School of Innovation, Design, and Engineering   **AstraZeneca**

Optimising the Planning- and Scheduling in a Complex Production

Discrete-Event Simulation in a pharmaceutical context

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Product- and Process Development

Paulina Boutros & Johan Börjesson

Hassanein Sater, Supervisor, AstraZeneca

Ioanna Aslanidou, Supervisor, Mälardalen University

Angelina Sundström, Examiner, Mälardalen University

ABSTRACT

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Authors:	Paulina Boutros Johan Börjesson 1st January 1998 15th April 1995
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Supervisor:	Hassanein Sater, AstraZeneca Ioanna Aslanidou, Mälardalen University
Keywords:	DES, Optimisation, Pharmaceutical industry, Product mix, Production planning- and scheduling, Resource allocation, Simulation.
Aim:	The aim of this study is to investigate the optimisation of production planning- and scheduling in a pharmaceutical facility using DES.
Research questions:	"How can DES be used to achieve flexibility and efficiency in a pharmaceutical facility?" and "How can DES be used to increase efficiency of the resource allocation in a pharmaceutical facility?"
Methodology:	This study has been compared to a deductive- and a quantitative research approach where a process simulation has been modelled. The theoretical framework was based on books and scientific publications. Empirical data was collected through unstructured observations at the production site, frequent meetings together with the company and through the company's database Discoverant. Based on the results from the simulation model conclusions could be drawn.
Conclusion:	The study concluded that there are bottlenecks at the beginning of the processes in all three production flows for Medicine A, Medicine B and Medicine C. If these are raised it would generate greater flexibility and efficiency in the production. There were also indications of a new allocation of resources that would raise efficiency in the production, thus making it possible to increase the output from the production.

SAMMANFATTNING

Datum: 5 juni 2022

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Författare: Paulina Boutros   Johan Börjesson
1 januari 1998   15 april 1995

Titel: Optimering av Produktionsplanering- och Schemaläggning i en Komplex Produktion – Diskret-Event Simulering i ett läkemedelssammanhang.

Handledare: Hassanein Sater, AstraZeneca
Ioanna Aslanidou, Mälardalens Universitet

Nyckelord: DES, Läkemedelsindustrin, Optimering, Produkt mix, Produktionsplanering- och schemaläggning, Resursfördelning, Simulering.

Syfte: Syftet med studien är att undersöka optimering av produktionsplanering- och schemaläggning inom en läkemedelsproduktion med användning av DES.

Frågeställningar: "Hur kan DES användas för att uppnå flexibilitet och effektivitet i en läkemedelsproiduktion?" och "Hur kan DES användas för att öka effektiviteten kring användandet av resurser i en läkemedelsproduktion?"

Metod: Denna studie har liknats vid en deduktiv- och en kvantitativ forskningsansats där en processimulering utformats. Den teoretiska referensramen baserades på böcker och vetenskapliga publikationer. Empirisk data samlades in genom ostrukturerade observationer i produktionen, regelbundna möten tillsammans med företaget och genom företagets databas Discoverant. Baserat på resultaten från simuleringsmodellen kunde slutsatser dras.

Slutsats: Studiens slutsats landade i att det finns flaskhalsar i början av alla tre produktionsflöden för Medicin A, Medicin B och Medicin C. Om dessa kan höjas skulle det generera en högre flexibilitet och effektivitet i produktionen. Det finns också tecken som visar på att en ny resursfördelning hade höjt effektiviteten i produktionen, därmed gjort det möjligt att producera mer produkter.

ACKNOWLEDGEMENTS

Paulina Boutros
Eskilstuna, juni 2022

Johan Börjesson
Eskilstuna, juni 2022

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ABBREVIATIONS

API	Active Pharmaceutical Ingredients
C/T	Cycle Time
DES	Discrete-Event Simulation
NP-hard	Non-deterministic Polynomial-time hard
R&D	Research and Development
VSM	Value-Stream Mapping

INTRODUCTION

In the following section, the studied problem area will initially be presented. The problem area studied is then summarised in the problem formulation, which then culminates in the study's aim and research questions. Finally, the scope of the study are presented to concretely present the area that has been studied.

1.1. Background

A large product mix is a challenging task for any producing company, and the larger the product mix, the more effort needs to be put into the production planning- and scheduling for the manufacturer to optimise the productivity and maximise the units produced (Badri et al., 2014; Sobreiro et al., 2014). The determination of an optimal product mix on production systems is one of the most important production planning decisions. Further, it is considered very important to determine the optimal product mix in relation to the output produced by the manufacturer (Ginting et al., 2018).

The pharmaceutical industry can be considered as a complex system consisting of processes, operations, and organisations that work with manufacturing, discovering, and developing medicines (Moniz et al., 2015; Marques et al., 2017). Consequently, the pharmaceutical industry has some exceptional challenges that are not as common in other industries (Kaylani & Atieh, 2016). Some of the challenges presented include a huge product mix with a variation in process times, batching of various lots that share common resources, industry standards that contain huge cleanliness and sterilisation regulations that incorporate campaign lengths, and can differ in accordance with product sequencing (Ghousi et al., 2012; Kaylani & Atieh, 2016; Hering et al., 2021). Production planning- and scheduling activities are thus two of the primary challenges in pharmaceutical industries (Ghousi et al., 2012). On the other hand, due to the growth in global competitiveness and the commitment to meet customer demand in a timely aspect, the pharmaceutical industry is compelled to improve their production planning- and scheduling and develop the utilisation of resources (Wattitham et al., 2015; Kaylani & Atieh, 2016).

Research and Development (R&D), construction and elaboration of Active Pharmaceutical Ingredients (APIs) and pharmaceutical manufacturing are parts of what a pharmaceutical company need to master in their everyday operations. Previously, the industry has had a timeframe of more than ten years to get a product from idea to market. However, the current paradigm of globalisation forces a drastic reduction of this time for the product to be competitive. Therefore, expanding R&D costs, high Cycle Times (C/T), and low anticipation of accomplishment are various challenges that the pharmaceutical industry is forced to overcome (Moniz et al., 2015; Marques et al., 2017). Furthermore, Moniz et al. (2015) state that regulators along with manufacturers have created an environment for operations management that heavily restrict the production planning- and scheduling activities. Ghousi et al. (2012) state that regarding the vagueness of production planning, forecasting methods could have an important part in decision making.

Production scheduling complications are observed as Non-deterministic Polynomial-time hard (NP-hard) because there is no common algorithm that can identify an optimal solution in any sensible time (Mönch & Zimmermann, 2011; Kaylani & Atieh, 2016). The current algorithms can control certain production systems, but algorithms become less effective when the extent of the system becomes greater, and variabilities increase. Most of the scheduling research does not clearly acknowledge execution problems such as unpredictability but consider that the global schedule will be accomplished precisely as it appears from the algorithm that creates it. Schedule modelling and execution will be an incredibly challenging work if the schedule is expanded and contain more limitations (Kaylani & Atieh, 2016). Traditional scheduling methods have shown results of 7,9% increase in efficiency in a pharmaceutical production (Eberle et al., 2016), however optimisation of scheduling through simulation has shown potential to generate up to 40% increase in efficiency (Spindler et al., 2021). Thus, Discrete-Event Simulation (DES) exploration becomes fundamental because of its capacity for investigating the complex dynamics of the system and its irregular action (Kaylani & Atieh, 2016).

1.2. Problem statement

The pharmaceutical industry is characterised by complex systems, operations, and development phases that are deeply linked with planning- and scheduling problems, leading to a low utilisation of resources (Moniz et al., 2015; Eberle et al., 2016; Marques et al., 2017). Some challenges that are common in the pharmaceutical industry and need to be addressed are large product mixes, batches that share resources, high regulatory demands, and sanitation procedures that can vary according to each specific product (Ghousi et al., 2012; Kaylani & Atieh, 2016; Eberle et al., 2016; Hering et al., 2021). However, one of the greatest challenges for any production company, including pharmaceutical productions, is the composition of a product mix (Badri et al., 2014; Sobreiro et al., 2014). In simpler productions scheduling issues can be handled with algorithms to optimise the production planning, however as the production complexity along with the product mix increases these algorithms loose accuracy in their optimisation (Kaylani & Atieh, 2016). These NP-hard problems need another solution that can handle the large complexity of the product mix (Mönch & Zimmermann, 2011; Kaylani & Atieh, 2016). DES has shown a good capability of handling these NP-hard problems by testing all possible scenarios and recommending the one where the desired outcomes are met (Triguero de Souca Junior et al., 2019).

The literature did however lack in how resources are to be considered in simulations. What is therefore interesting to know is to what extent the allocation of resources affects the flexibility and efficiency in a pharmaceutical production and how DES can be used to facilitate this situation. This is the literary gap that is going to be filled in this study.

1.3. Aim and Research questions

The aim of this study is to investigate the optimisation of production planning- and scheduling in a pharmaceutical facility using DES. Thus, the following research questions shall be answered:

1. *How can DES be used to achieve flexibility and efficiency in a pharmaceutical facility?*

2. *How can DES be used to increase efficiency of the resource allocation in a pharmaceutical facility?*

1.4. Scope

This study is directed towards the pharmaceutical industry through the examination of one pharmaceutical facility. Further focus is towards production planning where the efforts will be aimed at increasing flexibility and efficiency through DES. This study is also limited to only analysing processes at a scheduling level in the production process. That indicates that no analysis will be made on how the work is performed by the operators, nor any time the products would spend in a laboratory for analysis. Furthermore, this study will focus on the larger components in the production process that would be present in a production schedule. Therefore, information that would be included in an extended Value-Stream Mapping (VSM) such as activities between process steps or transportation times will not be a part of this study nor the simulation model.

2. THEORETICAL FRAMEWORK

In the following section, previous research and theories that will be useful for further development in the study will be presented.

2.1. Production planning- and scheduling in a pharmaceutical industry

The pharmaceutical industry performs in an extremely dynamic, highly regulated, and competitive business condition, being one of the main producing branches in Europe (Moniz et al., 2015; Eberle et al., 2016; Marques et al., 2017). The liberalisation of global trade with pharmaceuticals and the coercion from regulatory authorities to lower the price of medicine has led to an increase in generic competition. The price of imitation in the pharmaceutical industry is low in contrast to the price of innovation, which results in generic competition turning progressively harsh, especially concerning financial issues. Regarding that, the pharmaceutical industry is very contingent on patent effective life, being required to provide medicines rapidly and productively (Marques et al., 2017). Aside from this, the pharmaceutical industry has further exceptional challenges that are not as common in other industries (Kaylani & Atieh, 2016). Some of the challenges presented incorporate a huge product mix with a variation on process times, batching of various lots that share common resources, industry standards that contain huge cleanliness, and sterilisation regulations that include campaign lengths, that differ in accordance with product sequencing (Ghousi et al., 2012; Kaylani & Atieh, 2016; Eberle et al., 2016; Hering et al., 2021). Production planning- and scheduling activities are thus one of the primary challenges of pharmaceutical industries (Ghousi et al., 2012). Furthermore, Moniz et al. (2015) and Eberle et al. (2016) state that time-to-market is the most censorious problem in the pharmaceutical industry. To efficiently meet customer demand and sales order, improved and developed production planning and utilisation of resources is therefore necessary (Wattitham et al., 2015; Kaylani & Atieh, 2016). Production planning- and scheduling activities are intended to lower the costs and develop responsiveness of the manufacturing systems (Moniz et al., 2015). Kaylani and Atieh (2016, p. 412) define production planning- and scheduling as "allocating of shared resources during a planning period to competing products in order to meet production requirements."

Harjunkoski et al. (2014) and Eberle et al. (2016) claim that the critical aspects that operates the planning- and scheduling activities, in coherence of the pharmaceutical industry, can be categorised in three different sections: market, processes, and plants. The market aspect has a straight impact on the planning- and scheduling activities in the pharmaceutical industry, where this industry is very fragmented (Moniz et al., 2015). The pharmaceutical industry has a great variability on the demand, which results in a coercion generated by generic medicines, which in turn will lead to large production mixes in the production area. Operation flexibility is hence a necessity to suit the systems to the varying demand and in addition to that efficient production planning- and scheduling methods are necessary (Kaylani & Atieh, 2016). Manufacturing in a high adjusted market must consider further difficulties that do not obtain in less adjusted markets. Chemical processes are strictly supervised by the regulatory agencies that monitor the processes to confirm that the defined procedures are met in the transformation processes (Moniz et al.,

2015). Globally, the demand problem and the coercion to minimise costs are forcing operations to operate more efficiently, hence advanced production planning- and scheduling activities are required (Kaylani & Atieh, 2016). The production process topology dynamically considers the number of different planning- and scheduling models that can be introduced. When different APIs are produced, some manufacturing steps require for instance several production steps with tasks that include short- and long manufacturing times, often stretching over several work shifts. The rules and quality controls that take place in the manufacturing process control the transition requirements and batch size that need to be followed in the various steps of the process, which results in it becoming difficult to streamline the production time. Batch traceability needs to be verified because stable intermediaries and end products are manufactured in batches. However, it is more difficult to manufacture the first batches after a scaling up as these aim at utilising different processing units or changes in the manufacturing process. Hence, these flows require continuous reconciliations of the scheduling (Moniz et al., 2015). Production planning- and scheduling are also affected by the plant structure. Allocation of resources, operating situation, plant structure, and continuous manufacturing are aspects that also need to be considered in planning and scheduling. Continuous pharmaceutical production is a nascent manufacturing mode that relies on flow reactors rather than batch reactors, resulting in the manufacturing process going from a batch mode to constant operating conditions. Thus, in order to achieve full efficiency, coordination with advanced control systems should be implemented (Engell & Harjunkoski, 2012; Moniz et al., 2015).

2.2. Demand forecasting and production planning

Forecasting methods are used to develop decisions associated to production planning. Demand forecasting has an impact on several practical operations within an organisation including production planning and resource allocation (Ghousi et al., 2012). Production planning that is successful is contingent on the modelling quality of various problem-related features, involving demand uncertainty, production lead times, and capacity. Numerous types of research within inventory literature includes information about demand forecasting (Albey et al., 2015). On the other hand, there is limited information on demand forecasting in production planning research although demand forecasting is a crucial part within production planning (Bóna & Lénárt, 2014; Albey et al., 2015). Forecasts are reconsidered as added information and becomes accessible over the years (Aouam & Uzsoy, 2015). A time series is the primary source of information for forecasting, where this time series consists of a sequence of examinations obtained at frequent periods. The modelling simplifies system synthesis, involvement, and verification, while its forecast benefit planning operations (Box et al., 2015).

2.3. Theory of constraints

Theory of constraints is a philosophy within management that focuses on the weakest links in a chain to improve the performance of a system (Şimşit et al., 2014). The theory is based on the assumption that all systems have at least one bottleneck that constraints the performance of the system (Naor et al., 2012). The theory of constraints can be applied to many situations such as production, logistics, supply chain, project management, sales, and marketing. Because of this there are several definitions of what the weakest link in a system can be. However, most

companies strive for an increase in revenue and thus the best way to identify a bottleneck within this theory is to view everything that stands between the company and an increase of profits as constraints (Şimşit et al., 2014). If a company can manage its constraints, it can then implement a continuous improvement management system that in turn increases the profits. The simple idea is to identify the main constraint, and to elevate it so that the system runs smoother, thus eliminating this bottleneck. That would in accordance with the theory move the bottleneck to a new part of the system and then the procedure starts over, always improving itself (Naor et al., 2012).

2.4. Simulation

Simulation has been defined several times, but two frequently used definitions are:

> "The process of designing a mathematical or logical model of an actual real system and experimenting with the model on a computer to describe, explain, and predict the behaviour of the real system."

> (Kaylani & Atieh, 2016, p. 412)

> "The imitation of the operation of a real-world process or system over time. Whether done by hand or on a computer, simulation involves the generation of an artificial history of a system and the observation of that artificial history to draw interfences concerning the operating characteristics of the real system."

> (Banks, 2015, p. 1)

Once a simulation is built and validated it can be used to answer many *What if* scenarios about the real world (Banks, 2015; Triguero de Souca Junior et al., 2019). However, a simulation can also be used to investigate systems that are yet to be built in the real world and thus evaluate the process's infliction on the surrounding systems. By this assumption simulation can be useful both as an analytic tool for predicting effects and performances of existing systems, and as a design tool to predict the future effects of a new system before the investment is made. There are situations where simulation is not suitable and one of these situations is if the problem can be solved analytically (Banks, 2015). These situations are too simple for a simulation study to be performed but there are other situations when the number of variables increase, and the extent of the project gets too big for an analytical solution to provide a reliable result. These situations can be considered as NP-hard (Mönch & Zimmermann, 2011; Kaylani & Atieh, 2016). Analysing the results from a simulation model can expose the bottlenecks in a system and suggest ways to address these bottlenecks (Thenarasu et al., 2022). Riley (2013) discusses the possibilities and mentions the greatest challenge with simulation being optimisation. This is discussed by Dolgui and Ofitserov (1997) who explain that simulation combined with optimisation often provide a local optimum, thus sub-optimising the process. Simulation often aims to answer questions where different scenarios are presented to a system. Optimisation is defined as minimising or maximising desired parameters, or both. Thus, if a simulation has sufficient data to represent the

analysed system reliably, the scenario with the best suited outcome can be inferred as optimal (Triguero de Souca Junior et al., 2019).

2.5. The use of DES and its application in the pharmaceutical industry

A system can be defined either as continuous or discrete and this affects how to approach the problem. Continuous systems can often be approached with analytical methods and find a theoretical solution to the problem through a continuous simulation (Banks et al., 2015). There are also DES where variable changes occur at a discrete set of *Points* in time (Banks et al., 2015; Shoaib & Ramamohan, 2022). Since time is continuous in reality, a DES simulation makes an assumption and divides time into integer values. These values or *Points* are then analysed numerically, evaluating all changes from the previous value. Thus, DES often require the aid of computers to *Run* rather than *Solve* the scenario to find the best suited solution to a problem (Banks et al., 2015). Because of this, DES has been applied in many areas and has been proven to analyse performance indicators for instance queue statistics, inventory, utilisation of resources, and efficiency (Thenarasu et al., 2022).

There are different approaches to simulation (Shannon, 1975; Gordon, 1978; Law, 2007; Banks et al., 2015; Hering et al., 2021). Banks et al. (2015) has studied several authors and their research in order to conclude a twelve-step process for performing a DES project.

1. A *Problem Formulation* should be the start of every study. Often the problem is described by the customer, and in that case, there is a need for the analyst to completely understand the described issue and that the customer and the analyst share the same view of what the issue is (Banks et al., 2015).
2. *Creating a project plan and setting objectives,* so that the simulation answers the questions asked by the problem formulation. The project plan should include topics such as the cost of the study and how many people are going to be involved. Also included should be the number of days required for each phase to be completed (Banks et al., 2015).
3. Create a *Conceptual model* that states basic assumptions and characterises the system. The final model does not need to visually represent the model, only the essential results need to represent reality (Pritsker & Alan, 1998).
4. *Data collection* is a constant process in building a model, as the model grow so does the amount of data that needs to be put into the model (Shannon, 1975). The nature of the study will to a great extent dictate what kind of data that is going to be collected, and the selection of data needs to be thoughtfully picked out. This is a large part of building a simulation and should be begun as early as possible Henderson (2003).
5. In some situations, there needs to be a *Model translation* where the model can require to coding to function properly. However, if this step is possible to avoid with a specialised simulation software the development time is greatly reduced (Banks et al., 2015).

6. *Verification* needs to be tested several times in the simulation model to test if the model behaves as it should. This can be a difficult process in more complex models (Sargent, 2010).

7. Is the model *Validated* enough or does it require further calibration of the settings? This process is repeated until the results are sufficient for the purpose (Sargent, 2010).

8. The alternative scenarios need to be determined in an *Experimental design*. All system designs that are to be investigated need to be analysed and decide things such as number of runs, length of test period, length of initialisation period, and if there are other aspects to consider (Sanchez, 2020).

9. *Production runs and analysis* needs to be done to measure the performances (Banks et al., 2015).

10. Given the results from the nineth step *More runs* could be required (Banks et al., 2015).

11. *Documenting and reporting* are vital. Program documentation is important if the simulation is to be used again by another or the same user. The simulation would then be necessary to understand so that it could be operated again. This builds confidence in the program, but it could also be useful in a situation where the model is to be changed in the future. The final results of the analysis should be reported clearly and consistently in a report for decisionmakers to review (Musselman, 1998).

12. *Implementation* is the final step for a project and to be successful in the final step do heavily rely on how well the previous steps have been executed. It also relies on how involved the model user has been throughout the model development, where an involved model user will thoroughly understand the model and its intended benefits and thus the chance of a successful implementation drastically increases (Banks et al., 2015).

Compared to other industries where digital technologies have been adapted, there is a significantly slower pace in the pharmaceutical industry (Spindler, 2021). This can be a result of the strict regulations applied on the industry or as a consequence of the otherwise atypical nature of the pharmaceutical manufacturing process (Kaylani & Atieh, 2016; Spindler, 2021). Simulating different scenarios with DES, changing certain parameters, and comparing the outputs gives an opportunity for diverse testing without risk and thus DES is well suited for the pharmaceutical industry (Hering et al., 2021).

3. METHODOLOGY

In the following section, the study's choice of method during the work process will be presented. Initially, the study's research approach is presented, whereupon the selection of company, literature review, empirical data collection and the process of building the simulation model is described. The methodology section ends with an analysis implementation, types of errors in the simulation model and a reflection on the study's research quality.

3.1. Research approach

This study has been compared to a deductive research approach, which Bryman and Bell (2017) refer to existing theories. Erlam (2003) supports the explanation given by Bryman and Bell (2017) about a deductive research approach and adds that a deductive research approach ends up in something more specified. This study has been based on general science about production planning- and scheduling and simulation, where the outcomes resulted in several conclusions that were crucial to be able to answer the study's aim and research questions. This study was also based on a quantitative research approach, which Bryman and Bell (2017) describe as a research approach used in the collection of numerical data. This study was based on numerical data used for the simulation model. A quantitative research approach was chosen because the aim of this study was to investigate the optimisation of production planning- and scheduling in a pharmaceutical facility using DES, something is easier to achieve with a quantitative research approach. Eldabi et al. (2002) and Connelly (2004) state that studies using DES as a tool are generally known to use a quantitative research approach.

3.2. Selection of company

AstraZeneca is a globally innovation driven pharmaceutical- and biotechnic company with a focus on research, development, and provision of prescription medicines (AstraZeneca, 2022a). In terms of manufacturing, AstraZeneca is responsible for the entire process from chemical manufacturing, design and packaging to marketing, sales, and transportation (AstraZeneca, 2022). AstraZeneca works in an environment that is high-tech and Lean-oriented, where the focus is constantly on developing and identifying innovative solutions (AstraZeneca, 2022). The production facility in Södertälje is conductive and produces 40% of the company's medicines. AstraZeneca in Södertälje consists of 4,800 employees, of whom 700 work in production with 30 different drugs (AstraZeneca, 2022b). AstraZeneca was chosen as the company for this study as they have shown an interest in optimising production planning- and scheduling due to the large and complex product mix that is often difficult to handle in the pharmaceutical industry. Previous research indicates NP-hard problems need another solution that can handle the large complexity of the product mix (Mönch & Zimmermann, 2011; Kaylani & Atieh, 2016. Kaylani and Atieh (2016) further state that as the production complexity along with the product mix increases the algorithms loose accuracy in their optimisation (Kaylani & Atieh, 2016). Hence, DES was considered as an essential tool to conduct this study and thus optimise production planning- and scheduling at the production site. DES was chosen as previous research indicates that the tool has shown a good capability of handling NP-hard problems by testing all possible

scenarios and recommending the one where the desired outcomes are met (Triguero de Sousa Junior et al., 2019). By performing a more intensive and circumstantial analysis of the company, the DES tool will therefore be able to handle the large and complex product mixes and simplify production planning- and scheduling by having the opportunity to test different scenarios in the model.

3.3. Literature review

The literature review treats two main areas, namely production planning- and scheduling in a pharmaceutical industry and simulation including DES application in the pharmaceutical industry. The collected literature describes challenges within the industry together with the specific requirements and regulations placed on the pharmaceutical industry. Furthermore, the collected literature also describes why production planning- and scheduling has a major role in daily operations and how DES can be applied to thus optimise production planning- and scheduling. For the study to give a good understanding of the problem area, a literature review was initiated. The literature of the study was collected from books and scientific publications which included journals and published conference proceedings found through the databases at the library of Mälardalen University. The databases that were used to find relevant literature in the field were Scopus and IEEE Xplore combined with the search engines Google Scholar and Primo. This literary review was thus based on secondary data, which according to Bryman and Bell (2017) intends that the collected literature has been collected by others. The keywords that have been helpful when searching through databases to find relevant literature were "DES", "DES in a pharmaceutical production", "Pharmaceutical industry", "Pharmaceutical simulation study", "Production planning", "Production planning- and schedule optimisation", "Product mix" and "Resource allocation". As an initial test only the abstract and conclusion of the literature were read and if they were deemed suitable for the study a more thorough reading was needed.

3.4. Empirical data collection

To best explain the studied situation the collection of empirical data was gathered as primary data directly from the company, which according to Bryman and Bell (2017) intends that the collected empirical data is gathered by the researchers themselves. The data was collected through unstructured observations at the production site, frequent meetings with the head of production along with operators and production planners, and through the company's database called Discoverant.

During the four occasions that unstructured observations were performed at the production site the focus was on the flow of products and creating a picture of the situation that was true to reality. Bryman and Bell (2017) explain that unstructured observations are aimed at recording as much detail as possible with aim to develop a narrative for the situation that is being observed. For the study to represent the production in a simulation model there was a great need for details regarding how the products were processed, what steps were needed and in what order, what products have priority rules and what specified sequencing needed to be considered among the products. Parallel to the unstructured observations and along the entire process of the study there

was weekly meetings set up with the production to fill in the blanks of what was missed during the observations. These meetings were held with various line managers together with production planners and the head of production at the site. These meetings acted both as a source of information and also a form of validation throughout the process.

Through the database Discoverant production data that was relevant for the simulation could be collected. With aid from a process engineer expert at the company, the study could extract the relevant data and then process it in Microsoft Excel. After excluding the outliers and other faulty measurements from the collected data, the study could extract the following valuable data points: Maximum, Minimum, Average, Median, First- and Third Quartile.

3.5. Building the simulation model

The simulation model was built in ExtendSim10 since this was already in use at the studied company. ExtendSim10 is well suited for the situation as it is an established tool for conducting process simulations (Strickland, 2012). The approach used in this study was heavily influenced by the twelve steps provided by Banks et al. (2015) with some inspiration from Hering et al. (2021), see Table 1 and Figure 1.

Steps	Description
1. **Problem formulation**	*The study was defined and clear goals for the simulation were set up. This discussion was held with the supervisor together with the head of production at the site.*
2. **Creating a project plan**	*A Gantt Chart was created where larger checkpoints were included and described in detail.*
3. **Conceptual model**	*Inputs, assumptions, basic functionality, and goals were represented in a conceptual model for guidance throughout the study.*
4. **Data collection**	*By collecting data with Discoverant and organising it in Microsoft Excel the study could extract a Median, First- and Third Quartile of the production times that was used in the simulation model. This step was executed along with the process engineer expert at the company.*
5. **Building the model**	*Reoccurring meetings with the production team were scheduled once a week for continuous explanation and iteration of the progress. Through these checkpoints the simulation model grew forth over a few months. As a further support this step was*

	performed with help of the supervisor from the company.
6. Verification of the model	*Verification of data occurred through several test runs, along with an analysis of the simulation model logic, processing times and scheduling together with the supervisor from the company.*
7. Validation of the model	*Validation of the simulation model occurred by the supervisor together with the head of production from the company. Validation has been present to some degree in most steps of building the simulation model.*
8. Production run and analysis	*Test runs were made and analysed for further validation and comparison.*
9. Implementation as an analysis tool	*The simulation model could be used to analyse production runs and predict future improvements in the production set up.*
10. Implementation as a scheduling tool	*The simulation model could be used as a tool to find an optimised production schedule.*

Table 1 Action plan for the simulation (Source: Own construction)
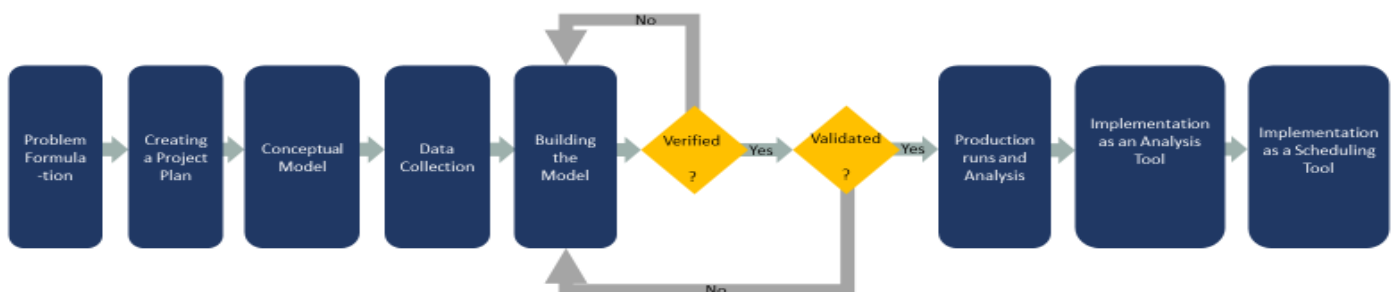
Figure 1 Simulation Process Flow (Source: Own construction)

At first there was a need for understanding the study and a solution to this was to divide the problems into chunks. Firstly, a simple process flow was created that showed how items moved through the processes. Secondly, a rudimentary VSM was created with an online software service called Miro board. The data was extracted from the company's own database using Discoverant, and the data was then processed in Microsoft Excel. The model was built on a Windows-based laptop with 8 GB RAM and a 64-bit processor using ExtendSim. The building of the simulation

model consisted of capturing the production process in a software program by connecting premade components, through drag and drop, in the simulation program based on the components functions and attributes. To get a reliable and valid representation of the production the supervisor from the company was regularly approached for feedback. The output of the simulation was analysed and judged based on production statistics collected from Discoverant, as well as the validation from the head of production.

3.6. Analysis implementation

The analysis was based on the results from the simulation runs. Each simulation scenario was aimed to explore different aspects of the production hence they were not all analysed in the same way and each scenario had specific demands for their reliability. The scenarios were run between several times depending on the expectations on the result. For example, the first scenario was run more times than scenario 3, since scenario 1 was more reliant on a statistical average that later could be used as a validation for the simulation. The simulation exported every scenario into a Microsoft Excel sheet after each run where the data was organised in tables, averages and totals were used to study the results. The most studied areas were the queues and the resources, since these areas could give a lot of information about how the production performed (see section 2.3). Queues that grew indicated a bottleneck and low utilisation of operators could indicate an ineffective use of the resources.

3.7. Types of errors

This study had to consider some potential errors that could occur and thus jeopardise the validity of the results. The errors have been categorised into the following categories: syntax errors, sematic errors, definition errors, and logic errors. Most simulation software has been built in checks that eliminate the first two error types, however in some situations these errors can still come up when running the simulations. Some errors are more difficult to detect, such as logical errors that will not be discovered until the simulation model goes through output analysis. Definition errors can also be difficult to detect until an output analysis is performed. Definition errors can be caused by incorrect inputs such as production times or average queue lengths (Woodward and Mackulak, 1997). The simulation model in this study has shown to be prone towards some logical errors. When the simulation is stress tested with several weeks of production planning that includes more than one shift of products, an error is likely to occur in one of the production lines. This occurs since one of the production lines had complicated sanitation rules combined with several different products. On the other hand, this was solved by duplicating the line and ensuring that only one of the duplicates was used at once. A result of this was that one of the sanitation solutions in the model was not reliable to the same level as the other two production lines when switching from one product type to another.

3.8. Research quality

The two parameters that this study has been evaluate are reliability and validity, which according to Bryman and Bell (2017) are prevalent parameters to measure in quantitative research. Since the simulation model required a reliable result, the study collected primary data from three

different sources: unstructured observations, frequent meetings and through the company's database Discoverant. According to Bryman and Bell (2017), the reliability of the study is strengthened when data collection and analysis takes place from different sources. In this case, the reliability of the study is strengthened by having the simulation model mimic the behaviour of the actual production in terms of design and data in order to obtain a reliable result. The reliability in the study was strengthened even further through continuously examination of the simulation model together with the supervisor and the head of production from the company. On the other hand, if the study was to be repeated there is a risk that some logical decisions could be made different because of the free nature of process simulation. Some solutions may be built in a different manner but if the logical assumptions are correct the outcome should however be the same result as the simulation model built for this study. There is also a risk that the simulation model may give some measurement errors because of missing data at some areas in the production. These areas had to be estimated by the operators. However, all measurements are treated the same thus all comparative measurements and calculations should be trustworthy.

Since the validity of the simulation model was of interest for all actors in the study there is no sign of any biases and thus the face validity could be considered high. The face validity is referring to whether a test measures what is to be measured (Bryman & Bell, 2017). All production data was collected over a long period in order to avoid any abnormal conditions that could otherwise affect the result of the study, and since all data was collected from previous productions it could then be tested against future production. This test would according to Bryman and Bell (2017) strengthen the predictive validity of the simulation model. Furthermore, the study's theoretical framework was mostly based on scientific publications. The validity of the theoretical framework was thus considered high, as the scientific publications were peer reviewed. The validity of the theoretical framework has been further strengthened as peer review has been performed by both course members and supervisor from MDU. This is something that is confirmed by Bryman and Bell (2017) who states that the possibility of strengthening the study's validity increases by using objective information and customary theory.

4. SIMULATION MODEL

This section will firstly present an explanation of the production environment where the study has taken place. After this the simulation model will be presented followed by the different scenarios that have been explored.

4.1. The production environment

The studied production produces medicines in tablet form in a production environment based on a cell layout. Three different APIs divided into 20 different variations are being processed by three production flows consisting of two or four steps depending on the medicine being produced. Each medicine and production step includes specific sanitation and production regulations including sequencing of products, campaign lengths, production times and lead times. In total there are 22 main processes and three preparatory processes that are included in the study where three are supporting activities, six granulation activities, two blending activities, ten compression activities, and four coating activities, see Figure 2 and Table 2. The three production flows are in this study called Medicine A, Medicine B and Medicine C and do not share any operators amongst each other in the current system.
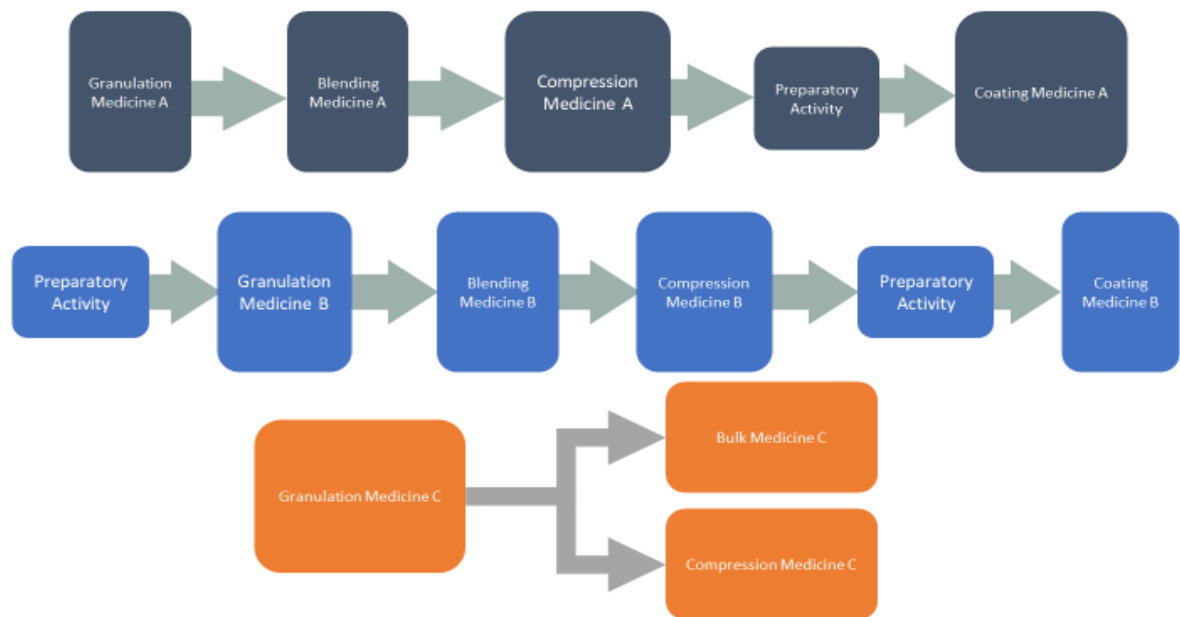
Figure 2 Schematic view of the production (Source: Own construction)

Process step	Granulation	Blending	Compression	Coating
Medicine A	2	1	4	3
Medicine B	3	1	2	1
Medicine C	1	-	3 or 4	-

Table 2 Number of machines for each process flow (Source: Own construction)

In the production environment there are three types of sanitation measures depending on the intensity of the sanitation. A- B- and C-sanitation, where A-sanitation is the highest level of

sanitation and the longest process. C-sanitation is the lowest level of sanitation measure and the quickest process.

	Medicine A	Medicine B	Medicine C
Granulation	4	6	2
Blending	2	2	-
Compression	3 or 4	2	2
Coating	3	3	-

Table 3 Number of operators in every step (Source: Own construction)

The number of operators required varies for the different steps in the process. The granulation step requires two operators each for the granulating machines and two operators for the blending machine, see Table 3. One operator is required for each compression machine and one operator each for the coating machines where the supporting activity is included.

4.1.1. Flow for Medicine A

The Medicine A flow consists of two separate variations that are being produced, with most of the demand being for the stronger variation. The granulation requires two operators per facility throughout the entire process, and there are four operators stationed in this area to handle two facilities. In this step, there are no regulations on the production sequence between the two variations. However, there are regulations constricting the process to only be operating for 21 days before a major sanitation, A-sanitation, is needed with a duration of 20 hours, see Table 4.

Medicine Type A	A-Sanitation (h)	B-Sanitation (h)	C-Sanitation (h)
Granulation	20	-	-
Blending	6	-	-
Compression	24	7	0.5
Preparatory	2	-	-
Coating	5	0.75	-

Table 4 Sanitation process times Medicine A (Source: Own construction)

After granulation there is a need for a final blending in the next step. The blending step serves under no specific requirements regarding sequence, but similarly to the previous step, there is a constriction so that every 14 days there is a mandatory A-sanitation for 6 hours and there is one single blender in this flow handled by two operators. Following this step is the compression step consisting of four tabletting machines that require one operator each, thus there are four operators stationed in this area. There are three types of sanitation measures depending on the input of products and time in this area. There is an A-sanitation that takes place every 28 days and lasts for 24 hours. If the medicine changes from one batch to another there is a requirement for a larger sanitation which includes changes of punches. This takes 7 hours to perform and is referred to as a B-sanitation. Because of this there is a need to schedule the production and avoid sanitation as much as possible. Lastly, there is a small C-sanitation measure of 0,5 hours that needs to be done after every batch if no changes are made. Finally, the Medicine A flow enters the coating step

which consists of a preparatory activity and three coating machines. The preparatory activity restricts by an A-sanitation with a duration of 2 hours every 26 hours. The three coating machines are on the other hand restricted by A- and B-sanitations. An A-sanitation takes place every 4 days and occupies 5 hours. The B-sanitation takes place every time there is a change of product and entails 0,75 hours of cleaning.

4.1.2. Flow for Medicine B

The Medicine B flow is very similar to the Medicine A flow. There are two variations of the medicine, and the more potent one is the more demanded product. Firstly, in this production flow there is a mandatory preparation step operated by one operator and every 7 days there is a mandatory A-sanitation with a 7-hour process time, see Table 5.

Medicine Type B	A-Sanitation (h)	B-Sanitation (h)	C-Sanitation (h)
Preparatory	7	-	-
Granulation	20	-	-
Blending	6	-	-
Compression	24	7	0.5
Preparatory	2	-	-
Coating	5	0.75	-

Table 5 Sanitation process times Medicine B (Source: Own construction)

After this follows the granulation step with three facilities to handle the products and two operators are required to run each facility. The preparatory step and the granulation step share the same operators, and thus this could become a restriction in the process. Thirdly there is a final blending step where the three granulation facilities need to share one blending facility which requires two operators. In the blending there is a requirement for sanitation every 14 days that takes 6 hours to perform. The following step is the compression step that consist of two facilities and two operators required per facility. The compression of Medicine B is restricted by three kinds of sanitation measures. The A-sanitation has a duration of 24 hours and is required every 28 days. The B-Sanitation is required when there is a shift in variation of the medicine from weak to strong variation, or the other way around. A B-sanitation is 7 hours long, and between every batch there is a shorter C-sanitation with a duration of 0,5 hours. Before the coating there is a need to prepare the solution. Also, once every 24 hours there is a need for a sanitation measure of 2 hours. Finally, the coating step is restricted by one A-sanitation every 4 days that has a duration of 5 hours, and a B-sanitation that is required when changing the recipe where this action is 0,75 hours long. The process is operated by one person and when this step is finalised the medicine can be sent to the lab for a final approval of the batch.

4.1.3. Flow for Medicine C

The Medicine C flow differs more from the other two production flows and includes its own set of constrictions. In the Medicine C flow there are two main types, one with only one API and one with two APIs combined, referred to as the Medicine C1 and the Medicine C2. These are also produced in different size tablets, which will affect the production flow. Medicine C1 has

five variations whilst Medicine C2 has seven different variations, both products are also produced in Bulk, with two variations each all of which affects the production flow. The flow itself exists of two activities. Firstly, there is the granulation step, where one machine handles the entire flow of products and is operated by two operators. The granulation step has no restrictions that affect the sequence however, the process is often adapted to the restrictions of the following compression step. The granulation is restricted by an A-sanitation that occurs every 10 days and occupies 14 hours of time, see Table 6.

Medicine Type C	A-Sanitation (h)	B-Sanitation (h)	C-Sanitation (h)
Granulation	14	-	-
Compression	14	4	1 or 1,5
Bulk	14	-	-

Table 6 Sanitation process times Medicine C (Source: Own construction)

The following step, and the last step in the production flow is the compression. In this cell there are three compression machines and one Bulk blender. The Bulk material is shipped in a powder form, and thus not compressed. This activity requires two operators and has a C/T of 2,5 hours. The other three machines have a compression element and because of this they run slower. These activities require two operators to start the activity and after this one operator can monitor the process alone. The compression machines have complex sanitation regulations that to a high degree affect the production. When handling the Medicine C1 type there is an A-sanitation and a B-sanitation. The A-sanitation is required when the colouring of the tablet is changed, which is between all but two tablets, and this A-sanitation has a duration of 14 hours. Between the two strongest variants there is a requirement for a B-sanitation, this is preferred to the A-sanitation since the process is shorter. A B-sanitation takes 4 hours to perform. If the same medicine is run in sequence, there is a required C-sanitation between each batch with a duration of 1 hour. For the Medicine C2 API there is another set of rules, and they include an A- and a C-sanitation. The seven variants are separated by variations, colouring and size. The ones with the least colour are required to go first in any production sequence. If the same medicine is run in sequence a C-sanitation is required with a duration of 1,5 hours, but if the medicine changes there is a need for an A-sanitation which has a duration of 14 hours. The Bulk process is restricted by an A-sanitation with a duration of 14 hours. This is required whenever the API is changed but can otherwise shift freely between the variations of the tablets.

4.2. Conceptual model

To design the simulation model, a conceptual model was initially constructed, see Figure 3. The conceptual model contains information about the simulation's model inputs, model outputs, model contents and assumptions.
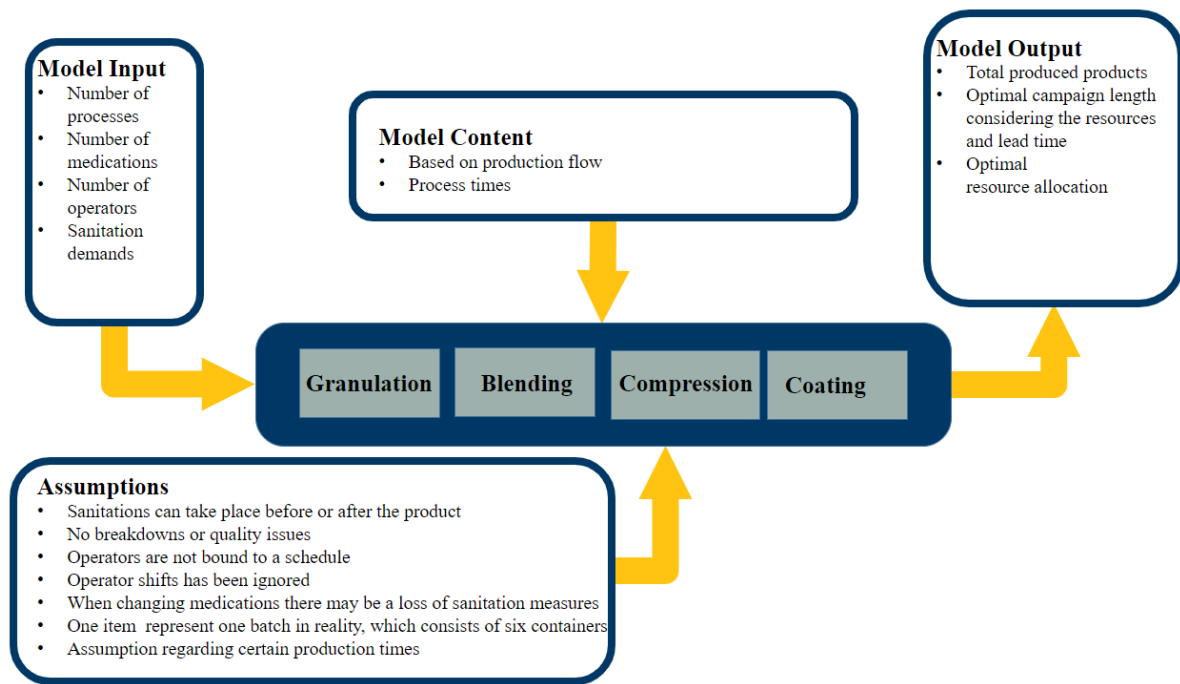
Figure 3 Conceptual model (Source: Own construction)

The inputs that have been considered to design the simulation model are number of processes, number of medicines, number of operators and sanitation demands. The outputs formulated in the conceptual model are total produced products, optimal campaign length considering the resources and lead time and the optimal resource allocation. The model contents that have been formulated in the conceptual model are that the simulation model is based on a production flow and based on process times. The assumptions that have been formulated in the conceptual model are:

- Sanitations can take place before or after a product
- No breakdowns or quality issues have been considered
- The operators are not bound to a schedule
- Operator shifts have been ignored
- When changing medicines, there may be a loss of sanitation measures
- One item in the simulation model represents one batch in reality, which consists of six containers.
- Assumptions regarding certain production times

In addition to these assumptions, certain production times for several machines could not be produced through Discoverant, which resulted in the production having to make an assumption regarding these production times.

4.3. Simulation model

The simulation model for this study has sought to represent reality and not recreate reality. In the simulation model there are three different APIs that are divided into 20 different variations of

medicines. In the simulation model, these 20 different variations of medicines are treated by three different production flows consisting of two or four process steps, depending on which API it concerns. In the simulation model, specific production- and sanitation regulations including sequencing of products, campaign lengths, production times and lead times have been included. In the simulation model there are 28 activities included, where three activities represent supporting activities, six activities represent granulation, two activities represent blending, 13 activities represent tablet compression, and four activities represent coating, see Appendix 1. The compression activities for the third API are in the simulation model three more in comparison to reality as the medicine variations differ with special production- and sanitation regulations. This was done as it has simplified the representation of reality in the simulation model. The activities for manufacturing in granulation, compression and coating have been doubled in the simulation model as production times differ depending on which variation of medicine is to be produced. The three production flows in the simulation model are Medicine A, Medicine B and Medicine C. Regarding sanitation measures, three different types of sanitation measures have been designed in the simulation model. As mentioned, these sanitation measures differ in intensity and are called A-, B-, and C-sanitation. It is important to consider also in the simulation that all three APIs require different time for A-, B-, and C-sanitation.

The process in the simulation model starts with a "create block", see Appendix 2 for specific blocks, where all information about the 20 different medicine variations is determined. The information in the "create block" creates a production schedule where several attributes are created to thus assign certain information. The attributes created in the "create block" are called *Create Time, Item priority, C/T, Medicine C type* (the blurred heading in Figure 4)*, and Medicine type*.

Figure 4 Information in the Create block (Source: Own construction)

The *Create Time* attribute sets a duration for when the item is to be introduced to the system. The medicine variations have also been assigned a priority through the *Item priority* attribute in

the "create block". This gives the possibility to decide in what order the medicine are handled in certain production steps, where those with the highest priority throughout the simulation always go first in the queue and those with the lowest priority always go last in the queue. An attribute for the sanitations has also been assigned as *C/T*, this attribute is needed to induce a sanitation if required. The attribute *Medicine C type* contains information about where the different medicine variations of the third API should be assigned in the process flow of Medicine C. The *Medicine type* attribute decides which medicine variation is to be produced. This *Medicine type* is used in the "select item out block" that detects what item is supposed to be processed in what production flow. The Medicine A variants are assigned the first output, the Medicine B variants are assigned the second output and the Medicine C variants are assigned the last output. Most of the activities are built in the same fashion, and most of the solutions are used several times throughout the simulation model.

4.3.1. Flow for Medicine A

Medicine A flow consists of two different variations of medicine that are manufactured. See Figure 5 for a detailed flow of the production for Medicine A.
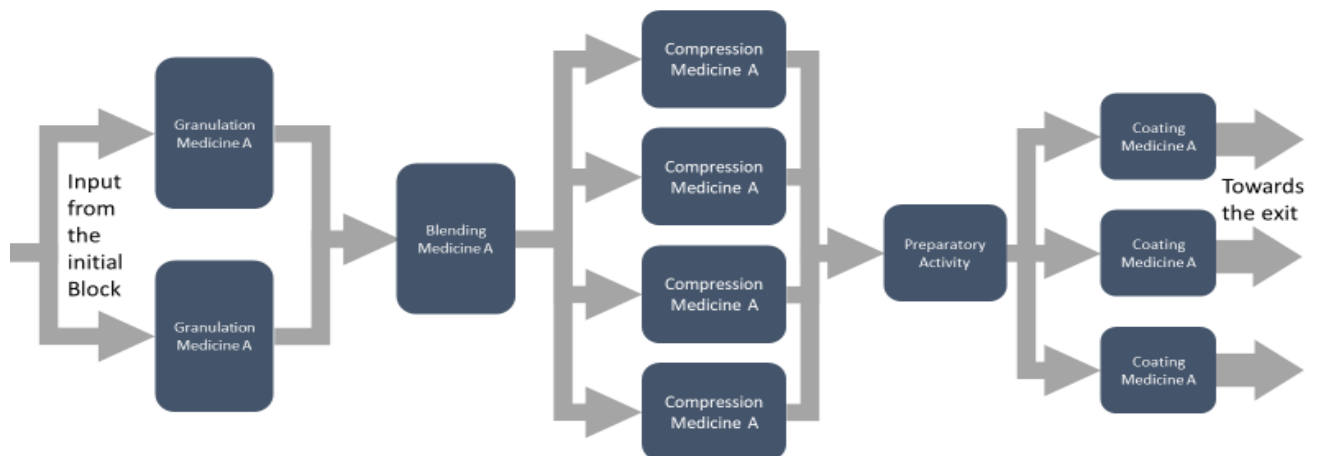
Figure 5 Detailed flow of Medicine A (Source: Own construction)

The granulation flow starts with a "gate block" that enables control for campaign lengths, see Figure 6. The two different variations are then evenly distributed between the two granulation machines via a "select item out block". In the granulation step for Medicine A, only A-sanitation takes place. In the next step in the simulation model, there is a "gate block" that halts the process

Figure 6 Granulation flow for Medicine A in the simulation (Source: Own construction)

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after 21 days for 20 hours to perform an A-sanitation. Then there is a restriction placed via a "gate block" that only allows one item in the process at a time. Two operators are then collected from a "resource pool queue block" that is connected to the "resource pool block". The number of operators required can be determined through the "resource pool block" and the "resource pool queue block". Depending on which variation of Medicine A is to be produced, it is distributed in a "select item out block", where it then proceeds to one of two "activity blocks" corresponding to what variant is being produced. For one medicine variation of Medicine A, the process time is a minimum of 9,75 hours, a maximum of 10,99 hours but the most likely process time is 10,37 hours. For the second variation of Medicine A, the process time is at least 13,99 hours, maximum 16,81 hours but the most likely process time is 15,36 hours. When the activity is completed, the set number of operators is returned to the "resource pool block" through a "resource pool release block". The granulation step has two identical facility's that handle the same process. The produced granulate is then collected in a common queue before the next step.

In the blending step, see Figure 7, there is first a "gate block" that enable control of campaign lengths. In this step, only an A-sanitation is performed here through a "gate block", but in the blending step it takes place after 14 days for 6 hours. Even here, it is important to consider that only one item enter the process at a time, which is controlled through a "gate block". After this step, two operators are picked up from a "resource pool block" to a queue that is set on "resource pool queue" which then starts the granulate in the blending activity. As previously mentioned, it is possible to change the number of operators required through the "resource pool block" and the "resource pool queue block". The blending process takes 3 hours and when the activity is complete, the number of set operators is returned to the "resource pool block" through a "resource pool release block".

Figure 7 Blending flow for Medicine A in the simulation (Source: Own construction)

The next step in the process involves tablet compression, see Figure 8. First there is the same control solution for campaign lengths. Thereafter, the variation of the medicine is evenly distributed on four different outputs through a "select item out block". In the compression stage, an A-sanitation also takes place here through a "gate block" every 28 days for 24 hours. Only one item goes through the process at a time after this step, which is managed with a "gate block".

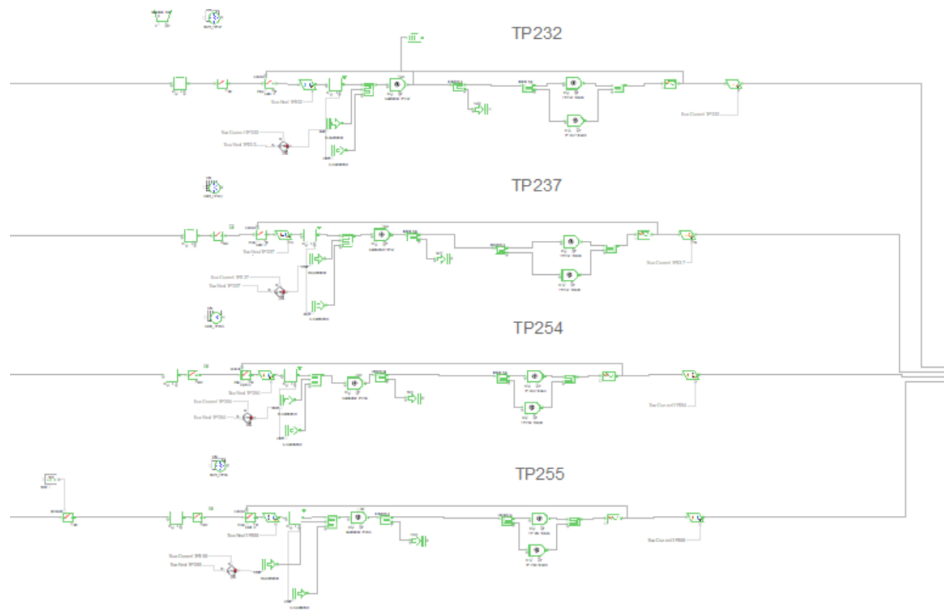*Figure 8 Compression flow for Medicine A in the simulation (Source: Own construction)*

After this step, an operator is picked up from a "resource pool block" to a queue set on "resource pool queue". The number of operators required can be changed through the "resource pool block" and the "resource pool queue block". If required, either a B- or C-sanitation are triggered from a "create block". If a change is detected by two "get blocks" that are set to detect the attribute *Medicine type* and a "decision block" that compares the two. If the item in the process is not the same as the item that is following, a B-sanitation is sent. A C-sanitation is sent every time a new item arrives. It is important to consider in this step that the time for a B-sanitation has been shortened, as a C-sanitation is deducted each time a B-sanitation is performed. In the simulation, a B-sanitation takes 6,5 hours while a C-sanitation takes 0,5 hours. A sanitation item is then sent to a "select item in block" that is set to "priority" and send a sanitation first. The sanitation is then sent to an "activity block" that is set to *C/T* and performs a sanitation for a certain time depending on which sanitation is required. Then, the items are sorted with a "select item out block" that detects if the item is a sanitation item or a real product. The real products carry on through the top output whilst the sanitations are sent downwards an "exit block" and then eliminated. To solve the issues of different production times, the items are sorted so that stronger variants are processed in one activity and weaker variants in another via a "select item out block". For one medicine variation of Medicine A, the process time is at least 23,24 hours, maximum 31,85 hours but most likely it takes 25,28 hours to compress the medicines. For the second medicine variant of Medicine A, the process time is at least 22,69 hours, maximum 46,84 hours but most likely it takes 26,01 hours to compress the tablets. After the compression activity is complete, the number of set operators is returned to the "resource pool block" through a "resource pool release block". All the compressed medicines are then collected in a common queue before the next step. The compression step has four identical facility's that handle the same process. However, the fourth facility is togglable between available and not available. This is done with a gate block and is necessary for one of the scenarios being performed by this study.

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In the last step of the Medicine A flow the coating takes place, see Figure 9. Before the coating activity itself, there is a supporting activity for coating that is performed. First there is the solution to enable campaign lengths for the following step. This step requires an A-sanitation through a "gate block" that is performed after 26 hours for 2 hours. The flow is restricted through a "gate block" so that only one item at a time enters the area.
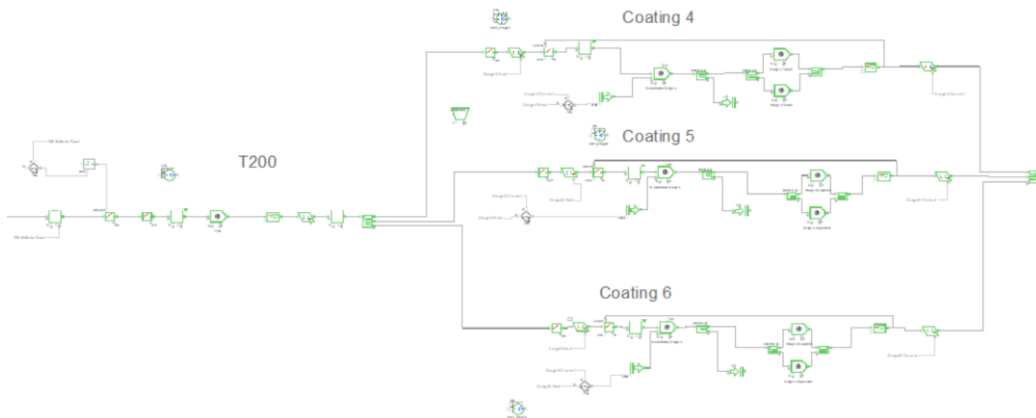

Figure 9 Preparatory- and Coating flow for Medicine A in the simulation (Source: Own construction)

After this step, an operator is picked up from a "resource pool block" to a queue that is set to "resource pool queue" for the supporting activity to continue. The supporting activity takes 2 hours and then the number of set operators is returned to the "resource pool block" through a "resource pool release block". Before the actual coating begins, what is produced is evenly distributed over three different outputs through a "select item out block". In the coating step there is an A-sanitation that is triggered with a "gate block" that opens after 4 days for 5 hours. There is a restriction on the process so that not more than one item is processed at a time with a "gate block". An operator is then picked up through a "resource pool block" to a queue set on "resource pool queue". Further in the coating step, a B-sanitation also takes place through a "create block" if required. To find out when a B-sanitation is to take place, the item that is already in the process is measured with the item that is to be received. The measurement takes place through two "get blocks" that are set to the attribute *Medicine type* and a "decision block" that determines whether the item that is in the process is not the same as the item that is to enter the process. If the item that is already in the process is not the same as the item that is to be in the process, a B-sanitation is sent. The sanitation is then sent to an "activity block" that is set to *C/T* and performs the sanitation for 0,67 hours. The "create block" that is connected to the B-sanitation is set to "priority" and sends a sanitation first in the queue if required. In the next step, items in a "select item out block" are distributed with two outputs, where one output receives the two variations of Medicine A and the other receives the sanitation that has been performed, which then goes on to an "exit block". To solve the issues of different production times, the items are sorted so that stronger variants are processed in one activity and weaker variants in another via a "select item out block". For one medicine variation of Medicine A, the process time is at least 7,08 hours, maximum 8,35 hours but most likely the coating takes 7,51 hours. However, for the second medicine variation of Medicine A it takes at least 8,14 hours, maximum 9,09 hours but most likely the coating here takes 8,71 hours. After the coating activity is complete, the number of set

operators is returned to the "resource pool block" through a "resource pool release block". After this step, the produced Medicine A medicines proceed to an "exit block". The coating step for Medicine A has three identical facility's that handle the same process.

4.3.2. Flow for Medicine B

The Medicine B flow also consists of two different variations of medicine that are produced. See Figure 10 for a detailed flow of the production for Medicine B.
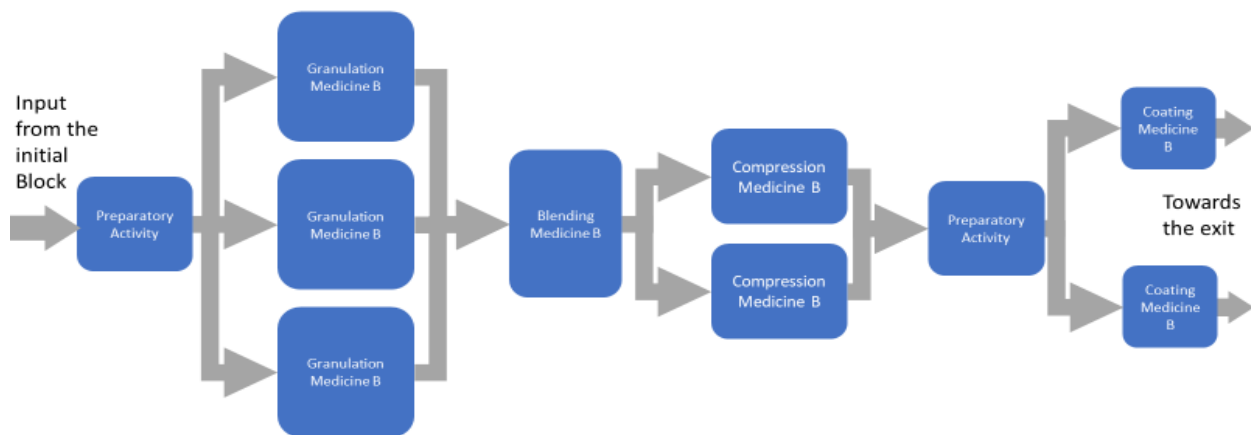
Figure 10 Detailed flow of Medicine B (Source: Own construction)

The flow in the simulation starts with several blocks that together enable control for campaign lengths, see Figure 11. In the next step, an A-sanitation is operated with a "gate block" that shuts down the flow every 7 days for 4 hours. Even here, it is important to consider that only one item enters the process at a time after this step, this is controlled with a "gate block". An operator is then collected from a "resource pool block" with "resource pool queue". However, the number of operators required can be changed in the settings of the blocks. This step refers to a supporting activity that takes 4 hours to manufacture and takes place before the granulation for Medicine B.

Figure 11 Preparatory- and Granulation flow for Medicine B in the simulation (Source: Own construction)

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The set number of operators is then returned to the "resource pool block" through a "resource pool release block".
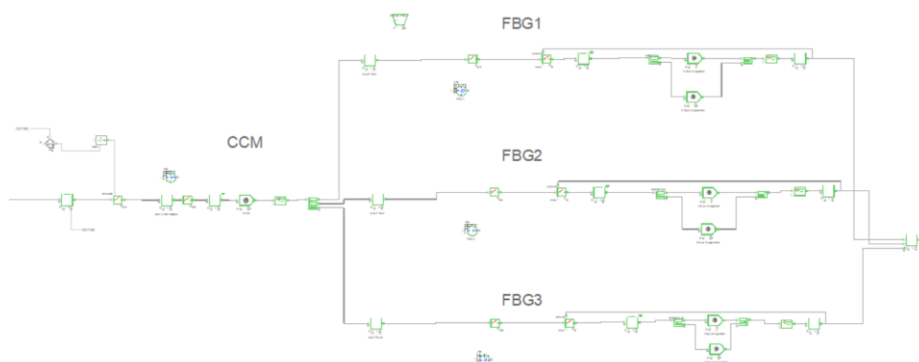
What has been produced is then evenly distributed over three outputs. In the granulation for Medicine B there is just an A-sanitation to consider that takes place after 7 days and lasts for 8 hours. The flow is controlled so that only one item is processed at a time through a "gate block". After this step, two operators are picked up from a "resource pool block" with a "resource pool queue". Depending on which variation of Medicine B is to be manufactured, this is distributed in a "select item out block". To solve the issues of different production times, the items are sorted so that stronger variants are processed in one activity and weaker variants in another via a "select item out block". For one medicine variation of Medicine B, the process time is a minimum of 14,44 hours, a maximum of 15,52 hours but the most likely process time is 14,8 hours. For the second variation of the medicine, the process time is at least 16,37 hours, maximum 17,35 hours but the most likely process time is 16,7 hours. When the activity is complete, the number of set operators is returned to the "resource pool block" thorough a "resource pool release block". The produced granulate are then collected in a common queue before the next step, the blending step.

In the blending step, the same solution for campaign length is used, see Figure 12. In the blending step, only an A-sanitation is performed with a "gate block" that takes place every 14 days for 6 hours. Only one item can enter the process at a time after this step, controlled with a "gate block". After this step, two operators are picked up from a "resource pool block" with a "resource pool queue" which then starts the granulate in the blending activity. The blending process takes 3 hours and when the activity is complete, the number of set operators is returned to the "resource pool block" through a "resource pool release block".
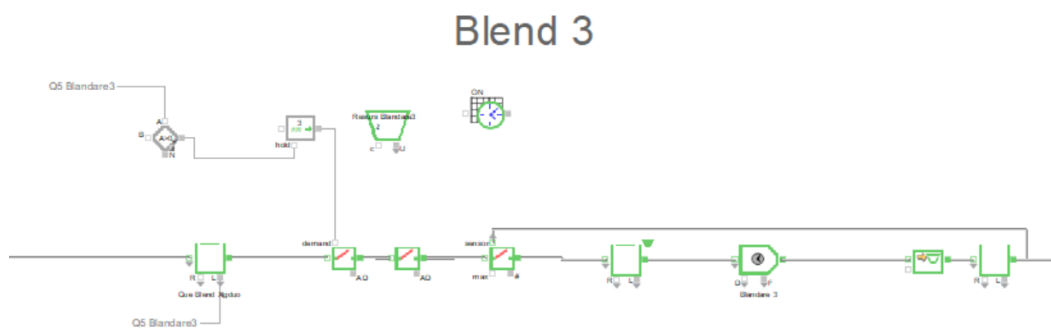
Figure 12 Blending flow for Medicine B in the simulation (Source: Own construction)

The next step in the process is tablet compression, see Figure 13. In this step, the process starts with blocks that together enable control of campaign lengths. The variations of the medicines are evenly distributed on two different outputs through a "select item out block". In the compression step, an A-sanitation takes place here through a "gate block" every 28 days for 24 hours. Only one item goes through the process at a time controlled by a "gate block".

Figure 13 Compression flow for Medicine B in the simulation (Source: Own construction)

After this step, an operator is picked up from a "resource pool block" with a "resource pool queue". If required, either a B-, or C-sanitation is triggered through a "create block". To find out when a B-sanitation is to take place, a measurement is done with two "get blocks" that are set to read the attribute *Medicine type* and a "decision block" that determines whether the item that is in the process is not the same as the item that is to enter the process. If the item that is already in the process is not the same as the item that is to be in the process, a B-sanitation is sent. A C-sanitation is sent every time a new item arrives and thus the time for B-sanitation has been shortened, as a C-sanitation is deducted each time a B-sanitation is performed. In the simulation, a B-sanitation takes 6,5 hours while a C-sanitation takes 0,5 hours. The sanitation is then sent to an "activity block" that is set to *C/T* and performs a sanitation for a certain time depending on which sanitation is required. In the next step, items in a "select item out block" are distributed with two outputs, where one output receives the two variations of Medicine B and the other receives the sanitation that has been performed, which then goes on to an "exit block". To solve the issues of different production times, the items are sorted so that stronger variants are processed in one activity and weaker variants in another via a "select item out block". For one medicine variation of Medicine B, the processing time is at least 8,92 hours, maximum 11,5 hours but most likely it takes 9,78 to compress the tablets. On the other hand, for the other medicine, the variation of Medicine B takes at least 9,25 hours, maximum 11,02 hours but most likely it takes 10,12 hours to compress the tablets. After the compression activity is complete, the set number of operators is returned to the "r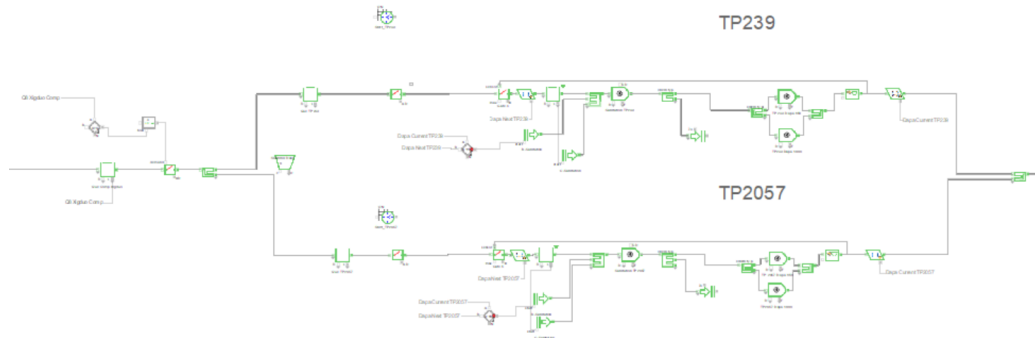esource pool block" through a "resource pool release block". All the compressed tablets are then collected in a common queue before the next step. The compression step has two identical facility's that handle the same process.

In the last step of the Medicine B flow, coating takes place. Before the coating activity itself, there is a supporting activity for coating that is performed, see Figure 14. This step also starts with several blocks that together form a function to enable control of campaign lengths. Furthermore, this step requires an A-sanitation through a "gate block" that is performed after 26 hours for 2 hours. Only one item enters the process at a time after this step, through a "gate block".
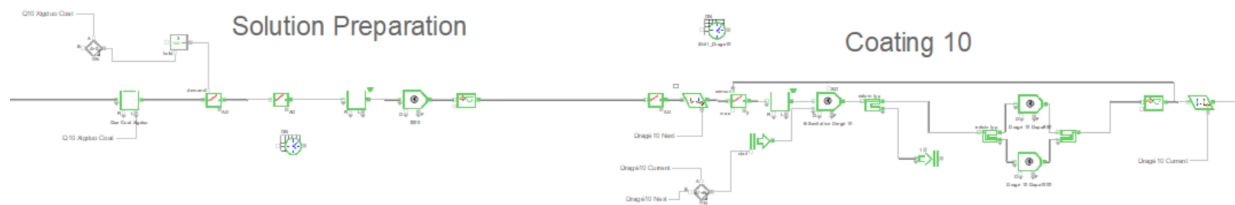
Figure 14 Preparatory- and Coating flow for Medicine B in the simulation (Source: Own construction)

After this step, an operator is picked up from a "resource pool block" with a "resource pool queue". The supporting activity takes 2 hours and then the number of set operators is returned to the "resource pool block". The items are evenly distributed on two different outputs through a "select item out block". Further in the coating step an A-sanitation also takes place through a "gate block" after 4 days for 5 hours. Only one item corresponding to a batch proceeds in the process at a time after this step. An operator is then picked up through a "resource pool block" to a queue set on "resource pool queue". Further in the coating step, a B-sanitation also takes place through a "create block" if required. To find out when a B-sanitation is to take place, the item that is already in the process is compared to the item that is to be received. If the item that is in the process is not the same as the item entering the process, a B-sanitation is triggered. The sanitation is then sent to an "activity block" that is set to *C/T* and performs the sanitation for 0,67 hours. The items are then sorted in a "select item out block" where the sanitations are sent to an "exit block" and the medicines are sent further in the flow. To solve the issues of different production times, the items are sorted so that stronger variants are processed in one activity and weaker variants in another via a "select item out block". For one medicine variation of Medicine B, it takes at least 2,62 hours to process, maximum 6,73 hours but most likely the coating takes 4,16 hours. However, for the second medicine variation of Medicine B it takes at least 2,66 hours, maximum 7,48 hours but most likely the coating for the second medicine variations takes 4,32 hours. After the coating activity is complete, the number of set operators is returned to the "resource pool block" through a "resource pool release block". After this step, the produced Medicine B tablets proceed to an "exit block".

4.3.3. Flow for Medicine C

The Medicine C flow in the simulation is more complex than the Medicine A and Medicine B flows are because Medicine C consists of several variations of medicines, namely 16 different variations. See Figure 15 for the production flow.
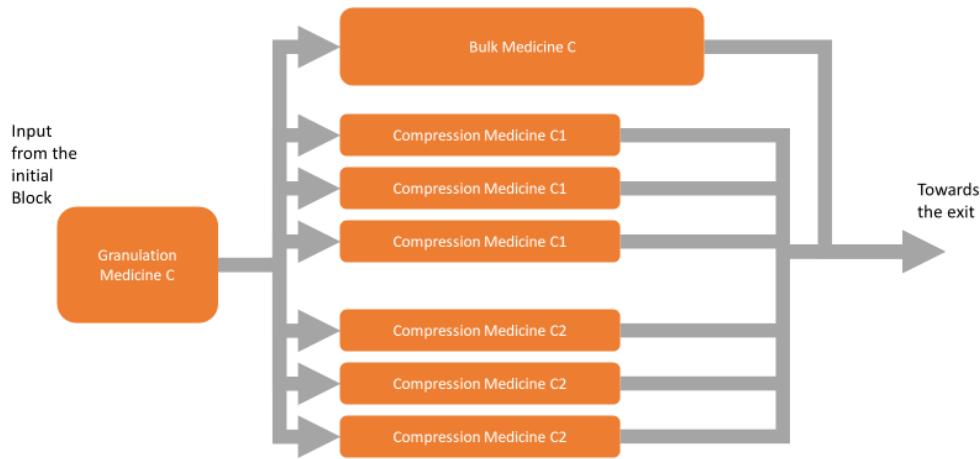
Figure 15 Detailed flow of Medicine C (Source: Own construction)

The flow in the simulation starts with a function to enable control for campaign lengths. The different variations are then divided into a "select item out block" consisting of two outputs depending on which *Medicine C type* it refers to. The different variations of Medicine C in the simulation divided into two different types of Medicine C, Medicine C1 and Medicine C2, see figure 16. Medicine C1 consists of one API and Medicine C2 has two combined APIs. Medicine C1 consists of five different variations while Medicine C2 consists of seven different variations.
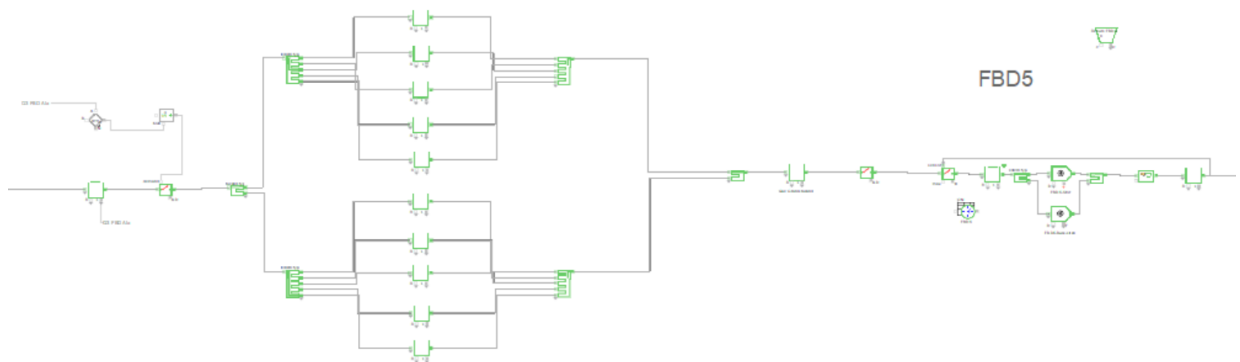
Figure 16 Granulation flow of Medicine C in the simulation (Source: Own construction)

Both Medicine C1 and Medicine C2 are also combined in a Bulk consisting of four different variations, two variations from Medicine C1 and two variations from Medicine C2. Furthermore, these variations are divided into another "select item out block" where Medicine C1 and Medicine C2 are divided into five different outputs each, depending on the type of variation it refers to. In the granulation step for Medicine C, see Figure 16, an A-sanitation takes place through a "gate block" that opens after 10 days for 14 hours. One item enters the process at a time after this step. Two operators are then picked up from a "resource pool block" to a queue set on "resource pool queue". Depending on which variation of Medicine C is to be granulated, this is distributed in a "select item out block", where it then proceeds to one of two "activity blocks" where one "activity block" receives Medicine C1 and Medicine C2 and the other

"activity block" receives the Bulk. The granulation for Medicine C1 and Medicine C2 takes a minimum of 8,96 hours, a maximum of 9,91 hours, but most likely it takes 9,45 hours to granulate. The activity for the Bulk only takes 3 hours to manufacture. After the granulation activity is completed, the number of set operators is returned to "the resource pool block". The produced granulate are then collected in a common queue before the next step.

The next step in the process concerns the compression- and the Bulk step, see Figure 17. These steps in the process begins with several blocks that together form a function to enable control of campaign lengths. In the next step, the different medicine variations are sorted in a "select item out block" where Medicine C1 and Medicine C2 go to one output and the Bulk goes to the other output. The Bulk is only granulated and blended and therefore the "select item out block" sorts out the Bulk from the compression step. In the Bulk step only one item enters the process at a time after this step, through a "gate block".
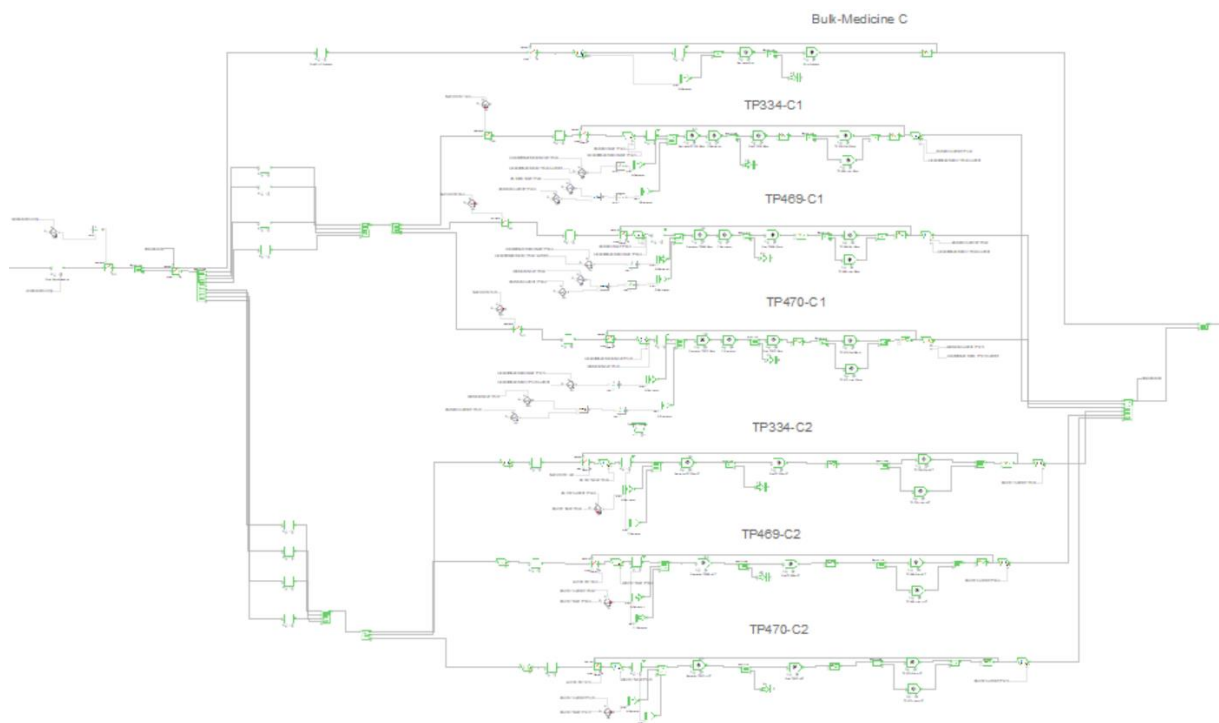
Figure 17 Bulk- and Compression flow for Medicine C in the simulation (Source: Own construction)

In the next step an A-sanitation is sent if required through a "create block". To find out when an A-sanitation is to take place, the item is measured through a "get block" that are set to the attribute *Medicine C type* and measures change through a "delta connector". If a change has taken place regarding the *Medicine C type*, a signal is sent to the "create block", which sends an A-sanitation. The sanitation is then sent to an "activity block" that is set to *C/T* and performs the sanitation for 14 hours. The "create block" that are connected to the A-sanitation are set to "priority" and send a sanitation first in the queue if required. Two operators are then picked up from a "resource pool block" to a queue set on "resource pool queue". Items are then sorted through a "select item out block" that send the medicines through the top output and the sanitation items are sent to an "exit block". The different Medicine C variations is then processed in an "activity block" for 2,5 hours.

After the Bulk activity is complete, the number of set operators is returned to the "resource pool block" through a "resource pool release block". After this step, the produced items proceed to an "exit block". At the same time as the Bulk is sorted out from the compression step through the "select item out block", Medicine C1 and Medicine C2 are further sorted into the compression step through the same "select item out block". For the simulation to handle the complexity regarding the sanitation regulations, the decision to double the production facilities was made. Since the regulations differ between the two variations of Medicine C, the simulation model chose to split the two into separate production lines and guaranteeing that no more than three activities are active at the same time. The simulation model could in this way guarantee that all sanitation rules where upheld without compromising the validity of the production times. The sanitation rules in this area for Medicine C variant are including an A-, B-, and a C-sanitation. The A-sanitation has a duration of 14 hours, the B-sanitation a duration of 4 hours and the C-sanitation 1 hour. An A-sanitation is triggered by rules appended in the products, if these are fulfilled a sanitation item will interrupt the production. B-sanitation is triggered between certain products if they are sent in sequence, this is preferred since the sanitation time is shorter. The C-sanitation is placed within the production activity and is going to occur every time a product enters the system. C-sanitation is an action that comes to affect when neither A-, nor B-sanitation is triggered. Because of this the duration of a C-sanitation has been subtracted from A- and B-sanitations and this leads to a correct total sanitation time. The Medicine C2 variation does not include a B-sanitation, only the A-sanitation and the C-sanitation. This in the simulation model has been solved by sending a C-sanitation for every product and subtracting that time from the A-sanitation that only triggers when certain rules are upheld. The sanitation times for the Medicine C2 variation is equal to the Medicine C1 sanitations, 14 hours and 1 hour for the A- and the C-sanitations respectively. After the compression step the product lines are merged and all products are sent to the "exit block".

4.4. Scenarios

This study has conducted four scenarios to answer the research questions. The scenarios are run over eight weeks, where a four-week schedule containing 125 items each is repeated twice. These scenarios are created in cooperation with the head of production to target different areas of the simulation model and showcase where the system is sub-optimal and can be improved. The different scenarios were partly created to both answer questions asked by the head of production and to answer the research questions formulated in this study (see Figure 18).

Scenario 1			
	W1	W2	W3	W4
---	---	---	---	---
Medicine A				
Medicine A	8	7	8	7
Medicine B				
Medicine B	18	18	18	18
Medicine C			1	
Medicine C				
Medicine C	1			
Medicine C	3			2
Medicine C				2
Medicine C				
Medicine C				
Medicine C		2		
Medicine C				
Medicine C		2		
Medicine C				
Medicine C				
Medicine C Bulk			6	
Medicine C Bulk				
Medicine C Bulk				
Medicine C Bulk		5		

Figure 18 Standard Production Schedule (Source: Own construction)

4.4.1. Scenario 1

The first scenario was created along with the head of production and is a real production schedule that will be used to compare the other scenarios. This scenario is investigating the current situation and what areas of production that today act as bottlenecks as well as investigating the value of one extra compression machine. In the compression step for Medicine A, there are either three- or four machines, depending on whether the completed compression machine is tested in the simulation. This is tested to thus determine which alternative creates the most efficient flow in terms of output and utilisation rate in the form of activities and operators.

4.4.2. Scenario 2

The second scenario is a stress test where the production schedule is doubled, whilst the extra compression machine is available. When twice the items are produced over the same time period, the aim is to investigate what activities act as bottlenecks. All-other settings are going to be identical to scenario 1. If any of the queues grow longer in this scenario, it will indicate a bottleneck.

4.4.3. Scenario 3

The third scenario is trying to create large inventories between each step. This is done in order to find the optimal campaign length in each activity, and it is done with the same standard production schedule. This test is also including the extra compression machine in the testing. The different scenarios are going to be compared internally as well as to scenario 1 to find correlations between performances in the system. The different campaign lengths that are going to be introduced are the length of 1, 2, 3, 4, 6 and 8 items, since these are deemed realistic campaign lengths to examine by the head of production. The simulation is going to test all combinations of campaign lengths, for example a campaign length of 2 can be introduced in one machine whilst

a length of 6 is introduced to another. This is going to be explored by the simulation programme and the results will be analysed.

4.4.4. Scenario 4

The fourth scenario is designed to test the allocation of operators between different production steps. This scenario is going to run three tests in the simulation where the operators are allocated in different combinations. The first test is combining the operators in the granulation step for Medicine A and Medicine C and combining all operators in the blending- and compression step for Medicine A, Medicine B and Medicine C, see Table 3 for number of operators that are combined. The second test is combining all operators in the granulation step for Medicine A, Medicine B and Medicine C and combining all operators in the blending- and compression step for Medicine A, Medicine B and Medicine C. Lastly, the third test is an original sharing of operators, but the blending operators can move freely between all activities. In the fourth scenario the extra compression machine is available. Resource allocation is also included in the preparatory activities that take place before the main activities. These three tests have chosen to be performed as these are the most realistic resource divisions that can be performed in the actual production at present. This test is intended to test which of these three is considered to be the most optimal resource allocation in terms of increased efficiency.

5. SIMULATION RESULTS

In this section the simulation results from every scenario are analysed according to the analysis implementation (see chapter 3.6), and the results are firstly presented separately and then comparatively to each other in the discussion section.

5.1. Scenario 1

The first scenario gave an output of 250 items, which means that all the medicines have been manufactured, see Table 7. In scenario 1 the Medicine B flow shows the highest utilisation in terms of activities, resources, and inventory in the granulation-, compression- and coating steps. However, the supporting activity for the granulation flow and the blending step of Medicine B does not have as high utilisation as the rest of the flow. The extra compression machine added to the simulation model showed lower utilisation in terms of activities, resources, and inventory in the compression step for the flow of Medicine B. The area with most waiting times is the Bulk. This Bulk activity has a utilisation of 4%, and at most the products wait in the queue for 78,4 hours. The average wait time of all queues was 4,19 hours with the extra compression machine and 4,4 hours without.

Input	250
Output	250
Average Wait	4,19h
Average Resource Utilisation	36 %

Table 7 Selection of results from Scenario 1 (Source: Own construction)

5.2. Scenario 2

The second scenario gave an average of 360 items produced, out of 500 items that entered the system, see Table 8. In this scenario the Medicine B flow achieves the highest utilisation out of the three. There is however an increase in the utilisation rate of the Medicine A specific resources, with an average increase of 35 percentiles compared to 13 percentiles in the Medicine B and 18 percentiles for Medicine C. The compressing activities from the Medicine A flow experience an increase of utilisation by an average of 35 percentiles whilst the Medicine B compression increased by 8 percentiles and 13 percentiles for Medicine C. In the queues there was an increase, because of the increased products that entered the system. From the second scenario it is possible to see a large strain on the queues placed before the Bulk activity, and queues placed before the granulation in all Medicine flows.

Input	500
Output (Average)	360
Average Wait	15,67h
Average Resource Utilisation	56 %

Table 8 Selection of results from Scenario 2 (Source: Own construction)

5.3. Scenario 3

This scenario did not yield a valid result. Due to the way the scenario was built in the simulation model this scenario did not test the campaign length as intended as there was a logical error in this situation. Instead, it created unwanted stocks that hindered the flow of products and slowed the production. The results from this scenario will thus be ignored.

5.4. Scenario 4

The first test combined the operators in the granulation step for Medicine A and Medicine C and combined all operators in the blending- and compression step for Medicine A, Medicine B and Medicine C. This resulted in an output of 250 items produced, meaning that all the medicines have been manufactured, see Table 9. In this test the Medicine B flow achieved the highest utilisation rate in terms of activities, resources, and inventory in the granulation-, compression- and coating steps. On the other hand, there was no difference regarding the utilisation of the supporting activity and the blending activity for the Medicine B flow between scenario 1 and test 1 in scenario 4. The average wait time in this scenario is 2,79 hours for the queues and the longest wait times where experienced in the granulation step for Medicine B with an average over the three granulation processes of 69,8 hours at most.

Input	250
Output	250
Average wait	2,79h

Table 9 Selection of results Scenario 4 Test 1 (Source: Own construction)

The second test combined all operators in the granulation step for Medicine A, Medicine B and Medicine C and combined all operators in the blending- and compression step for Medicine A, Medicine B and Medicine C. This resulted in an output of 250 items produced, meaning that all the medicines have been manufactured, see Table 10. Also, in this test the Medicine B flow achieved the highest utilisation rate in terms of activities, resources, and inventory in the granulation-, compression- and coating steps. On the other hand, there was no difference regarding the utilisation of the supporting activity and the blending activity in the Medicine B flow between scenario 1 and test 2 in scenario 4. The average wait time in this scenario was shorter than the previous test with an average of 2,61 hours. The longest wait times where experienced in the granulation step for Medicine A with 70 hours, whilst the Medicine B is second with an average of 60 hours in the granulation step.

Input	250
Output	250
Average wait	2,61h

Table 10 Selection of results Scenario 4 Test 2 (Source: Own construction)

The third and the last test were an original sharing of operators, but the blending operators were able to move freely between all activities. This resulted in an output of between 17 and 24 produced products out of 250 products, see Table 11. The granulation step for Medicine A and

the granulation step including the supporting activity for Medicine B had the highest degree of utilisation in terms of the activities. In contrast, the utilisation rate for the remaining activities from Medicine B decreased by approximately 50% compared to scenario 1, while the utilisation rate for the activities in the granulation step for Medicine A was almost unchanged compared to the result in scenario 1. In terms of the utilisation rate of the resources, it turns out that the blending operators were used the most during this test, with a utilisation rate of approximately 75%. The average wait in this test was 3,5 hours with a maximum wait time of 71,3 hours in the granulation step of the Medicine B flow.

Input	250
Output	17-24
Average wait	3,5h

Table 11 Selection of results Scenario 4 Test 3 (Source: Own construction)

6. ANALYSIS AND DISCUSSION

In this section, the literature has been linked to the results from the simulation for further discussion.

6.1. Scenario 1

From the first scenario it is clear that the production has the capacity to produce the number of products that is expected from it, since all 250 products that enter the system also exit the system every time the simulation is run. When examining the data further it indicates that the preparatory activity before the granulation step for Medicine B is not utilised to its full capacity. However, since all products are processed there is no need for it to improve either in the current set up. This does indicate that the flexibility that Kaylani and Atieh (2016) inquire for is present in this production, and there is potential to cover for other facilities in the process if they lack the flexibility. The extra compression machine made a difference in the production times however, with an average wait time in all queues between the activities of 0,21 hours faster if it was used which further strengthens the flexibility in the production and freeing of resources that is sought after by many (Engell & Harjunkoski, 2012; Moniz et al., 2015; Kaylani & Atieh, 2016). The Bulk activity in the Medicine C flow is experiencing longer queues compared to the other activities. This could be an area for improvements since there is nothing hindering the production except the availability of operators. The efficient utilisation of resources is mentioned as a key aspect when increasing the efficiency of a production and the utilisation in this area should thus be examined to see if it is possible to raise the utilisation level (Wattitham et al., 2015; Kaylani & Atieh, 2016). The result from scenario 1 is reasonable and corresponds to the expected outcomes of the actual production. This indicates that the iterative process of validating the model in every step has resulted in a valid model.

6.2. Scenario 2

The second scenario did not produce all items that were sent into the system, and this is exactly what was expected from the test. Simulation can be used to identify bottlenecks (Thenarasu et al., 2022) by showing the areas that underperform. The area that turned out to be the most visible bottleneck was the granulation step in the Medicine B flow. This was shown by a growing stock between the preparatory activity and the granulation, from the theory of constraints it is possible to identify this as a bottleneck (Naor et al., 2012; Şimşit et al., 2014; Thenarasu et al., 2022). In the Medicine A flow 68 products were entered and 60 excited the flow. All eight products that stopped in the flow were hindered by the first step, granulation. This indicates that granulation is the bottleneck in this flow, since all other processes could handle what came out of that process (Naor et al., 2012; Şimşit et al., 2014). From the Medicine C flow a pattern is starting to appear, the granulation process is the bottleneck and there are four items that do not get processed in this area. It can also be worth observing that the queue before the Bulk activity has an average waiting time of 33 hours and a maximum of 76 hours, this could thus be an area where improvements can be made if the flexibility was higher amongst the operators.

6.3. Scenario 4

As for scenario 4, test 1 and test 2 have received the same number of products, which means that everything has been manufactured. However, test 2 has a lower average wait time for the queues of 18 minutes. This indicates that test 2 is in this case more optimal. Medicine B received a wait time of 60 hours in the granulation step for test 2, which corresponds to a difference of ten hours comparing to test 1. This indicates that test 2 also in this case is more optimal. To further compare test 2 that showed the best results together with scenario 1 where the extra compression machine is included, scenario 1 also has manufactured all products. Furthermore, scenario 1 showed a higher average wait time than test 2, which represents a difference of 1,58 hours. Without the extra compression machine scenario 1 resulted in an average wait time of 4,4 hours which is also a higher average wait time than test 2. This indicates that test 2 still are better than the other results. The third test in scenario 4 had an output of between 17 and 24 produced products out of 250 products, which is a major difference from the other results. However, test 3 had a lower average wait time than scenario 1 with a difference of 0,69 hours and 0,9 hours, respectively, depending on whether the compression machine is included.

The results indicates that test 2 is still more optimal than scenario 1 and test 1 and 3 as everything has been manufactured at the same time as it has increased the resource efficiency. Furthermore, test 2 is considered to be most optimal as there is a very low average wait time on the queues in comparison with scenario 1 and test 1 and 3. This goes in line with what Wattitham et al. (2015) and Kaylani and Atieh (2016) state who claim that to efficiently meet customer demand and sales order, improved and developed production planning and utilisation of resources is therefore necessary (Wattitham et al., 2015; Kaylani & Atieh, 2016). In this case, test 2 has a developed production planning by improving utilisation of resources and reduce inventory handling as well as everything has been manufactured. This can thus increase efficiency in the form of meeting customer demand and sales orders. Furthermore, Kaylani and Atieh (2016) claim that the demand problem and the coercion to minimise costs are forcing operations to operate more efficiently, hence advanced production planning- and scheduling activities are required (Kaylani & Atieh, 2016). This further proves that test 2 is in this case most optimal in order to streamline the flow in the production. Advanced production planning by, for example, allocating resources in a more efficient way and reduce inventory use is required to thus meet customer demand and reduce costs. Ghousi et al. (2012) claim that demand forecasting has an impact on several practical operations within an organisation including resource allocation for instance. This indicates that demand forecasting is important to consider in production in order to achieve a positive impact regarding, among other things, the allocation of operators in production.

Box et al. (2015) states that modelling simplifies a system synthesis, involvement, and verification and this study has provided a possibility to involve and create an overview of the entire production flow. It has created the possibility to answer several *What if* scenarios and has answered some as well, which was one of the arguments for the benefits of a simulation study presented by Banks (2015) and Triguero de Souca Junior et al. (2019). As Banks et al. (2015) proposed, this simulation has been able to investigate some future situations that are not included in the current system and drawn conclusions from this. Because of the simulation there is also a

possibility to test different production schedules and through this evaluate what schedules are better than others. The weight of an efficient production schedule was lifted by Moniz et al. (2015) in order to lower costs and create a more efficient production. The simulation has thus approached the issues of an NP-hard problem (Mönch & Zimmermann, 2011; Kaylani & Atieh, 2016) and eased the scheduling process by creating possibilities for evaluation of production schedules despite of the large product mixes and strict regulations that were presented by Mönch and Zimmermann (2011) and Kaylani and Atieh (2016).

7. CONCLUSIONS

The aim of this study was to investigate the optimisation of production planning- and scheduling in a pharmaceutical facility using DES. The aim of the study has thus been met by answering the research questions. The research questions answered what would happen if more facilities were added and if allocation of operators could affect the results in production. This goes in line with previous research that suggested that many *What if* scenarios can be answered about the real world through a validated simulation model (Banks et al., 2015). Previous research also predicted that bottlenecks could be discovered when performing a simulation model (Thenarasu et al., 2022), which also found to be true in this study. This study has thus strengthened the arguments for DES to be a valuable tool within manufacturing industries.

How can DES be used to achieve flexibility and efficiency in a pharmaceutical facility?

For DES to answer the first research question several scenarios were run and experimented with flexibility and efficiency. The extra compression machine in Medicine A flow would increase the flexibility in the production to some degree but the efficiency would not be affected much. The current set up can handle the production flow without the extra machine and since this is not the bottleneck of the production it is not where the efforts should be made. The real bottlenecks however were found to be the granulation processes for all medicine flows. These activities would require more support than other activities and that could in turn increase the flexibility and efficiency of the production flow. A different allocation of operators in the simulation has generated an increase of efficiency via the increased flexibility provided by the more flexible resources. The best result was when all operators are allocated amongst all six granulation processes share their resources, all operators in the two blending and the nine compression processes share their resources and all operators in the four coating processes share their resources. This turned out to increase the flexibility in the flow, which led to an increase in efficiency as an outcome.

How can DES be used to increase efficiency of the resource allocation in a pharmaceutical facility?

To answer the second research question in the study, the aim was to increase the efficiency of the resource allocation through DES. The simulation showed that combining all operators in the granulation-, blending- and compression- and coating step results in the most increased efficiency. This conclusion is drawn as all products were manufactured as well as the average queue lengths in the simulation were lower in comparison to the other results for scenario 4 as well as scenario 1. Furthermore, this combination will result in that the operators for granulation are learning all the different steps in the granulation step, the operators for blending and compression are learning all the steps for blending and compression and all operators for coating is handling the coating step.

7.1. Suggestion for future research

This simulation project was restricted by computing power. A more sophisticated computer would be able to test more solutions, and to combine solutions in a more efficient way than was possible in this study. It would be interesting to investigate the same or a similar production with more computing power and thus being able to execute all the tests that this study did not have the resources for. Simulation as a tool is very powerful, and there are still many tests to run. For example, a test where campaign lengths are introduced would be very interesting to build correctly as this could generate large gains for the production. It would require some effort but is possible to build that scenario on to the current model. If that is successful it would be interesting to test it together with a different resource allocation, however, the test grows very large very quick and thus the test would be demanding to perform. The same principle applies to a potential test where all items are introduced at random times to the simulation. To analyse the results from that test could give what would be called the optimal production schedule. Unfortunately, the scale of this test would entail the need for a very sophisticated computer to run these tests since the number of scenarios would increase exponentially for every new item introduced to the system. The results however would be very interesting to see.

7.2. Recomendations to the Company

Firstly, the simulation model gave no indication for a need of an extra compression machine in the Medicine A flow. The current situation is well adapted for compressing all products without the extra machine; thus, a recommendation would be to focus the efforts in other areas rather than implementing a new and costly machine. Further recommendation to the company is to improve the granulation activities, these steps are identified as the bottlenecks and thus they need support from the other activities. Further recommendation is to educate all granulation operators to handle all granulation steps and educate all blending and compression operators to handle all blending and compression. This is a recommendation to the company as the result from the simulation model indicated that this would streamline the production flow in terms of manufacture all products, resource allocation and minimised inventory handling. Another recommendation is since the company are to inherit the simulation from this study, they should continue testing other combinations of resource allocations. For example, the batch production of Medicine C show examples of very long waiting times, along with low utilisation of the operators in the production step before. A test where the operators in the Medicine C flow could share responsibilities may solve this issue.

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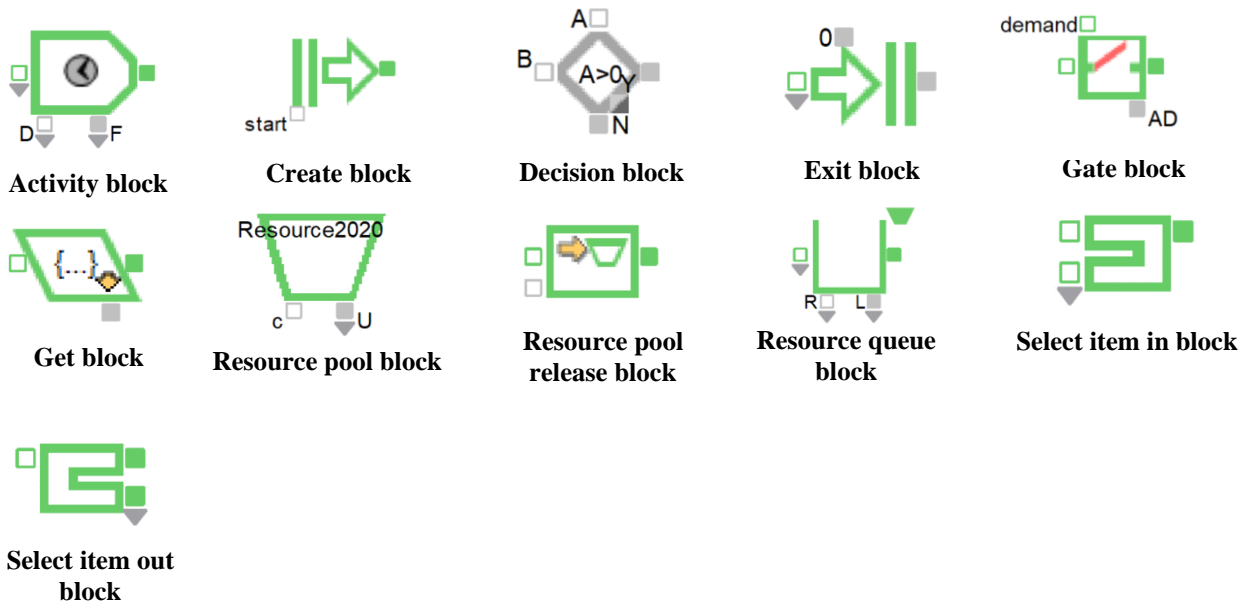
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APPENDICES

Appendix 1: Overview of the simulation model

Appendix 2: Overview of the different simulation blocks described in the study

Activity block	**Create block**	**Decision block**	**Exit block**	**Gate block**
Get block	**Resource pool block**	**Resource pool release block**	**Resource queue block**	**Select item in block**
Select item out block				

Appendix 3: Results Scenario 1

The results from scenario 1 is removed due to secrecy from AstraZeneca.

Appendix 4: Results Scenario 2

The results from scenario 2 is removed due to secrecy from AstraZeneca.

Appendix 5: Results Scenario 3

The results from scenario 3 is removed due to secrecy from AstraZeneca.

Appendix 6: Results Scenario 4

The results from scenario 4 is removed due to secrecy from AstraZeneca.