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POTENTIAL INTEGRATION OF MACHINE LEARNING ALGORITHM AND MANUFACTURING EXECUTION SYSTEM IN THE LEAN SIX SIGMA METHOD TO IMPROVE OPERATIONAL EXCELLENCE AT ABC FARMA COMPANY

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ABSTRACT

This research focuses on the implementation of Operational Excellence (OE) in the pharmaceutical industry, especially in companies that transformed from PT Askes (Persero) to the Health Insurance Organizing Agency (BPJS). With the entry of the COVID-19 pandemic in early 2020, the need for industry readiness in the face of unexpected changes was further exposed. One approach adopted is Lean Six Sigma (LSS) which is supported by the Manufacturing Execution System (MES) to improve the efficiency and quality of the production process. This research takes a case study on product A with a focus on improvements to hardness issues. Through the Define, Measure, Analyze, Improve, and Control (DMAIC) stages, traditional methods and advanced analysis based on Machine Learning (ML) algorithms are used to improve production processes. The results showed success in achieving significant improvements in the productivity index and quality of product A production processes, making a valuable contribution in the context of Operational Excellence research in the pharmaceutical industry. The LSS method, which has been modified by integrating with ML algorithms and MES, provides productivity aspects consisting of LT, PCE and TD, as well as quality aspects consisting of better Pp, Ppk and sigma levels. The modified LSS method also provides the potential for COGM savings of 2,66 billion Rupiah and reduces the risk of production process failure to less than 200 batches for every 1 million production batches. Based on this, it can be concluded that the development of the Lean Six Sigma method which has been integrated with ML and MES algorithms has the positive potential to increase OE at ABC Farma.

KEYWORDS *Pharmaceutical Industry, Operational Excellence, Lean Six Sigma, Machine Learning Algorithm, Manufacturing Execution System*

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INTRODUCTION

Based on Rokom, 2012 and Humas Kemenko Kesra, 2013, it has been known that there was a significant event in Indonesia in the health aspect, which is starting from January 1, 2014, PT Askes (Persero) transformed into the Health Insurance Organizing Agency (BPJS). One of the impacts of this event is that pharmaceutical companies are required to provide affordable and competitive drug prices without neglecting the safety and quality aspects of the drugs. Therefore, based on internal marketing intelligence data, pharmaceutical product sales until 2021 have always been dominated by generic drugs by more than 50%.

Despite many pharmaceutical industries striving to produce drugs related to COVID-19, according to Riana & Amirullah, 2021, in mid-July 2021, stocks of drugs related to COVID-19 treatment were found to be empty in several pharmacies. This indicates a shock effect for the pharmaceutical industry, which is required to operate swiftly and excel operationally, whether due to government mandates, social responsibilities, or not wanting to miss opportunities to increase sales. Although COVID-19 has somewhat subsided and improved, other pandemics and extraordinary events could occur without careful anticipation from the industry. From these research findings, it can be concluded that an industry must have operational excellence to act quickly and accurately in facing unforeseen changes.

According to (Carvalho et al., 2021), operational excellence plays a crucial role in an organization's ability to develop agile capabilities. One proven approach to achieving operational excellence is using the lean six sigma framework, commonly abbreviated as DMAIC (Rüttimann & Stöckli, 2015). Lean is a term coined by James Womack with a broad meaning, representing a business transformation methodology derived from the Toyota Production System. Lean focuses on understanding customer value and its enhancement by reducing the cycle time of providing products or services (Skalle & Hahn, 2013).

Six Sigma is a concept developed by Bill Smith of Motorola in 1985, which led Motorola to win the US Malcolm Baldrige National Quality Award in 1988. It is a business transformation methodology that maximizes profits and adds value to customers by focusing on reducing variation and eliminating defects using various statistical and data-based tools and techniques (Skalle & Hahn, 2013).

In addition to lean and six sigma, actions that can be taken to improve processes by providing process transparency, responsiveness, and cost efficiency are the implementation of Manufacturing Execution Systems (MES) (Berres et al., 2007). MES can also assist in production planning and optimization using data-based planning algorithms with realistic work plans. MES also allows various parts of the company to be involved in the production process and provides suitable tools to perform tasks effectively (Meyer et al., 2009).

In the era of Industry 4.0, many approaches can be used to analyze various variables, including operational management variables such as man, method, machine, material, and their impact on operational excellence indicators. One of these methods is the approach using machine learning algorithms.

Machine Learning (ML) is a branch of Artificial Intelligence that is a method of mapping mathematical models used to learn or uncover underlying patterns embedded in data. Machine learning involves a set of computational algorithms that can recognize patterns, classify, and predict data by learning from existing data in the form of a training set (Abraham et al., 2020). The company ABC Farma, whose name is disguised in this study, was selected as the study location because ABC Farma is one of the largest pharmaceutical industries and is at the forefront of health resilience. ABC Farma has large and diverse assets and products. Therefore, ABC Farma is the right research location for a pilot project study in developing new methods to achieve Operational Excellence.

Previous research has highlighted the potential integration of Machine Learning (ML) algorithms in Lean Six Sigma (LSS) methods in the pharmaceutical industry, especially in drug formula development and production process optimization (Jariwala et al., 2022). Similarly, efforts to utilize ML for business process reengineering, inspired by LSS methodology, aim to reduce waste and variation and accelerate production performance (Al-Anqoudi et al., 2021). Other studies have focused on integrating ML and LSS in developing models to gain insights into core concepts driven by practitioners, although there are still challenges in reaching a consensus on these core concepts (Perera et al., 2021). Meanwhile, ML has also proven to be an effective tool in mitigating risks and supporting the development of solid oral dosage products in the pharmaceutical industry (Lou et al., 2021).

The application of AI and ML in digitizing pharmaceutical research also shows significant progress, with the potential for routine use in the future (Nagaprasad et al., 2021). However, research also notes challenges in implementing ML in manufacturing industries, such as model complexity and lack of relevant data (Weichert et al., 2019). The integration of Manufacturing Execution System (MES) with LSS methodology has also been proven to provide efficient and accurate results in process improvement projects (Hwang, 2006), while the role of MES in realizing Industry 4.0 opportunities also becomes an important highlight in the context of manufacturing process optimization (Arica & Powell, 2017). With these various findings, this study aims to combine these concepts in the context of the pharmaceutical industry, particularly in ABC Farma, to enhance Operational Excellence.

This research aims to examine the potential contribution of integrating Machine Learning algorithms and Manufacturing Execution System in Lean Six Sigma methods at ABC Farma, as well as the development of Lean Six Sigma methods integrated with both technologies to improve Operational Excellence. The benefits for the company include providing a better understanding of methods that can be used to achieve operational excellence in the digital era, helping optimize production processes, and achieving Operational Excellence sustainably. For academics, this research contributes to the development of analysis methods in Lean Six Sigma by utilizing the potential of machine learning and manufacturing execution systems to address current industry challenges, especially in the pharmaceutical sector, and provide references for further research. With the potential for integration, this research is relevant in efforts to achieve operational excellence at ABC Farma.

RESEARCH METHOD

This research employs the research and development (RnD) method with the aim of developing methods to enhance operational excellence (OE) at ABC Farma Company. Experiments are conducted to integrate Manufacturing Execution System (MES) and Machine Learning (ML) algorithms in the Lean Six Sigma (LSS) stages to evaluate their contributions to OE. Quantitative data used are sourced from the MES application and observations in the production facilities of ABC Farma Company's CCB. The LSS method is utilized with the DMAIC framework (Define, Measure, Analyze, Improve, Control) to manage and analyze data. The method development process involves data collection, analysis using Pareto Analysis, initial condition measurement with Value Stream Mapping and Process Capability Analysis, analysis of relationships between variables using Tukey Pairwise Analysis and ML algorithms, and process improvement implementation with the assistance of MES and ML. The Control phase is used to validate the effectiveness of the new method with Value Stream Mapping and Process Capability Analysis.

The integration of MES and ML algorithms in the Improve phase is the main focus of this method development. MES is used for documentation and communication of the production process, while ML algorithms are used for process optimization. Two ML algorithms are selected after validation and discussion using Rsquared indicators that produce the best results in predicting production process outcomes. The results of this method development are then analyzed to assess their contribution to OE, particularly in terms of productivity and quality. The integration of MES and ML algorithms shows potential to reduce time and increase flexibility in the production process, which directly impacts the improvement of OE at ABC Farma Company.

RESULT AND DISCUSSION

Results of LSS Method Development in the Define Stage

Analysis of the Results of the Define Stage Development

The overall data production collection process in the business is conducted in two ways: (1) previous business process (PBP) by collecting deviation data conventionally and (2) results of business process re-engineering (RBP) by collecting deviation data using MES.

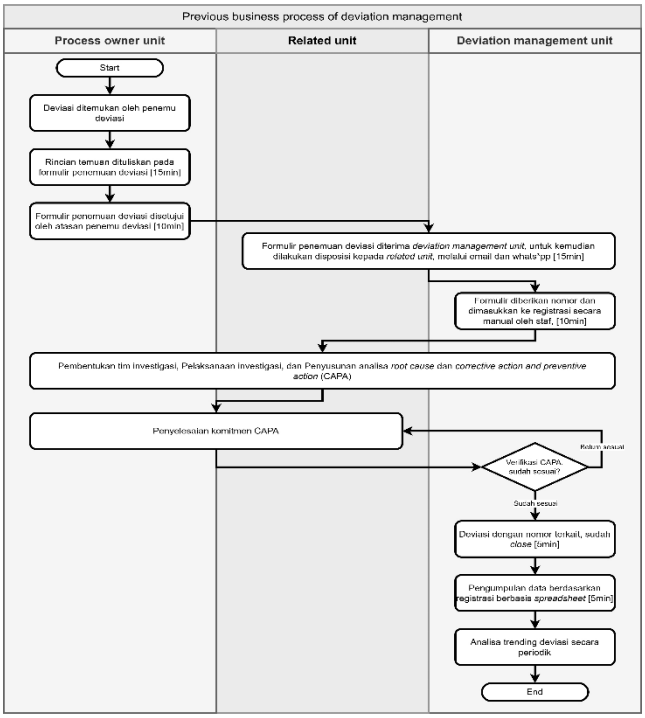


Figure 1 PBP from deviation management

Both business processes can be seen in figures 7 and 8. The difference between the two business processes lies in several aspects, including:

- In PBP, Deviation details are written on a deviation discovery form, while in RBP, deviation details are written on a deviation discovery form available on MES. Both PBP and RBP in this aspect require approximately 15 minutes.
- In PBP, the deviation discovery form is manually approved by the supervisor of the deviation discoverer on paper, requiring approximately 10 minutes due to document delivery activities, while in RBP, the deviation discovery form is approved by the supervisor of the deviation discoverer through MES, which can be directly accessed on their respective devices, requiring approximately 5 minutes.
- In PBP, the deviation discovery form is received by the deviation management unit, then disposition is made to the related unit through email and WhatsApp, requiring approximately 15 minutes, while in RBP, the deviation discovery form is received by the deviation management unit, then disposition is made to the related unit through a single-platform, namely MES, thus requiring only 10 minutes.
- In PBP, deviations with related numbers are closed on manual records, while in RBP, deviations with related numbers are closed through MES. Both PBP and RBP in this aspect require approximately 5 minutes

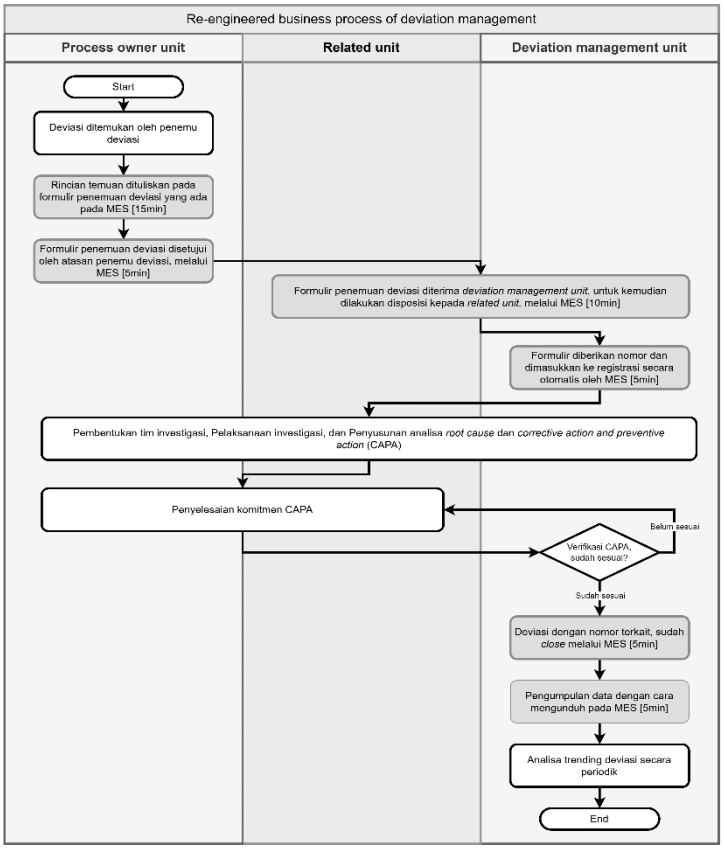


Figure 2 RBP from deviation management

- In PBP, data collection is based on online spreadsheet registration, while in RBP, data collection is done by downloading from MES. Both PBP and RBP in this aspect require approximately 5 minutes.

Based on the time or duration required for the define stage, the time difference between PBP and RBP is only about 15 minutes for each deviation, because MES will have a significant impact on risk reduction. The risk assessment based on FMEA from PBP, which then becomes risk mitigation in RBP, is outlined in Appendix 1. Some potential failure risks examined are as follows:

- Deviation detail writing: The potential failure risk is writing errors on deviations due to human error, potentially causing the information provided to be questionable and resulting in deviation follow-up being off-target. This risk has a severity level of 7, occurrence level of 3, and detectability level of 1, resulting in an RPN value of 21 and a major risk category. RBP changes the risk control by making deviation forms based on the poka yoke principle and conducting socialization regarding the completion of deviation forms, transforming the form into a digital format on MES, significantly reducing human error potential using data validation. This improves the occurrence value to 1, resulting in an RPN of 7 and a minor risk category.
- Deviation approval: The potential failure risk is signature forgery by unauthorized personnel, potentially leading to off-target deviation follow-up. This

risk has a severity level of 7, occurrence level of 3, and detectability level of 3, resulting in an RPN of 63 and a major risk category. RBP changes the risk control by requiring every leader to monitor the circulation of deviation detail forms, changing the form into a digital format on MES, significantly reducing signature forgery potential using registered accounts and unique codes for approval instead of wet signatures. This improves the detectability value to 1, resulting in an RPN of 21 and a major risk category.

- Deviation acceptance and disposition: The potential failure risk is giving disposition to unrelated departments, potentially causing not all considerations to be included in the investigation. This risk has a severity level of 7, occurrence level of 3, and detectability level of 3, resulting in an RPN of 63 and a major risk category. RBP changes the risk control by requiring disposition approval from the head of the deviation management unit, changing the disposition process from paper-based to following the deviation detail form, which will be in digital form on MES. This improves both occurrence and detectability values to 1, resulting in an RPN of 7 and a minor risk category.
- Deviation registration and numbering: The potential failure risk is errors during deviation registration and numbering, potentially causing deviations to not be properly registered, which complicates deviation data analysis and audits. This risk has a severity level of 1, occurrence level of 7, and detectability level of 7, resulting in an RPN of 49 and a minor risk category. RBP changes the risk control by providing guidelines for deviation numbering and registration, transforming the previously manual registration and numbering activities into an automated system according to predefined algorithms. This improves both occurrence and detectability values to 3 and 1 respectively, resulting in an RPN of 3 and a minor risk category.
- Deviation closure: The potential failure risk is erroneous status changes in deviations, potentially causing inaccurate status leading to inaccurate data analysis. This risk has a severity level of 3, occurrence level of 3, and detectability level of 7, resulting in an RPN of 63 and a minor risk category. RBP changes the risk control by requiring status changes to be approved by the head of the deviation management unit, changing the status change process from manual to automated through MES. This improves both occurrence and detectability values to 1 and 3 respectively, resulting in an RPN of 9 and a minor risk category.
- Deviation data collection: The potential failure risk is a data collection process that takes a long time, potentially causing delays in data analysis. This risk has a severity level of 3, occurrence level of 3, and detectability level of 1, resulting in an RPN of 9 and a minor risk category. RBP changes the risk control by storing data in the MES database instead of periodic downloading, improving the occurrence value to 1, resulting in an RPN of 7 and a minor risk category.

Overall, based on the risk assessment using FMEA, RBP provides significantly better risk categories and RPN values compared to those generated by PBP.

Results of the LSS Method in the Measure Stage

Results of Measure Stages

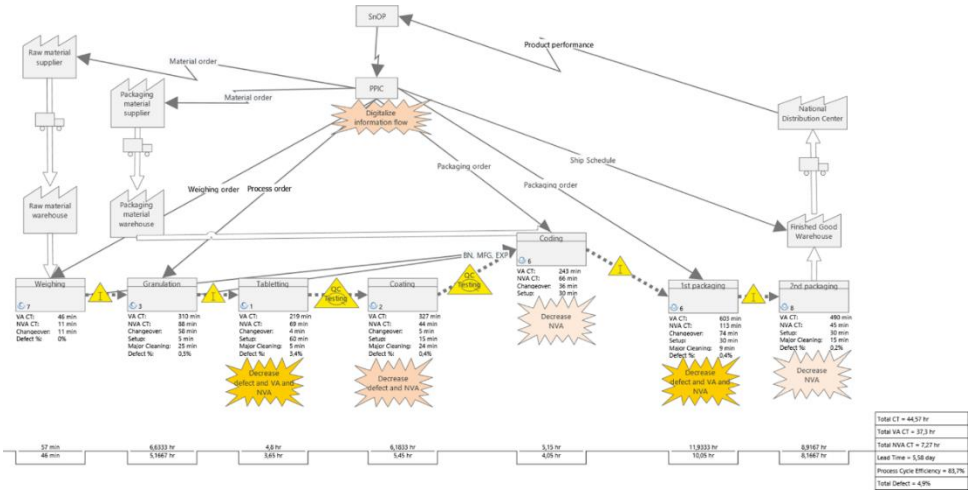


Figure 3 VSM of PBP production product A

In the define stage, the product and the problem to be addressed for the project to enhance OE using the LSS method have been determined, which is product A with the issue of tablet hardness. In the subsequent measure stage, mapping of the previous business process (PBP) for the production process of product A is conducted.

Production planning at ABC Farma begins with interpreting the sales performance of products in the market, which then flows into Sales and Operation Planning (SnOP). From SnOP, breakdowns are made based on products and their production locations and provided to Production Planning and Inventory Control (PPIC). PPIC schedules production through process orders and material orders to relevant parties.

There are several stages in the production process of product A, which generally consist of weighing, tabletting, coating, coding, primary packaging, and secondary packaging. Lead time (LT), process cycle efficiency (PCE), and total defects (TD) are measured by mapping the production process flow using a value stream mapping (VSM) diagram. The results of mapping and analyzing the PBP of the production process of product A using VSM can be seen in Figure 9.

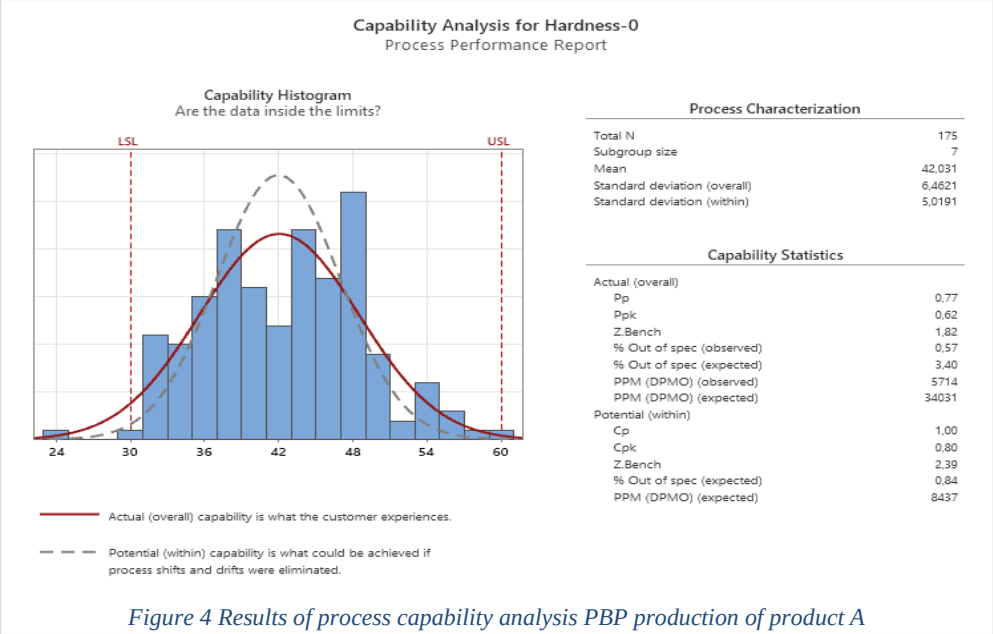


Figure 4 Results of process capability analysis PBP production of product A

In addition to metric measurements from VSM, measurements are also carried out on process reliability parameters (*process capabilty analysis*) which is carried out by measuring the values of Pp-0, Ppk-0 and *sigma* value-0 in the initial conditions, especially for the problem of tablet hardness in product A. The characteristics of tablets in the form of hardness in product A, are expected in the range of 30 to 60 N. Evaluation *of process capabilty analysis* from the hardness of the tablet (*hardness*) of product A that is still in production with PBP, carried out in 25 batches. The results of the evaluation can be seen in figure 10.

Analysis of Measure Stage Results

The VSM of the PBP for the production of product A has a total cycle time (CT) of 44.57 hours, within which there are 7.27 hours of activities that do not add value, known as non-value-added cycle time (NVACT), but these activities cannot be avoided. The total CT and NVACT values provide an LT-0 of 5.58 days, assuming one day consists of 8 working hours, and a PCE-0 value of 83.7%. Information regarding the % defect at each stage of the production process also yields a TD-0 value of 4.9%.

Based on the mapping results of the PBP using VSM, the LT-0, PCE-0, and TD-0 values are then used to create a kaizen star as a marker for the stream or stage of the production process that will undergo improvement, along with a brief description of the improvement plan in that stream. Improvement plans for the PBP of the production process of product A include the following:

- Digitizing the flow of information from PPIC to process owners
- Reducing defects, CT from VA and NVA in the tabletting process
- Reducing defects and CT from NVA in the coating process
- Reducing CT from NVA in the coding process
- Reducing defects, CT from VA and NVA in the 1st packaging process
- Reducing CT from NVA in the 2nd packaging process

Evaluation of the process capability analysis of tablet hardness for product A still in production with PBP yields a Pp-0 value of 0.77 and a Ppk-0 value of 0.62. Based on this evaluation, it is also found that the total DPMO in PPM units, in its actual overall, is 34031 PPM, which according to table 3 means the sigma level of tablet hardness for product A produced using PBP is equivalent to 3.25 sigma. This sigma level value indicates that the process is not yet optimal in terms of its reliability because in every one million bets of product A production, there is a potential to produce more than thirty-four thousand defective units.

Analysis of the Results of the Development of the Analysis Stages

Table 1 Differences between TPCA and TPCA+ML on product hardness A

Poin	TPCA	TPCA+ML
Penggunaan	Sangat sederhana dan mudah dipahami.	Perlu keterampilan khusus untuk *tuning* dan interpretasi.
Interpretasi	Mudah diinterpretasikan perbedaan antar kelompok.	Memberikan visualisasi untuk interpretasi yang lebih baik.
Analisis	Memungkinkan analisis antara setiap kombinasi faktor.	Mengidentifikasi fitur penting dan hubungan yang kompleks.
Hubungan Antar Faktor	Fokus hanya pada perbandingan antar kelompok dan tidak memodelkan hubungan.	Risiko *overfitting* dan kompleksitas model yang lebih sulit diinterpretasikan.

Correlation analysis was conducted in two ways: TPCA and TPCA+ML. The differences between these two methods can be seen in Table 4. Risk-based FMEA analysis from TPCA, which then transitioned to TPCA+ML, for risk mitigation is presented in Appendix 3. Some potential failure risks examined are as follows:

- Inability to Detect True Correlation between Variables: The potential failure involves the analysis failing to detect significant relationships between the analyzed aspects, which could lead to inaccurate decisions in product quality improvement. This is due to the variables analyzed possibly being uncorrelated or having weak correlations. This risk has a severity level of 7, an occurrence level of 7, and a detectability level of 7, resulting in an RPN value of 343, categorizing the risk as critical. TPCA+ML changed the risk control from using Tukey pairwise comparison for correlation analysis to using decision tree regression model for additional correlation analysis to validate the findings from Tukey pairwise comparison. This improvement resulted in severity, occurrence, and detectability values of 3 each, leading to an RPN value of 9 and categorizing the risk as minor.
- Overinterpretation of Analysis Results: The potential failure involves drawing incorrect conclusions based on correlation analysis results, which could lead to ineffective or irrelevant implementation of improvements. This is due to a lack of understanding or incorrect interpretation of the analysis results.

This risk has a severity level of 10, an occurrence level of 7, and a detectability level of 7, resulting in an RPN value of 490, categorizing the risk as critical. TPCA+ML changed the risk control from interpreting the results from Tukey pairwise comparison to validating and interpreting the results with the help of decision tree regression model. This improvement resulted in a severity value of 7, and occurrence and detectability values of 3 each, leading to an RPN value of 63 and categorizing the risk as major.

- Suboptimal Selection of Analyzed Variables: The potential failure involves selecting variables that do not reflect key factors influencing product quality, which could lead to ineffective or insignificant improvements. This is due to a lack of understanding of crucial factors in the production process. This risk has a severity level of 7, an occurrence level of 7, and a detectability level of 7, resulting in an RPN value of 343, categorizing the risk as critical. TPCA+ML changed the risk control from selecting variables based on technical and operational considerations to further analysis with decision tree regression model for identifying variables most influencing product quality. This improvement resulted in severity, occurrence, and detectability values of 3 each, leading to an RPN value of 9 and categorizing the risk as minor.

In general, based on risk assessment using FMEA, TPCA+ML provides significantly better risk categories and RPN values compared to those produced by TPCA.

Results of the Improve Stage Development

The overall production data collection business process is conducted in two ways: (1) previous business process (PBP) by collecting deviation data conventionally and (2) the result of business process re-engineering (RBP) by collecting deviation data using MES.

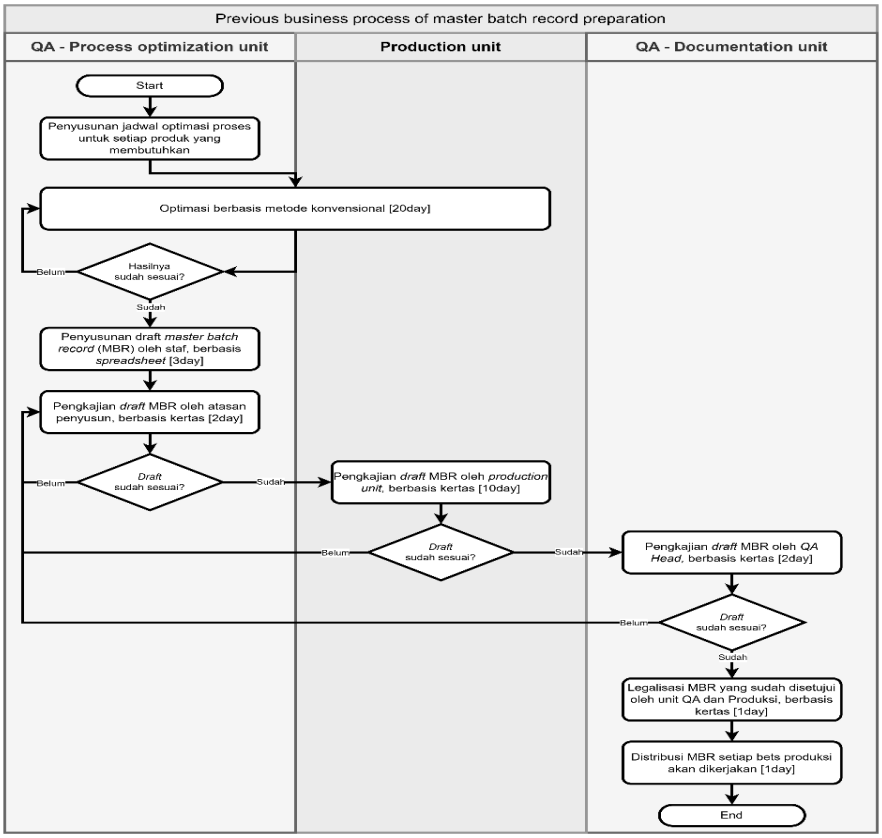


Figure 5 PBP from MBR preparation

Both business processes can be seen in figures 15 and 16. The differences between the two business processes lie in several aspects, including:

- In PBP, Optimization based on conventional methods takes about 20 working days due to numerous repetitions in the optimization activities to achieve the desired settings. In contrast, in RBP, Optimization is based on Artificial Intelligence - Machine Learning methods, allowing the optimization results to be predicted earlier by ML algorithms via computers. After obtaining the expected results, the optimization process is carried out in the production facility, reducing the optimization time to 10 working days.
- In PBP, Draft master batch record (MBR) compilation by staff, based on spreadsheets, takes about 3 working days. Whereas in RBP, Draft master batch record (MBR) compilation by staff, based on MES, which provides templates for each product type and its process type, reducing the processing time to 2 working days.
- In PBP, Review of draft MBR by the compiling supervisor, paper-based, while in RBP, Review of draft MBR by the compiling supervisor, based on MES. Both PBP and RBP have a processing time of about 2 working days.
- In PBP, Review of draft MBR by the production unit, paper-based, takes about 10 working days due to the number of parts in the production unit, requiring a long time. Whereas in RBP, Review of draft MBR by the

production unit, based on MES, which offers the advantage of simultaneous or parallel review, reducing the processing time to 5 working days.

- In PBP, Review of draft MBR by the QA Head, paper-based, while Review of draft MBR by the QA Head, based on MES. Both PBP and RBP have a processing time of about 2 working days.
- In PBP, Legalization of MBR approved by QA and Production units, paper-based, while Legalization of MBR approved by QA and Production units, based on MES. Both PBP and RBP have a processing time of about 1 working day.
- In MBR distribution, each production batch will be processed, taking about 1 working day in PBP. In contrast, in RBP, MBR is automatically generated before production, eliminating the need for specific time for this task, reducing the processing time to 0 working days.

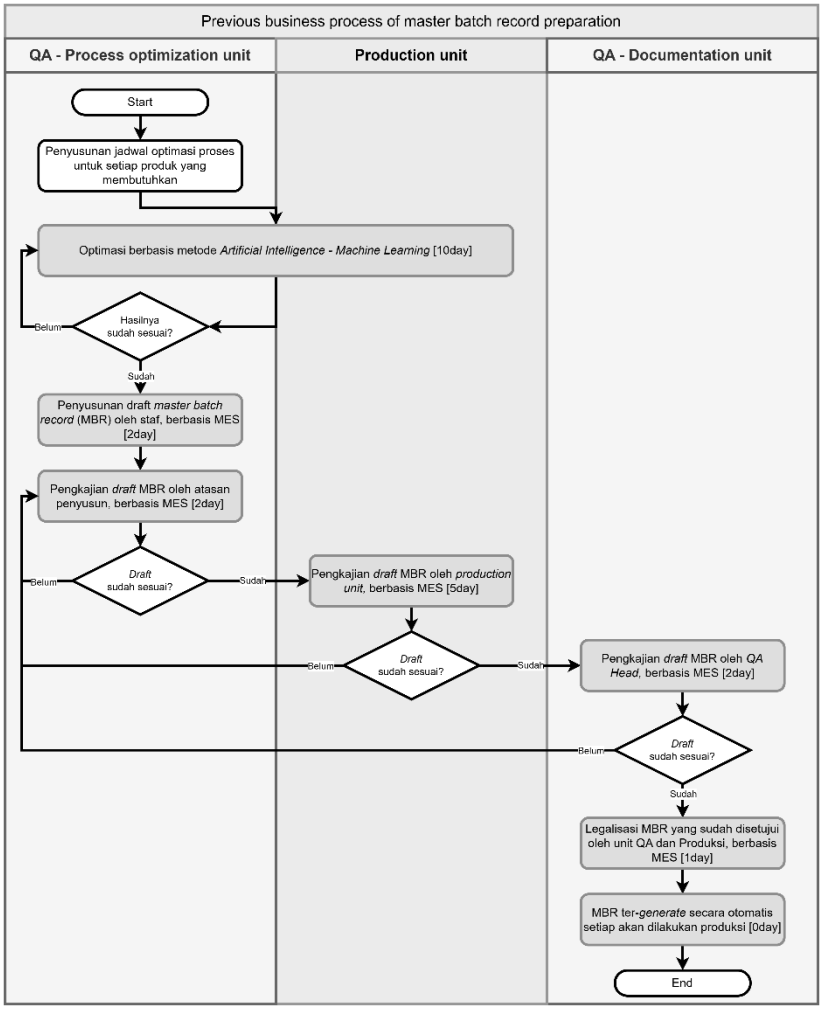


Figure 6 RBP from MBR preparation

Based on the time or duration required for the Improve stage, the difference in time between PBP and RBP is approximately 17 working days for each MBR, proving the significant impact of combining ML algorithm for optimization and

MES for MBR preparation acceleration. Apart from the time aspect, this combination also has an impact on risk reduction.

The risk-based FMEA study from PBP, which then transformed into RBP, is presented in Appendix 4. Several potential failure risks analyzed include:

- Process Optimization: The potential failure is the need for time and cost-consuming optimization, potentially causing delays in product initiation due to the long time required to achieve optimal processes. This is caused by using conventional optimization methods. This risk has a severity level of 1, occurrence level of 7, and detectability level of 7, resulting in an RPN value of 49 and a minor risk category. RBP transforms risk control by evaluating optimization results not only at the end but also at each process stage to expedite optimization. It is based on ML algorithms before actual optimization in the production facility, improving occurrence and detectability to 3 each, resulting in an RPN of 9 and a minor risk category.
- MBR Preparation and Review: The potential failure includes (1) lengthy drafting process, (2) time-consuming review of draft MBR, and (3) misalignment of production process stages, potentially causing delays in product initiation and incorrect production processes. This is caused by drafting MBR based on standard office software, requiring printing for review. This risk has a severity level of 3, occurrence level of 3, and detectability level of 3, resulting in an RPN value of 27 and a minor risk category. RBP transforms risk control by using MES-based MBR drafting with pre-existing templates for faster preparation and parallel reviews, reducing occurrence and detectability to 1 each, resulting in an RPN of 3 and a minor risk category.
- MBR Legalization: The potential failure includes lengthy approval processes, potentially causing product initiation delays due to unapproved MBRs. This is caused by paper-based legalization review, leading to prolonged review and approval. This risk has a severity level of 3, occurrence level of 3, and detectability level of 3, resulting in an RPN value of 27 and a minor risk category. RBP transforms risk control by allowing parallel reviews based on MES applications without the need for dedicated administrative personnel, reducing occurrence and detectability to 1 each, resulting in an RPN of 3 and a minor risk category.
- Batch Record Usage: The potential failure is the difficulty in tracking and ensuring the use of the latest batch record revisions, potentially causing uncontrolled document quantities and incorrect production processes. This is caused by paper-based batch record management with manual revision tracking. This risk has a severity level of 7, occurrence level of 3, and detectability level of 7, resulting in an RPN value of 147 and a major risk category. RBP transforms risk control by automatically disposing batch records via MES, ensuring only the latest revisions are used. This reduces occurrence to 1 and detectability to 3, resulting in an RPN of 21 and a minor risk category.

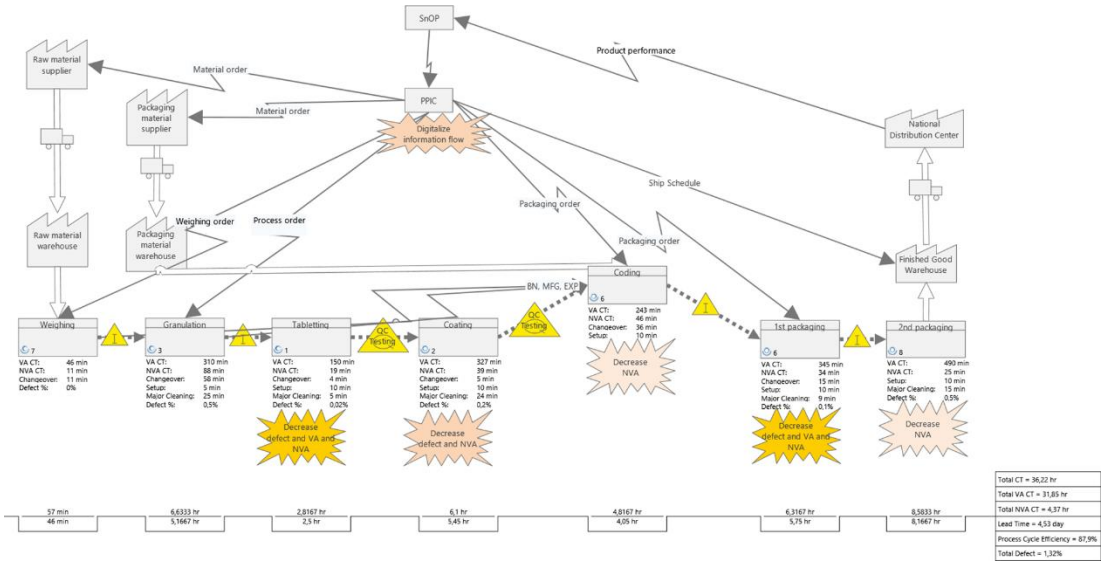
Overall, the risk assessment using FMEA from RBP provides significantly better risk categories and RPN values compared to those generated by PBP.

Results of the Lean Six Sigma (LSS) Method in the Control Stage

Control Stage Results

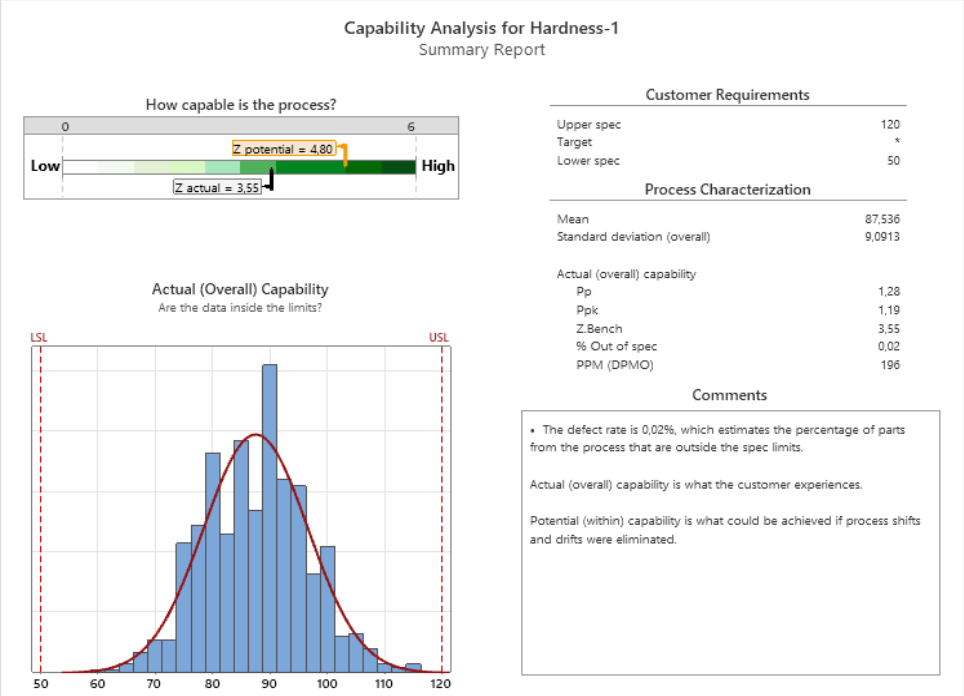
In the improve stage, the impact of the improvements made is measured on OE metrics whose previous values have been measured in the measure stage. Measurements of LT-1, PCE-1, and TD-1 conducted in the measure stage by mapping the production process flow using a value stream mapping (VSM) diagram, as well as the values of Pp-1, Ppk-1, and sigma value-1, are verification and control activities aimed at assessing the condition after improvements have been made to the production process of product A.

In this control stage, measurements are conducted again to control the OE metrics, which should have shown improvement after passing through the improve stage. The mapping results and analysis of the RBP production process of product A using VSM can be seen in figure 17.



Gambar 7 VSM dari RBP produksi produk A

Measurements (measure) on process reliability parameters (capability process analysis) are conducted by measuring the values of Pp-1, Ppk-1, and sigma value-1 in the condition after improvement, especially for the tablet hardness problem in product A. The tablet characteristics in product A, in terms of hardness, are expected to be in the range of 50 to 120 N. Process capability analysis evaluation of tablet hardness for product A still in production with RBP is conducted on 72 batches. The results of this process reliability evaluation can be seen in figure 18.



Gambar 8 Hasil process capability analysis RBP produksi produk A

Analysis of Control Stage Development Results

VSM of the RBP production process of product A has a total cycle time (CT) of 36.22 hours, within which there are 4.37 hours of activities that do not provide value, known as non-value-added cycle time (NVACT), but these activities cannot be avoided. The total CT and NVACT values provide an LT-1 of 4.53 days, assuming one day consists of 8 working hours, and a PCE-1 value of 87.9%. Information related to the % defect of each production process stage also provides a TD-1 value of 1.32%.

The results of the RBP mapping using VSM with LT-1, PCE-1, and TD-1 values are derived from activities based on kaizen star, which serves as a marker for the stream or stage of the production process that has been improved, along with a brief description of the improvements in that stream. The details of these improvements include:

- Digitization of information flow from PPIC to process owners, previously manual, now done digitally using MES.
- In the tabletting process:
  - Defects reduced from 3.4% to 0.02%.
  - VACT reduced from 219 minutes to 150 minutes.
  - NVACT reduced from 69 minutes to 19 minutes.
- In the coating process:
  - Defects reduced from 0.4% to 0.2%.
  - NVACT reduced from 44 minutes to 39 minutes.
- In the coding process:
  - NVACT reduced from 66 minutes to 46 minutes.

- In the 1st packaging process:
  - Defects reduced from 0.4% to 0.1%.
  - VACT reduced from 603 minutes to 345 minutes.
  - NVACT reduced from 113 minutes to 34 minutes.
- In the 2nd packaging process:
  - NVACT reduced from 45 minutes to 25 minutes.

Process capability analysis evaluation of tablet hardness for product A still in production with RBP resulted in a Pp-1 value of 1.28 and a Ppk-1 value of 1.19. Based on this evaluation, the total DPMO in PPM units, in its actual overall, is 196 PPM. Referring to Table 3, the sigma level of the tablet hardness of product A produced using RBP is equivalent to 5.04 sigma. This sigma level indicates that the process is much more optimal in terms of process reliability because for every one million bets of product A production, less than two hundred bets may be defective.

Discussion on Lean Six Sigma (LSS) Method Development

Potential Contribution of Integrating ML Algorithm into LSS Method

The single contribution of integrating ML Algorithm into the LSS method lies in the analysis stage, providing additional analysis after using TPCA. TPCA, which can only provide analysis of aspects influencing the hardness of product A, the issue resolved for OE improvement at ABC Farma. The ML Algorithm provides further analysis to prioritize each aspect, making the improvements in the improve stage more targeted.

From the FMEA risk assessment results, the ML Algorithm significantly contributes to reducing the RPN value in the analysis stage of the LSS method. Details of the reduction in RPN values can be seen in Table 7.

Tabel 2 Kontribusi algoritma ML pada penurunan risiko di tahapan analyse pada metode LSS

Risk	RPN of LSS Analyse stage without ML algorithm	RPN of LSS Analyse stage with ML algorithm
Tidak Dapat Mendeteksi Korelasi Sebenarnya antara Variabel	343	27
Overinterpretasi Hasil Analisis	490	63
Tidak Optimalnya Pemilihan Variabel yang Dianalisis	343	27

Based on the differences between TPCA and TPCA+ML in Table 4 and the summary of risk reduction contributions in the analysis stage as per Table 7, it can be concluded that the ML Algorithm has the potential to positively contribute to the LSS method, particularly in the analysis stage at ABC Farma.

Potential Contribution of Integrating MES into LSS Method

The single contribution of integrating MES into the LSS method lies in the define stage, providing alternatives in production data management and recording of non-conformities. The results of the reengineered business process (RBP) in

deviation management using MES provide a reduction in time of about 15 minutes for each deviation compared to its previous business process (PBP).

From the FMEA risk assessment results, MES significantly contributes to reducing the RPN value in the define stage of the LSS method. Details of the reduction in RPN values can be seen in Table 8.

Table 3 MES contribution to risk reduction at the define stage of the LSS method

Risk	RPN of LSS Define stage PBP deviation management	RPN of LSS Define stage RBP deviation management
Penulisan rincian deviasi	21	7
Persetujuan rincian deviasi	63	21
Penerimaan dan disposisi deviasi	63	7
Registrasi dan pemberian nomor pada deviasi	49	3
Penutupan deviasi	9	3
Pengumpulan data deviasi	9	3

Based on the reduction in deviation management time from the RBP results using MES and the summary of risk reduction contributions in the define stage as per Table 8, it can be concluded that MES has the potential to positively contribute to the LSS method, particularly in the define stage at ABC Farma.

Potential Contribution of Integrating ML Algorithm and MES into LSS Method

The contribution of integrating ML algorithm and MES into the LSS method lies in the improve stage, providing alternatives in process optimization and MBR preparation. The results of the reengineered business process (RBP) in deviation management using MES provide a reduction in time of about 17 working days for each MBR compared to its previous business process (PBP).

From the FMEA risk assessment results, the combination of ML algorithm and MES contributes significantly to reducing the RPN value in the improve stage of the LSS method. Details of the reduction in RPN values can be seen in Table 9.

Tabel 4 Kontribusi algoritma ML dan MES pada penurunan risiko di tahapan improve pada metode LSS

Risk	RPN of LSS Improve stage PBP of process optimization and MBR preparation	RPN of LSS Improve stage RBP of process optimization and MBR preparation
Optimasi Proses	49	9
Penyusunan dan pengkajian MBR	27	3
Legalisasi MBR	27	3
Penggunaan batch record	147	21

Based on the reduction in deviation management time from the RBP results using ML algorithm and MES and the summary of risk reduction contributions in the improve stage as per Table 9, it can be concluded that ML algorithm and MES have the potential to positively contribute to the LSS method, particularly in the improve stage at ABC Farma.

Potential Contribution of Modified LSS Method on OE

The modified LSS method developed by integrating ML algorithm and MES at various stages has contributed to improving OE. The OE indices used for ABC Farma in this study are lead time, process cycle efficiency, and total defect for productivity aspects, as well as Pp, Ppk, and sigma level for quality aspects.

Product A at ABC Farma has been measured for all these indices, both in terms of productivity and quality, in its baseline condition and also after improvements.

The improvement in OE indices at ABC Farma starts from determining the product and its issues, which is product A with the issue of tablet hardness during production. The hardness issue in product A is analyzed for its causes by five aspects (5M): man, method, measurement, machine, and material. The analysis revealed that the method and material aspects are crucial in addressing the hardness issue in product A. Improvements are focused on these two aspects using ML algorithm and MES, resulting in significant improvements in OE indices. A summary of the improvement results based on OE indices can be seen in Table 10.

Tabel 5 Perbandingan indeks OE sebelum dan sesudah perbaikan menggunakan LSS yang telah dikembangkan

Aspect	OE Index	Before Improvement	After Improvement
Productivity	Lead Time (day)	5,58	4,53
	Process cycle efficiency (%)	83,7	87,9
	Total defect (%)	4,90	1,32
Quality	Pp	0,77	1,28
	Ppk	0,62	1,19
	Sigma Level	3,25	5,04

Product A manufactured by ABC Farma has a cost of goods manufactured (COGM) of Rp 380 per tablet, so for a box containing 30 tablets, the COGM of product A is Rp 11,400. Like products in the pharmaceutical industry, product A at ABC Farma is also produced in batch units. The batch size for product A at ABC Farma is 15,500 boxes, so the COGM of product A for one production batch is Rp 176,700,000 under the conditions before improvement.

After improvement, the COGM value is Rp 308 per tablet, so for a box containing 30 tablets, the COGM of product A is Rp 9,255. Similarly, product A at ABC Farma is produced in batch units, and the batch size for product A is 15,500 boxes, so the COGM of product A for one production batch is Rp 143,450,000 under the conditions after improvement. Based on these conditions, the potential annual savings in COGM for product A amount to Rp 2.66 billion. A summary of the potential annual COGM savings for product A can be seen in Table 11.

Tabel 6 Potensi penghematan COGM produk A

Condition	Unit		COGM
Before Improvement	per tablet	Rp	380
	per dus (30 tablet)	Rp	11.400
	per produksi (15.500 dus)	Rp	176.700.000
	per tahun (asumsi 80 kali produksi)	Rp	14.136.000.000
After Improvement	per tablet	Rp	308
	per dus (30 tablet)	Rp	9.255
	per produksi (15.500 dus)	Rp	143.450.000
	per tahun (asumsi 80 kali produksi)	Rp	11.476.000.000
	Potensi penghematan pada produk A per tahun	**Rp**	**2.660.000.000**

Another benefit of using the modified LSS method integrated with ML algorithm and MES is the reduction in production process failure risk, depicted by the sigma level for every one million production batches. Under the conditions before improvement with a sigma level of 3.25, there is a potential for over thirty-four thousand batches of production process failure for every one million production batches, while after improvement with a sigma level of 5.04, there are less than two hundred batches of potential production process failure for every one million production batches. A summary of the potential reduction in production process failure risk for product A can be seen in Table 12.

Tabel 7 Potensi penurunan risiko kegagalan produksi produk A

Condition	Index	Value
Before Improvement	Sigma Level	3,25
	Defect Per Million Opportunities	34.031
After Improvement	Sigma Level	5,04
	Defect Per Million Opportunities	196

CONCLUSION

This study concludes that the integration of Machine Learning (ML) algorithms and Manufacturing Execution Systems (MES) into the Lean Six Sigma (LSS) method at ABC Farma contributes positively. The ML algorithm in the LSS analysis stage provides deeper analysis and reduces risks, while MES in the definition and improvement stages provides faster processing times and reduces risks. The integration of these two technologies enhances productivity and quality aspects, as well as the potential for cost savings and reducing the risk of production process failures. The policy implications of this research highlight the potential use of modified LSS methods in the pharmaceutical industry to improve production effectiveness and efficiency, which at a national scale could contribute to Indonesia's health resilience. Suggestions for further research include considering the addition of other products based on matrix and bracketing methods, while limitations of the study include focusing on one company in Indonesia and the potential differences in results when applied to other companies within and outside the pharmaceutical sector.

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