must comply with the regulations of AIFA for the Italian market and FDA for the American market, as well as the GMP procedures that direct the compilation of production documents and all the practices for the good realization of the products.

The plant is divided into several departments and prepares two storage warehouses each connected to at least one of the production departments.

As for the project in question, the department of interest is the packaging.

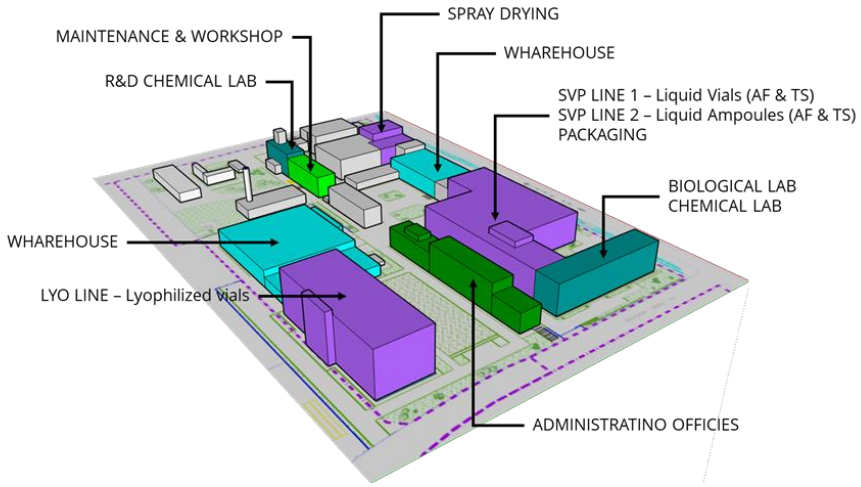


Exhibit 1 - Avara site and departments

In the packaging's department come vials and/or ampoules of the product and bulks of packaging material, including cases, PVC for the construction of trays for multipack ampoules or multipack vials, package leaflet, primary packaging boxes, secondary packaging boxes for serialization.

The materials and people who enter the department, for compliance with the aforementioned rules, by procedure must follow a specific process of dressing for people and storage of the goods in specific areas delimited by demarcation lines. In fact, for example, warehouse-13, which is the warehouse connected to the packaging department, once the material is requested, this is deposited in the stock room in communication with the department, from which the department operator will be able to recover the material.

At this point, the material is introduced into the department and brought to the line of interest or other internal areas dedicated to the stock.

The company has four complete packaging lines located in different dedicated areas. Specifically, three lines are close to the room connected with the warehouse, while one line is arranged a little bit distant. However, a warehouse access room has been set up.

The lines carry out the activities of vial or ampoule labelling, the arrangement on PVC trays for the multipack case, the insertion of the product with the package leaflet in dedicated cases, the polygraphic sticker or tamper evident (if required) and finally the stacking and insertion of the cases in the packaging cardboard.

In some cases, the above activities can be carried out on other specific individual machines, such as the labelling machines or the sticker machines. In extreme and purely temporary cases, some actions can be carried out manually. This is due to a lack of equipment of the machines to package a type of format or the inability of a supplier to create specific cases.

At the end of the packaging in the carton boxes, if requested by the customer, they are moved on to the serialization activity which consists in printing the serial number on each case and assigning this to the reference labelled box.

Serialization is a fundamental step for the guarantee of production and compliance with regulations and product tracking. This procedure is for anti-counterfeiting purposes of delicate products such as pharmaceutical drugs.

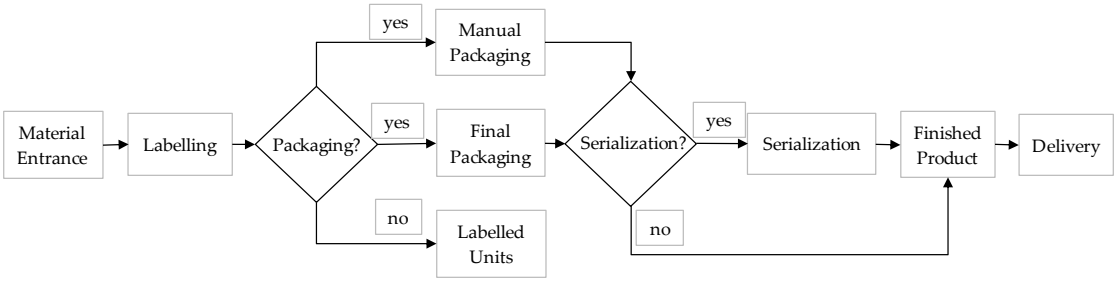


Exhibit 2 - Packaging process flow

The objective of the project is the improvement of productivity in packaging lines, providing a monitoring tool and the application of lean techniques. Some techniques including specifically the use of SMED starting from the analysis of the OEE that will be introduced as a tool of performance monitoring. In addition, the techniques of 5S, poke yoke, and finally, because of a continuous improvement, the techniques of kaizen and visual management will be used.

In addition to the description of the individual techniques, a case study will be used to verify and test the use of these techniques in similar situations.

In addition, the A3 scheme will be used to summarize the evolution of the steps of the project and have an immediate view of the progress achieved.

3. Background knowledge

The following briefly describes lean techniques and their importance in their application.

A3 thinking

A3 thinking[2] is the basis of lean management. It is one of his most effective practices to be able to exhibit any project in all its criticalities, developments, and final results.

The A3 thought was born in Japan from Toyota's studies, it is divided into 8 steps able to highlight the problem, the analysis, the corrective actions, and the action plan on a single sheet of A3 format, precisely.

A3 is therefore an approach that helps to collect and use data, understand the real problem to be solved and identify the best countermeasures to be implemented later to achieve the final goal.

Being a tool for lean management, the information collected is synthesized preferring a graphic display of the information itself. It is a tool applicable in different areas not only at an industrial level, but also at an organizational and functional level.

The compilation of this document starts from the identification of the team responsible for the project, the stakeholders to be satisfied, the definition of the topic and the duration of the project.

A3 model follows the logic of Deming's Plan Do Check Act (PDCA) cycle. This is because the A3 model is constantly changing at the same time as the project is carried out. The problem is observed with different techniques that are recorded on the A3 until the project is completed and the problem is solved. Thanks to these continuous revisions, improvements and adjustments, strategies can be found to approach and achieve the goal.

In detail, for the Plan section of the PDCA, there are classified the first 5 steps:

1. Clarify the problem/Problem background/Current situation: description of the reason why this project is assigned, with a brief description of the

problem encountered by the client. To better find or describe the problem, it can be used the IS/IS NOT analysis.

2. Breakdown the problem: consists of the collection of data related to the problem highlighted, data analysis and extraction of information that highlights the critical issues of the problem itself. This section also recognizes indicators that will be used throughout the entire execution of the project to monitor any improvements or worsening.

3. Set the target: once the key to the problem and the key indicators have been identified, in this section the goal to be achieved is set, establishing a must-have and, where possible, a nice to have. In this way, there is a specific reference achievable and a better secondary goal if the implementations of countermeasures prove to be very efficient.

4. Analyse the root causes: For root cause analysis, several methods can be used. The best known and most used methods are the analysis of the 5 whys and the fishbone analysis (Ishikawa Diagram). In the first method, it is possible to identify the root causes starting from an effect and going backwards wondering why that phenomenon occurred. In the second method, on the other hand, the effect is defined as the head of the fish and it goes to search through the 4M (Machine, Man, Material, Method) or by functionality, the causes that caused it.
   In some cases, it may be necessary to use both methods.

5. Develop countermeasures: it is a hint of the Do phase in which, once all the factors have been analysed, for each cause, specific countermeasures are hypothesized and how they impact the target. Once the list of countermeasures has been drawn up with the respective estimates of costs and efforts/resources to be used, a priority matrix is created to establish which according to the stakeholders and the project owner is the most feasible countermeasure.

Once the planning is finished, then the phase of implementation of the countermeasures starts, and this phase belongs to the Do.

At this stage, the countermeasures to be applied have been decided and it is possible to proceed in the construction of the timing forecast for implementation completion and the impact of the countermeasure on the target.

Note the division of countermeasures into three categories:

- Quick Win: high-benefit solutions with the use of little or no resources. They are the best solutions from an economic and implementation point of view. It is quickly visible the impacts on the target.

- Light intervention: they are solutions with medium-high benefit with the use of medium-low resources both in terms of time and cost. They can be implemented in the short to medium term and therefore the results are also visible within a short time of implementation.

- Structural intervention: solutions with a high benefit but which requires high resources in terms of time, cost, and necessary information. These are solutions that distort the present environment and that in most cases lead to the introduction of innovations. This requires a lot of effort including economic expense, installation time, operator training and more.

So, it is clear that the quick wins are the preferable solutions in any type of project while structural intervention can be suggested as a project to be done in the future.

After that, there is the penultimate step "monitor results and process" that belongs to the Check phase. In fact, at this stage, the results obtained from the implementation are verified after a monitoring period. In this phase, it is visible how to implement small adjustments and how to achieve the nice to have target.

Finally, the last step belonging to the Act phase is "standardize and share the success". In this step, the standards of the processes implemented (or modified ones) are defined and the success is made known throughout the company to create the sense of belonging and fulfilment of the efforts made. In addition, in this step it is possible as mentioned before, to suggest those more challenging countermeasures or even the opening of new projects for other areas tangent to the problem solved with the current project.

In summary, the A3 has as its main purpose Problem Solving through planning and the involvement and development of the thinking of people connected to the project.

A3 can exist at different levels of a lean organization, they can be strategic, value stream and operational. They can generate multiple A3s considering different aspects of the main problem.

Kaizen

Kaizen[3] is considered in the lean philosophy as a means for the company organization, in particular, to make production lean and agile. It was also born in Japan in the Toyota factories after the Second World War and the introduction of the Marshall Plan.

It consists in "changing for the better" (translation of the word itself) through the continuous improvement of processes and attitudes of people towards this philosophy.

To achieve Kaizen, it is necessary to adopt the practice of self-criticism to find a margin for improvement starting from the operator himself who is responsible for the errors and puts ideas to improve. As a result, the culture of small improvements and standardization leads to significant changes in productivity, all starting with the monitoring of events and results.

In these terms, one can connect the Kaizen principle with the famous Deming cycle or PDCA cycle:

- PLAN: Plan your improvements, including goal setting.
- DO: Implement the necessary actions for improvement.
- CHECK: Test your success against your baseline.
- ACT: Corrective activities to improve.

Repeating this virtuous cycle begins the continuous progress on which kaizen is based.

With the kaizen method, it is, therefore, possible to obtain benefits both at the production level and at the level of personal growth since the operator feels part of the improvement process.

Focus of the project – OEE

Overall Equipment Effectiveness [4] is a tool related to monitoring the efficiency of a plant, a machine or at a general level, the production system.

It is a percentage indicator that represents the overall performance of a productive resource or a set of resources, be they human or technical, during the time in which they are available to produce.

Therefore, the OEE investigates all types of inefficiencies that lead to lower productivity: from lack of materials to poor planning, from setups to downtime, from micro-stops to failures, from rework to non-conformities.

In particular, any inefficiency is limited to three factors: Availability, Performance, and production Quality.

These three elements include what are traditionally referred to as the " Six Major Losses ". Among these it is possible to classify as follow:

- Availability: Breakdowns; Setup times
- Quality: Scraps and rework; Startup time
- Performance: shutdowns due to minor inconveniences; reduced processing speed

To apply the OEE it is necessary to visualize and monitor the main losses up to define the factors used for its calculation.

Therefore, for Availability, it will be found the operating time used for production on the net operating time, that is, the time considered useful for production.

For Performance, it will be calculated as the ratio between real production and planned production, where real production depends on changes in speed or rhythm of the machines

Finally, Quality is considered as the sum of the good pieces destined for the customer on the number of pieces produced in total, therefore compliant and non-compliant pieces.

In the end, it will come out as formula for the OEE[5]:

$$OEE\ (\%) = Availability * Performance * Quality * 100$$

$$OEE\ (\%) = \frac{operating\ time}{theoretical\ operating\ time} * \frac{real\ production}{theoretical\ production} * \frac{good\ pieces}{overall\ production} * 100$$

The losses caused by these three elements reduce the number of compliant parts that a machine can produce.

Losses due to availability are mainly due to inactivity, caused by failures and time required to setup the machines. Where the setup is defined as the time necessary to prepare a certain machine for the production and is measured by timing the time that elapses from the last good piece of the previous production to the first good piece of the subsequent production after the tooling. Other additional losses can be caused by cutting tools and start-up times.

The performance losses are mainly due to the reduced speed of the machines. Internal interruptions (events that interrupt the production flow without making the machines stop) and reduction of the working speed (the machines often work at lower speeds than those for which they were designed), all lead to the decrease in real production.

The quality factor is negatively affected by the production of defective parts, which can be produced in the start-up phase, in many cases necessary to bring the machines to optimal operating conditions. Scraps and rework are other losses caused by errors in production or by defects in the machines themselves.

The project activity is therefore based on the collection of OEE data, identifying the processes and interferences that cause problems to the production equipment. And finally, evaluate if the interventions put in place to improve the performance of the machines have given positive results. Operationally, this activity will be supported by operators to find any feedback that may positively influence the improvement in performance in general.

Documentation about OEE

The choice of a tool such as OEE requires documentation (generally paper), to effectively collect production data. Therefore, after data collection, it will be necessary to proceed with data cleaning and extraction of information.

Thanks to the digitalization increasingly present in industries, some software can help for the calculation of values and the organization of data to make their use quick and intuitive. Reporting data to tables in the workplace is one way to improve future outcomes. Operators must be informed about the results of the OEE. Sharing information is a crucial aspect of reducing losses.

The collection of data will bring after some time visualization of productivity and critical areas on which to intervene, thanks to a broader view of any accidents, maintenance and generic activities that are carried out on production lines.

From the information obtained, it will continue with the classic forms of root cause analysis to intervene in the most inefficient point.

SMED

The Single-Minute Exchange of Die[6] tools was born between the 50s and the 60s, from Shigeo Shingo within Toyota factory to produce economic batches with maximum efficiency. It was understood that to optimize the batch change with a different product from the previous one, it was necessary to intervene with the tooling phases or better defined as setup times. Since during the setup times there is no production, this activity is necessary but does not bring any value to the product. Inefficiency occurs when the setup time is excessively high compared to the production time.

The SMED, therefore, deals with the investigation of setup times and their classification in internal and external times of a machine. To obtain a rapid changeover and to be able to increase the production yield.

As mentioned above, the setup occurs every time the production batch is changed. In the case of very small batches, the change will be made several times, especially with products very different between themselves. This is the case, for example, of a pharmaceutical-type production.

Going into detail, the phases of the SMED consist of:

1. Observation and study of the activities carried out in the process
2. Make the distinction between activities IED and OED, where IED means installation or equipment change activities, which can only be carried out when the machine is turned off; instead, OED is the machine setting

activities that can be done simultaneously with the operation of the machine.

3. In the third phase, the aim is to remove all non-value-added activities and turn IED activities into OED where possible.
4. Then proceed with an Improvement of internal setup operations
5. Next, an Improvement in External Setup Operations

All these activities can be achieved thanks to the adoption of standardized operations for example with the use of the 5S technique (described below).

Finally, the results from the application of the SMED find:

- Greater flexibility
- Very short set-up times/set up
- Increase productivity in less time
- Increased customer satisfaction
- Absence of production excesses
- Better organization of work for operators

5S

5S[7] is a simple procedure for managing order and cleaning workstations. The 5S was born in Japan and stand for:

- Seiri – Sort. Delete anything you don't need in your workplace.
- Seiton – Set in order. Efficiently arrange tools, equipment, materials, etc.
- Seison – Shine. Check the order and cleanliness created.
- Seiketsu – Standardize. Maintain the order and cleanliness created, try to improve by continuous repeating of the phases Seiri, Seiton, Seison.
- Shitsuke – Sustain. Impose discipline and rigour for the continuation of improvements.

These are the pillars of the improvements to be adopted to make the workstations and operations of an operator fast and streamlined. Important is the teaching to operators of the importance of using these tools as an aid/support.

Some tools that can be useful in support of the maintenance of the 5S system are Slogans, Posters, demonstrative photos, Newsletters, Small manuals.

Poka Yoke

Poka Yoke[8] is a tool used to reduce defects to zero and limit quality control inspections. From the Japanese language, Poka means involuntary error, Yoke comes from the verb Yokeru that means to avoid.

The basis of the success of the application of Poka Yoke depends on the managers. Business leaders need to build the culture and provide support in terms of time and resources. All this is accompanied by talent scouting and the possibility of people expressing their knowledge in their field of work.

Thanks to the Poka Yoke, the operator can reduce unnecessary time and prefer those activities that give added value to the production itself.

With Poka Yoke you try to achieve perfection in production, this means a 100% reduction in waste. By experience and empirical observation comes out that the sources of the main defects could be the following ones:

- Omitted processing
- Machining errors
- Error in fine-tuning of the workpieces
- Missing part
- Wrong part
- Machining the wrong part
- Error in operation
- Error in adjustment and calibration
- Incorrectly tuned equipment
- Tools and formats prepared not adequately.

Nowadays, automatic signalling mechanisms through visual, sound or line block sensors are used to design a "perfect" system.

Visual management

Visual management[9] is the set of tools to make a process fluid thanks to the non-verbal communication established by visual standards. Thanks to these tools everyone is put in a position to understand any activities to be carried out or understand alarms without the need for previous explanation.

In particular, with the use of Visual Controls, for example, you have the potential to help identify problems, reduce waste, reduce production costs, shorten lead times, reduce inventory, create a safe working environment, and consequently increase your profits. Visual Controls standardise decision making based on facts.

The easiest form of visual control to apply is colour coding, where there is the use of colours to communicate status.

Another tool can be the use of Standard Work that show the tasks to be carried out in sequence clearly and simply.

Finally, it is possible to use quality standards to give operators a demonstration of defects and leave a basis for making their decisions regarding the goodness of the product.

Therefore, it can be summarized that the essential tools of Visual Management can be traced back to three main categories, based on function and type:

- Viewers: graphs and functional diagrams for the best performance of practical work always within the worker's reach, which provide him with immediate indications on how to perform certain tasks. Viewers can also be used as tools to stimulate results through successfully achieved goals and performance.

- Visual controls: tools at the service of workers within the company that allow you to understand when and how to carry out a given action. e.g., traffic lights and Kanban signs.

- Visual process indicators: This category includes all the reports that facilitate the performance of the work through precise indications of areas and processes, guiding the correct flow of materials or information quickly and intuitively.

The use of these tools ensures an increase in efficiency in terms of waste reduction, employee work effectiveness and standardization of processes.

4. State of art - Literature review – A case study

Studying the literature there is a wide range of discussions about the different techniques of lean management not properly concerned in the pharmaceutical sector. Probably the reason is that the pharmaceutical sector is too much regulated to be free of using all the lean advice. But with this thesis, the aim is to dare all the limitations and show how lean management is applicable everywhere.

One point of beginning to understand how to apply the lean management in the pharmaceutical sector is given by M. Bevilacqua, F.E. Ciarapica, I. De Sanctis, G. Mazzuto and C. Paciarotti's article "A Changeover Time Reduction through an integration of lean practices: A case study from pharmaceutical sector" [10] (2015). There, the authors analyse the packaging line of a pharmaceutical company using lean techniques to reduce batch change time and changeover time up to 50%, increasing overall equipment effectiveness (OEE) by 25%.

Within the study, the approaches of SMED in combination with suppliers, inputs, process, outputs, and customers (SIPOC), Kanban, 5S techniques and Total Productive Maintenance (TPM) are used.

The aim is to eliminate the non-value-added activities that can cause the lengthening of the change-format times, all those following the rules of Good Manufacturing Practice (GMP) that limit some activities of improvement/conversion of internal times to external.

In particular, from the article, it was decided to continue in stages the improvement of the OEE and Changeover time indicators.

1. Measurement: video making and time monitoring.
2. Analise: video analysis, then through brainstorming the definition of a setup baseline worksheet and the creation of a spaghetti diagram.
3. Implementation: implementation of SMED, SIPOC, Poka Joke and critical path method techniques.
4. Improvement: use of 5S techniques, Kanban, and standardization to achieve continuous improvement.
5. Test.

During the first phase, it turned out that the cleanliness and change format activities required about three times more than all other material production or

preparation activities. In addition, analysing the efficiency of the line appears that some defects create delays on the lines. The biggest category of defects is the so called "closure of houses".

In the analysis phase, there is a detailed analysis and verification of the theoretical time and the real time of the operational phases. Creating a baseline worksheet setup and the consequent classification of the same in internal and external setups.

Once identified where to intervene, the SMED is implemented with the use of spaghetti diagrams on the lines and the definition of solutions by category:

- Preparation and check-up of materials and equipment
- Cleaning and washing parts
- Removal and installation of parts used in production
- Documentation, regulation, and instructions.

A handbook is then released for the changeover of each line.

For the implementation, standards are defined for the format of the materials.

For the improvement, a kanban system is created combined with visual management where the level of reordering of the material is indicated through coloured labels.

At the end of the case study, the results are monitored after the application of the improvements, and they achieved a 61% improvement in the changeover and the 10% reduction in the space allocated for the materials. OEE also sees an increase from 18% to 26%.

In conclusion, this article introduces the steps that can be adopted in this project and that with a different focus can bring results in the application of the lean techniques in pharmaceutical companies.

5. Problem background

As discussed before, to better manage the project stages, it is used the A3 framework. Starting from the definition of the problem perceived by the company and their real needs, it is possible to collect and analyse data, highlighting the root causes of the problem. After that, some possible countermeasures are developed and prioritized till their application. Finally, a stage of monitoring is performed to observe the impacts on the target and the achievements through a KPI dashboard.

Avara believes that the packaging time for a batch of products is excessively long, especially the initial setup time. However, the company is not able to indicate why there is this lengthening due to the lack of a monitoring system. An improvement intervention is therefore required on two of the packaging lines. They are the most widely used in the department and consist of a single vial packaging per carton on the MAR line and a multipack packaging of 10 vials per carton on the BA50 line.

Therefore, the lean project consists in the creation of a monitoring system of the lines to be used also in the long term and the introduction of improvement's techniques to reduce setup times and increase the efficiency of the lines themselves.

Tangentially to efficiency activities, it is asked to review the documents of the processing procedures (Batch Record) to make their compilation lean and fast.

6. Current situation and breakdown the problem

The observation of the operation of the packaging lines started from a Gemba Walk with which the movement of the operators and materials introduced in the department was observed to interpret the activities and look for possible improvements. As a first step, the operativity of the lines was analysed, subsequently, the process flow was drawn and the critical activities in terms of machine malfunctions and excess waste production were highlighted.

MAR

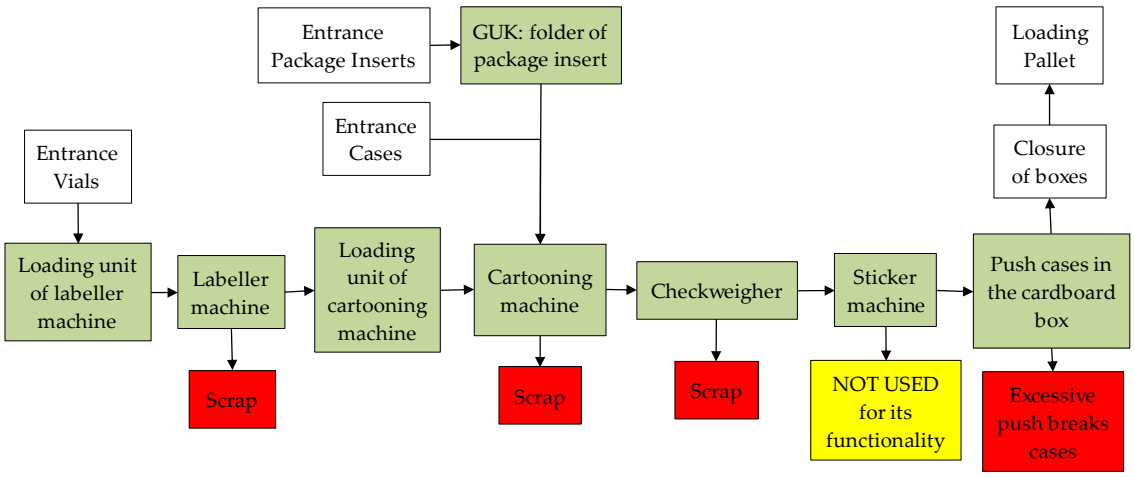


Exhibit 3- MAR process flow

This line has been modified over the years depending on the company's product portfolio. Lately, under the ownership of Avara, the MAR line is composed of a loading unit of the vials without the label, called Anonymous. This unit is filled manually by the operators. The vials are then taken to the conveyor guide for entry into the labeller. The labeller is composed of an electrical system called Libra from which the recipes of the product to be labelled are selected, as well as all the in-process information. The recipe indicates information such as product type, format and set speed, while during operation the actual speed, the number of pieces processed and the reporting of any errors and alarms are shown.

From the labeller come out the vials labelled and stamped with the variable data corresponding to the batch and the expiration date, some sensors recognize the presence of these and discard the vial without this information. Among other rejects, anonymous vials or incorrect reading of the label barcode can occur.

At the exit of the labeller, the good vials are collected in a second loading unit that will transport the vials to the entrance of the cartooning machine. The vial is detected by a photocell that allows the passage of the vial in the cartooning phases. In particular, the vial is stretched out and, in the meantime, a case is taken, which is opened and brought into the upper chain for the insertion of the vial, at the same time, a package leaflet is taken and folded into a machine named GUK, which provides the folds to the sheet, which once ready is placed in the picking pliers of the cartooning machine. At this point, the vial is pushed against the folded package leaflet and inserted directly into the carton. The product is closed through the flaps of the case and if it complies with the code, presence of sheet and vial, it is carried forward, otherwise, it is discarded. The good cases are then weighed on the checkweigher (commonly called libra) which recognizes in a range the total weight of the product and discards it if it is out of range.

The boxes are then brought into the sticker machine that is currently used once and therefore acts in most cases, the role of a conveyor belt. The product then reaches the stacking hopper of the vials for the insertion of 40 boxes per shelf of the box. Finally, once the box is complete, the PRB lets out the open cardboard from the top and bottom side and slid on the final rollers. At this point, the operator observes that the box is complete and closes both sides with scotch tape. In the end, the operator places the closed box on the pallet. At the end of the pallet, the boxes are packed together and stored in the dedicated waiting areas for the serialization phase.

As you can see from Exhibit 3 it should be noted that the most critical issues occur on the labeller, on the cartooning machine (in particular, the GUK) and finally, the PRB.

As for the MAR labeller, some employees don't know how to select recipes or reset data. This lack corresponds to a waste of time as only the experienced operator knows how to intervene and must therefore instruct and help the colleague.

The cartooning machine and the GUK are the fundamental parts of the line and create many problems and interventions during production. In particular, the GUK causes problems both in the picking and folding of the package leaflet and in the consequent hindrance of the carton chain. This occurs when a package leaflet is not placed in the carton and therefore gets stuck in the sampling pliers.

The callipers carry the prospectus until the chain makes the turn and if this does not detach itself by gravity or if the operator does not notice its presence, this is then accumulated under the chain creating a deviation and in worse cases the exit from the tracks of the chain. This problem also impacts the performance of the cartooning machine itself, causing a series of adjustments to the chain itself.

Finally, the PRB is a very old part of the line and the risk of error in the stacker counts is very high, for this reason, the sides of the boxes are left open. In addition, the boxes many times are not taken correctly from the machine, and this causes stops in which the operator must intervene to force the machine to a subsequent withdrawal or simply the removal of that cardboard. However, the main problem occurs when the cartons get stuck in the guides of the machine and for this reason, their forced transport causes the box to break and the consequent breakage of the finished product (cartons and vials).

Exhibit 3 represents the process described above. Starting from the left, the first activity is the "Entrance Vials", instead, the last activity, with which the process ends, is "Loading Pallet". About the use of colours, The Green parts represent the activities done automatically by the line, instead, the White parts must be done by the operators. The Red cells represent the criticalities due to the possibility to make scraps and finally, in Yellow is indicated a note of use.

BA50

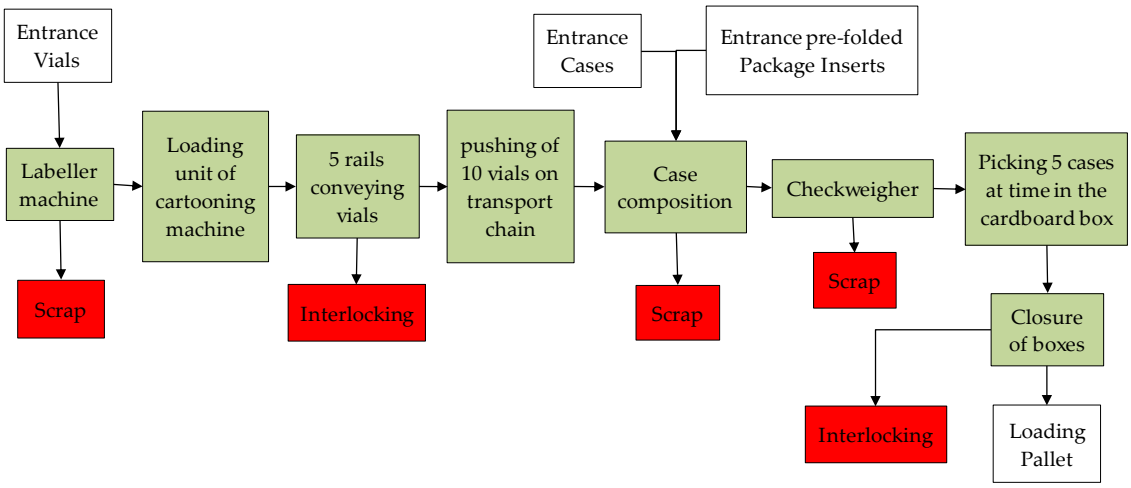


Exhibit 4 - BA50 process flow

The BA50 is a young line within the department, less than ten years old, and was initially used to produce only one format of products with format Ø26mm. Subsequently, it was decided to expand its production, adding other formats such as Ø24mm. This line also produces multipack boxes, which means that inside the single case there are ten vials of product. The line consists of the Neri RL300 labeller in which the vials are loaded and as for the MAR process, a label is attached with the variable data printed on the vial. If a label is found to be non-compliant with the data or the barcode, the vial is discarded. Therefore, at the exit from the labeller, the good vials are conveyed to a collection unit.

Unlike MAR, this unit must collect the vials in the five guides to form the withdrawal of the ten vials at the end of the stroke. The vials arrive at the entrance of the cartooning machine in blocks of ten vials, which placed on the transport chain pass several photocells that detect the presence of all the vials. Meanwhile, a case is taken from the machine and opened. Once the vial and the carton are aligned and ready for insertion, a package leaflet already folded by the supplier is also taken and the vials are pushed against this to facilitate the insertion in the case. The case continues the stroke inside the cartooning machine and is closed using a glue jet. If the product complies, it is taken to the checkweigher, otherwise, it is discarded. From the libra, only the product is passed in the weight range and then ends up in the buffer corridor of the case packer.

In this case, a suction cup arm collects five cases at a time and places them inside the cardboard box. Once the cardboard is saturated, it is closed independently with scotch tape from the machine itself.

Now the finished box is unloaded along the rollers and picked up by the operator who will make sure to put it on the pallet.

From Exhibit 4 of the BA50 line, it can be observed that the critical issues are like those found in the MAR. However, for the Neri RL300 labeller, the problem is electrical, in fact, during the observation, a phase reordering error is often reported. This problem can only be solved with the intervention of the mechanic and consists of adjustments of phase settings.

There is criticality in filling the five product guides. As long as all five guides do not have vials, the cartooning pusher will highlight a problem and stop itself. This is because the loading unit is structured to fill the second corridor first and then the next ones. In this way, the outermost corridor often remains empty until

the unit is fully loaded and therefore the vials are easily pushed towards that guide. After the pushers of the cartooning machine, a further criticality is given by the probes inside it. In fact, in case of inconsistent adjustments, the push of the vials combined with an incorrect withdrawal of the package leaflet and a wrong position of the case, causes an excessive push that goes to destroy the case and the vials.

In addition, the use of glue for closing the case can give problems as a result of a non-use over the weeks. If the machine is not used but is left active, the glue carbonizes and dries. A mechanical intervention is therefore necessary to purge the glue pump and change the nozzle now obstructed by dry glue.

Subsequent critical issues are found on the case packer because if the guides of the exhaust channels for closing the boxes are too narrow or poorly adjusted, this causes the box to break and damage some cases and the possible breakage of vials.

Finally, a problem that occurs in both lines is the blocking of the checkweigher at the time when more than three scraps are made. In fact, to continue it is necessary to unlock the shutdown through the operator's log-in. However, operators run many times on the lines and from production, it is probable that a line is not used frequently. For this reason, after 60 days the log-in password expires.

In this way, to be rehabilitated, the intervention of an external department called MQA (Manufacturing Quality Assurance) is needed to rehabilitate the user. This causes a waste of time as the MQA agent is not inside the department.

In conclusion of the lines' descriptions, Exhibit 7 represents the process of BA50. As for the Mar, starting from left, the first activity is the "Entrance Vials", instead, the last activity is "Loading Pallet". As before, the Green parts represent the activities done automatically by the line, instead, the White parts are the ones done by the operators. Finally, the Red cells represent the criticalities due to the possibility to make scraps and some interlocking.

OPERATORS AND MECHANICS

Once the machines have been analysed, it is possible to enter into the details of the activities carried out by the line operators.

The operators present in the department are twenty divided into two teams of eight for the morning (6 a.m. till 2 p.m.) and afternoon (2 p.m. till 10 p.m.) shifts, and two other teams of two people, one for the night shift (10 p.m. till 6 a.m.) and one for rest day. In fact, for the management of shifts, a slipped system is used for which part of the operators starts the working week on Monday and ends on Friday while the other begins on Monday and ends on Saturday with a rest day within the working week. Teams are minimally variable depending on limitations (some can only do the morning shift or otherwise they can only do the afternoon shift).

However, the operators present in line are at least two, the number may increase depending on the urgency of the lot and the number of people present in the shift.

It is also noted that the line can be managed by a single operator if the colleague is in break or lunch break, with the particularity that the production of the line is divided into phases to be able to control all the machines. This means non-continuity of the line and production at 50% of the real capacity.

About the mechanical field, two mechanics are available for the maintenance of the entire department, one for the first shift and the other for the second shift.

Every week they make the shift change that theoretically is reported by the head of maintenance to the head of the packaging department.

OEE MODEL

At this point to monitor the performance of production, an OEE scheme has been introduced. An extract of it is shown below (Exhibit 5). All times are expressed in minutes and the pieces correspond to the number of complete cases.

Day (dd/mm/yy)	Lot (A00000xxxxx)	Line	Format	Shift	Operators	Theorical available time	**TOT SET UP**	T-clearance	T-cleaning	T-starting checks	T-Lot preparation	T- functionality checks	T-start up	T-light adjustment machine	T-changes	T- operators	T- micro stop < 5 min

T- stand-by	T-Maintenance	**SUM time loss**	Effective time	Availability	LOT Availability	Theorical case	Effective case	Cumulative case	Performance	Lot Performance	Reworked	Scraps	Scraps code	Not-compliant vials	Good case	Quality	Lot Quality	OEE

Exhibit 5- Extract of OEE model used

As can be seen, the scheme used starts from the insertion of the day on which the data collection is done, the batch to be produced, the line used, the format of the product, the shift, and the line managers (operators). These are informative data to identify how many days have been used, more precisely the number of shifts, to complete the packaging of a batch, and highlight any adjustment times or actual format changes.

Next, there is the compilation of data for OEE factors. In particular, the entire shift (480 minutes) is considered as theoretical available time and alternatively, in some cases, the time in which the shift operator occupies the line or the splitting of the shift in case of the start of a second batch on the same line.

However, the **total of the setups** considers the following times:

- Clearance time: consists of the time necessary to remove the materials from the line and subsequently from the processing room at the end of lot production. In parallel, the compilation time of the Batch Record is considered regarding the material reconciliation part.

- Cleaning time: it is the time required for cleaning the line using industrial solvents and other products, as well as the time of compilation of the Batch Record, the Logbook (document about the specific production area) and the attachments to be displayed in the room to witness the cleaning of the machine and the processing area (which is then transformed "into processing" when starting with a new batch).
  Generally, this activity is carried out immediately after clearance at the end of the batch.

- Time of the starting checks: this is the time that is used to check the cleanliness of the line and the area when the operators are about to start a new batch. It is clear that in case the batch starts immediately after the cleaning of the previous batch, the starting control is reduced or null.

- Lot preparation time: it is the most important activity that consists of the introduction of materials in the work area, the control of the identification codes of the materials concerning the Transfer Order (TO) delivered from the warehouse and the verification of the specific material. To verify the material, a sample of the case and prospectus are also taken in which the identification codes are checked and finally signed and countersigned by the operators. A similar process regarding the creation of the stamp of variable data. The stamp is mounted, the correctness of the data entered, and the quality of the print is verified, then the Batch Record is filled in by hand, reporting twice, lot number and expiration date. This is to confirm the sample label pasted on the Batch Record.
  As the last activity considered in this measurement of time, the loading of materials on the line is also considered. That is the loading of the labels reel, vials, cases, package leaflet and cardboard boxes for packaging.

- Time for checking line operation (functionality check time) consists of the time to check that the operation of the sensors of the labeller, the cartooning machine and the libra. This time is therefore considered the time necessary to prepare the waste tests.

- Start-up time: it is the time for which the first product box has been assembled and then controlled for its completeness.

- Times for light machine adjustments: this is the last intervention in which the mechanic or possibly the authorized operator makes adjustments on the line.

- Change or tooling time refers to any changes in the reel of the labels or foil change for the stamp.

As has been said above, these are the setup times in which corresponds to the time necessary to prepare a given means of production, timing the time that

elapses from the last good piece of the previous production until the first good piece of the next production concluded the tooling.

Subsequently, there are other times related to operators, materials, or mechanical interventions, in fact:

- Operator absence time concerns the time for which the line remains unsupervised by at least one operator. In this case, during the breaks of an operator, the colleague must remain on the line and alternates with the other colleague on his return.
  Therefore, if both operators are far from the field of action of the line, the absence is considered.

- Micro stop time corresponds to the sum of all machines' stops less than 5 minutes.

- Stand-by time: unlike micro-stops, these stand-by correspond to stops greater than 5 minutes for which the machine is available but is not used.

- Maintenance times collects all the mechanical interventions due to the restoration of the operation of the line. The intervention time depends on the severity of the failure or the ability of the mechanic to identify the problem and intervene with the right means.

Therefore, the sum of all these times is defined as the sum of time loss that is subtracted from the theoretical time available, this difference is therefore the actual time of production.

In this way, it is possible to check the availability of the single shift and the average availability for the completion of the lot. Using the formula:

$$Lot\ Availability\ [\%] = \frac{\sum effective\ time}{\sum theoretical\ available\ time} * 100$$

Next, it is possible to move on to the performance section in which must enter the number of theoretical pieces calculated as:

$$Theoretical\ cases\ [pieces]\ =\ bottleneck\ speed\ \left[\frac{pieces}{min}\right] *\ actual\ time[min]$$

Instead in the cases produced, the total of good pieces is added to the number of scraps of that shift. For the cumulative cases, it can be verified that the final production number of the batch is corresponding to the number given by the Process Order (PO).

At this point the performance of the single shift is calculated as $\frac{cases\,produced}{theoretical\,cases}$, while for the average performance referred to the completion of the lot it is used:

$$Lot\ Performance\ [\%] = \frac{\frac{\sum cases\ produced}{bottleneck\ speed}}{\sum effective\ time} * 100$$

Finally, to complete the OEE, the quality factor is considered. In this factor, the number of non-compliant pieces is considered as the sum of the number of reworked and the number of scraps. So, their sum is added to the good pieces represented as good cases produced. In this way, it is possible to calculate the quality as:

$$Quality\ [\%] = \frac{good\ cases}{total\ cases\ produced\ (compliant\ and\ non\_compliant)}$$

For the average quality referred to the lot, the sum of good pieces on the total of pieces produced in the lot is considered.

Finally, in this case, the OEE is considered on the realization of a lot calculated on the number of shifts used for the completion of it.

OEE ANALYSIS

From the observation of about three weeks, in correspondence with the functionality of the lines, the trend is reported in the following tables.

In the specific case of the MAR (Exhibit 6), the analysis presents over 11 days corresponding to 22 shifts 9 lots were completed. The respective average OEE values are:

A = 38.26%

P = 68.33%

Q = 97.12%

OEE = 25.39%

Day	Lot A00004	Ø	Shift	Th.av.time	Tot. Setup	T-Op.absence	T- micro stop	T- stand-by	T-maintenance	SUM time loss	Effective time	Lot Availability	Th. cases	Effective cases	Cumulative cases	Lot Performance	Reworked	Scraps	Lot Quality	OEE
14/09	1695	36	2	480	203				15	218	262	54.5 %	16866		17354		0	18		
21/09	1792	26.5	2	340	65				20	85	255	61.3 %	15300	5000	5000	42.8 %			100 %	26.2 %
22/09			1	480	0	5	3	9	98	115	365		21900	9970	14970					
			2	290	53	3	7	128	39	230	60		3600	2500	17470			5		
22/09	1890	26.5	2	190	50					50	140	39.4 %	8400	6000	6000	75.0 %			99.2 %	29.3 %
23/09			1	480	25	35	15	112	126	313	167		10020	7000	13000					
			2	300	60	70	11	37	47	225	75		4500	4194	17194		138	5		
23/09	1919	30	2	180	153	5	5	15		178	2	29.2 %	120	30	30	75.7 %	9		99.3 %	22.0 %
24/09			1	480	121	4	15	64	85	289	191		11460	8739	8769		41	10		
24/09	2119	26.5	2	480	99	5	13	116	15	248	232	29.4 %	13920	6660	6660	79.0 %			99.4 %	23.1 %
27/09			1	480	100	20			360	480	0		0	0	6660		0	0		
			2	300	121			10	30	161	139		8340	10927	17587		95	16		
27/09	2122	30	2	180	70			75	35	180	0	26.0 %	0	0	0	63.6 %			98.7 %	16.3 %
28/09			1	480	93	5	6	106	72	282	198		11880	7000	7000			19		
			2	210	94	32	5	24	27	182	28		1680	1631	8631		92	4		
28/09	2130	30	2	270	83			100		183	87	59.5 %	5220	2726	2726	32.8 %	15	3	99.2 %	19.3 %
29/09			1	480	86			35		121	359		21540	6051	8777		44	6		
08/10	2358	26.5	1	480	165	17	3	95	115	395	85	27.1 %	5100	5036	5072	99.5 %	117	36	97.0 %	26.2 %
			2	480	27	18	7	228		280	200		12000	11987	17066		359	6		
11/10			1	90	80	10				90	0		0	0	17066		0	0		
11/10	2397	26.5	1	390	86	39		130	35	290	100	32.4 %	6000	4772	4803	88.3 %	96	31	95.3 %	26.1 %
			2	480	0	20		100	133	253	227		13620	12497	17300		723			
12/10			1	170	150	10				160	10		600	577	17811		25	25		

Exhibit 6- Data collection MAR

As for the BA50 (Exhibit 7), however, it presents an analysis on the operation of 10 days of production for a total of 20 shifts. In this time, 8 lots with average OEE values were completed:

A = 29.08%

P = 50.39%

Q = 85.58%

OEE = 12.54%

Day	Lot A00004	Ø	Shift	Th.av.time	Tot. Setup	T-Op.absence	T- micro stop	T- stand-by	T-maintenance	SUM time loss	Effective time	Lot Availability	Th. cases	Effective cases	Cumulative cases	Lot Performance	Reworked	Scraps	Lot Quality	OEE
14/09	1668	24	1	480	99	x	x	x	381	480	0	14.4 %	0	0	0	64.2 %	0	0	99.5 %	9.2 %
15/09			1	480	131	5	10	31	167	344	136		2720	2000	2000		0	0		
			2	160	80	22	2	13	18	135	25		500	67	2067.3		0	103		
15/09	1698	24	2	320	108	15	5		140	268	52	32.3 %	1040	1000	1000	47.5 %	0	0	99.7 %	15.3 %
16/09			1	480	98	x	15	33	105	251	229		4580	1688	2688.4		0	84		
			2	75	73					73	2		40	0	0		0	0		
16/09	1714	24	2	405	126	15	1	0	64	206	199	52.5 %	3980	1400	1400	31.1 %			99.5 %	16.2 %
17/09			1	480	110	4	10		90	214	266		5320	1490	2889.8			13.8		
27/09	1910	23.75	1	480	101			64	315	480	0	19.3 %	0	0	0	55.3 %			47.3 %	5.0 %
			2	480	115	15		165		295	185		3700	2048	2048		1060	20		
28/09	1920	23.75	1	480	196	10	26	81		313	167	34.8 %	3340	1942	1942	80.9 %	177	31	89.3 %	25.1 %
30/09	2247	26	1	480	153	10			317	480	0	29.1 %	0	0	0	41.0 %	0	0	89.1 %	10.6 %
			2	480	105	10	14	64	90	283	197		3940	1219	1219		42	2		
01/10			1	480	0	10	15	218	60	303	177		3540	1680	2899		0	0		
			2	480	0	10	14	137	135	296	184		3680	1676	3356		1540	0		
08/10	2356	26	1	480	150	20			270	440	40	19.9 %	800	510	5132	90.4 %		32	98.2 %	17.7 %
			2	480	35	15	16	211	52	329	151		3020	2943	34598		510	36		
11/10	2398	26	1	480	83	15	20	70	70	258	222	41.1 %	4440	2980	29831	60.8 %	240	31	99.0 %	24.8 %
			2	215	123	5		23		151	64		1280	498	34830		30	19		

Exhibit 7- Data collection BA50

As it turns out, the BA50 line has worse results.

However, for both lines, it turned out that availability is the most inefficient factor that severely impacts the OEE.

In fact, generalizing it can be said that the factors of OEE correspond to:

A = 33.79%

P = 59.36%

Q = 89.73%

OEE = 19.56%

Therefore, the availability of the lines corresponds to just over a third of the shift.

To identify the activities on which to intervene, a Pareto analysis is carried out.

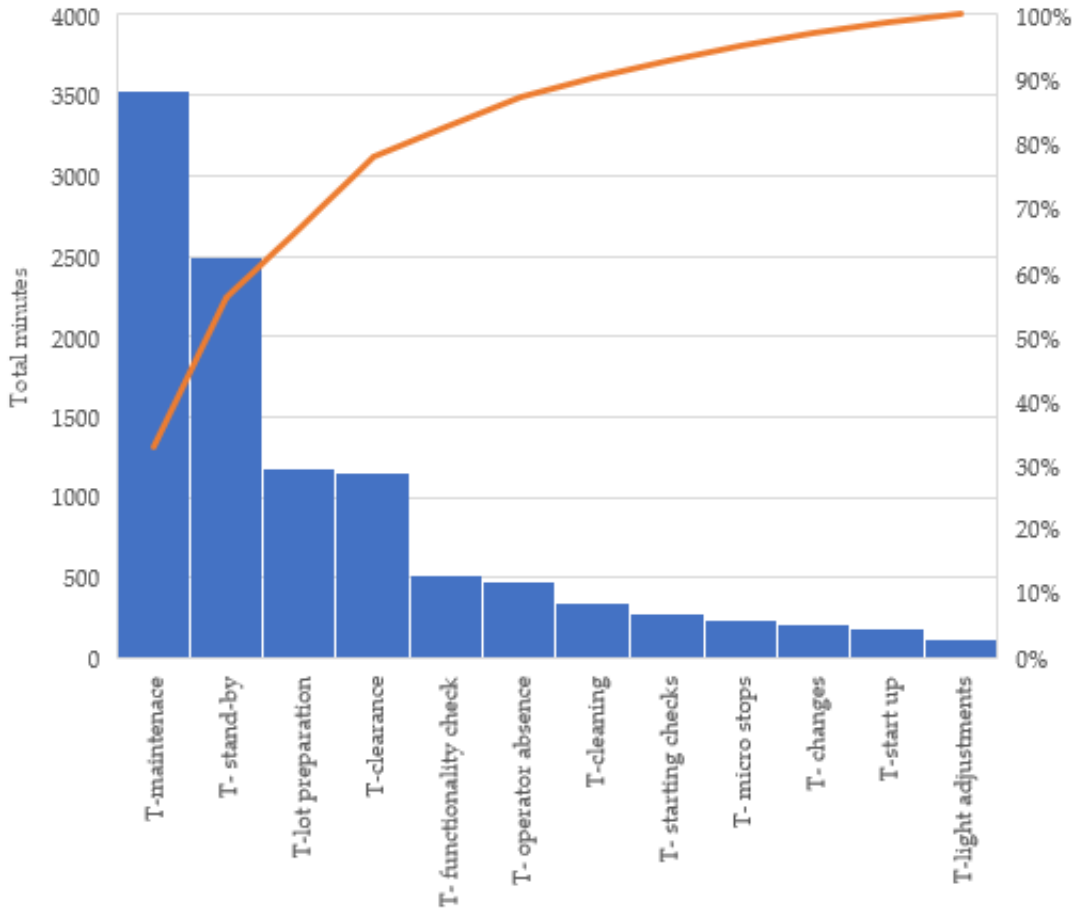


Exhibit 8- Pareto analysis

As you can see, the longest tasks are maintenance, stops of more than 5 minutes (stand-by) and almost equal lot preparation and clearance. However, the latter activity is more significant in terms of time as described above, the number of

tasks to be carried out in the clearance is lower than in the preparation of the batch. For this reason, at the same time, clearance is the most inefficient.

In fact, from the **clearance** times it appears that although the removal activities of the materials and accounts for reconciliation can be done in parallel, some operators are in difficulty in filling out the Batch Record cards with the correct accounts. This happens because the operators who compile the Batch Records change from time to time, moreover the operators assigned to the line are not always the same, the department head opts for versatility so that all operators know how to approximately put into operation and work on all the machines. This round system sometimes leads operators in difficulty in recognizing which fields of the Batch Record to fill in and which not, so it is necessary to research and ask the most experienced colleagues in the compilation what information to enter. Sometimes, however, there is also a lack of material such as calculators.

Entering instead, in detail of **maintenance** times, it was analysed the frequency of the intervention on the single part of both the lines and the mean time of repairing. The following exhibit shows the results:

Line	Machine	Frequency	Mean time [min]
MAR	Loading unit labeller	0	0
MAR	Labeller	5	12
MAR	Loading unit cartooning machine	1	14
MAR	GUK	8	29
MAR	Cartooning machine	12	49
MAR	Libra	1	10
MAR	Sticker machine	1	4
MAR	PRB	2	40
BA50	Labeller	9	65
BA50	Loading unit cartooning machine	1	5
BA50	Cartooning machine	19	111
BA50	Libra	0	0
BA50	PRB	0	0

Exhibit 9 - Frequency and mean time of mechanics' intervention on different machines of the line

As noticed, the machines that need more intervention was for both the cartooning machine and the time necessary for repairing is very long, going in case of BA50 near to two hours.

Especially, analysing the type of activity done, the most impactful in terms of time is the change of formats and the following phase of adjustments before the functionality of the line.

It is known that the head of the packaging department leaves one shift for the changeover of the line, once the machine has the right mechanical part for the incoming product, he sent the materials to the lines. If the materials are ready to be used, it means that the product doesn't need to be dried, the mechanic starts the adjustments in terms of good processing given by the right friction regulation.

The time for the changeover can be extended due to the lack of materials or the impossibility of using the vials wet. This situation occurs especially on MAR where the products come from the cold room with temperature about 2°C till 8°C.

Then focusing on the intervention on the machine the problems on the MAR are linked to the GUK machine. If the package leaflet is not properly picked up and folded, it destroys the case in which it must be inserted. Alternatively, if the package leaflet is picked up by the callipers but there is not the case, it can follow the entire course of the chain of transportation till it goes under the chain itself and it causes the misalignment from the track and the break of the belt. This incident causes a very long time for repairing and substitution of the components.

For the BA50, instead, the problems in the cartooning machine are caused by a wrong inserting of the vials into the case. In particular, the vials are pushed with high strength giving an opposite reaction that to the inserting, leaving one vial not properly inside the case. With this, the case is not able to be closed and the case gets stuck. The force of the movement causes the break of the vials and the following stops for cleaning of the machine and the mechanical adjustments. In addition, the use of glue for the closing of the cases requires many interventions for the regulation of the jet. On the other hand, if the machine is not used for a long time but is taken functioning without utilizing it, that causes the carbonization of glue and accumulation of dry glue in the nozzle, so it is necessary a purge.

Although, BA50 is the most critical line due to the multipack system. It means that if one vial is not completely inserted, the effects are very dangerous on the

cartooning machine. In addition, if the format used is not properly conformed to the product to process, the interventions for regulations will be very frequent.

Another important point for the lengthening of the maintenance time is that, in some cases, the mechanic is not present in the department but is in the workshop. This workshop is located in another building for which the intervention time is dilated for the arrival in the department and the dressing time. It should be noted that the department mechanic is one per shift. However, the lines can work simultaneously, but in case of failure on both, in this case, the mechanic will have to prioritize one intervention over another causing a waiting time on the non-prioritized line.

As for the **stand-by** times, the frequency and mean times of each activity are observed. Below, the detail of each:

Activity	**Frequency**	**Mean time [min]**
Case closure	3	11
Reworked vials loading	9	15
Unlock libra's password	2	29
Lack of material load	5	9
PRB recovery of broken full boxes	6	19
Count labels and search of missed label/vial	26	26
Loading unit empty	6	27
Material waiting	4	34
Line reorder	1	10
Vials drying	3	66
Label reel breakage	9	17
Change of foil and label reel	4	20
Machine adjustments	5	33
Vial breakage	3	25
Vial interlocking	1	16
Documents compilation	1	8
Opening of the boxes for glue control on boxes	1	200
Problem exiting vials from cartooning machine	1	10
Problem exiting vials from labeller	1	10
Drop of heat sensor in PRB	1	5
Warming of glue and stamp	1	30

Exhibit 10 - Stand-by causes with their frequency and mean time considering the whole time of observation

In red are highlighted the most frequent activities that are made at least once a shift. The most critical is the count of labels, which is the activity done when a pallet is fully loaded. At this time, the operators empty the line and count the entire production till that moment, and they verify the number of labels consumed is the same as the produced. If the result of the count is less than the expected, starts the search of the missed label, instead, if the count is more than expected means that maybe a vial has not the label and it is packed anonymous. In this case, the worst that can happen, the team start the search and in case the label does not appear, there is the opening of all the boxes and the cases to find the anonymous.

The other "red" activities are the loading of the vials considered good for the reworking and the change of the broken reel of the labels.

The first is an activity that normally is done every time during the normal processing of the line. In this case, this activity is done just to feed the loading unit and there is no count of how many vials are reworked.

The second activity, instead, is a problem linked to the quality of the suppliers' materials. In this case, the reel of the labels is delivered with many additions that creates problems with the sensors of the labeller machines. For example, some labels are not pasted on the vials, and it creates scraps. If the reel is broken, the operator must refill the unloading part of the reel in the labeller machine. If this activity is done in parallel with the normal functioning of the cartooning machine, it is not a real stop, but in case the operator is alone on the line, this means a waste of time to restore the line.

However, in yellow are represented the activities less frequent but that consume more time. As said before, the activity of opening the boxes described in Exhibit 10 for the check of the quality of glue in the closed cases, is a non-recurring activity depending on missed attention of the operator of the outputs of the cartooning machine in BA50, after a mechanical intervention. When the operators realise the poor quality of the output cases, was too late, and quite 120 boxes of 10 cases were opened and checked cause 200 minutes of wasted time.

For the other three "yellow" activities, the time of warming of glue and stamp must be considered any time the labeller and the cartooning machine are off before the starting of the lot. In particular, if the stamp is not ready, the operators cannot go on with the lot preparation and the check of sensors.

Then the vials drying is referred to the vials coming from the cold room and as said before, for this activity is considered the time to put the bulk vials in their containers on pallet allocated all over the working area to give more air to the vials and try to dry quickly for the production. This activity is repeated every Monday if there is the launch of the Process Order or in case there is an immediate launch without preventive communication. What happens in this specific scenario because in the first case nobody is present in the company during the eight hours before the expected time of processing of the lot. On the other hand, the time from the exiting from the cold room and the arrangement in the room is less than eight hours. It is important to specify that eight hours are the minimum time lapse for obtaining a good level of drying of the vials for been processing.

The aforementioned activity can be also related to the last yellow activity, the waiting of materials.

Since some communications are done contemporarily to the start of the lot preparation, can happen that the warehouse has not ready the material requested. In particular, if it does not receive the Process Order with the Transfer Order related to the lot, the warehousemen cannot start to pick the materials. In this way, the delays affect not only the ordinary activity of packaging but also the changeover one. As said before, if the materials are not available, the mechanic is not able to perform the friction adjustment on the machines. This affects consecutively the starting of the lot production.

Another critical activity that is impactful on the production and, it is not so essential, is the use of a password on the checkweigher. The password is asked after three consecutive scraps, or to recall the right recipe of the product under process. The operators cannot change the recipe or change any parameter of the libra, for this activity is necessary the intervention of the mechanics.

In any case, the password expires after 60 days and in case the operator has not refreshed it, it is necessary the intervention of an agent of the MQA department. It means as shown in Exhibit 10, 29 minutes of waiting.

7. Set the target

From the analysis of the data, it can be observed that among the three factors of OEE, availability is the most impactful. For this reason, it was decided to improve by 25% as a must have and 50% as a nice to have. Specifically, a reduction of about 30 minutes is proposed for the must have and 192 minutes for the nice to have. In detail, it will impact maintenance times, clearance times and stand-by times. Secondly, further simplifications will be found for the lot preparation time.

It is also important to define a target linked to the visibility of information regarding the performance of the line. For this reason, the filling in of the OEE register has been divided according to the person responsible for the activities:

for the operator

- Withdrawal of documents 5%.
- Correct compilation 15%: insertion of the required information
- Complete compilation 20%: insertion of all activities

for the coordinator and supervisor of the day

- Correct classification 10%: time allocation
- Complete classification 15%: feasibility check of total times

for the database

- Enter data in the register correctly 20%.
- Fully entering data into the register 15%.

Considering the percentages represented by the importance of the phases, it is proposed a must-have target of 65% and 100% for the nice to have.

It is specified that the classification and data entry part in the register will be activities carried out by the department coordinators at the end of the project. In this way, the continuation of performance monitoring is allowed, having objective evidence for data collection.

8. Root cause analysis

For what regards the root cause analysis, starting from the observations and the gathered data, it is used for the identification of the macro causes, an Ishikawa diagram (fishbone diagram) based on the 4M: Machine, Man, Material and Method.

From this, it has identified the low availability as an effect of downtime of machines, inefficiencies of men, low quality, or lack of materials and finally a lack of organization, communication classified as lack of a proper method.

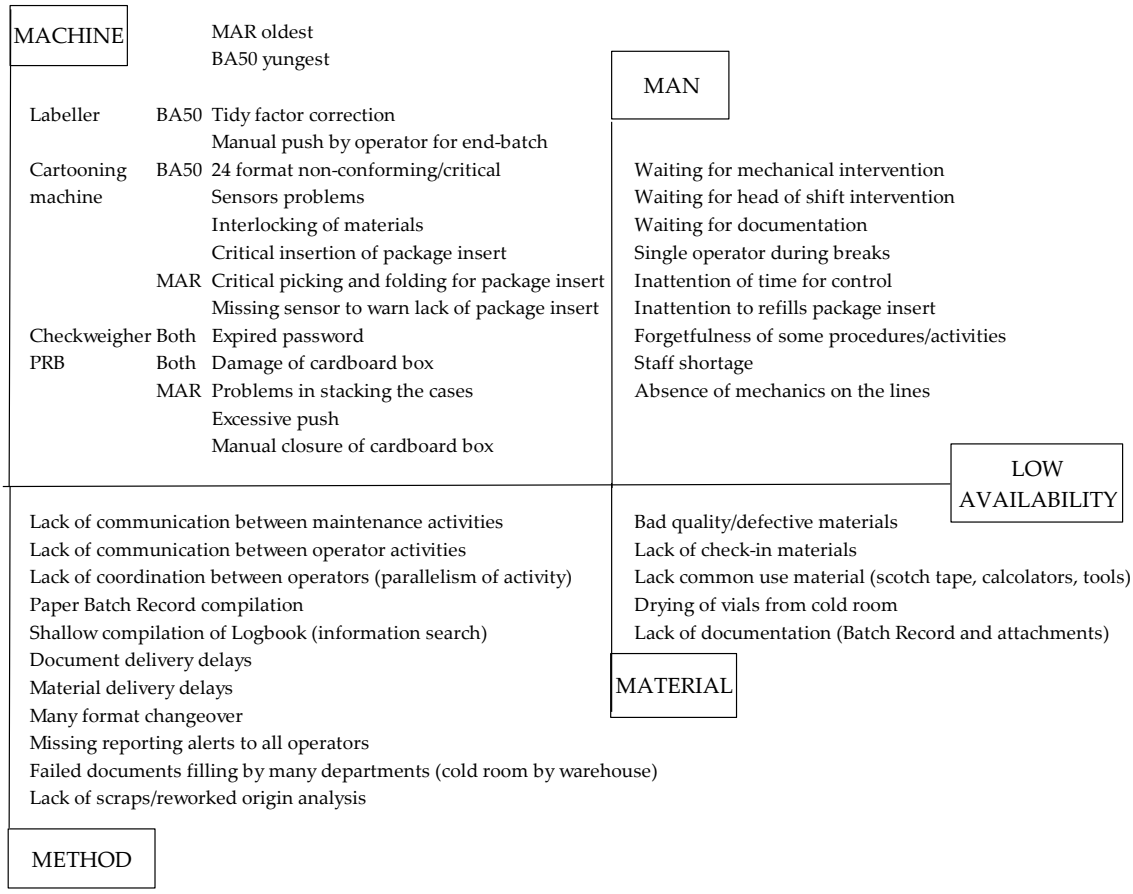


Exhibit 11- Ishikawa diagram - 4M model

Going into the specifics, as far as the **machines** are concerned, in addition to the problems of functionality, there is also non-compliance of format and activities for which the operator must remain in the station. The 24 format in the BA50 is

not performing the maintenance times during its use are much more frequent. However, in general, it is reported by mechanics that the machine itself has always had problems. For the MAR line, on the other hand, the problems are related to the package leaflet of some products for which the excessive thickness causes friction in its grip and bending. The operator must then carry out the activity of checking the presence of cases before closing the box.

In the **men** category, on the other hand, there are three subcategories of criticality:

- Waiting for maintenance and coordinator intervention and presentation of documentation to start production.

- A limited number of personnel (operators and mechanics)

- General errors of inattention and forgetfulness on how to fill out documents or carry out activities for which it is necessary to ask for the intervention of colleagues or the coordinator to continue.

Materials, on the other hand, meant as semi-finished or packaging materials, are often deformed or poorly performing, which interfere with the operation of the machines. As for commonly used materials, they are not always present in the processing room and therefore frequent movements occur.

The most critical issue is the absence of documentation to be able to start quickly and take advantage of the entire shift of the packaging operators. Similar is the problem of drying the vials that occurs mainly at the beginning of the week since the materials are not extracted from the cold room at least eight hours before. This is because it is not possible to leave the product thawed for more than some hours indicated in the Batch Record and view of problems on the lines, refreezing would damage the product. For this reason, the extraction of the material from the cold rooms is carried out only when they are sure to process the batch.

However, the most important category that creates intense reductions in time and that also impact the performance of operators and machines, is the **method**.

The main difficulty is the organization of the department. in particular, the lack of communication between operators of the same shift and subsequent shifts, and also between mechanics and coordinators that causes delays in activities, repetition of interventions and incorrect compilation of documents or incorrect execution of an activity.

Even the superficial compilation of some documents causes a lack of visibility and subsequent search for information by colleagues.

The organization also means the coordination of activities and the visibility of information between different departments. The delay in the delivery of materials or documents occurs due to the failure to communicate the stages of production and its planning. The delays of the departments before packaging affect the time available to package and serialize and finally a possible delay on delivery to the customer. In addition, not having departmental planning, it is not possible to know in advance how to distribute products on the lines and the possibility of working in the campaign with the same format. Therefore, the times are lengthened to be able to make different format changes that despite consisting in the replacement of mechanical components, there is also the adjustment phase that is carried out only in the presence of the materials of which there is never a certainty of their immediate availability.

9. Develop countermeasures

Once defined the root causes of the problem, observing the activities and having a brainstorm with the operators, head of the department and the other managers, many possible solutions were collected for each of them, and then with a priority matrix was defined the best ones.

For **Machines**, it is mainly proposed to unlock the checkweigher because entering the log-in causes delays in case of an expired password. Eventually, create a single operator profile with a single password known by all operators, and a reminder for coordinators to be used to prevent the password from expiring.

About the MAR line, on the other hand, it is proposed to restore the photocell of the minimum load of the package leaflet. This was removed but it is not clear why, however, it is asked to reinsert it in such a way as to reduce the number of stops of the cartooning machine due to the lack of the package leaflets. Instead, for the interlocking of the package leaflets, a revision of the case of a product that reports more this problem is proposed and finally, analyse any solutions for adapting the format. In addition, it is proposed to remove the sticker machine since it is not used and carries out the activity of the transport belt between the libra and the PRB. However, in the case of searching for labels or vials, that part of the machine is an extra one to check as the cartons with the vials can often hide in that area. In addition, if not used for a long time, the thermal sensor inside the machine shutdowns and a mechanical intervention is needed to make it start again. Therefore, the time and effort spent on this machine could be greatly reduced if it were removed.

It is then suggested the insertion of the closure with scotch tape in the PRB of the MAR, however, it is explained that by causing several errors in stacking the cases inside the box, the use of scotch tape would preclude the visual inspection to make sure that all the cases are inserted. For this reason, the solution is not applicable.

Instead, for the BA50 it is suggested the insertion of a loading unit at the entrance of the labeller, allowing a reduced refill frequency and greater control of the other parts of the line. In this way, a line like the configuration of the MAR is created.

Additional suggestions were shown for the critical format, in detail a revision of the 24 format on the BA50 or the purchase of a new more performing one is requested, while secondly the creation of a modified thrust is proposed for those lines that do not have a loading unit and must push the vials at the end of the batch towards the labeller.

Instead, for other interventions related to the functionality of the lines, it is proposed to bring a toolbox and the manuals of the specific line in its proximity (Machine kit). In this way, long journeys to collect the necessary material are avoided. This, in particular, concerns the BA50 as it is located in another room far from the maintenance area of the department.

As for general improvements on the lines, it is proposed to add a video-camera at the entrance to the cartooning machine or better to place it above the system of inserting the vial into the case, in this way it is possible to verify that the vial inserted has the label. In fact, in the case of reconciliation of the labels, if an anonymous vial is packed, with the camera it would be possible to immediately identify if the anonymous vial has actually been inserted into the case. In this way, you should avoid the unpacking of pallets of the finished product to search for the anonymous vial.

As for the category of **Men**, procedures have been revised, in particular, those concerning the BA50 to make explicit some steps for the correct functioning of the machines, therefore, it is asked to make them official. Subsequently, a re-training is proposed for those operators who do not know how to put a line into operation or are not autonomous in managing it. In this way, a reduction in time is expected due to the inability to activate the line or request assistance from colleagues.

For continuous processing and to ensure greater control of the line by the operator, it is proposed to be able to lower the speed of the machines when the operator remains alone during the breaks of the colleague. Instead, to help them carry out in-process checks about every three hours and avoid forgetting about it, it is suggested the purchase of a timer to set every time they have to check.

For the operators, finally, it is suggested a rebalancing of the teams both in terms of capacity and in terms of the number of presences per team, in fact, nowadays

one team is more performing than the other and the number of absentees is greater in one of the two. However, these absences or incompetence in some cases are justified by the lack of recognition of the skills of some employees. For this reason, to solicit a good performance and motivate already competent employees, the inclusion of a meritocratic reward system is suggested.

Finally, it is proposed to leave the mechanic in the department to have an immediate intervention on the lines.

For coordinators, on the other hand, it is suggested to create a mask for the creation of packaging labels. This task requires pc entry of lot number and expiration date from two to four times for the same label. For this reason, the creation of a single form would lead to the automatic compilation of the fields and the subsequent control done with the use of bar code reading. In this way, the coordinator would take less time for this activity and would be immediately available in the event of a call by the operators.

For the **Method** issue, in particular concerning the compilation of the batch record, after a careful study of the document and the perplexities or compilation errors by the operators, it is proposed the removal of redundant parts belonging to the cleaning section and check flags. This is because if there is no flag, a compilation error is reported and therefore the operator is considered inattentive. With this change instead, the operator after having made the list of activities indicated in the Batch Record signs only once ensuring the compliance (OK) of the items indicated in the Batch Record. If there is the presence of something non-compliant (NON-OK), the shift leader will be called, and he will fill in a notes field indicating what is not compliant.

As for the sampling of the label and the stamp with variable data, the proposed solution is the insertion of a representative layout of the label with FPO barcode, the orientation of the batch setting and expiration and vision notch verification of variable data entry. These are enough to indicate how to enter the data correctly on the label. Finally, replace the hand-filled part of batch and expiration date verification, which is repeated twice, one for those who make the stamp and one for those who check the stamp, with the withdrawal of the first good label printed and showing all the required data, sign it and countersign it only. This step is possible thanks to the fact that at the delivery of the Batch Record there

are other parts of the same that report the lot and the expiration date. So, the creation of the stamp should only be a consequence of those documents. Then it is requested to add in the Batch Record the example of the pallet configuration for the delivery of the finished batch to the customer.

Also in the Batch Record, other printed parts are currently obsolete or used once; therefore, if these sheets are not used during the batch the coordinators will have to cancel them according to GMP standards when the Batch Record is revised; Therefore, it is suggested to turn those parts of Batch Record into standard attachments to be used only when necessary. In this way, the control of the Batch Record also becomes faster.

Finally, many of the compilation problems could be solved with the introduction of an electronic Batch Record. In this way, an immediate reception of the Batch Record by the documentation department would be guaranteed, avoiding long waits for the delivery of the same and the compilation by the other departments.

Concerning the coordination of processes on the line, it is proposed to develop standards for the activities to be carried out on the lines, this following a SMED analysis on the activities that in the analysis have been defined as longer and impacting on availability (i.e., Format-changeover and Clearance).

About improving communication between mechanics and the department, it is proposed to build a register of maintenance activities, also linked to the opening of the maintenance notification. At the moment, this activity is carried out by the coordinators, however, the mechanics should also be able to fill it out to help the coordinators identify the problem for which the intervention took place.

Finally, the introduction of an OEE register which indicates the productivity of the lines is considered. In it will be indicated the production (good pieces and scraps) for each shift and how long it was made. In addition, to classify the waste, it is suggested the use of identification trays of the discarding machine, in which the waste of the machines is deposited and then at the end of the shift or in the downtime available, operators proceed with the account of them and therefore record the origin of the reworked.

As for the information necessary for the compilation of the BR, it is suggested to enter on the logbook a more detailed compilation of the mounted format and the theoretically set speed for that product. Then turn the logbook also into a record

of production speeds so as not to run into compilation problems on the Batch Record. Finally, add the information of the number of the machine on the wall in such a way as to facilitate the compilation of the Batch Record and the attachments of the working area.

To solve the problem of lack of materials during the format changeover and therefore the creation of delays on the conclusion of the activity, it is proposed the creation of format changeover kits equipped with all the required materials: vials, cases, package leaflets and cardboard boxes.

But the most useful countermeasure for the coordination of activities in the department and between departments is the creation of a schedule for packaging and the sending of automatic communication of the availability of a batch ready for packaging. Nowadays, there is "lot tracking", a database that is discussed every day for an hour via online meeting. However, it is superficial or inefficient because all notifications made during the meeting are not indicated anywhere. So, they repeat the communications every time and they don't have a clear idea of the production order.

Finally, to improve the flow of materials within the department, it is proposed to move the BA50 to the main production room and where possible, break down the separation walls to expand the area, have greater visibility on the lines and create additional material storage areas (structural change).

As for the **Materials**, focusing on the documents, it is proposed an improvement of some attachments such as, for example, the attachment for the collection of waste labels by adding a grid that helps operators in counting the labels and then the change of colour of the "labelled" labels that can be easily confused with the "cleaned" ones to be added on the dedicated attachment. In addition, it often happens that operators fill out a document called Semi-finished instead of the Labelled, for this reason, an analysis is being carried out to transform these attachments into a single one and use the "status labels" as the only indication of the processing changes on the product.

In addition, it is proposed to duplicate all commonly used documents and prepare them directly in the vicinity of the lines. The same thing to make it for

stamps. In this way each line has in its area, all the materials avoiding unnecessary movements.

As for the commonly used materials, however, it is proposed to duplicate some of them and make them personal (i.e., calculators), to guarantee the timeliness in continuing with their activities and the parallelization of the activities themselves.

The analysis also shows that waiting for the drying of the vials coming out of the cold room, requires a lot of time and space, for this reason, it is proposed to purchase or create a multi-shelf trolley on which to place the vials and leave the product as ventilated as possible.

Finally, in some cases there have been problems with the materials delivered to the department, so it is suggested an improvement in the check-in control of the materials and verify their quality.

In the end, once were highlighted all the possible countermeasures, an efforts-benefits analysis was done trying to classify each solution as "Quick-Win", "Good to Do", "Future" and "Not Feasible".

In the following Exhibit, all the countermeasures are summarized.

ID	Countermeasure	Benefits	Efforts
A	Unlock checkweigher	19	7
B	Package leaflet minimum loading photocell (MAR)	34	6
C	Case change	28	13
D	Removal of the sticker machine from MAR	29	13
E	PRB scotch recovery (MAR)	27	15
F	Loading unit for labeller of BA50	30	13
G	Revision format 24	28	15
H	Thrust bank	30	12
I	Machine kit on the line	19	9
J	Video-camera in entrance of cartooning machine or above vial insertion	34	18
K	Add parts in BA50 procedure	27	6
L	Re-training operators	32	9
M	In-line single operator speed change	28	6
N	Timers' purchase	33	10
O	Rebalancing the team group	18	8
P	Meritocratic operators' system	24	14
Q	Mechanic in the department	17	6
R	Packaging labels by coordinator	27	12

S	Cutting in cleanup pages	29	11
T	OK and NON-OK changes	35	11
U	Stamp/label test and layout	29	11
V	Pallet configuration representation	30	10
W	Bb003/01 and /02 turn them into standard attachment	29	9
X	Electronic batch record	40	18
Y	SMED	32	9
Z	Standardize activities	26	11
AA	Opening maintenance notification/maintenance register	17	8
AB	Productivity account per shift (scraps and vouchers) - OEE register	16	6
AC	Waste trays	24	10
AD	Put on logbook the type of format	27	6
AE	Production speed register	27	6
AF	Put the number of the machine on the wall	34	6
AG	Format changeover kit	31	6
AH	Creation of packaging scheduling	36	12
AI	Coordination of documents and production	28	12
AJ	Structural change: local union and lines	28	18
AK	Change format of label scraps document	29	8
AL	Change colour label "labelled"	30	10
AM	Make the semi-finished and labelled attachment unique	26	8
AN	Common attachments on each machine	23	13
AO	Duplicate the stamps and put them in place.	27	13
AP	Duplication of commonly used materials	25	9
AQ	Trolleys for drying vials	29	10
AR	Material control check-in	25	12

Exhibit 12 - List of countermeasures and related benefits-efforts evaluations

Three drivers are defined for the effort: info collection, cost, and time consumption; then increasing info visibility, time, cost, and errors reduction are defined as the drivers for the benefits. After that, a prioritization matrix based on the AHP method with "Borda count" and weighted sum approach is built. Creating the plot of the results, it is assessed as Quick Wins (in green) the solutions with high benefits and low efforts, Good to Do (in blue) if low efforts and low benefits, finally, Future improvement (in orange) if both the criteria are high. The last quadrant represents a solution not worthy or feasible to be considered.

Based on this plot, with the company, it is decided to focus first on the solutions

B – L – N – S – T – U – V – W – Y – AF – AG – AH – AK – AL – AQ, then on A – I – K – M – O – Q – Z – AA – AB – AC – AD – AE – AI – AM – AP, and finally for the future, the other projects all C – D – F – G – H – J – R – X.

Following this flow of solutions, it will start from "quick wins" and "good" solutions that do not require high expenses, high-tech knowledge, and much operative time. After that, will be possible the introduction and integration with technologies.

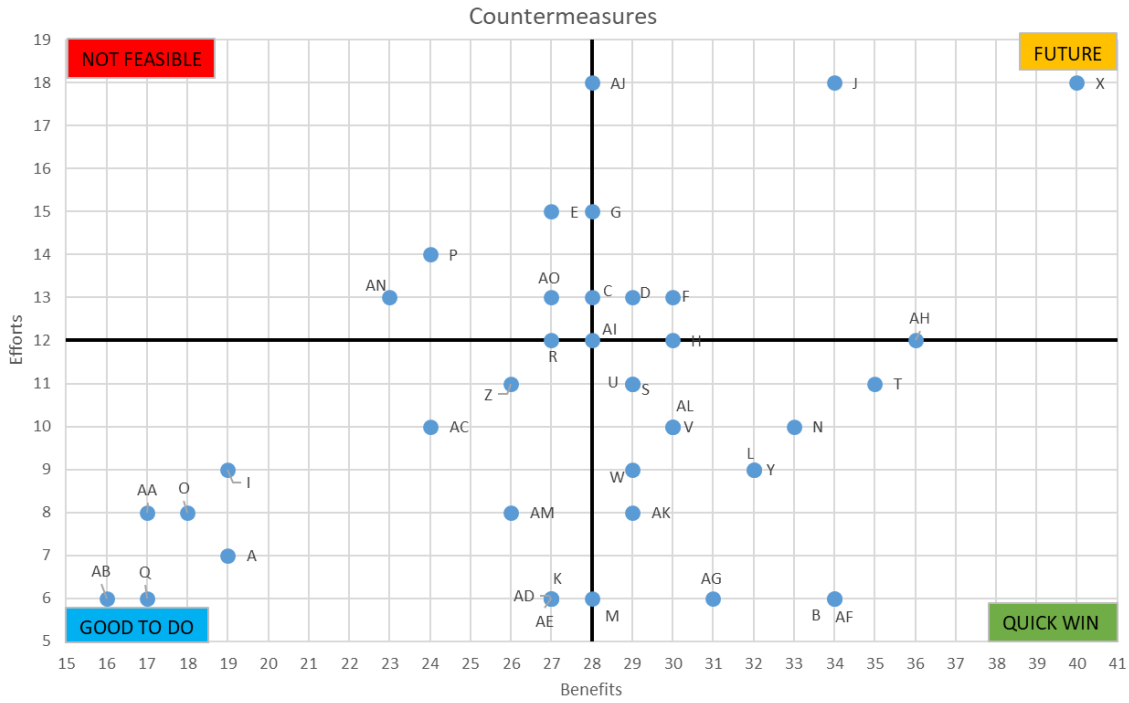


Exhibit 13- Plot of countermeasures

Summary

In conclusion, from what has been analysed and proposed, there is a forecast of reducing the waste of time for an average of 28 minutes. In this way, the availability would rise from 33% to 40% (+25%).

ID	Indicator	Mean Actual value	Expected value	Delta	Gain
AG	Waste time reduction	82 min	22 min	60 min	73%
AH	Waste time reduction	120 min	Max 30 min	90 min	75%
AI	Increase of information	Time to call responsible of launch	Immediate notification		100%
AK– AL –T– U– V–W–AM	Waste time reduction	10 min	6 min	4 min	40%
AQ	Waste time reduction	120 min	60 min	60 min	50%
B	Waste time reduction	10 min	3 min	7 min	70%
L – K	Waste time reduction	20 min	10 min	10 min	50%
N – AP – I	Waste time reduction	15 min	5 min	10 min	67%
Y – Z	Waste time reduction	90 min (for clearance) 60 min (for lot preparation)	75 min (Worst case) 53 min	15 min 7 min	17% 12%
AA– Q	Increase of information	Uncertain information about activities performed	Awareness of activities performed		70%
AB– AC– AE	Increase of information	No monitoring	Awareness about performance		100%
AD	Increase of information	Uncertain information	Completeness of information		100%
M	Productivity	Half production during breaks	Continuous production during breaks		50%
A– O	Waste time reduction	20 min	3 min	17 min	85%
D	Waste time reduction	30 min (For downtime of heat sensor)	0 min	30 min	100%
F	Productivity	2 bulks loaded	3/4 bulk loaded	1/2 bulks	50%

Exhibit 14 - Summary of estimated gains

10. Implement countermeasures

Entering in the details of the implementation of countermeasures, looking at Exhibit 15, the solutions considered quick wins or good to do are the most impactful and important to work on.

At this stage, the owner, the start date, and the estimated due date of the countermeasure's implementation were defined. To show the progress of the countermeasure each of it is divided into four phases and their completion is highlighted in **bold**.

ID	Countermeasure	Owner	Start date	Due date	Phase 1	Phase 2	Phase 3	Phase 4
AF	Put the number of the machine on the wall	Coordin.	02-nov	12-nov	**Write**	**Stamp**	**Put on the wall**	**Use**
AG	Format changeover kit	Leoni	28-oct	25-nov	**Take materials**	Fill vials	Create kit	Use
AH	Creation of packaging scheduling	Riello – Cenci	30-oct	26-nov	**Make the scheduling**	**Fill with data**	Test of functionality	Application on field
AK	Change format of label scraps document	Valenti	27-oct	20-nov	**Agreements**	**Approval**	**Training**	Operative
AL	Change colour label "labelled"	Valenti	27-oct	20-nov	**Agreements**	Approval	Training	Operative
AQ	Trolleys for drying vials	Leoni - Cremaschi	02-nov	TBD	**Approval**	**Features' definition**	Building	Use
B	Package leaflet minimum loading photocell (MAR)	Cremaschi-Cavicchini	28-oct	08-nov	**Guk tech's vision**	**Restore**	**Check functionality**	**Use**
L	Re-training operators	Cremaschi-Leoni – Coordin.	02-nov	TBD	**List**	**First training**	Second training	Third training
N	Timers' purchase	Leoni	02-nov	08-nov	**Put in list**	**Purchase**	**Delivery**	**Use**
S	Cutting in clean-up pages	Leoni - Valenti	27-oct	20-nov	**Agreements**	Approval	Training	Operative
T	OK and NON-OK changes	Leoni - Valenti	27-oct	20-nov	**Agreements**	Approval	Training	Operative
U	Stamp/label test and layout	Leoni - Valenti	27-oct	20-nov	**Agreements**	Approval	Training	Operative
V	Pallet configuration representation	Leoni – Valenti	27-oct	20-nov	**Agreements**	Approval	Training	Operative
W	BB003/01 and /02 turn them into standard attachment	Leoni - Valenti	27-oct	20-nov	**Agreements**	Approval	Training	Operative
Y	SMED	Cenci	02-nov	15-nov	**Videorecording**	**Video analysis**	**Activities' classification**	**Standards' definition**

A	Unlock checkweigher	Riello – Baiocchi – Varesi	TBD	TBD				
AA	Opening maintenance notification/maintenance register	Cremaschi-Leoni – Coordin.	02-nov	TBD	**Register creation**	Inform personnel	Training	Application
AB	Productivity account per shift (scraps and vouchers) - OEE register	Cenci	02-nov	TBD	**Folder creation**	Folder sharing	Training	Implement
AC	Waste trays	Leoni – Coordin.	02-nov	TBD	**Find them in the warehouse**	Bring them in packaging	Training	Use
AD	Put on logbook the type of format	Cremaschi	02-nov	08-nov	**Training**	**Implement**		
AE	Production speed register	Leoni	02-nov	TBD	**Register creation**	Training	Implement	
AI	Coordination of documents and production	TBD	TBD	TBD				
AM	Make the semi-finished and labelled attachment unique	Valenti	27-oct	20-nov	**Agreements**	Approval	Training	Operative
AP	Duplication of commonly used materials	Leoni	02-nov	15-nov	**List**	**Purchase**	**Delivery**	**Use**
I	Machine kit on the line	Coordin.– Leoni – Cremaschi.	02-nov	15-nov	**Agreements**	**List**	**Move materials**	**Use**
K	Add parts in BA50 procedure	Valenti	27-oct	20-nov	**Agreements**	**Approval**	Training	Operative
M	In-line single operator speed change	Coordin. – Mechanics	02-nov	03-nov	Inform personnel			
O	Rebalancing the team group	Leoni	TBD	TBD	Team creation	Inform personnel		
Q	Mechanic in the department	Cremaschi	02-nov	03-nov	**Agreements**	**Inform personnel**		
Z	Standardize activities	Cenci	02-nov	25-nov	**video SMED**	**Analyse the video**	**Definition of standard**	Application
D	Removal of the sticker machine from MAR	Leoni – Cremaschi - Valenti	27-oct	TBD	**Agreements**	Approval	Change	Validation
F	Loading unit for labeller of BA50	Cremaschi	TBD	TBD	**Alternative proposal**	Check feasibility	Building	Assembling

Exhibit 15 - planned and/or implemented countermeasures

About the owners:

- "Coordin." Means the head of shifts.
- "Leoni" is the head of the packaging department.
- "Riello" is the company tutor alias leader manufacturing.
- "Valenti" is the product specialist, and she is allowed to open changes in procedures.
- "Cremaschi" is the head of maintenance and engineering.
- "Cavicchini" is the project engineer.
- "Baiocchi" is the CEO of the company.
- "Varesi" is the head of quality department.

Some countermeasures are still to be defined due to overlapping and waiting to finish the already started.

Below, a Gantt chart is drawn to highlight the activities that are conducted simultaneously and the expected time of conclusion.

In green is highlighted the completed countermeasures, in orange are the "work in progress" ones.

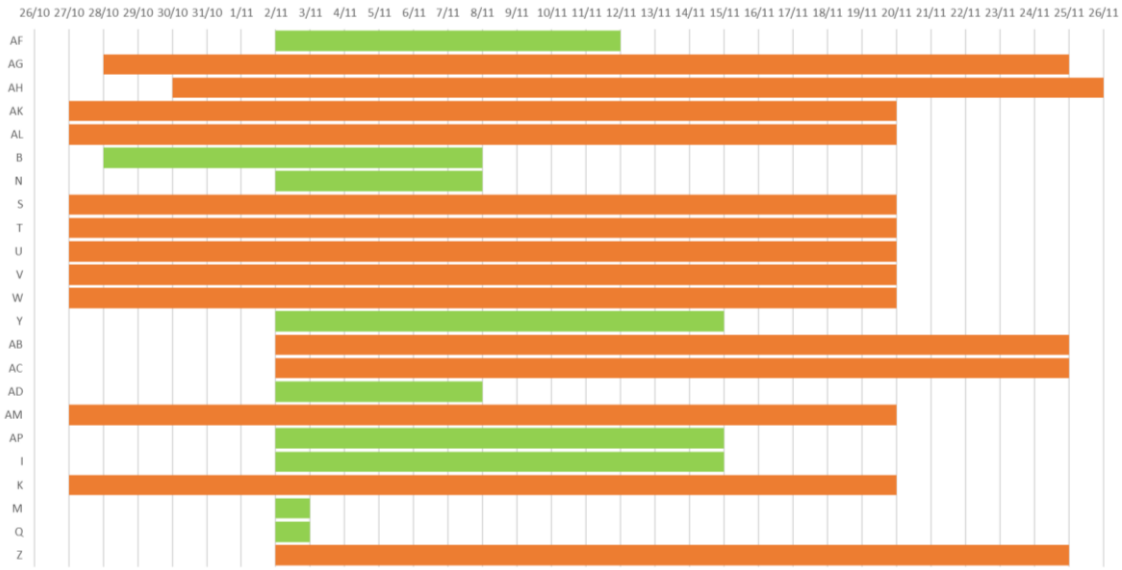


Exhibit 16 - Gantt chart about implemented countermeasures

Now, the details of each countermeasure are explained below.

AF. Put the number of the machine on the wall

Following the concepts of visual management, it was considered useful to make clear and immediately identifiable the number of machines to be marked on the different documents that operators must fill out. For this reason, they were printed and hung on the walls of the rooms where the lines are arranged.

AG. Format changeover kit

The format changeover kit becomes of fundamental importance to impact the format changeover times and therefore on the increase in the availability of the line.

At the moment, it was decided to focus on one of the products that are most packaged on the lines. Once the product for MAR and BA50 had been established, the packaging materials (cases, package leaflets and cardboard boxes) were collected, subsequently, the production of 100 vials of the specific format of both products was requested. These vials are filled with WFI (Water For Injection), purified water used to dilute drugs. The choice to use this water is made to avoid product contamination in case of breakage of the vials during the format changeover tests. In addition, to avoid the framing of vials with the real product that will have to be packaged, the vials will be numbered.

Once the use of the kit is finished, the vials will be placed in the appropriate container while the packaging materials will be restored at the end of the first batch made. In fact, at the end of the lot, a hundred boxes and package leaflets and a couple of cardboard boxes will be taken.

The kit will be stored in the office to avoid unauthorized withdrawals by operators or mechanics. The collection and return of the material will be tracked.

The mechanic will care to point out any loss or breakage of the vials of the kit.

With this system, it is estimated a reduction of at least 60 minutes as it is not necessary to wait for the arrival of the materials to begin the friction adjustments or the drying of the vials in case of material coming from the cold rooms.

AH – AI. Creation of packaging scheduling and Coordination

The creation of a schedule for the packaging department is based on the distribution of production monitored by "Lot Tracking" and applied to the availability and timing of packaging of the lines.

The plan collects the estimated monthly production with the indication of the bulk lot, product name, client's country, and code of the finished batch. Each product is already assigned the standard production times of the categories: labelling, packaging, stickering, serialization. These phases are evaluated by shifts and the sum of them divided by the three shifts indicates the total days of packaging.

From the "Lot Tracking" the lots are then divided by delivery date, and it has proceeded with the creation of the scheduling.

First, it is necessary to put in ascending order the number of bulk batches, since a FIFO logic is followed for the consumption and packaging of products. Generically, if a risk event is not opened, the bulk lot is unlocked and can be approved and assigned to a finished lot code. So, once the Batch Record is created, this batch can be packaged.

So, following a logic of packaging in campaign, where, if possible, there is a reduction of the number of format changeovers. In this way, for example, it is avoided the loss of at least one shift to make the change twice within the same week.

Subsequently, there is the necessity to combine the serialization phase since it is a single line and it must operate on almost all products with a standard speed at 18 pieces/min, where pieces are meant the cases.

Once all the packaging phases have been adjusted, obviously avoiding the overlapping of batches on the same line, the number of people needed for production is considered. Once this is done, it is verified that the available people are sufficient. The available people are calculated by removing from the number of people per team, the operators assigned to the night, rest, on vacation and sick. In this way, you indicate the people available for the month.

This scheduling must be considered by the planning department to avoid the arrival of orders greater than the actual production capacity. In fact, with the

planning department, it will be estimated two months before the production. So, the planning department will look for a monthly schedule while the packaging department will receive the packaging plan every week.

With this system, the waiting for warehouse materials is avoided and continuous production of the lines is carried out. It will also balance the workload over the entire month, avoiding overloads at the end of the month as it is present in the as-is situation.

This solution combined with the communication system of the AI solution will allow the head of the department to know in advance the availability of materials and therefore the preparation of the same in the warehouse.

Avoiding the loss of maximum hours for the arrival of the Batch Records and materials.

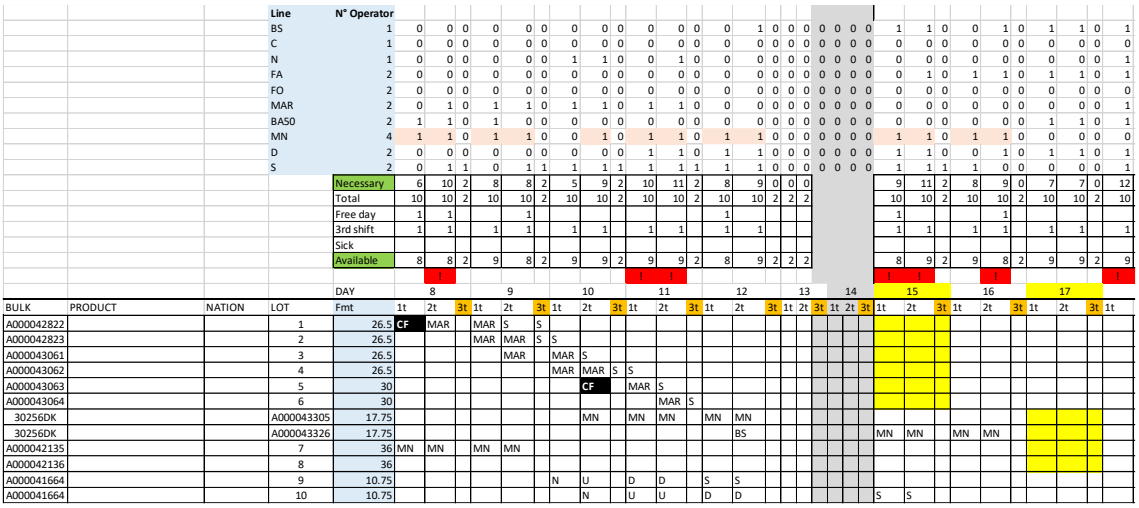


Exhibit 17 - Example of the scheduling system

In Exhibit 17, from the top, it is possible to identify the assignment of operators for line (in light blue), in particular, in the case of MN, which means Manual packaging, it is highlighted in light orange due to the fact, operators from other departments can hold this activity. Below that the evaluation of the personnel necessary for the activities compared with the available one (in green). Where there is the red alarm, it means that there is overcapacity to fill, so it is necessary to find people to do the activities.

In grey are represented the non-operative days, instead, in yellow are represented the due dates of the lots. That means the operations must finish before that date. In orange is represented the night shift due to the presence of

only two operators and so the only activities that can be done are the manual packaging or the serialization.

Finally, in black is represented the Changeover Format that requires, generally, one shift and it is evaluated thanks to the column of the format in light blue.

Documents Improvements: AK – AL – T – U – V – W – AM

Following the Poka Yoke and Kaizen concepts, these solutions concerning the compilation of documents would make it easier and free of "uncertainty" the compilation by operators. In this way, the activities would continue as they are now, and a signature would be enough to indicate that the activity has been done and no problems have occurred.

To proceed with these changes, the same products designed for the format changeover kit have been considered, in this way the effectiveness of these cutting is verifiable.

For the implementation, a meeting with the responsible for opening the changes and with the representatives of the documentation department was taken. once the reasons and extent of the changes were presented with the explanation of the impact they would have on the activities, and the awareness of complete compilation by the operators, an example of Batch Record was created.

If these changes will be approved, a CAPA (Corrective Action and Preventive Action) will be opened. So, the new Batch Record will be tested on the lines for two months and if the test result is positive, they will proceed with the opening of a change and the extension on all the Batch Records.

However, before using the test, first, this must be approved and then they will upload a training to the operators to inform them of the changes.

Finally, with the opening of the change, the document can eventually become operative.

As for the AK solution (Change format of label scraps document), this would also have a positive impact on the label account as if filled correctly, a sheet collects a maximum of 30 labels. So, it would be enough to count the number of complete

sheets used to have the number of total scraps and add the number of scraps on the partial sheet.

With these changes, it is estimated a reduction in the time of compilation and account of the labels of more than 4 minutes.

AQ. Trolleys for drying vials

This countermeasure involves the reuse of some of the trolleys abandoned by the company. The aim is to modify these trolleys equipped with guides. In particular, it is needed the insertion of a support consisting of a steel base between the guides so that the plastic bulk of the vials can be arranged above, without the risk of falling. The steel base must be drilled to ensure the aeration of the vials and therefore a faster drying.

Considering the size of the lots and the number of plastic bulk of vials, it is suggested the creation of two trolleys. For the creation of this structure has already been sent a quote that is around € 4820. This expense has been budgeted; therefore, it is awaited the handover to the company responsible for the improvement of the trolleys.

Figure 1 – Base of the trolley structure

As for the benefits of this countermeasure, it is noticed the reduction in the space used to unload the material, therefore an increase in mobility in the area, a reduction in waiting times for drying estimated at 50% as it is estimated 30 minutes to unload the bulks on the trolleys (it remains unchanged) and less than an hour for the total drying of all the vials. Nowadays, they wait even 2 hours before having the vials completely dry.

B. Package leaflet minimum loading photocell (MAR)

This solution involves the restoration of the photocell of the minimum load for package leaflets. For its restoration, a technician from the manufacturer GUK verifies that the photocell is still working and restores the component that had been removed in the past. Once this check has been carried out, the technician makes sure that the number of package leaflets that can be loaded is at least more than one block (about 250 package leaflets) so that the alarm does not sound too often. At the end of this adjustment, it is also indicated the correct way to enter the prospectuses and reduce the number of interlocking or non-withdrawal by the machine.

Finally, the effects on operators must be verified during the production of a batch.

It is estimated a reduction in waiting times for non-loading prospects of at least 7 minutes considering the set of all the micro-stops recorded.

L – K. Re-training operators and Add parts in BA50 procedure

Retraining becomes of fundamental importance to support the versatility of the operators in the department. Being in small numbers, all operators must be able to work on the lines.

Many operators have doubts about some lines and for this reason, they are asked which are the machines on which they have the most difficulty and then retraining is planned.

Training consists of:

- Reading the procedure for machine functionality.
- Compilation of Batch Record of the machine.
- Q&A.
- Explanation by the mechanics of details for the operator's use. Explanation of where the operator can intervene in autonomy.

The machines selected at the moment are linked to the project and the most used. Therefore, the selected order is as follows:

- B+S (vials' labeller stand-alone)
- BA50

- MAR
- SERIALIZATION (no need for mechanics)

The training is subjected to the people who have answered the questionnaire of competence with NO and NA (NO- not capable; NA- not autonomous). The results are shown below in Exhibit 18.

	NERI	CORIMA	B+S	Dividella BOL.	E. MAR	MAR	FAMAR	E.BA50	BA50	UHLMANN	FARMORES	SERIALIZZAZIONE
Operatore	no	NO	NO	OK	NA	OK	OK	NO	NA	OK	NO	OK
Operatore	NO	NO	NA	OK	OK	OK	NA	NA	NA	ok	NO	OK
Operatore	OK	NO	OK	OK	OK	OK	OK	OK	OK	OK	NO	OK
Operatore	OK	OK	OK	OK	OK	OK	OK	OK	OK	OK	NO	OK
Operatore	OK	OK	OK	NA	OK	OK	OK	OK	OK	OK	NA	OK
Operatore	NO	NO	NO	OK	NO	OK	OK	NO	NA	OK	NO	NA
Operatore	NO	NO	NO	OK	NA	OK	OK	OK	OK	OK	NA	OK
Operatore	OK	NO	OK	NO	NO	NA	OK	NA	NA	OK	OK	NO
Operatore	NO	NO	NO	OK	OK	OK	OK	OK	OK	OK	NA	NA
Operatore	OK	NA	OK	NO	OK	OK	OK	OK	OK	OK	NO	OK
Operatore	NA	OK	OK	OK	OK	OK	OK	OK	OK	OK	OK	OK
Operatore	OK	OK	OK	OK	OK	OK	OK	OK	OK	OK	NO	OK
Operatore	NO	NO	NO	NO	NO	NA	OK	NA	NA	OK	NO	NO
Operatore	NA	NO	NA	OK	OK	OK	OK	NA	NA	OK	NA	NA
Operatore	no	OK	NO	NO	NA	OK	NA	OK	OK	OK	NO	OK
Operatore	NO	NO	NO	NA	OK	OK	OK	NA	OK	OK	NA	OK
Operatore	OK	OK	OK	NA	OK	OK	OK	OK	OK	OK	NA	OK
Operatore	NO	NO	NO	OK	NO	NO	OK	NO	NA	OK	NA	NA
Operatore	NO	OK	OK	OK	OK	OK	OK	NO	NA	OK	NO	OK
Operatore	NO	NA	NA	OK	OK	NA	NA	OK	OK	NO	NA	OK

Exhibit 18 - Operators' competencies questionnaire

The training is repeated every month (if necessary, the employees of the first training will be asked if they need the second). Confirming that they do not need the second training means that the subject goes from NO or NA to OK (= capable).

With OK, the employee is considered autonomous on the operation of the line. In case of subsequent re-training, it is carried out a maximum of three consecutive times, beyond which the employee is considered, by default, able to make operative the machine.

After the first three months of continuous training, a test is established in which all employees (even OK ones) will participate to verify the actual knowledge of the machine.

The results will help in the evaluation of the frequency of the trainings. By default, it is proposed one training every six months for everyone.

Operatively, the coordinator will fill the training document highlighting the number of training performed: 1 of 3, 2 of 3, 3 of 3.

The trainings are distributed as follows:

Day	Machine	Trainers	Operators	Supervisor
26/10/21	B+ S	Shift 1: Head of shift Mechanic	Name Surname 1 … Name Surname N	Head of the department
		Shift 2: Head of shift Mechanic	Name Surname 1 … Name Surname N	
….	….	Shift 1 …	Name Surname 1 … Name Surname N	
		Shift 2 …	Name Surname 1 … Name Surname N	

Exhibit 19 - Example schedule of trainings

Retraining is also effective for the control of procedures as in some cases they are superficial and not very intuitive for operators. With this re-reading, the lack of a fundamental step for the check of the BA50 sensors is noticed.

Following this observation, a change of procedure was opened and made explicit with visual examples of how to carry out a correct sensor check. As with any opening change, an approval period is required, followed by the training of the operators and finally the making operative of the change in the procedure.

For these countermeasures, a reduction in setup times of about 5 minutes and another 5 minutes is expected concerning the uncertainties on the compilation of the Batch Record.

N – AP – I. Material purchase

These solutions follow the kaizen principles for which the workstation is optimized. All materials are provided for operators. In particular, black markers for check sensors and calculators are purchased, then they will be distributed personally to the operators, following, tools such as scotch dispensers to close the packaging and scissors, are bought and assigned to each line. Timers are also

bought to ensure in-process control. Often, happen that they are skipped due to inattention to the time.

Instead, mechanics are asked what are the first aid materials needed for the BA50 and MAR lines. subsequently, an ad hoc toolbox was created for the line that together with the instruction manual of the machines is brought to its proximity.

In this way, there is an overall reduction in wasted time of about 10 minutes, especially for the case of the BA50, dedicated to the recovery of materials and/or manuals from the maintenance area.

Y – Z. SMED and Standardize activities

Following the phases for the realization of the SMED, the first step starts with the video recording of the activities, to ensure correct recognition of the activities especially in the case of two operators per line.

Subsequently, the video is analysed indicating the operator, the activity, the beginning and the end of the activity, the difference of these two times (elapse time) and finally calculate the cumulative time for each operator. At this point, the activity is classified as IED or OED starts.

In this third step, possible groups of activities that can be transformed from IED to OED are identified.

Then, it is possible to draft the standardization of the activities.

As the last step, standardization is shown to operators, the result is implemented and monitored.

Following, in Exhibit 20 the representation of one SMED analysis about the lot preparation and in Exhibit 21 is represented the Gantt chart of activities performed by operator 1 and Exhibit 22, in a Gantt chart, is represented the activities performed by operator 2.

set up time		1	internal time	01:03:31	78.72%		
		1	external time	00:17:10	21.28%		
		2	internal time	01:09:00	85.52%		
baseline set up	01:20:41	2	external time	00:11:41	14.48%		
Operator	activity	start time	end time	elapsed time	cumulative	internal / external	possible switch?
1	preparazione BR e logbook	00:00:00	00:14:11	00:14:11	00:14:11	I	X
1	break	00:14:11	00:38:42	00:24:31	00:38:42	I	X
1	attende istruzioni	00:38:42	00:39:00	00:00:18	00:39:00	I	X
1	monta bobina e preleva timbro	00:39:00	00:49:34	00:10:34	00:49:34	I	X
1	compila doc per timbro	00:49:34	00:50:36	00:01:02	00:50:36	I	X
1	va a fare il timbro	00:50:36	00:55:30	00:04:54	00:55:30	I	X
1	monta timbro	00:55:30	00:57:09	00:01:39	00:57:09	I	X
1	compila doc etichette e assembla BR	00:57:09	01:03:04	00:05:55	01:03:04	I	X
1	prelievo etichette check stampa	01:03:04	01:06:36	00:03:32	01:06:36	E	
1	prepara check sensori	01:06:36	01:07:03	00:00:27	01:07:03	I	X
1	carico flaconi	01:07:03	01:08:13	00:01:10	01:08:13	E	
1	attende partenza E	01:08:13	01:08:45	00:00:32	01:08:45	E	
1	prende prova scarti	01:08:45	01:09:00	00:00:15	01:09:00	E	
1	cerca sacchetto	01:09:00	01:09:31	00:00:31	01:09:31	E	
1	controllo flaconi stampati	01:09:31	01:10:11	00:00:40	01:10:11	E	
1	stacca etichette bianche da bulk	01:10:11	01:11:24	00:01:13	01:11:24	E	
1	carico flaconi	01:11:24	01:13:33	00:02:09	01:13:33	E	
1	sposta vasche bulk vuote	01:13:33	01:13:47	00:00:14	01:13:47	E	
1	compila doc e assembla BR	01:13:47	01:15:55	00:02:08	01:15:55	E	
1	firma campioni e assembla BR	01:15:55	01:17:21	00:01:26	01:17:21	E	
1	chiamato dal collega per problemi PRB	01:17:21	01:17:50	00:00:29	01:17:50	E	
1	sistema scrivania e assembla BR	01:17:50	01:18:50	00:01:00	01:18:50	E	
1	guarda meccanico per PRB	01:18:50	01:20:41	00:01:51	01:20:41	E	
2	break	00:00:00	00:08:47	00:08:47	00:08:47	I	X
2	attesa istruzioni	00:08:47	00:10:11	00:01:24	00:10:11	I	X
2	presa materiali 1	00:10:11	00:11:23	00:01:12	00:11:23	I	
2	porta via pallet con vasche bulk vuote	00:11:23	00:13:27	00:02:04	00:13:27	I	X
2	presa materiali 2	00:13:27	00:15:15	00:01:48	00:15:15	I	
2	prende bancali vuoti e mette su transpallet	00:15:15	00:15:52	00:00:37	00:15:52	I	X
2	presa materiali 3 con stacco foglio	00:15:52	00:17:41	00:01:49	00:17:41	I	
2	presa materiali 4	00:17:41	00:19:01	00:01:20	00:19:01	I	
2	presa pallet vuoto di legno per bulk	00:19:01	00:20:40	00:01:39	00:20:40	I	X
2	presa materiali 5	00:20:40	00:22:10	00:01:30	00:22:10	I	
2	presa materiali 6	00:22:10	00:22:58	00:00:48	00:22:58	I	
2	presa materiali 7	00:22:58	00:23:57	00:00:59	00:23:57	I	
2	posiziona primo bancale bulk	00:23:57	00:24:24	00:00:27	00:24:24	I	X
2	solleva bancale 7	00:24:24	00:25:28	00:01:04	00:25:28	I	X
2	controllo doc	00:25:28	00:26:43	00:01:15	00:26:43	I	X
2	controllo materiali	00:26:43	00:50:04	00:23:21	00:50:04	I	
2	sposta bancale vuoto in posizione uscita sc	00:50:04	00:50:46	00:00:42	00:50:46	I	X
2	sistema e rcupera fogli da rifiuti	00:50:46	00:52:00	00:01:14	00:52:00	I	X
2	toglie imballo bancali bulk	00:52:00	00:54:40	00:02:40	00:54:40	I	X
2	butta sacco plastica e ne apre uno nuovo	00:54:40	00:55:20	00:00:40	00:55:20	I	X
2	sposta cestini per riconciliazione	00:55:20	00:56:01	00:00:41	00:56:01	I	X
2	preparazione check sensori astucci e prosp	00:56:01	01:03:00	00:06:59	01:03:00	I	X
2	carico scatoloni	01:03:00	01:05:24	00:02:24	01:05:24	I	X
2	attesa istruzioni	01:05:24	01:06:02	00:00:38	01:06:02	I	X
2	compila doc timbro	01:06:02	01:09:00	00:02:58	01:09:00	I	X
2	attesa polmone A pieno	01:09:00	01:10:29	00:01:29	01:10:29	E	
2	check sensori A e bilancia	01:10:29	01:12:44	00:02:15	01:12:44	E	
2	inserimento astucci in bilancia	01:12:44	01:13:24	00:00:40	01:13:24	E	
2	butta astucci e prospetti usati	01:13:24	01:13:56	00:00:32	01:13:56	E	
2	attende istruzioni	01:13:56	01:14:47	00:00:51	01:14:47	E	
2	compila doc sensori	01:14:47	01:15:00	00:00:13	01:15:00	E	
2	recupero campione astuccio e prospetto	01:15:00	01:15:52	00:00:52	01:15:52	E	
2	compila doc sensori	01:15:52	01:16:34	00:00:42	01:16:34	E	
2	carico astucci e spegne A	01:16:34	01:16:52	00:00:18	01:16:52	E	
2	problemi PRB	01:16:52	01:17:45	00:00:53	01:17:45	E	
2	sblocca bilancia	01:17:45	01:19:00	00:01:15	01:19:00	E	
2	aiuta meccanico	01:19:00	01:20:36	00:01:36	01:20:36	E	
2	guarda output A	01:20:36	01:20:41	00:00:05	01:20:41	E	

Exhibit 20 - SMED analysis

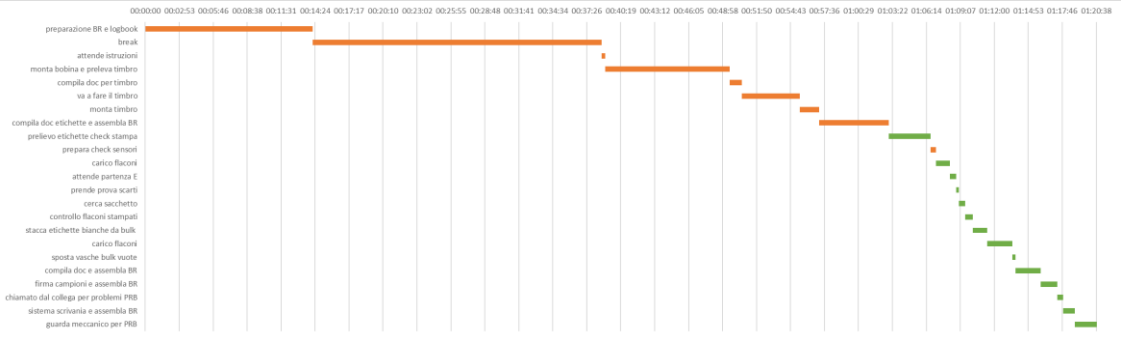


Exhibit 21 - Gantt chart of the activities for Operator 1

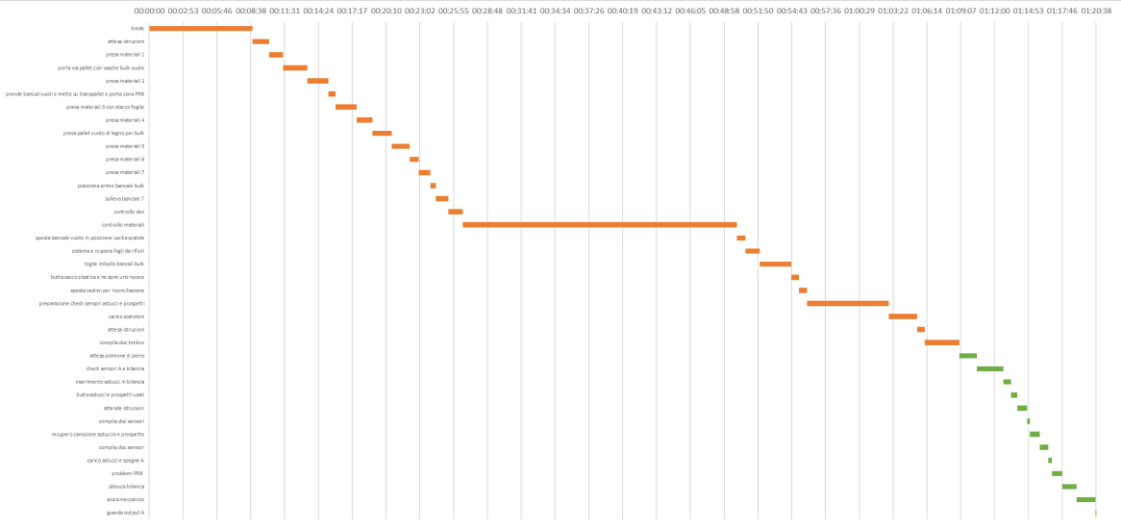


Exhibit 22- Gantt chart of the activities for Operator 2

It is estimated that about clearance times including accounts and cleaning on both lines, tasks can be completed in about 45 minutes. In case of problems related to lack of labels or searches for vials, the time can be extended by another 30 minutes.

Therefore, considering the worst case analysed, there is a gain of 15 minutes (-17%), otherwise, it is estimated to gain close to 45 minutes or 50% of the time used nowadays.

As for the preparation of the lot instead, the activities can be carried out in about 53 minutes having a gain of about 7 minutes (-12%)

AA – Q. Mechanics' management

discussing with the head of maintenance, it was decided to opt for the creation of a register of maintenance activities. In the created form, it is indicated the type of activity carried out, the line on which is done the activity and whether it is necessary to make the handover from one mechanic to another and the shift coordinator. This register is managed by the mechanics and handed over to their chief once the shift or activity is over.

For the opening of the maintenance notification instead, it is explained that the mechanic is not authorized to fill it out since it is a production document. However, this activity is therefore compensated with the register itself.

In this case, the benefit obtained is at the level of information. As to date, it is not always clear the maintenance activity carried out on the machines and there is no documentation to establish a statistic. With this register, on the other hand, it is possible to monitor the problems of the lines and find the best activity to make the lines more performing.

Finally, the constant presence of the mechanic in the department guarantees greater monitoring of the performance of the post-maintenance lines.

AB – AC – AE. Productivity's management

All these three countermeasures will always contribute to the monitoring of production. Continuing the work done with the OEE, it is possible to indicate productivity both in terms of quality and machine performance linked to speed.

The OEE register is assigned to the coordinators and the head of the department. It is told them how to compile it and how to interpret the values obtained.

In this way, it is possible to intervene directly on any inefficiencies. This activity can be carried out monthly to verify continuous improvement.

In particular, by indicating the origin of the waste with the waste trays, it is possible to interpret isolated cases of poor quality or a worsening trend of the machines or others.

AD. Put on logbook the type of format

Always to increase the visibility of the information necessary for the compilation of the documents, it is decided to establish a standard for the compilation of the logbook about the change of format. It is established to indicate the product and the diameter of the installed product format, and the product and diameter of the format mounted for subsequent production. In this way, operators can also verify that the indications on Logbook and Batch Record are consistent and can start with production. If deemed necessary, it is possible to consider making changes to the format of the logbook to ensure the inclusion of the information mentioned above.

M. In-line single operator speed change

Regarding the productivity of the single operator on the line, it is proposed to be able to lower the speed of the line during the breaks of the operators. In this case, the coordinator is authorized, if required by the operator, to lower the speed momentarily. Following the pause, the speed of the regime is restored.

However, other tests will be developed to evaluate the optimal speed for good performance by analysing productivity if the operators' breaks are alternated and if they are simultaneous.

A – O. Unlock checkweigher and Rebalancing the team group

For the good to do A and O activities, they are evaluated by the managers and in the first case, a meeting between the selected team is expected to understand their impact while for the second one the end of the year is expected to make the changes.

D. Removal of the sticker machine from MAR

For the MAR sticker machine, the change has been opened and now is waiting for the details for the change with a possible conveyor belt. This is because moving the PRB would also create additional labour to make the changes to the electrical system. However, a tape is already present on the site, it is evaluated if

it is compliant or if it is necessary to buy a new one of which the estimated cost is € 5000.

The next step is to wait for confirmation from the validation department to start the changes. It should be considered that the removal of the sticker machine must take place in a period of production downtime on the MAR, to be able to operate without creating inconvenience. For this reason, the intervention may take place during August 2022.

F. Loading unit for labeller of BA50

For the last countermeasure studied, it is believed that the loading unit is excessively bulky to be inserted into the room currently available to the BA50. For this reason, it is proposed as an alternative to inserting a plane near the beginning of the conveyor belt. In this way, the operator can place an extra bulk of vials and fill 100% of the short conveyor belt that the labeller has. In this way, it is avoided to fill the conveyor every two minutes and have more elasticity to control or intervene on the other parts of the BA50 line.

Then talking to the person in charge of the countermeasure, he will study the structure project in which the possibility of inserting this component without having to open a validation notification. Above all, the anchoring system for safety regulations is evaluated.

11. Monitor results and processes

In this phase, the results and progress of the implemented countermeasures are analysed. However, to meet the company's priorities, it was decided to continue monitoring during December, as the post-expiry period of the thesis. Analysing the period after analysis and implementation of some of the countermeasures, you can notice improvements in the indicators of the target.

In the specific case of the MAR (Exhibit 26), observing 9 days corresponding to 13 shifts, 9 lots were completed. The respective average OEE values are:

INDICATOR	**RESULTS**	AS-IS	DELTA IMPROVEMENT
Availability	40.22%	38.26%	+ 5.1%
Performance	74.77%	68.33%	+ 9.4%
Quality	97.37%	97.12%	+ 0.25%
OEE	29.29%	25.39%	+ 15.4%

Exhibit 23- MAR's OEE indicators improvements

As for the BA50 (Exhibit 27), instead, the observation 12 days of production for a total of 22 shifts. In this time, 11 lots with average OEE values were completed:

INDICATOR	**RESULTS**	AS-IS	DELTA IMPROVEMENT
Availability	32.43%	29.08%	+ 11.5%
Performance	68.52%	50.39%	+ 36%
Quality	96.61%	85.58%	+ 12.9%
OEE	21.47%	12.54%	+ 71.2%

Exhibit 24 - BA50's OEE indicators improvements

Generalizing it can be said that the factors of OEE correspond to:

INDICATOR	**RESULTS**	AS-IS	DELTA IMPROVEMENT
Availability	35.48%	33.79%	+ 5%
Performance	71.30%	59.36%	+ 20.1%
Quality	96.63%	89.73%	+ 7.7%
OEE	24.44%	19.56%	+ 24.9%

Exhibit 25 - Overall OEE indicators improvements

Day	Lot A00004	Ø	Shift	Th.av.time	Tot. Setup	T-Op.absence	T- micro stop	T- stand-by	T-maintenance	SUM time loss	Effective time	Lot Availability	Th. cases	Effective cases	Cumulative cases	Lot Performance	Reworked	Scraps	Lot Quality	OEE
15/10	2725	30	1	480	91	5	13	34	200	343	137	28.5%	8494	8446	8446	99.4 %	53	9	99.3 %	28.2%
18/10	2726	30	1	480	160	15	21	30	110	336	144	29.8%	8640	5216	5216	62.3 %	162	10	94.5 %	17.5%
18/10	2726	30	2	285	78	20	9	94		201	84		5040	3301	8517		291	6		
19/10	2740	30	2	435	124	10	X	75	105	314	121	27.8%	8712	8595	8595	98.7 %	21	3	99.9 %	27.4%
20/10	2756	30	1	480	150	25	11	90		276	204	37.1%	14280	7051	7051	51.8 %	68	3	99.9 %	19.2%
20/10	2756	30	2	150	90	10	X	20		120	30		2100	1435	8486		38	5		
20/10	2759	30	2	330	85	10	X	69	19	183	147	44.5%	11172	8681	8681	77.7 %	186	8	97.8 %	33.9%
21/10	2820	26.5	1	480	140	17	33	48	105	343	137	36.0%	10412	5526	5526	95.2 %	382	24	99.0 %	33.9%
21/10	2820	26.5	2	270	80	5	9	43		137	133		10108	12474	18000		183	163		
08/11	3266	36	1	480	182	20	40	43	57	342	138	35.2%	10626	10485	10485	88.1 %	84	3	63.6 %	19.8%
08/11	3266	36	2	255	56	18	5	25	30	134	121		9317	7093	17578		178	24		
08/11	3267	36	2	225	165	5	X	35		205	20	45.1%	1200	517	517	77.0 %	37	3	97.7 %	33.9%
09/11	3267	36	1	480	0	23	5	79	66	173	307		18420	13575	14092		312	3		
09/11	3267	36	2	140	86	x	x	x	X	86	54		3240	3511	17603		62	1		
09/11	3284	36	2	340	85	10	x	28	55	178	162	79.4%	9720	5973	5973	83.7 %	108	3	98.9 %	65.8%
10/11	3284	36	1	480	15	20	10	45	x	90	390		23400	11313	17286		70	3		

Exhibit 26 - Post-analysis MAR data collection

Day	Lot A00004	Ø	Shift	Th.av.time	Tot. Setup	T-Op.absence	T - micro stop	T - stand-by	T-maintenance	SUM time loss	Effective time	Lot Availability	Th. cases	Effective cases	Cumulative cases	Lot Performance	Reworked	Scraps	Lot Quality	OEE
18/10	2754	26	1	350	184	X	20	7	139	350	0	22.0%	0	0	0	65.4%	0	0	96.7%	13.9%
18/10	2754	26	2	195	8	25	x	12	74	119	76		1520	922	922		1050	105		
19/10	2754	26	1	480	14	20	23	211	38	306	174		3480	2372.6	3294.6		188	86		
19/10	2754	26	2	185	155	11	3	x	x	169	16		320	186.7	3481.3		20	1		
19/10	2755	26	2	295	124	10	10	60	X	204	91	30.9%	1820	1800.3	1800.3	78.0%	0	3	99.9%	24.1%
20/10	2755	26	1	420	195	59	x	36	x	290	130		2600	1645.9	3446.2		60	29		
21/10	2826	26	1	280	91	5	31	43	50	220	60	44.3%	1200	705.8	705.8	50.2%	70	28	99.8%	22.2%
21/10	2826	26	2	480	97	15	10	36	45	203	277		5540	2679	3384.8		1230	50		
22/10	2899	26	1	480	185	19	82	104	20	410	70	28.9%	1400	1122	1122	57.1%	250	30	99.8%	16.5%
22/10	2899	26	2	480	0	15	31	141	62	249	231		4620	2313.4	3435.4		970	54		
25/10	2899	26	1	80	70	10	x	x	x	80	0		0	0	0		0	0		
25/10	3012	26	1	400	40	10	10	122	155	337	63	25.9%	1260	1241.3	1241.3	76.1%	820	33	99.4%	19.6%
25/10	3012	26	2	480	0	10	22	90	193	315	165		3300	2228.1	3469.4		1230	191		
26/10	3034	26	2	420	113	5	x	47	55	220	200	30.3%	3600	2335.6	2335.6	65.1%	1400	6	99.7%	19.7%
27/10	3034	26	1	460	125	15	x	x	253	393	67		1139	1138.8	3474.4		1150	88		
27/10	3035	26	2	480	147	33	2	30	160	372	108	33.0%	2160	1450.3	1450.3	80.5%	900	3	99.7%	26.5%
28/10	3035	26	1	165	50	10	X	x	x	60	105		1995	1978.1	3428.4		300	111		
28/10	3053	26	1	315	108	5	13	51	20	197	118	29.3%	2242	1064.4	1064.4	68.0%	690	34	94.6%	18.9%
28/10	3053	26	2	480	0	20	8	221	114	363	117		2223	2205.9	3270.3		900	119		
28/10	3053	26	N	75	45	10	x	x	x	55	20		380	200.3	3470.6		210	3		
02/11	3419	26	1	480	125	15	11	92	x	243	237	46.2%	4503	2420	2420	56.0%	1000	40	99.8%	25.8%
02/11	3419	26	2	195	74	20	13	13	x	120	75		1425	1071.9	3491.9		30	19		
04/11	3279	26	N	370	125	80	5	10	X	220	150	37.4%	2850	1433.6	1433.6	52.0%	40	36	99.6%	19.4%
05/11	3279	26	1	480	109	47	34	90	15	295	185		3515	2049.8	3483.4		60	93		
05/11	3279	26	2	45	25	20	x	x	x	45	0		0	0	3483.4		0	0		
05/11	3281	26	2	435	230	10	x	10	x	250	185	42.5%	3515	3451.5	3451.5	98.2%	300	55	99.0%	41.3%

Exhibit 27 - Post-analysis BA50 data collection

These results are due to the awareness of the operators and therefore better attention to their duties. In particular, some operators appreciated the initiative to record data, precisely to make their work objective.

As for maintenance interventions, thanks to the presence of the mechanic in the department, the preparation of the machine kit, the foresight of the elderly maintainer and the skills of the new mechanic, it can reduce intervention times. In particular, thanks to the toolbox placed in the room of the line, about 6 minutes were saved.

Moreover, with the specific maintenance interventions, it is possible to reduce the reworked vials and so indirectly impact the quality factor, gaining 7.7% of improvement as shown in Exhibit 25.

In addition, the implementation of some countermeasures including Photocell package leaflet minimum load (MAR), the first retraining and the purchase of commonly used materials have brought these results.

Thanks to the presence of the photocell and the increase in the load capacity of the package leaflets, the frequency of restoration has decreased, and the refill time has become about 1 minute. While thanks to the training and the explanation of the correct steps to check the sensors on the machines, about 7 minutes were saved. Indeed, the reduction of the frequency indirectly also impact the performance factors due to the continuous rhythm of production.

So, it is possible to conclude, for what regards to the processes, that work focused on just one factor of the OEE, which can also bring improvements on all the others. As demonstrated in that case, improving the availability, and trying to work in a continuous allows good performance due to the continuous rhythm and on the other hand, working on the time of maintenance and on the specificity of the intervention can slightly improve the quality.

As for the compilation of the documents, it is possible to say that the operators have collaborated to reach a level equal to 35% reaching part of the complete compilation. In fact, to date, some fields are still not filled in. For the part dedicated to the coordinator and the compilation of the database, practical training is still necessary that will take place in December.

The other solutions require the collaboration of the company to buy the trolleys, unlock the checkweigher, remove the sticker machine and finally the improvement in the IT system for the communication between departments. Nonetheless, these implementations have been structured and clearly defined in terms of activities to do, responsible for the implementation, planning and scheduling, and has been already evaluated and considered in the operative yearly budget. It means that the company is in charge to buy the required resources and then implementing the solutions.

12. Standardize and share

Once the set objectives have been achieved, with a view to continuous improvement, for the processes and the operation of the lines, it is suggested to continue with the implementation of countermeasures for the future.

In particular, start with the revisions of the machines and the opening of changes and validations for the format 24 and the addition of the loading unit to the BA50 labeller. To do this it will be necessary to move the entire line to another wider area.

Subsequently, when the company has the necessary funds, it will be possible to consider installing an inkjet printing system on the most used labellers, this would lead to savings on the purchase of the foil and greater management of the "characters" for printing variable data. For this innovation, an expense of about € 70k is estimated, but based on the payback, the investment will be healed after just under 10 years.

As for the interlocking of the package leaflets, it is suggested to discuss with the supplier of the cases to enlarge all those critical cases for which the entry of the package leaflet is difficult and causes greater stops to remove the residues.

Finally, to limit Batch Record compilation errors and reduce the time spent by both employees in the build and coordinators for reviewing them, the implementation of the electronic Batch Record is strongly suggested.

This last integration mostly allows the visibility of information and obligated the operators to fill all the fields of the documentation. Since this solution is not implemented, as a transitional phase is important that the coordinators and the head of the department often check that the operators compile entirely the documents. With this first attempt of monitoring, also the following steps of classification and upload of data on the database will be easy and fast.

Moreover, it is important to continue monitoring the performances of the lines with the OEE method, especially with the introduction of the OEE register, this highlights the trend of the factors and gives a continuous improvement view to find further actions to increase the yield of the production.

At the conclusion of the A3 flow, Exhibit 28 represents the completed A3.

A3 No. and Name	Team members
1	Cenci Giulia

Team Leader (name & 'phone ext)
Cenci Giulia 3406426558

Stakeholders (name & role)	Department
1. Riello Vincenzo - Tutor/manufacturing leader	1 Packaging
2. Leoni Giordano - Client/Packaging responsible	2 Documentation
3. Baiocchi Andrea - CEO/final client	3 Maintenance
4. Cremaschi Luca - Maintenance responsible	4 Production

Organisation objective
improvement productivity of packaging lines

Start date & planned duration
2nd September 2021 till 20th December 2021

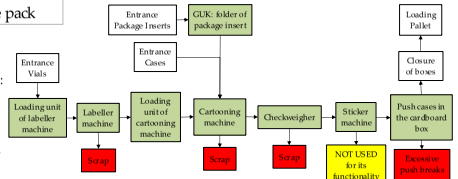
1. Problem Backgroud

There is an evidence of extension of time for the packaging of single lots. in addition there are delays between receiving of documentation and beginning of activities on the lines.
It is requested a monitoring of the lines MAR and BA50 in terms of performance for machines, operators and mechanicians

2. Current situation and breakdown the problem

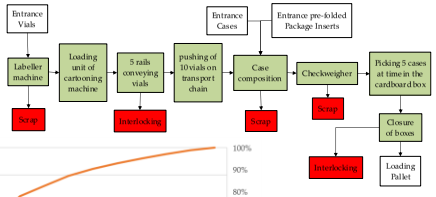
MAR: single pack

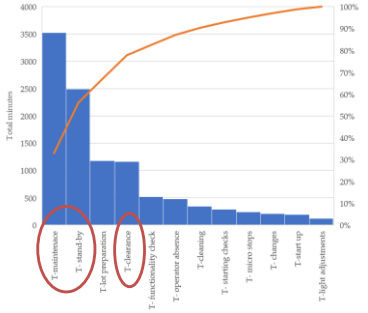
11 days (22 shifts) 9 completed lots:
A = 38.26%
P = 68.33%
Q = 97.12%
OEE = 25.39%



BA50: multi-pack

10 days (20 shifts) 8 completed lots:
A = 29.08%
P = 50.39%
Q = 85.58%
OEE = 12.54%



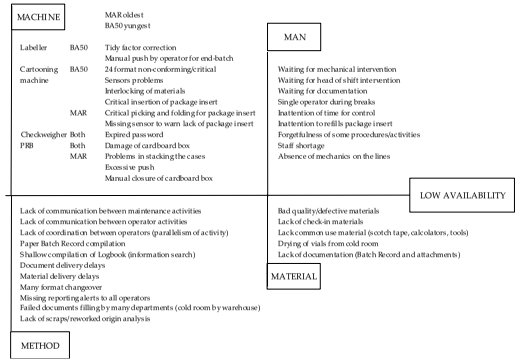


Overall mean OEE's factors:
A = 33.79%
P = 59.36%
Q = 89.73%
OEE = 19.56%

3. Set the Target

1	MUST HAVE: increasing of overall Availability from a mean of 33% To 40% (+25%)
2	NICE TO HAVE: increasing of overall Availability from a mean of 33% To 50% (+50%)
3	MUST HAVE: increase visibility by compiling of OEE register from 20% to 65%
4	NICE TO HAVE: increase visibility by compiling of OEE register from 20% to 100%

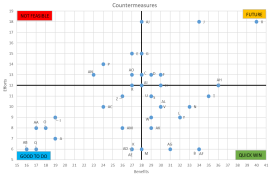
4. Analyse the Root Cause



5. Develop Countermeasures

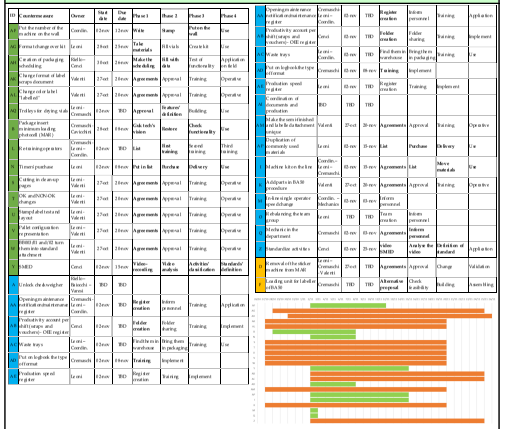
ID	Countermeasure
A	Unlock checkweigher
B	Package insert minimum loading photocell (MAR)
C	Case change
D	Removal of the sticker machine from MAR
E	PRB scotch recovery (MAR)
F	Loading unit for labeller of BA50
G	Revision format24
H	Thrust bank
I	Machine kit on the line
J	Video-camera in entrance of cartooning machine or above vial insertion
K	Add parts in BA30 procedure
L	Re-training operators
M	In-line single operator speed change
N	Timers' purchase
O	Rebalancing the team group
P	Meritocratic operators' system
Q	Mechanic in the department
R	Packaging labels by coordinator
S	Cutting in cleanup pages
T	OK and NON-OK changes
U	Stamp/label test and layout
V	Pallet configuration representation
W	Bb003.01 and .02 turn them into standard attachment
X	Electronic batch record
Y	SMED
Z	Standardize activities
AA	Opening maintenance notification/maintenance register
AB	Productivity account per shift (scraps and vouchers) - OEE register
AC	Waste trays
AD	Puton logbook the type of format
AE	Production speed register
AF	Put the number of the machine on the wall
AG	Format changeover kit
AH	Creation of packaging scheduling
AI	Coordination of documents and production
AJ	Structural change: local union and lines
AK	Change format of label scraps document
AL	Change color label "labelled"
AM	Make the semi-finished and labelled annexes unique
AN	Common attachments on each machine
AO	Duplicate the stamps and put them in place.
AP	Duplication of commonly used materials
AQ	Trolleys for drying vials
AR	Material control check_in

Prioritization using BORDA COUNT method and Weigthed Sum criteria.



ID	Indicator	Mean Actual value	Expected value	Delta	Gain
AG	Waste time reduction	82 min	22 min	60 min	73%
AH	Waste time reduction	120 min	Max 30 min	90 min	75%
AI	Increase of information	Time to call responsible of launch	Immediate notification		100%
AK - AL - T - U - V - W - AM	Waste time reduction	10 min	6 min	4 min	40%
AO	Waste time reduction	120 min	60 min	60 min	50%
B	Waste time reduction	10 min	3 min	7 min	70%
L - K	Waste time reduction	20 min	10 min	10 min	50%
N - AP - I	Waste time reduction	15 min	5 min	10 min	67%
Y - Z	Waste time reduction	90 min (forclosance)	75 min (Worst case)	15 min	17%
		60 min (forlot preparation)	53 min	7 min	12%
AA - Q	Increase of information	Uncertain information about activities performed	Awareness of activities performed		70%
AB - AC - AE	Increase of information	No monitoring	Awareness about performance		100%
AD	Increase of information	Uncertain information	Completeness of information		100%
M	Productivity	Half production during breaks	Continuous production during breaks		50%
A - O	Waste time reduction	20 min	3 min	17 min	85%
D	Waste time reduction	30 min (for downtime of host sensor)	0 min	30 min	100%
F	Productivity	2 bulks loaded	3/4 bulk loaded	1.2 bulks	50%

6. Implement Countermeasure



Gantt chart: In green is highlighted the completed countermeasures, in orange the work in progress ones.

7. Monitor Results & Process

Resalts are extrapolated from 15/10 till 10/11

INDICATOR	RESULTS	AS-IS	DELTA IMPROVEMENT
Availability	35.48%	33.79%	+ 5%
Performance	71.30%	59.36%	+ 20.1%
Quality	96.63%	89.73%	+ 7.7%
OEE	24.44%	19.56%	+ 24.9%

Employing 9 countermeasures out of 32 --> increase in the availability of 5%.

As for the compilation of the documents, it is possible to say that the operators have collaborated to reach a level equal to 35% reaching part of the complete compilation

8. Standardise & Share Success

Implement solution:

C Case change
D Removal of sticker machine in MAR
F Loading unit for BA50
H Thrust bank
J Video-camera for cartooning machine/ new system for labeller
X Electronic Batch Record

Especially, focus on development of electronic documentation

13. Discussion and conclusion

After about two and a half months to date, from the thesis work and the analyses carried out it has emerged that using a performance monitoring system, it is possible to make productivity in an objective way. As demonstrated, the use of methodological approach as A3 thinking and lean techniques can provide visibility of criticality of processes, thank the collection and study of the data. With this approach also the company realises concretely its efficiency that before the introduction of those tools were only estimated.

Therefore, thanks to the analysis of the different factors of the OEE, it is possible to identify where to intervene while with the observation in the field and the analysis of the activities through the SMED strategy it is possible to say how to improve the chosen OEE factor. It is believed that the OEE is a good tool for a poorly automated department to be able to identify how to intervene in supporting the activities of the operators. In particular, in the study present here, by intervening on the processes and at the same time on the related documentation, it is possible to reduce the lost time and guide the operators towards continuous processing.

While the analysis of maintenance activities has guaranteed a detailed study of the frequency and cause of the interventions, allowing specific maintenance to solve the problem.

In addition, as can be seen, initially employing 9 countermeasures out of 32 or about a third of the suggestions for improvement, there is already an increase in the availability of 5%. So, from the nice-to-have target of 25%, there is the necessity to expect the developments of the other countermeasures to see the estimated results.

Therefore, it is possible to say that in a controlled sector where every change must be processed and written in procedures, applying improvements on different fields, and providing collaboration and coordination with other departments, it is possible thanks to the monitoring of activities, to obtain positive results to increase productivity.

Indeed, thanks to the above lean techniques, after an in-depth analysis of the production processes, it is possible to standardize and make fluid the

continuation of the processes, making operators aware of their task and their ability to intervene on the line in a fast and targeted way.

In conclusion, this experience was a good introduction to the working world, especially, for the development of problem-solving capabilities. In particular, the use of a logic flow, well sequenced, allows me and the company how to study, analyse, and organise all the elements for this "first" conclusion of the project.

Moreover, considering the sector and the limitations to which the company is subjected, the finding of some countermeasures was sometimes hard. However, I realize that there is always an alternative applicable and collaboration with the personnel is very important to guarantee success.

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