



Getting in control of workload

Analysing and redesigning a production planning and control system of a Make-to-Order general flow-shop for potential improvements, guided by simulation

Master Thesis

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Master of Science in Business Administration
Course Operational Excellence at Rotterdam School of Management (RSM), Erasmus University



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Preface

Hereby, I present the final report of my study Business Administration. I could not have finished this thesis without the support of some people that I would like to thank.

First of all, I would like to thank my coach Dr. Roelof Kuik and co-reader Prof. Dr. Fabian Sting for their support, supervision, suggestions and comments, throughout this research. Especially the friendly and inspiring meetings with Roelof were of big help to give direction to the thesis.

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Gratefulness goes to the company BaseClear in Leiden and in particular to Bas Reichert and Erna Barél for giving me the opportunity to study again and to perform this research within the company. I want to thank my colleagues at BaseClear for their help, support and interest. I hope that the outcome of this research will contribute to a further growth of the company.

Finally, special thanks to my family and friends for their support and sympathy throughout the last two exciting years. I am glad there is more time for you guys again.

Leiden, October 2017

Jan Peter Heutink

Abstract

Production planning and control is of great importance for the competitive position of companies and is about managing the flow of materials and goods as well as capacity utilization. An important problem area of production planning and control systems concerns the scheduling and capacity planning decisions. Recently Small-Medium-Businesses face several challenges with their production scheduling. Increased complexity in production layouts and product variety can have an impact on manufacturing service performance measures.

One company that must deal with increasing variability in order flow, product variety and complexity in production layouts is BaseClear, a service provider in the field of DNA analysis. BaseClear can be typed as a Small-Medium-Business general flow shop in the MTO industry. BaseClear encounters an unbalanced workload regarding its NGS production department which results in variable Work-In-Process and excessive lead-times. The goal of this thesis is to find possible solutions for this business problem. An answer to the following research question is formulated:

How should BaseClear improve the production planning and control of its NGS department to achieve overall balanced Work-in-Process and reduced lead times?

The operational performance of the production planning and control of the core-business process of BaseClear, Next-Generation-Sequencing (NGS), is analysed and possible improvements for decision-making support based on production planning and control theory proposed to balance Work-In-Process and reduce lead times. After a thorough operational performance analysis structural exceeding lead times and unbalanced Work-In-Process have been determined for the NGS production process. About 10% of all orders have been delivered late in 2016 in comparison to customer agreements and there is variation visible in lead times. Work-In-Process is equally distributed over the NGS production process and waiting time contributes to 67% - 80% of the total lead time on average in 2016.

A general finding for all NGS process flows is that sample arrivals are unequally and randomly distributed over the year. No pattern between increasing sample arrival and exceeding lead times could be determined. Lead times are randomly distributed over the year, but in general the variability in sample arrival has an impact on the stability of the production process performance. In 2016 production scheduling is based on the actual sample arrivals and needed data output per period. These two figures determine the number of process steps that are scheduled and performed each week. No impact of sequencing capacity on lead time and Work-In-Process could be distinguished. The sequencing capacity is not limited and no after-ebony effect on lead time is observed.

After theoretical and empirical research, it can be concluded that there is overlap with the factors found in practice and the dominant factors found in literature on medium term production planning and control level. Poor insight in operational performance corresponds to the need of capacity control measures and possibility of backlog of work in the shop. Limited capacity equipment, personnel and space corresponds to the need for controlled capacity utilization, workforce availability and flexibility. Lack of a standardized ERP with feedback relates to the need for a capacity planning method. A complex production layout with custom services and high variability relates to type of work content and processing time variation. And finally, variable workload with high peaks and poor insight in customer enquiries for medium-term planning, relates to order arrival variability.

After a literature review it has been determined that a balanced order arrival and controlled capacity planning and utilization helps to ensure Work-In-Process balancing and the ability to control and reduce lead times. Total workload must be controlled and should not exceed pre-set maximum limits and a workload input/output control method is needed to manage lead times. It is concluded that

workload control in combination with COBACABANA are suitable production planning and control concepts for the high-variety and variable context like in the case company BaseClear. Lead time allowance can be divided into an allowance for the pre-shop pool waiting time and an allowance for the shop floor throughput time.

Based on empirical research, guided by a simulation study, the effect of a better-balanced order arrival and an increased number of production batches until the sequencing step is evaluated. The following solutions are proposed that can possibly contribute to accomplish the business goal:

- Decrease order arrival variability by realising a constant sample arrival rate.
- Increase production batch scheduling from order registration until the sequencing step.

Based on theoretical research, the proposed solutions can be made effective in practise by:

- Improving the customer enquiry stage (order acceptance/job entry stage) to control the input of work to the job pool.
- Determine optimal and maximum levels of WIP for the job pool and shop floor.
- Implementation of a dynamic visual workload input/output decision capacity control method, like COBACABANA, by introducing a centralised planning board for an overview of the current workload situation in the job pool and the shop floor, can help to control order arrival and to maintain a minimal workload level in the shop. The number of cards should be set equal to 100% of the workload norm and the number of cards in circulation should be controlled.
- Determine optimal release frequencies for the work orders to keep Work-In-Process at the pre-determined level in the shop.
- Introduction of the anticipated new lower level NGS service with longer promised lead times can help to stabilize the workload of the job pool and the shop.
- Introduction of centralized order release control at the job release stage as the main control point can simplify the remaining planning and control process.
- Implementation of a standard production schedule with increased number of batches until the sequencing step.
- Sequencing run scheduling based on capacity utilization and due dates expiration measures for lowest operational costs.

Keywords: Production Planning and Control, Workload Control, COBACABANA, General flow shop, lead time reduction, Work-In-Process balancing, Simulation Modelling

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List of abbreviations

BPS	Business Problem Solving
COBACABANA	Control of BALance by CArD BAsed Navigation
ConWIP	Constant Work-In-Process
CRM	Customer Relationship Management
DBR	Drum-Buffer-Rope
DNA	DesoxyriboNucleic Acid
ERP	Electronic Resource Planning
FTE	Full Time Equivalent
GB	Gigabases
GMP	Good Manufacturing Practises
ISO	International Organization for Standardisation
JIT	Just-In-Time
KPI	Key Performance Indicator
LIMS	Laboratory Information Management System
LT	Lead times
MB	Megabytes
MRP	Material Requirement Planning
MRPII	Manufacturing Resource Planning
MTO	Make-To-Order
MTS	Make-To-Stock
NGS	Next-Generation-Sequencing
OM	Operations Management
POLCA	Paired cell Overlapping Loops of Cards with Authorization
PPC	Production planning and control
QC	Quality Control
RBC	Repeat Business Companies
SMB	Small-Medium-Business
SME	Small-Medium-Enterprise
TOC	Theory of Constraints
VMC	Versatile Manufacturing Companies
WIP	Work-In-Process
WLC	Workload Control
WS	Workstation

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1 INTRODUCTION

1.1 Motivation

Production planning and control (PPC) is of great importance for the competitive position of companies and is about managing the flow of materials and goods as well as capacity utilization (Vollmann, Berry and Whybark, 1988). There is a need for high logistical performance (on-time delivery of services) and high efficiency (low costs) to remain competitive. Lead time (LT) is an important strategic Key Performance Indicator (KPI) and lead time reduction has become an imperative to improve companies operational and financial performance (Azizoglu, Cakmak and Kondakci, 2001; Salmasi, Logendran and Skandari, 2010). Yet, it has been highlighted that a controlled and consistent lead time is even more important than a short but highly variable one (Bozarth and Chapman, 1996). In Make-to-Order (MTO) policies, achieving short and stable lead time is key to for a low and reliable customer order fulfilment time. However, it is difficult to achieve lead time consistency since its components are related to several drivers that vary across products and times. Poor PPC can result in long and unreliable lead times and high levels of Work-In-Process (WIP). Less WIP contributes to a better efficiency of a company. To remain competitive, companies need to improve their performance on a continuous basis. Therefore, companies need effective production planning and control to guarantee highest operational performance.

An important problem area of PPC systems concerns the scheduling and capacity planning decisions. Recently Small-Medium-Businesses (SMB) face several challenges with their production scheduling. Increased complexity in production layouts and product variety can have an impact on manufacturing service performance measures (Soepenbergh, Land and Gaalman, 2012). The Workload Control (WLC) concept was developed to overcome the “lead time syndrome” (Mather & Plossl, 1978). Literature shows that ‘Workload Control’ (WLC) is regarded as the most suitable PPC concept for many companies in the Make-to-Order (MTO) industry (Stevenson et al., 2005). The core of the WLC concept consists of controlled release of customer orders to the shop floor, while maintaining an order pool prior to release to buffer against many uncertainties involved with MTO companies. By keeping the queues of orders on the shop floor at an acceptable level, throughput times are controlled and delivery dates can be met (Kingsman and Hendry, 2002). Many studies of the WLC concept have been performed within job-shopping. However, few empirical studies have been done in general flow-shops. Besides this, further action research into how WLC can be effectively implemented in practice and feeding back empirical findings to simulation-based WLC research to improve the applicability of WLC theory is needed (Thürer, Stevenson and Silva, 2011).

One company that must deal with increasing variability in order flow, product variety and complexity in production layouts is BaseClear, a service provider in the field of DNA analysis. In this thesis the operational performance of the production planning and control of the core-business process of BaseClear, Next-Generation-Sequencing (NGS) will be analysed and possible improvements for decision-making support based on production planning and control theory proposed to balance Work-In-Process (WIP) and reduce lead times. The research contributes to opportunities for a better strategic competitive position of the company.

The first chapter of the thesis is an introduction of the business problem to which this Business Problem Solving (BPS) project applies. In Section 1.2 the context of the case company in which this BPS project is performed will be described. The section thereafter (Section 1.3) discusses the problems encountered in this context, followed by the resulting research objective in Section 1.4 and the research questions with relevance for management practice of this project (Section 1.5) that form the basis of this BPS project. Finally, section 1.6 provides an outline of the content of the thesis.

1.2 Problem context

This section begins with a brief description of the case company BaseClear, discussing the corporate history, its products and departments that are most relevant for this BPS project (Section 1.2.1). After that a more in-depth description of the company's core business, the NGS production process, is given in Section 1.2.2. An introduction to the material flow and order handling as well as the current planning and control system makes part of this section. The aim of this section is to provide a global impression of the case company and its internal processes, forming the basis for further discussion of the company's problem.

1.2.1 Case company description

BaseClear is an independent service provider, founded and owned by Bas Reichert (CEO) and Erna Barél (CFO), and located on the Bio Science Park in Leiden. For all areas in which DNA plays a key role, BaseClear has been offering convenient and high-quality solutions since 1993. The company is specialised in DNA analysis for the Life Science sector with a focus on DNA sequencing. A technique to unravel the genetic code of DNA. The clients are working in the field of biotechnology, food- and pharma industry or research institutes. Since technological developments in the DNA sequencing market are rapid and unpredictable, equipment maintenance and training of employees is very expensive, in many cases it is more cost efficient for customers to outsource their sequencing projects than to buy their own DNA sequencing equipment. Lead time is one of the most important Key Performance Indicators (KPI) within the highly competitive sector and is mainly influenced by workload, available capacity of the analysis equipment, resources and amount of data that needs to be produced for each sample.

BaseClear distinguishes itself by having a highly customer-oriented approach, which means direct communication and a close collaboration with its customers to develop solutions specifically matched to their needs. Customers can rely on a top-level molecular biology lab infrastructure including the latest sequencing technologies offered by Illumina and Pacific Biosciences. The BaseClear team takes care of the full process from customer enquiry to data delivery. BaseClear strive for the highest quality of its services. Therefore, different quality systems have been introduced in the company based on ISO 17025 and Good Manufacturing Practices (GMP).

Over the years BaseClear extended its service package, although all services are still routine DNA tests. A detailed overview of the development of services can be found in appendix A. The core business of BaseClear is now based on Next-Generation sequencing (NGS), a technique to unravel the nucleotide order of DNA samples with use of the latest technology. BaseClear offers complete service packages based on innovative NGS technologies. These technologies make it possible to sequence for instance complete genomes within weeks at a fraction of the costs of conventional sequencing technologies like Sanger. BaseClear offers sequencing services on Illumina platforms (HiSEQ2500 and MiSEQ) as well as the Sequel system from Pacific BioSciences. With these technologies, an unmatched combination of read lengths, data output and short delivery times can be accomplished. These systems have the power and flexibility to enable a wide range of genome-scale applications at the lowest cost.

The organisation of BaseClear consists of about 60 employees and is subdivided into several functional departments of which the most relevant for this research are displayed in this thesis. The Marketing & Sales department is responsible for managing the (key)accounts. They are in direct contact with the customers to settle their enquiries and compose year contracts or specific quotes for standard or custom requests. The Operations department is responsible for the primary production processes and needs to make sure lead times and quality of the work is accomplished as agreed with the customer. Finally, the raw data that is generated is carefully processed and analysed by a specialized bioinformatics team within the Bio-IT department, thus offering a complete analysis solution from wet lab to data interpretation. This department releases the data to the customer. A chart of the company in 2017 can be found in appendix B.

1.2.2 NGS production process

The workflow of the NGS production process is discussed in more detail in this section. The DNA samples are processed in a push driven Make-to-Order (MTO) general flow-shop process which is operated every Monday to Friday. The main objective of all services is to readout the nucleotide order of DNA samples and deliver raw or analysed digital data to the customer. The customer can make a selection out of different services. For each service, unique protocols are used that influence the read length and in general the amount of data that is generated. There are several steps involved in this NGS process. Some steps are performed manually and others automatically by dedicated equipment. BaseClear has several dozens of customers who make use of its NGS services. The first step is a customer enquire phase where a contract or quote is agreed with the customer. After that the customer places the order in a digital web portal of the company. Samples that are used as input are delivered as liquid DNA in small plastic tubes or as raw material that needs to be purified on forehand. The samples are sent together with an order form and quote that describes the service that needs to be performed. Every working day orders are received. Other inputs in the process are specific reagents for the equipment and consumables. Normally, the number of orders in production vary between 30 and 80. Each order can consist of one sample up to multiple plates with 96 samples. After receiving the material, an order is created in the Laboratory Information Management System (LIMS) and each sample is marked with a unique storage code. This registration step is checked by a second employee to avoid any mix-up errors in the downstream process. After registration, the concentration and quality of each sample is determined (sample QC step). This go/no-go step is most important for creating a flow in the process. When the measures meet internal criteria, the samples are prepared for sequencing (sample prep). Here the DNA is fragmentized into smaller pieces and specific DNA tags are added to each sample to be able to identify them in a batch. The quality of the sample prep is checked (library QC step) to make sure it meets the internal criteria for sequencing. After that multiple samples are batched in a sequencing run to make sure the capacity of the sequencing equipment is used at the most. Before the samples are run on a sequencer they are diluted to a proper concentration to meet the amount of data that the customer has ordered. During the sequencing step, the DNA fragments of each sample are read and transformed into digital data. The size of each fragment differs from 50 nucleotides to more than 10k nucleotides per read-out dependent on the protocol and reagents that are used. The total amount of data that is sent to the customer differs from several hundred MB to a couple GB of data per sample. In the final step, the quality of the data is checked and released as raw or analysed data to the customer. A simplified scheme of this process can be found in figure 1.

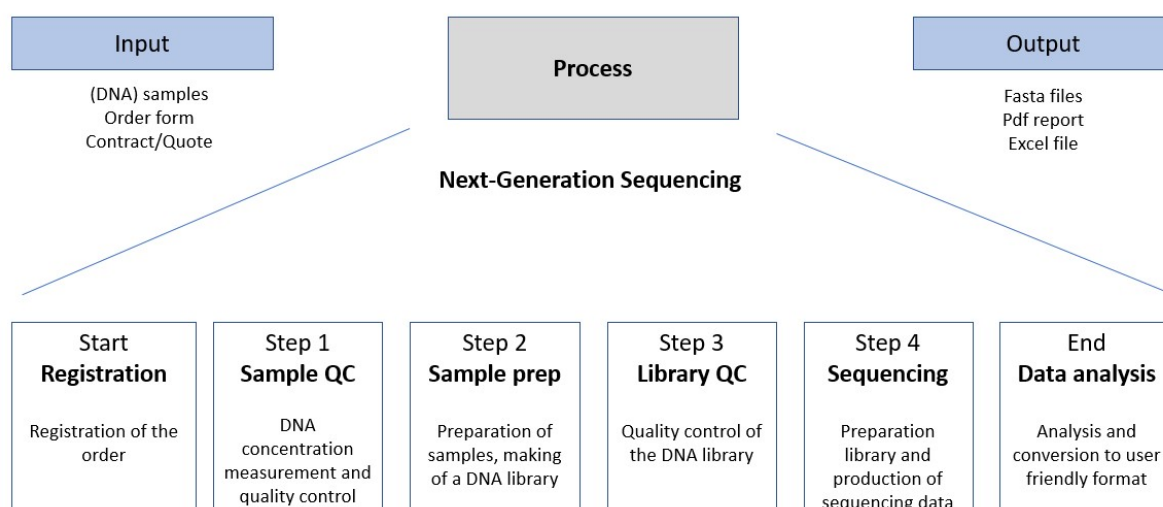


Figure 1: Simplified workflow of the NGS process.

When a closer look is taken at the NGS process a multi-production line can be determined. Each sample flow is based on a sample type and service that the customer can order. The path that is followed depends on the type of sequencing run that needs to be performed. There are three different types of sequencers used (Sequel, MiSeq and HiSeq). The actual sequencing runs (sequencing step) on the Sequel system are outsourced to another organisation. On the HiSeq sequencer two different protocols are run. Sometimes a sample needs to be run on the HiSeq as well as the Sequel. So the same sample will be analysed in two different processes. The run type that needs to be performed in combination with the run length (PE300, PE125 or SR50) determines which process flow is followed and thus which type of sample prep (NexteraXT, 16S profiling, TruSeq, Sequel or amplicon) is performed. Each sample flow uses its own specific equipment with limited sample or data capacity for each step. The bioanalyzer is used for DNA quality control purposes in multiple steps. Each machine in the process uses its own specific reagents. This inventory flow of reagents is outside the scope of this research project. The theoretical, most optimal, total time needed to run a complete NGS sequencing process from order registration until data analysis varies between 6 and 10 days dependent on the sequencing run type that is performed. For each process an urgent, standard and custom variant are offered to customers. The current lead-times that are offered are 4 weeks for standard services, 6 weeks for custom services and 1 week for fast orders. In figure 2 a detailed overview of the NGS production process of BaseClear can be found. Within this multi-product production line a dominant flow can be determined. The NexteraXT route (blue/green) and 16S profiling (yellow) are the most common.

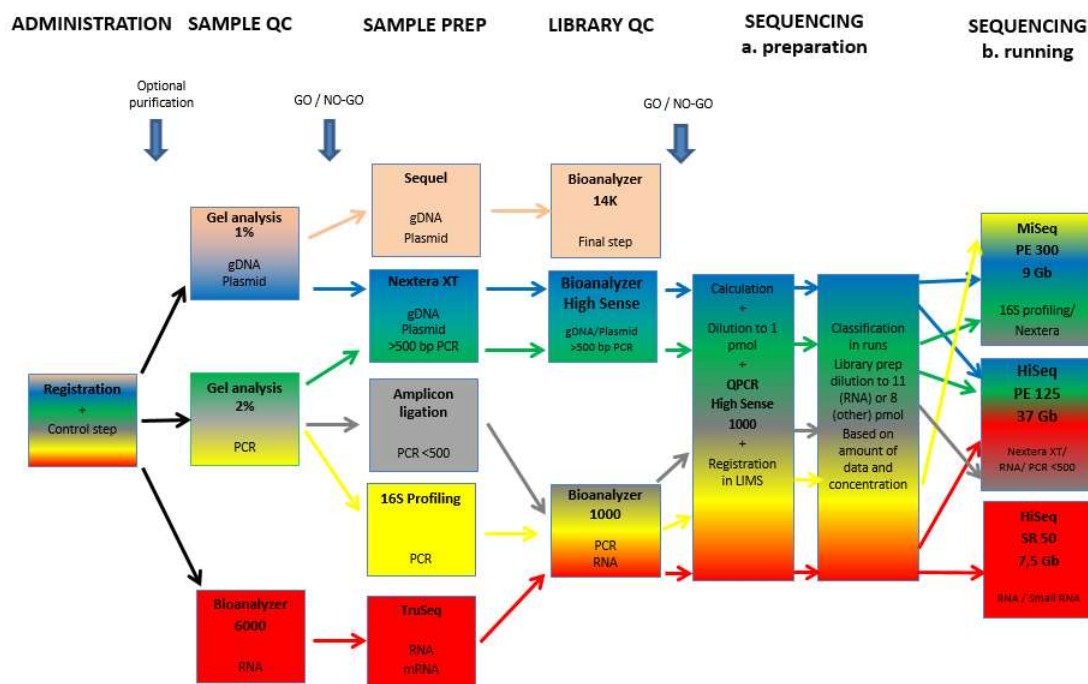


Figure 2: Detailed overview of the NGS process (final step: data analysis not included).

On an organisational level, there are three different function profiles within the NGS department each with its own responsibilities. There are five technicians (4.7 FTE) that perform all activities in the laboratory that are needed to process the samples. Some of the technicians can perform all specific steps of each process, others are only qualified to perform some of the steps. There are two senior technicians (1.3 FTE) that are involved in optimization projects to improve efficiency or quality of the services. They are also involved in project management, like sending project updates to the customer and they function as a back-up for the production manager. The senior technicians are also qualified for the primary laboratory activities so they are a back-up for the technicians as well. The production manager (1 FTE) is responsible for quality, customer satisfaction and accomplishing lead times of all orders. Besides project management the manager does the planning and control of all sequencing orders. After the samples are sequenced the manager Bio-IT (1 FTE) is responsible for the analysis of

the generated data. The actual analysis is performed by bio-informaticians (3 FTE). They release the data to the web portal and inform customers that the data is ready for further downstream applications. The current planning and control system of the NGS process is described in more detail in the next section.

1.2.3 NGS planning and control

After the customer order has arrived and registered in the LIMS a due date is manually added to the LIMS by a technician based on information in a quote that is sent along or on internal terms and conditions of the service that is requested. By the end of the week the production manager makes a manual production schedule for each employee in Excel format. Each production step is elaborated into a time block based on an average historical time estimation of each step. The outstanding work is visualised in LIMS. The first step in making a production schedule is checking if raw material needs to be purified before it can be released to production. In a second screen in LIMS the due date and run type of all samples that needs to be processed are visualised. These are all samples that passed the sample QC step. So the actual planning of the production processes starts after the sample QC step. A selection for each sequencing run type is made in LIMS and samples are scheduled into run batches. During this planning, quality control on the measured DNA concentration and QC results, based in the information in LIMS, is performed by the manager as well. Orders that are already late at hand are manually put on top of the priority list. After a sequencing run batch is completely full or when due dates of samples impend to exceed a sequencing batch is finalized, even when it is not completely full, and the deadline for the sequencing run is added to the Excel schedule. All production steps that are needed are randomly added to the planning schedule based on other production work that needs to be performed and considering available personnel and equipment capacity as well as laboratory space. For each employee, specific tasks for each week are assigned in Excel. An example of a production schedule is given in Appendix C.

1.3 Problem description

The motivation for this research is based on practical findings. BaseClear encounters several problems regarding its current planning and control system of its NGS department, as described in the previous section. This section will discuss the present problems. From a business perspective, there is a need for shortest lead times in the market and a need for highest efficiency which means performing completely full sequencing runs to minimize operational costs. Feedback from customers obtained from yearly satisfaction surveys show that the lead times of the NGS services vary and the agreed due dates sometimes are exceeded. Besides this, feedback from the production manager is that several sequencing runs are not completely full when they are processed, runs are not scheduled in a systematic way and theoretically more runs can be performed within a certain timeframe.

An explorative analysis on the lead-times of 20 orders that have been processed in Q4 2016 confirm a variability in lead time and WIP. If all steps in the NGS process including data analysis are performed in one flow a total lead time of 11-15 days is possible, dependent on which sequencing run type is performed. The measured lead times of the 20 orders varied between 10 and 34 days and there is no flow in the process. The results of this orientation study are visualized in a value stream map in figure 3.

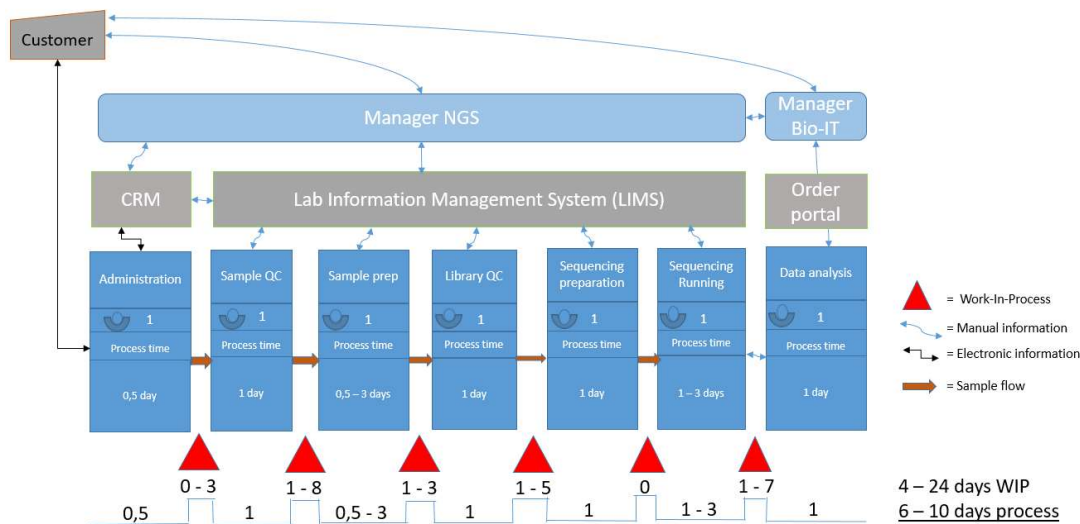


Figure 3: Value stream map – NGS production performance (20 random orders processed in Q4 – 2016).

This exploratory study shows that the current planning and control system of the NGS department within BaseClear is inadequate. The problems are subdivided into two main aspects:

1. The production planning and control system is suboptimal to handle the sample flow which leads to variable and exceeding lead-times.
2. The NGS resources are not used in the most efficient way which results in unbalanced Work-In-Process.

These problems have been discussed with the production manager of the NGS department of BaseClear and the following root causes have been outlined. There is a growth of the order flow and the total number of orders and samples that are in process vary a lot over time which causes peaks in workload. There is limited equipment, personnel and laboratory space available and some steps are performed manually and are hard to automate. This makes it difficult to handle the peaks in workload in a flexible manner. There is a poor information flow between the Marketing & Sales and Operations department which makes it difficult to gain insight in customer enquiries and therefore medium-term planning. There are no clear definitions made what is standard or custom services which results in much communication between departments to get clarity about the work that needs to be performed for orders that are not standard. The current planning schedule is made manually and there is no standardized electronic resource planning with feedback (ERP) between the LIMS and the planning system. Finally, there is poor insight in performance measures which makes it hard to track, control and report the actual lead times. In figure 4 the main causal relationships among the problems as discussed above are visualized.

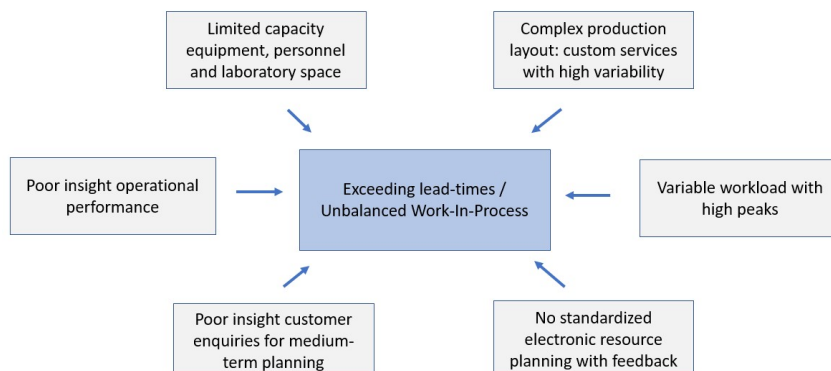


Figure 4: Preliminary cause and effect diagram.

Besides the problems mentioned above BaseClear's customers are offered more and more possibilities for customised NGS projects. BaseClear is planning to introduce a new sales model within the NGS department in 2017. It is a so-called 'airplane' concept. The specific characteristic of this model is an extreme easy and fully automated online service for the independent customer who doesn't need additional high-end support or expertise, but only cost efficient high-quality data and a user-friendly experience. The customer buys samples that will be collected in a pre-pool batch and released to production after a batch of 95 samples is completely full or when the capacity in the process is sufficient. This model is a cheaper variant of the current traditional model where the samples are released to the process directly after the order is placed by the customer and processed in batches. The introduction of this new sales model will give an extra challenge for planning and controlling the NGS production.

1.4 Problem formulation

In view of the problem description described in the previous section, the problem can be formulated as follows: "BaseClear encounters an unbalanced workload regarding its NGS production department which results in variable and exceeding lead times".

1.5 Research objective

The Chief Executive Officer of BaseClear (Drs. Bas Reichert) has asked to redesign the planning and control of the NGS department based on theoretical and empirical findings. The objective of this practice-oriented research project is a contribution to opportunities and knowledge of how BaseClear can re-design the production planning and control of its NGS department to improve the operational performance in terms of more balanced WIP and reduced lead times. The characteristics of the new service model that will be implemented during 2017 within the NGS department can be used to accomplish this goal. It is important for the case company that the resulting recommendations are practically implementable, meaning that the proposed improvements must be simple to implement and easily understood. From a theoretical perspective, this research contributes to knowledge how workload control concepts can contribute to possibilities for optimizing production performance in a Make-to-Order general flow-shop environment.

1.6 Research questions

With respect to the problem formulation and the objective of this BPS project, the main research question and related sub questions are stated below. The following research question will be answered:

How should BaseClear improve the production planning and control of its NGS department to achieve overall balanced Work-in-Process and reduced lead times?

The following sub questions have been formulated to answer the main research question in a step-by-step manner:

1. What factors of production planning and control theories are applicable in the context of BaseClear to balance WIP and reduce lead times?
2. What are, according to theory, suitable solutions that BaseClear can introduce to its current production planning and control that can contribute to achieving overall balanced WIP and reduced lead times?
3. How does the current production planning and control of the NGS production process of BaseClear perform in terms of WIP and lead times?
4. What is the simulated effect of implementing theoretical solutions to the production planning and control on WIP and lead times of the NGS department?

5. What solutions should the NGS department of BaseClear introduce to its production planning and control for possible contributions to better balanced WIP and reduced lead times based on simulated findings?

1.7 Research approach

The aim of this BPS project is to conduct empirical research with a design-oriented research objective, namely to design a solution for a business problem. Van Aken et al. (2007) state that a BPS project differs from a research project when it comes to the objective. The purpose of research is to solve a knowledge problem in the immaterial world of knowledge, whereas the purpose of a BPS project is to solve a business performance problem in the material world of action. It is aimed at actual change and improvement in this material world. This design-oriented research is based on a combination of theory and practice, following the intervention cycle, also called the problem-solving or regulative cycle (Van Strien, 1997). The extended intervention cycle, or intervention cycle ++ (Wynstra, 2011), has five stages (see figure 5).

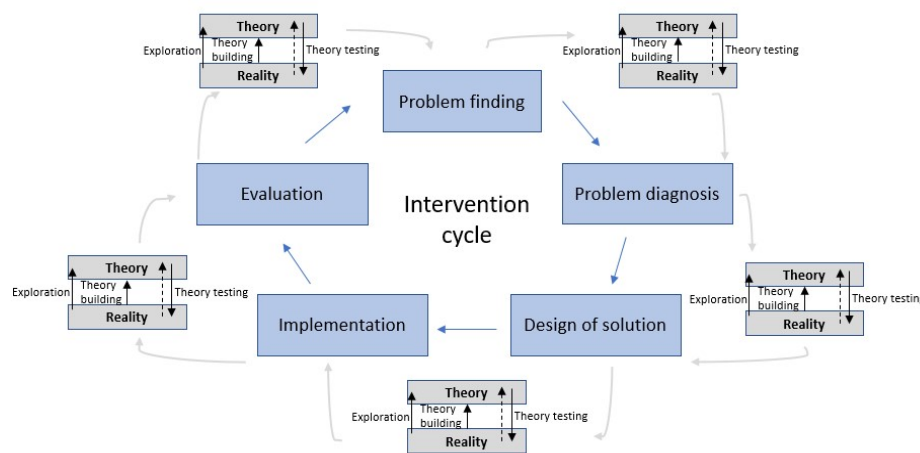


Figure 5: Representation of the intervention cycle++ (Wynstra, 2011).

During and in between each of the stages of the extended intervention cycle, theory and reality are compared to ensure a well-founded research. Van Aken et al. (2007) underline the need for this comparison. A continuous discussion between theory and practice is required to exploit the theory-based approach to problem-solving. Besides a comparison between theory and practice, the confrontation may also mean that the current situation is interpreted using theoretical concepts or evaluated from a theoretical perspective. During this BPS project, the first three stages of the intervention cycle ++ will be covered completely. The actual implementation of the solution, the fourth stage of the cycle, will not be executed at the case company due to the limited amount of time available. Evaluation will therefore only be performed based on theoretical outcomes.

1.8 Thesis structure

The structure of the thesis is as follows. A detailed introduction of the business problem finding is introduced in this chapter (Chapter 1: Introduction). The following chapters are aimed at contributing to the research objective. To this end a literature review of production planning and control and workload control theories and performance areas of flow-shops is given in the second chapter (Chapter 2: Literature Research). At the end of this literature research an outline of potential solutions is formulated which serves as a basis to solve the business problem. In the next chapter, the research methodology is given (Chapter 3: Research Methodology). The fourth chapter elaborates on the information from chapter 1 and contains a thorough analysis of current practices at the case company and corresponding performances to diagnose the problem areas (Chapter 4: Problem Diagnosis). Based on the findings of chapter 4 possible solutions are theoretically applied, after which the outcomes are analysed and conclusions drawn in the next chapter (Chapter 5: Design of Solution). Additionally, the research in general and possible outcomes of implementing the

solutions are discussed in chapter 6 (Chapter 6: Discussion). The thesis will be finalised with recommendations for further research (Chapter 7: Recommendations), an overview of the literature that is used and appendices. A schematic overview of the chapters of this thesis can be found in figure 6.

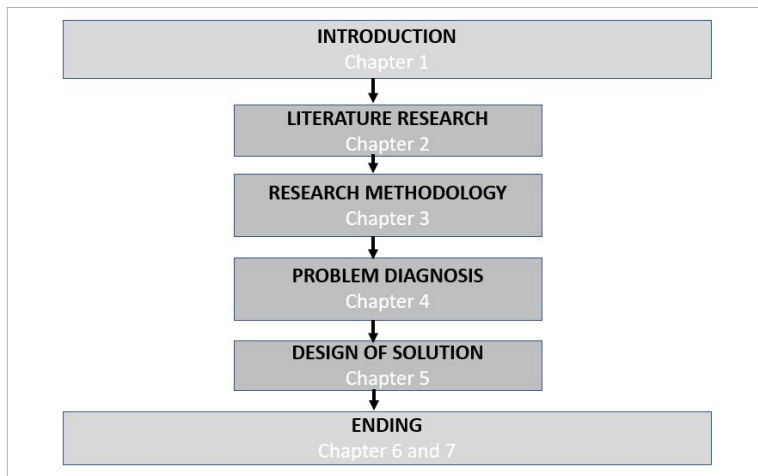


Figure 6: Schematic overview of the thesis structure.

2 LITERATURE RESEARCH

The goal of this chapter is to find an answer to sub research question 1 and 2. To this end a literature review will be performed on theories and concepts of production planning and control (PPC) to discuss what factors are applicable in the context of the general flow-shop of BaseClear to balance WIP and control lead times. In the first section 2.1, general theory of PPC will be explored. Section 2.2 will give an outline of the difference between pull and push based production systems. In section 2.3 a classification of companies within the Make-To-Order (MTO) industry will be outlined. In section 2.4 a more in-depth review will be performed on PPC concepts in the MTO industry, including Material Requirements Planning, Theory of Constraints and Workload Control. In section 2.5 an overview of four main card-based production control concepts will be discussed. These are Kanban, CONWIP, POLCA and COBACABANA. In section 2.6 the applicability of PPC systems in the case company will be discussed. In section 2.7 areas of production performance optimization, including WIP balancing and lead time reduction of general flow-shops will be discussed. The literature research will be summarised in section 2.8 and a theoretical model of factors to balance WIP and control lead times presented. The final section will give an outline of potential suitable solution concepts that can be used in the context of BaseClear which will serve as a basis to solve the business problem.

2.1 Production Planning and Control

Production is regarded as a transformation process that takes inputs and transforms them to outputs that are of a higher value than the inputs. A crucial aspect for any production input/output model is that the time that the transformation process takes is a very important factor. This is because the finished product is being delivered to a customer who requires receiving that product or information by a promised delivery date. Failure to meet this promised delivery date could affect the amount of future business likely to arise from that customer and the prices that can be secured. The ability to be able to carry out the necessary transformation processes is an essential qualifier in a market, but price and delivery lead time quoted are crucial order winning factors. This is particularly applicable in most of the manufacturing and service companies within the MTO sector. PPC is of great importance for the competitive position of manufacturing firms (Zäpfel and Missbauer, 1993). Empirical studies show that enterprises with short delivery times grow faster and earn higher profit than their slower competitors (Stalk and Hout, 1992; Rommel et al., 1993). Van Dierdonk and Miller (1980) discuss that PPC is basically an exercise in information and decision making and not solely a production activity.

One of the primary functions of production planning is to match market demands with manufacturing and to control the resultant flow of goods and materials. The relationship between a firm's environment and strategy and its production control system is a complex one. For over thirty years many PPC systems have been on offer. These systems are designed to solve many problems that arise in managing the flows of materials and goods as well as capacity utilization (Vollmann, Berry and Whybark, 1988). PPC systems are crucial tools for meeting increasingly high customer demands and expectations in the present competitive manufacturing climate. Typical functions of a PPC system include planning material requirements, demand management, capacity planning and the scheduling and sequencing of jobs. Two of the key purposes of such functions include to balance WIP and reduce lead times. These are important objectives and therefore choosing the right PPC system is a crucial strategic decision. Stevenson et al. (2005) conclude that all PPC approaches can be effective under the right shop conditions. However, there is no perfect PPC that will fit for all situations (Plenert, 1999). As a result, applicability depends on the individual characteristics of a company and success is dependent upon several factors. Managers of the company must play a large role during implementation by 'championing' the project, giving their specialist opinion and setting parameters through facilitating organizational change. Neely and Byrne (1992) conclude that an organization needs a combination of production control methods to take advantage of the strengths of each system. PPC approaches do not have to be mutually exclusive and at times can be hard to isolate.

The need to make the right choice for a specific PPC system within a company is particularly important given that implementation can be an expensive and timely process requiring a change of culture, philosophy and working practices. This issue is particularly acute for the MTO environment. Many of these companies are Small and Medium sized Enterprises (SMEs), like the case company BaseClear. Small companies, with limited financial resources, are in danger of suffering the consequences of implementing an inappropriate and unsuccessful contemporary PPC approach. Because of the great importance of PPC and because of the evident problems companies have achieving the desired goals, many control systems have already been developed. Graves et al. (1995) reviewed literature on ten manufacturing control systems with variations. Gstettner and Kuhn (1996) classified different pull production systems. Bonvik et al. (1997) also compared production-line control. Zäpfel and Missbauer (1993) performed a notable review of PPC methodologies. However, this study does not focus primarily on MTO production. The growth and importance of MTO industries, coupled with a growth of new planning and control methodologies, contributed to a need to undertake a critical assessment from a MTO perspective which has been performed by Stevenson et al (2005). The findings of these studies will be deepened in the following sections.

2.2 Push and Pull production systems

In the MTO industry two types of production systems, push and pull, can be determined (Monden, 1983). Both systems operate equally in opposite sense and have their own merits and demerits (Ramiro et al., 1988). Push is a conventional system of production. When a job completes its process in a workstation (WS), then it is pushed to the next workstation where it requires further processing or storing. In this method, due to unpredictable changes in demand or production problems, the job happens to deviate from its schedule and it causes accumulation of WIP.

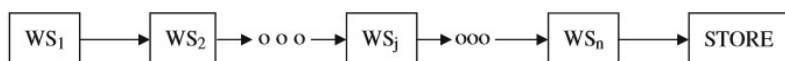


Figure 7: Example of a push production system.

A pull type production system consists of a sequence of workstations involving value addition in each workstation. In the pull system, from the current workstation, each job is withdrawn by its succeeding workstation. In other words, the job is pulled by the successive workstation instead of being pushed by its preceding workstation (Kong and Allan, 2007). Pull systems are here defined in

accordance with Hopp and Spearman (2004) as control systems that explicitly limit WIP that can be in the system. So the primary advantage of the pull system is reduced WIP.

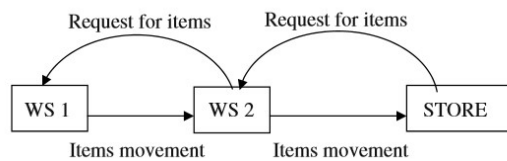


Figure 8: Example of a pull production system.

Push systems schedule releases, while pull systems authorize them. As a result, push systems control release rate and observe WIP while pull systems control WIP and observe throughput (Hopp and Roof, 1998). Karmarkar (1991) distinguishes between a push and a pull system by looking at the order release process. In a pull system, an order release occurs due to physical removal of finished products, while in a push system production is authorized in advance of the actual realization of demand. According to Bonney et al. (1999), the British Standards Institution defines a push system as “a system of ordering in which orders are issued for completion by specified due-dates based on estimated lead times”. In the same work a pull system is defined as “a system of ordering in which a fixed stock is held and orders are issued for the immediate replacement of any products which are removed from stock”. Simchi-Levi et al. (2009) give a similar description by stating that in a push based production system, decisions are based on long-term forecasts whereas a pull-based production system is demand driven so that they are coordinated with true customer demand rather than forecast demand. A comparison between the performance of both push and pull systems is made in several studies (Krajewski et al., 1987; Sarker and Fitzsimmons, 1989). Bonney et al. (1999) investigated the effect that push and pull information flows have on a production system performance under a variety of conditions by means of simulation study. They concluded that push systems perform better under demand uncertainty and order size variability. The mean waiting time for demand to be satisfied appeared to be longer for pull systems than for push systems. Another study by Spearman and Zazanis (1992) based on mathematical models shows that less congestion results in pull systems because WIP levels are limited and WIP variability is reduced. Furthermore, they suggest that the effectiveness of pull systems results from limiting WIP and WIP variability. Finally, they show that both from a practical standpoint and with respect to an optimal policy, a pull system is easier to control than a push system. Simchi-Levi et al. (2009) state that a pull-based system shows a significant reduction in WIP level, enhanced ability to manage resources, and a reduction in system costs when compared with an equivalent push based system. On the other hand, they argue that pull based systems are often difficult to implement in case of long lead times and that it is frequently more difficult to take advantage of economies of scale in manufacturing.

A strategy that takes advantages from the best of both is the hybrid push-pull strategy. In this strategy, some stages of the production system are operated in a push-based manner, while the remaining stages employ a pull-based strategy. Bonney et al. (1999) acknowledge that most practical systems consist of both push and pull. Takahashi and Soshiroda (1996) distinguish two types of integration of push and pull. One is the vertical integration, which implies that the system consists of two levels, the upper level consisting of a push-type production ordering system and the lower level consisting of a pull-type production ordering system. The other type of integration is the horizontal integration, which implies that all the stages are not ordered by either of the production ordering system, but that some stages are ordered by a push type production system and the other stages are ordered by a pull-type production system. In contrast with the results of the study performed by Bonney et al. (1999), Simchi-Levi et al. (2009) argue that higher demand uncertainty leads to a preference for managing the production system on realized demand, i.e. a pull strategy, while smaller demand uncertainty leads to an interest in managing the system based on a long-term forecast, i.e. a push strategy. Many of the emerging approaches are hybrid methods based on established concepts. In addition, there is increasing attention being focussed on hybrid production environments in the MTO sector (Chang et al. 2003, Soman et al. 2004).

2.3 Classification of companies in the MTO industry

MTO is a manufacturing process in which manufacturing starts only after a customer's order is received. Apart from the Make-to-Stock (MTS) industry, companies within the MTO industry can be divided into Repeat Business Customizers (RBCs) and Versatile Manufacturing Companies (VMCs) based on order volume and variety as discussed by Amaro et al. (1999). RBCs produce customised products for each of its customers on a continuing basis, with a regularity of demands. RBCs tend to have a relatively small customer base and compete for the initial order of a continuing supply contract. A RBC provides customized products on a continuous basis over the length of a contract. Goods or products are customized but may be made more than once permitting a small degree of predictability. RBC can generate more stability by enticing customers into a more predictable and committed relationship. In a general flow shop work travels in one direction but jobs can visit a subset of work centers, permitting limited customization, relevant to a RBC (Stevenson et al, 2005). In figure 9 a classification of companies is given based on product volume vs variety.

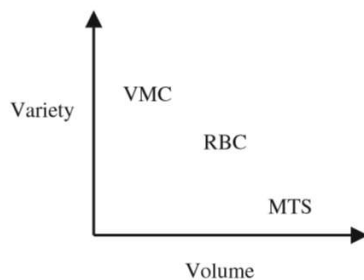


Figure 9: Classification of companies within the MTO industry based on Volume vs Variety.

2.4 PPC systems in the MTO industry

In this section three of the main PPC systems from MTO perspective which has been stated by Stevenson et al (2005) will be discussed in more detail, including Material Requirements Planning, Theory of Constraints and Workload Control.

2.4.1 Material requirements planning (MRP)

Volmann et al (1997) gave a complete description of Material Requirements Planning (MRP) and Manufacturing Resource Planning (MRP II). MRP is a periodic push-based system designed for complex production planning environments. MRP can provide significant benefits such as improved customer service, better production scheduling and reduced manufacturing costs. Despite being labelled a 'legacy system', MRP is still an important PPC approach. Sower and Abshire (2003) found that one-third of manufacturing companies studied use packages such as MRP. MRP II offers greater functionality than MRP, integrating a wider number of modules and company operations. MRP is very widely used, partly due to its universalistic approach, but this does not mean a wide applicability. There is a clear progression in increased functionality from MRP to Electronic Resource Planning (ERP) especially with large companies. However, this increase does not seem to have eased the problem of integration and implementation. There are reservations for criteria regarding the use of MRP-based systems in the MTO industry. Company size has been identified as an important factor in implementation strategy and success. It may be possible to tailor the design of MRP systems to the needs of MTO companies to some extent, however this would further add to the expense. Capital investment and the impact on SMEs of a failed ERP implementation strategy may be an entry barrier for ERP into SME. ERP-based approaches are an option for both RBC and VMC companies whatever the shop floor configuration and may be a potential solution for at least some of the concerns of the MTO sector. In isolation MRP is a shop floor production control mechanism and require a higher-level collaboration to be used in the MTO industry. ERP is applicable to all company types but this is due to its wide availability.

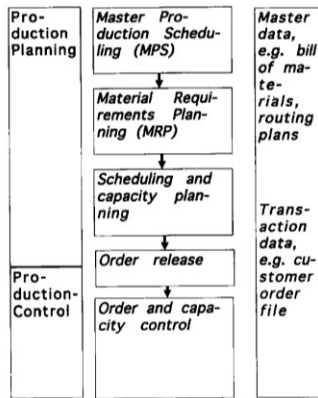


Figure 10: Framework of a traditional PPC system with MRP.

2.4.2 Theory of Constraints (TOC)

Theory of Constraints (TOC) is a bottleneck-oriented concept. The approach is commonly attributed to the work of Goldratt (Goldratt and Cox 1984, Goldratt 1990). It is now more commonly known as the Drum–Buffer–Rope (DBR) approach. Under the TOC philosophy, the production process is scheduled to run in accordance with the needs of the bottleneck(s), as the bottleneck (constraint resource) determines the performance of the whole production system. Mabin and Balderstone (2003) explain that TOC has been developed into a management theory of theoretical frameworks, methodologies, techniques and tools. Based on analysis of mainly manufacturing-based companies, applications of TOC show that companies benefit from lead time reduction and increased revenue. TOC can be used within small organizations, demonstrating its apparent applicability to the MTO industry. Wahlers and Cox (1994) discuss the use of TOC, highlighting its applicability to highly customized industries, where the company was able to reduce lead times and improve delivery performance. Duclos and Spencer (1995) compare MRP scheduling with that of DBR scheduling in a flow shop, where it was concluded that DBR performed better, with the constraint buffer used in DBR useful in increasing system output. Based on this study it has been shown that TOC can have a beneficial impact on performance in the flow shop, confirming its relevance to both the RBC and VMC sectors of MTO industries.

However, TOC has received a large amount of criticism in the literature. Early criticisms focus on a lack of disclosure of the full details of TOC (Duclos and Spencer, 1995; Wiendahl, 1995) and claims of optimality (Wiendahl, 1995). Explanations have shown that TOC is not an optimal approach (Goldratt, 1990). Duclos and Spencer (1995) are also sceptical of the achievements of TOC, highlighting the confusion resulting from a TOC performance measurement system with distinct differences to traditional Operations Management (OM) performance measurement systems making comparisons and objectivity difficult. In the general flow shop it is likely that bottlenecks will remain relatively stationary and deterministic. Rahman (1998) comparisons of TOC with alternatives suggest TOC will outperform MRP when there is a dominant bottleneck, but that MRP performs better when there are highly customized products. The TOC system is more complete than the Just-In-Time (JIT) system, see Plenert and Best (1986), Rahman (1998) and Plenert (1999). This further suggests that it is important to determine bottleneck resources for TOC. Rahman (1998) states that it is difficult to conclude that one system is better than the other.

The literature has highlighted the use of TOC in MTO production scenarios where variable routings and non-repeat production exist, including use in SMEs. The stationary positioning of bottleneck resources may be a requirement for effective use and this is a realistic assumption in general flow shops, like the case company BaseClear. However, as with MRP, TOC does not directly cater for the importance of planning and control at the customer enquiry and job entry stages in MTO production. It could be argued that these planning processes are simplified as the workload need only be estimated for constrained resources. This may be of benefit in highly customized industries where

estimating required processing times in advance can be difficult. TOC continues to be an option widely considered by practitioners and has been used effectively in highly customized environments. New PPC concepts such as JIT and TOC do not have the type of repetitive manufacturing that enables dedicated facilities to be set up in a simplified shop floor layout. Thus, they cannot rely on the more visible 'situational management' on the shop floor, as described by authors such as Johnston (1995), which has led to a decrease in the importance of higher level planning in many firms.

2.4.3 Workload Control (WLC)

Workload Control (WLC) is a sophisticated PPC solution specifically designed for the needs of the MTO Industry. WLC has been described as one of the new PPC concepts available for practical operations. WLC concepts buffer the shop floor against external dynamics by creating a pool of unreleased jobs making the shop floor more manageable. This approach stabilizes the performance of the shop and makes it independent of variations in the incoming order stream (Bertrand and Van Ooijen, 2002). The use of workload norms should turn the queueing of orders on the shop floor into a stationary process which can be characterised by an equilibrium (Land and Gaalman, 1996). The true objective of WLC is to process jobs to meet the promised delivery dates with the machine and workforce capacities and capabilities available. The job release stage can itself only be fully effective if the queue of jobs in the pool is also controlled. Otherwise, jobs may remain in the pool for too long so missing their promised delivery dates. A workload control system must include the customer enquiry stage, (the job entry stage), to control the input of work to the pool as well and plan the capacity to provide in future periods so the shop floor queues are also controlled. If manufacturing lead times are to be controlled then the total workload has also to be controlled, not only overall but its occurrence over time as well.

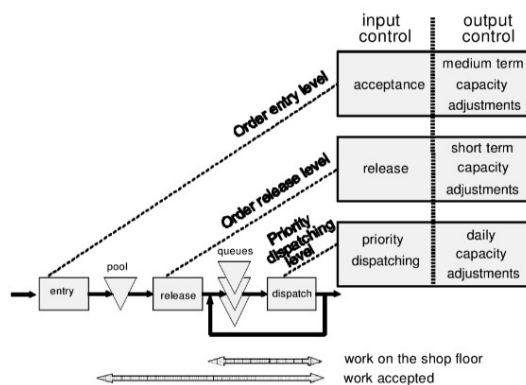


Figure 11: The general framework of the WLC concept (Breithaupt, 2002).

Irastorza and Dean (1974) were the first to develop a sophisticated release method, which balances and limits the queues of jobs on the shop floor. More comprehensive control concepts and load-orientated release methods were developed in the eighties. The main three branches of WLC are covered by Bechte (Load Oriented Manufacturing Control: LOMC), Bertrand and the Lancaster School (Land and Gaalman, 1996), Probabilistic (for example, Bechte 1988, 1994, Wiendahl 1995). Oosterman et al. (2000) consider several WLC concepts and show that the performance varies depending on shop configuration. However, in general as variability increases, WLC becomes more applicable (Henrich et al., 2002) and WLC can lead to the reduction of WIP (Land and Gaalman, 1996). WLC is designed to achieve the same levelling of workload to capacity that is achieved in repetitive manufacturing using lean tools, but it does so while allowing the customers of MTO companies to obtain highly customized products (Thürer et al., 2012). Hence, it reduces the variability of the incoming workload that results from product customization, rather than limiting variation in the product mix itself (Thürer et al., 2017). WLC typically controls the incoming workload of the shop using continuous workload measures or calculations. The complexity of implementing workload calculations affect WLC applicability, particularly to small shops with limited resources. As a result, many studies have found implementing WLC in practice to be extremely challenging (e.g. Stevenson, 2006; Hendry et al., 2008; Stevenson et al., 2011).

WLC is designed for MTO type production environments and can be an effective method of controlling WIP and reducing lead times, accommodating non-repeat production and variable routings. This has been demonstrated through simulation and empirical research. Oosterman et al. (2000) evaluated the use of various WLC concepts under different shop conditions and found that the performance varies with the environment, explaining part of the poor performance of controlled release methods reported in many simulation studies. Wiendahl (1995) has reported successful implementations of WLC concepts. Land and Gaalman (1996) provide a good critical assessment of the various WLC concepts used for order release and presents a more sophisticated release mechanism. Within WLC there are four levels at which the control of queues can be attempted. These are on priority dispatching level, order release level, order acceptance and order entry at customer enquiry level, see figure 12, and will be discussed in more detail in the following sections.

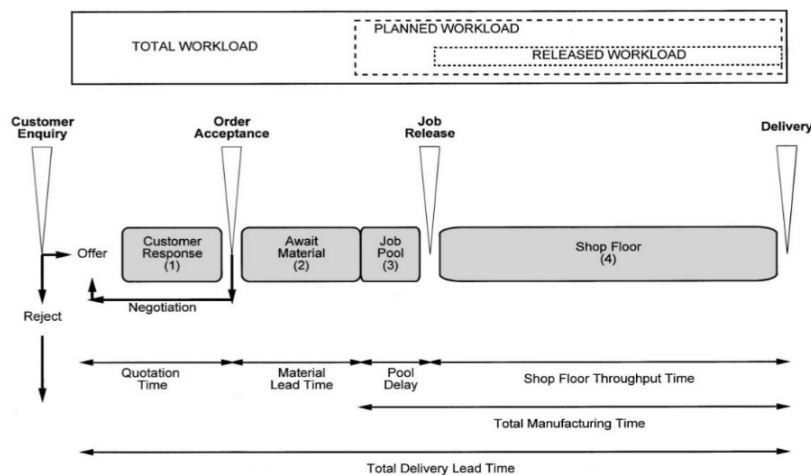


Figure 12: Components of the WLC concept (Kingsman, 2000).

2.4.3.1 Customer enquiry and order acceptance

The first input control decision is order acceptance and delivery date promising. This control decision deals with customer enquiries. Customer enquiries can arise in a variety of ways. Sometimes customers completely determine the delivery dates of orders, in other situations the company has a strong influence on the promised delivery dates (Park et al., 1999). Dealing with customer enquiries entails a complex process of decision making. Kingsman et al. (1996) gives an extensive discussion on relevant acceptance and due date promising decisions for MTO companies. The process will result in orders to be produced in a certain period with a promised delivery date for each order. Average lateness is the difference between the average realised throughput time and the average promised delivery time. The average lateness will increase when a larger number of orders must be produced in a certain period assuming both capacity and promised delivery dates to remain the same. So increased waiting times will result in a longer average realised throughput time. The average lateness will also increase if tighter delivery dates are promised for the same set of orders, because in this situation the average promised delivery time component decreases. The variance of lateness is more specifically influenced by the characteristics of the accepted orders. For instance, orders with a larger number of operations to be performed will generally require larger throughput times. If throughput times of individual orders are insufficiently, the variance of lateness will also likely increase.

Production planning and order acceptance are difficult management problems in MTO companies, because the arrival of orders into the company is a stochastic process. The arrival of enquiries cannot be predicted in advance. Furthermore, each order can be different, requiring different amounts of processing work on the work centers and in a different routing sequence. Managing lead times using workload input/output control methods based on controlling a hierarchy of aggregate loads of work is a better approach than using forecast lead times (Kingsman, 2000). However, the customer enquiry stage and order acceptance point (job entry) may be better as the main control point. It has

been shown that job entry can control WIP and lead times with the same workload (Haskose et al., 2002). Without control at the customer enquiry and job entry stages, power will have been lost before reaching the job release or shop floor dispatching stages causing pre-shop pool times to escalate. These stages are the least elaborated areas (Land and Gaalman, 1996), but have received attention recently (Enns and Prongue Costa, 2002; Kingsman and Hendry, 2002). At these stages input and output control can be used together, coping with the same workload but with shorter lead times (Kingsman and Hendry, 2002). When customers enquires cannot be determined, this research shows that when WLC is employed at the customer enquiry stage, due date quotations can be made with confidence by stabilizing lead times and controlling WIP.

2.4.3.2 Order release control

The next input control decision is the release of orders. When order release control is applied, orders do not enter the shop floor directly, but they are retained in a pre-shop pool and released in accordance with certain performance targets, e.g. to restrict the level of WIP and/or maximize due date adherence (Thürer, 2013). Order release is one of the main functions of PPC (Bertrand and Wijngaard, 1986; Zäpfel and Missbauer, 1993). Henrich et al. (2002) consider the decision of job release to be the main control point crucial to the simplification of the remaining process. Releasing mechanisms have a significant effect on the performance of the production system, including balancing WIP and controlling lead times (Hendry and Wong 1994). Results show that controlled release deteriorates flow time, lateness and tardiness performance. Controlled release appears to work best in situations of low load and tight due dates. Because capacity is often restrictive, it is important to select those orders for release that provide capacity groups in the shop with a good load balance. This will support the control of the average lateness (Land, 2004). Balance of loads results in smooth flows on the shop floor and avoids congestion in front of certain capacity groups. The release decision can also contribute to a low variance of lateness. This is achieved by considering relative urgency of orders in selecting the orders to be released next. To be able to accurately determine this urgency, reliable throughput times are required. The control of these throughput times is another function of the release decision. For most WLC concepts, jobs are only released onto the shop floor if released workload levels will not exceed pre-set maximum limits, while ensuring jobs do not stay in the pool too long to reduce lead times and meet due date objectives. While jobs remain in the pool, unexpected changes to quantity and design specifications can be accommodated at less inconvenience. Land and Gaalman (1998) suggest that the procedure to release jobs is basically the same in each WLC concept.

Land and Gaalman (1994) conclude that the three most comprehensive WLC concepts are those proposed by Bertrand and Wortman (1981), Bechte 1988) and Tatsiopoulos (1983). The first of these concentrates on the job release stage and is not a full WLC system. The second addresses both the job entry and the job release levels, and has been tested using case study research. It was concluded that a comprehensive WLC system of this type enabled the factory studied to reduce lead times, reduce WIP, meet planned due dates and guarantee a high work center utilization. However, as this research only addresses one factory, it is not clear whether these improvements could be achieved in other companies. Some authors claim that controlled releasing mechanisms enhance the performance of the shop (Plossl and Wight (1973); Melnyk and Carter (1987); Ragatz and Mabert (1988)). However, other studies found that controlled order releasing was counterproductive. They argue that order releasing has an inherent disadvantage since it removes some of the dispatching options by restricting the set of jobs available for dispatching (Baker (1984); Kanet (1988). Salegna and Park (1996) argue most of this research has concentrated on simple decision rules at the job release and job entry levels using simulation experiments that model a hypothetical job shop. There has been very little research into the effectiveness of more comprehensive decision rules.

2.4.3.3 Priority dispatching

The last input control decision is priority dispatching or production scheduling. Baker (1974) defined production scheduling as 'the allocation of resources over time to perform a collection of tasks'.

Production scheduling has received much attention until 1990 and yet few systems have proved to be successful in practice. The work by Shimoyashiro et al. (1984) suggests that if the workload balance and the amount of work input is controlled at the release stage, then good shop performance can be obtained no matter which shop floor dispatching rules are employed at the scheduling stage. Similar conclusions were given by Browne and Davies (1984) highlighting the importance of controlling the releasing of jobs from the pool onto the shop floor. Kingsman and Hendry (2002) and Haskose et al. (2004) found that priority dispatching is a relatively weak input control decision when used alone. As the performance of release increases, the impact of shop floor dispatching rules diminishes (Wein 1988). Once an accurate release decision has been made, priority dispatching has a limited influence on the average lateness and the variance of lateness. However, some dispatching rules exist that still improve the average lateness (Land, 2004). Dispatching rules do not provide a schedule of jobs through the shop. They can only be used to choose which job should be processed next, from the queue of jobs waiting at a work center (Hendry, 1989). Priority dispatching can only change the order in which each job emerges out of the work center. It cannot change the time before the work center is free and available to start processing further jobs. If it is an overloaded situation where there is too much work to do every job in time, it can help to select which jobs should be delivered on time, by giving them priority for processing at the work center and which will be allowed to be late. It cannot in these circumstances provide any assistance on ways to deliver all jobs on time.

Research by Pappas concluded that no sophisticated priority rule should be used since the interruption of the 'natural' flow of work in the shop adds more problems than it solves. With a release method in place, only a simple shop floor dispatching rule such as First-in-System-First-Served (FSFS) or First-at-Work-centre-First-Served (FWFS) is needed (Kingsman 2000). The dispatching rule typically applied with card-based production control systems is first-in-first-out (FIFO). There appear to be two reasons that justify this choice of dispatching rule. First, there is typically no or little processing time variability in the environments where card-based systems were originally developed, which makes the application of load-based dispatching rules not meaningful. Secondly, card-based systems were generally developed for to stock production environments and FIFO is a suitable time-based dispatching rule for shops where jobs do not have individual due dates. When there is high processing time variability a load-oriented dispatching rule is more justified and when jobs have individual due dates a due date-oriented dispatching rule is more suitable than FIFO dispatching to indicate the urgency of jobs.

2.5 Card based PPC systems

Card-based systems are simple, effective means of controlling production. All card based control systems use information on output from the system to control input to the system, so they are input/output control systems (Wight 1970; Plossl and Wight 1971). This control cycle also makes them pull systems. The information on output that is used to control input to the system is usually provided via cards. Card-based control systems provide a simple, visual approach to controlling production. A critical review on the control mechanisms underpinning four key card-based control systems will be given. These are Kanban (Sugimori et al. 1977; Shingo 1989), Constant Work-In-Process (ConWIP; Spearman, Woodruff, and Hopp 1990; Hopp and Spearman 2001), Paired-cell Overlapping Loops Of Cards with authorisation (POLCA; Suri 1998; Riezebos 2010) and COntrol of BALance by CArd BAsed NAVigation (COBACABANA; Land 2009; Thürer, Land, and Stevenson 2014). These four key systems build the foundations for all card-based control systems available in the literature to date. Card-based solutions are often adopted in practice to signal the release of orders onto the shop floor or to coordinate the flow of orders between work centers as they are simple, visible means of controlling production. Card-based control systems are relatively straightforward to implement and are effective in stable production environments, like flow shops (e.g. Stevenson et al., 2005). Thürer, Stevenson, and Protzman (2016) argue that the following three factors have the greatest impact on which card-based control system should be chosen for a given context: routing variability, processing time variability and WIP inventory vs order release control.

2.5.1 Kanban

Kanban is a pull and card-based production system that aims to cut inventory and flow times, where the start of one job is signalled by the completion of another. There are many variations but in its simplest form, cards are part number specific. Determining the number of Kanban cards is a major strategic decision for balancing WIP, flow times and utilization. Kanban needs a continuous flow or large batches, a limited number of parts, few set ups and low demand variability to be an effective system, making it suited to repetitive manufacturing. Kanban has been highlighted because it can be used as a simple shop floor signal in conjunction with more sophisticated MTO applicable approaches involving centralized planning. Kanban relies on the use of Just in Time (JIT), which does require advanced planning, rare in the MTO sector. Hendry (1989) concludes that JIT as a system has been designed for the MTS sector and is inapplicable to the MTO sector. Although some of the elements may be appropriate, the vital control modules required at the customer enquiry and job release stages are not offered by the JIT system. However, aspects of the JIT philosophy and lean thinking approach, such as attitude towards waste and stockholding, could be adopted. Conventional Kanban and MRP controlled production systems are both special cases of a general approach to production control. The key feature of this approach is the control of release of jobs to each production stage by limiting the number of jobs in process at the stage or at a group of adjacent following stages.

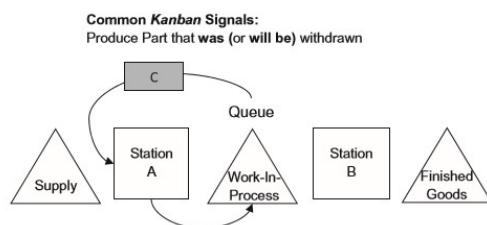


Figure 13: Example of a common Kanban system used for coordinating two workstations.

The 'traditional' Kanban system is well known to PPC researchers and cannot cater for the routing variability and lack of repetition predominant in MTO manufacturing. In isolation, the Kanban is a decentralized shop floor signalling system and lacks control at the customer enquiry stage, job entry and job release stages. Despite this, it may be possible to use Kanban on the shop floor in conjunction with a higher-level planning tool such as WLC, however this would still need a way to accommodate product variation, while the WLC job release function means that the shop floor can be controlled through simple priority dispatching without the need for Kanban signals. Krishnamurthy et al. (2004) has shown that Kanban systems are not effective in the case of MTO companies. The main reason is that the number of products in the assortment of these firms is generally high, while at the same time the frequency of demand is low. Together, these effects lead to a strong inefficiency of such pull systems. Kanban systems suffer from a lack of load balancing capabilities, which hinders their application even to pure flow shops if there is variability. In environments with custom products, changing product mix, infrequent orders, or highly variable demand, Kanban is not a reasonable assumption (Krishnamurthy and Suri, 2009). Shingo (1989) concluded as well that Kanban is not suitable for high variety production environments and this is recently confirmed by Harrod and Kanet (2013). Adding load balancing capabilities may be a potential key to improving the performance of Kanban-like systems in shops that feature variability. Much of the available literature addresses one of the main weaknesses of Kanban systems and that is sensitivity to processing time variability. The main means of accommodating processing time variability have been to adjust the number of Kanban's allowed in the system (see, e.g. Takahashi and Nakamura 1999; Dallery and Liberopoulos 2000; Tardif and Maaseidvaag 2001; Takahashi 2003). However, it has recently been argued that an increase in the number of Kanban's when the workload increases is counterproductive since it leads to the well-known 'lead-time syndrome' (Mather and Plossl, 1978).

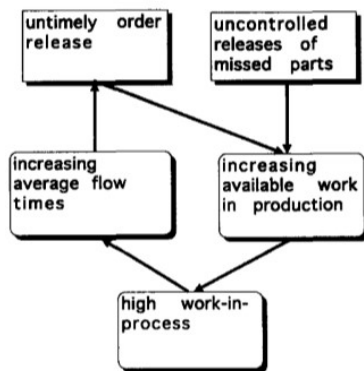


Figure 14: The lead-time syndrome (Mather and Plossl, 1978).

2.5.2 Constant Work-In-Process (ConWIP)

The basic idea of the pull based ConWIP is to keep WIP at each production routing at a constant level where WIP is measured in capacity demand of the bottleneck resource of the line (Spearman et al., 1989). So each routing becomes a constant work-in-process (or ConWIP) line. Once the WIP level for each line is determined, orders are released to a line only if old orders have been finished by the line. This can be interpreted as a pull system and, as in Kanban cards, can be used to trigger the release decisions. Like Kanban, ConWIP is a variant of workload control. Since the WIP level is measured in capacity units, the product mix may change and the assumptions concerning the production environment are less restrictive than for Kanban. ConWIP is a continuous shop floor release method. Cards regulate the flow of work, but are not 'part number specific'. Instead they are 'job number specific' staying with a product or batch through the whole length of the process, making it a more manageable method when there is high variety.

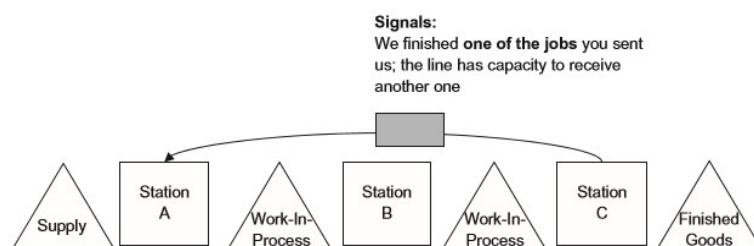


Figure 15: Example of a ConWIP PPC system.

ConWIP is a straightforward solution for controlling the flow of jobs. However, there are important restrictions on its applicability. Since there is only one loop, all jobs need to enter the shop at the same station and leave the shop at the same station. The flow should also not be split and the number of stations in the loop should not be too long (Hopp and Spearman 2001). As a result, ConWIP essentially only applies to a pure flow shop where all jobs visit all stations in the same sequence. ConWIP does not apply to shops with high processing time variability since it does not support load balancing (Germs and Riezebos 2010). ConWIP does not apply if stations are decoupled since this would require a WIP limit for each station. ConWIP only provides a limit for the shop in the form of the number of cards or jobs. Therefore, ConWIP only applies to an order control problem. Fowler et al. (2002) consider Kanban to be throughput control oriented while ConWIP is naturally more focussed on WIP. Nevertheless, ConWIP can provide a greater throughput than Kanban (Spearman and Zazanis 1992). In comparing ConWIP with push alternatives, Spearman et al. (1989) conclude that the stability of ConWIP is preferred at the expense of a slightly higher average level of WIP, since WIP in the push system fluctuates and its performance deteriorates more quickly when control is reduced. Gaury et al. (2000) consider modelling and optimization to be much easier for ConWIP than for Kanban. ConWIP only requires the determination of one parameter (Tardif and Maaseidvaag, 2001), since a single level of WIP is set for the whole system. Under ConWIP, some standardization of products is needed because if the number of cards is to regulate the level of WIP, the workload represented by each card will have to be similar. Gaury et al. (2000) conclude that a

disadvantage of ConWIP is that WIP levels inside the system are not controlled individually. ConWIP as an approach is of greater applicability to the MTO industry than Kanban. However, it is again questionable whether the hierarchical control system can provide the necessary control at the customer enquiry, job entry and job release stages. Kanban is most useful for the pure flow shop, while CONWIP may be of more relevance in the general flow shop.

2.5.3 Paired cell overlapping loops of cards with authorization (POLCA)

Paired cell Overlapping Loops of Cards with Authorization (POLCA; e.g., Suri, 1998; Riezebos, 2010) is a hybrid push–pull card-based signalling system emphasizing the reduction of lead times, cutting product costs and increasing due date adherence. Using the POLCA philosophy, cards are placed in pairings where jobs travel in one direction and information returns in the other. It is aimed at highly engineered production, small batches and high product variety (Suri 1999). The system was designed to cope with more variability than Kanban and ConWIP and only accounts for routing variability. Suri (1998) argued that to achieve efficient control in production environments with high variety or custom engineered products, new strategies that combined the features of push/MRP and pull/Kanban were needed. He proposed the POLCA system as an effective material control system for such environments. POLCA represents an extension of a Kanban system that allows a station to enter into a control loop with more than one station but, in a pure flow shop, POLCA and Kanban systems are the same. POLCA was argued to be an alternative to Kanban specifically for the context of Quick Response Manufacturing or time-based competition (Suri, 1998). It is different from the other card-based systems in the sense that it combines a card-based component with a material requirement planning (MRP) system. It is therefore described as a push/pull system. POLCA cards are ‘cell specific’ operating between pairs of cells staying with a job on its journey between them and can belong to more than one fixed pairing, allowing routing flexibility. Suri (1999) explains that the cards bring back information signalling the capacity at the partner cell so the destination cell will always have capacity.

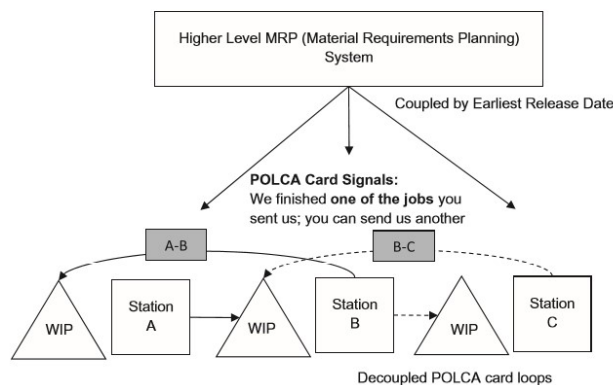


Figure 16: Example of a POLCA PPC system (decoupled POLCA loops coupled by an MRP system).

Several researchers have investigated the benefits of the POLCA system. Pieffers and Riezebos (2006) provide a critical description of the main features of POLCA, and Vandaele et al. (2008) provide details on the design and performance analysis of a system operating under POLCA control. Fernandes and Carmo-Silva (2006) conduct simulation experiments to compare performance of POLCA with other systems. POLCA links MRP with the shop floor, thus the reservations described earlier regarding MRP apply here too, although without higher level planning its applicability would be limited. Limited discussion suggests that POLCA may be of relevance to the MTO industry based on its allowance for non-repeat production. As with other production signalling methods, POLCA relies on assistance at the higher planning levels to determine delivery dates based on workloads and capacities at the customer enquiry stage. Similarly, it needs to be incorporated with other methods if it is to address job entry and job release. Lödding et al. (2003) and Harrod and Kanet (2013) showed that POLCA leads to blocking when there is high routing variability. If routing variability is high, two work centers can block each other whereby neither is able to free up the cards that the other

requires. So POLCA appears to be more suited to a flow shop rather than a job shop and hence is only a solution for a RBC company.

POLCA has remained largely unchanged since its introduction (Riezebos 2010). One of the few improvements reported has been the introduction of colour-coded cards by Pieffers and Riezebos (2006). Stations are given a specific colour, meaning each POLCA card consists of two colours. Meanwhile, Vandaele et al. (2008) presented an approach for setting the number of POLCA cards in accordance with expected demand in the context of an electronic POLCA system. There exists no simulation study assessing the actual performance of a (complete) POLCA system. Analysis of the underlying control mechanism reveals that POLCA is equivalent to a Kanban system with job-anonymous cards. This means that largely the same limitations apply. Each routing step should be represented by a POLCA loop. So routing variability must be low for POLCA to be effective. In addition, POLCA may lead to blocking if there are feedback loops in the routing. POLCA systems should only be applied to production lines with simple, directed routings. POLCA systems do not incorporate load balancing, which impedes their application if processing time variability is high (Germs and Riezebos 2010).

2.5.4 Control of Balance by Card Based Navigation (COBACABANA)

Most card based systems concentrate on controlling the shop floor. They neglect other planning tasks, like estimating short, feasible due dates during customer enquiry management. A card-based version of WLC, COBACABANA (Control of BALance by CARD-Based Navigation), was proposed by Land (2009) to overcome this shortcoming. COBACABANA uses cards for due date setting and order release, making it a potentially important solution for small shops with limited resources for implementing the core principles of WLC in practice. Many of such firms operate as flow shops rather than job shops. COBACABANA includes two control stages, order acceptance and order release. COBACABANA establishes card loops between the planner responsible for order release and each work center. The availability of cards authorizes the planner to release new orders onto the shop floor feeding back information about production from the shop floor to a central planner, providing a visual control mechanism for the shop floor. Since card loops are decoupled from the routing characteristics of jobs, all possible routing permutations can be accommodated. COBACABANA creates a mix of jobs on the line that balances the workload across stations. This is supported by release cards on a planning board. The use of a centralised release function avoids problems with the propagation of information that is inherent to a Kanban system in the order control problem. COBACABANA was developed independently from the literature on card-based control systems. So it emerged from the separate stream of WLC literature. It is specifically suited for order control in high-variety contexts and it allows processing time variability to be accommodated.

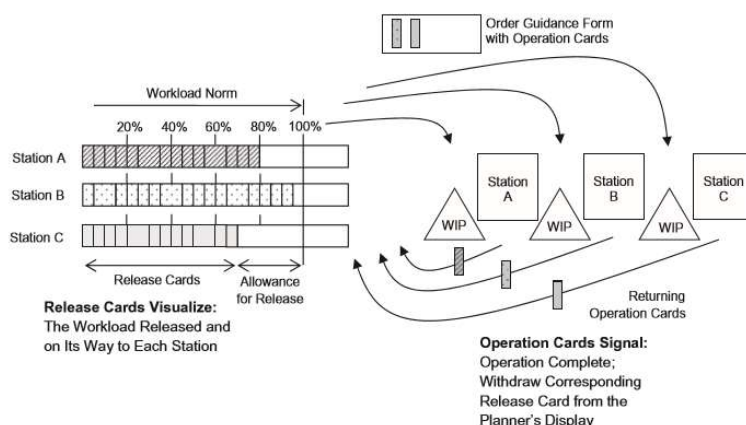


Figure 17: Example of COBACABANA PPC system.

Different cards are maintained for each work center. For example, cards can be colour coded with a different colour used for each work center (Riezebos, 2010). Under COBACABANA, cards represent a certain amount of workload. Each card represents the same amount of workload, but multiple cards

can be assigned so that the workload of each operation in the routing of an order is accurately represented. Orders are considered for release at periodic time intervals. To release an order, the planner must attach the right number of cards for each work center in the routing of an order to an order guidance form that travels with the order. The cards related to a certain work center return to the planner after the completion of the corresponding operation. An order can only be released from the pool if sufficient cards are available for each of the work centers in its routing. By controlling the number of cards in circulation and set them equal to 100% of the workload norm, the workload is controlled. Thus, COBACABANA balances the workload as part of the order release decision making process. This load balancing, or workload smoothing, corresponds to one of the main principles of heijunka in lean operations (Marchwinski et al., 2008) and prevents surges in work that temporarily deplete the capacity buffer and increase the inventory buffer in the form of WIP. COBACABANA is based on the WLC concept, which has been shown to significantly improve the performance of shops both through simulation (Thürer et al., 2012, 2014, 2015) and in practice (Hendry et al., 2013). WLC and COBACABANA were designed to achieve the same levelling of workload to capacity that is achieved in repetitive manufacturing using lean tools, but while also allowing the company to offer highly customized products to its customers. It reduces the variability of the incoming workload that results from product customization rather than limiting variation in the product mix itself (Thürer et al., 2014). COBACABANA has the potential to improve flow shop performance, but its due date setting procedure should be adapted compared to job shops. In a flow shop, due date estimation can also be further simplified by considering the load awaiting release to the first station only while maintaining most performance benefits. COBACABANA could result in many cards, as cards are related to workloads rather than products and so many cards may be required to represent all possible processing times. The original COBACABANA concept was presented prior to recent advances in WLC theory (Thürer et al., 2012) that have significantly enhanced the potential of WLC to improve performance.

Two main weaknesses have been identified with the original design of COBACABANA. Multiple cards were required to represent the workload of one operation of an order, which may lead to a substantial number of cards having to travel with an order through the shop. Secondly, it was based on WLC using periodic releases only, which may lead to premature work center idleness (Land and Gaalman, 1998). COBACABANA incorporates both a periodic and a continuous release time element. Periodic release allows the workload to be balanced, while continuous release avoids premature work center idleness or starvation. COBACABANA uses load balancing to avoid starvation while simultaneously reducing and stabilizing WIP levels, thus aligning input with output. COBACABANA is argued to yield the most benefits compared to 'traditional' card-based systems in pure flow shops (Thürer, Stevenson and Protzman, 2015). Performance improvement in flow shops can be obtained by just considering the load waiting in the pool that is to be released to the first (gateway) station (Land, 2009). This makes COBACABANA even simpler and further enhances its applicability to shops in practice. Pure flow shops will benefit the most from the unique load balancing capabilities of COBACABANA's release method (Thürer et al, 2016). Small shops with limited resources often struggle to implement Manufacturing Resource Planning (MRP) or Enterprise Resource Planning (ERP) software for higher level planning (e.g. Aslan, Stevenson, and Hendry 2015). The simple card-based solution provided by COBACABANA could potentially take over this role in the future.

Customer enquiry management performs two functions within COBACABANA. First, it stabilises the planned workload by controlling the acceptance of orders. Second, it ensures short, feasible delivery time allowances or due dates. Thürer et al. (2014) demonstrated that these two functions can be combined if due dates are feasible and reflect a company's actual operational capabilities. Order release divides the planned workload into two parts, the load in the pre-shop pool and the load on the shop floor. The delivery time allowance can be divided into an allowance for the pre-shop pool waiting time and an allowance for the shop floor throughput time. COBACABANA uses the order release mechanism to control the amount of work on the shop floor. Variability in the planned workload is shifted from the shop floor to the pre-shop pool (Melnik and Ragatz 1989; Thürer et al.

2012). Therefore, only the pre-shop pool waiting time is considered to vary. Since the shop floor workload is stabilised, the allowance for the shop floor throughput time (i.e. the time from release to completion) is a constant. COBACABANA originally integrated order release with an order acceptance stage has not been tested through simulation yet.

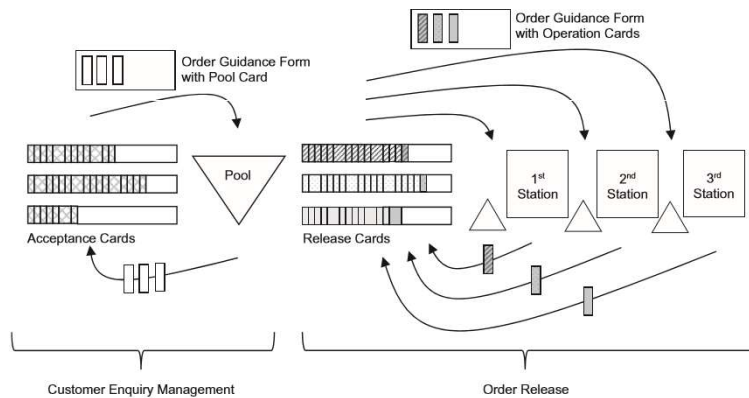


Figure 18: Example of integrated COBACABANA card loops between customer enquiry/order release and order release/stations on the shop floor (Thürer et al, 2015).

2.6 Production performance optimization

For any production system, the efficiency is measured through a function of related factors. These factors must establish close relationship with the focused problem. These factors individually or jointly represent the performance. From the study of Berkley (1992) it is inferred that the average WIP, average flow time, mean cumulative throughput rate and weighted earliness of the job are frequently used as performance measures. Yavuz and Satir (1995) have used seven factors in their study and includes the factors given by Berkley. In the following table 1 the factors that have been found in literature involving manufacturing operational performance are defined and optimisation of any of these measures will improve production performance.

Table 1: Definitions of performance measures involving production efficiency.

Nr.	performance measure	definition
1	mean cumulative throughput rate	ratio of total satisfied demand to the total generated demand
2	mean total production lead time	average amount of time spent by an order from entering the system until completion
3	mean total demand satisfaction lead time	ratio of orders that are delivered on time to the total delivered orders
4	mean utilization of line	mean utilization of the last station in the line
5	mean setup/run time ratio of line	ratio between the setup time and the run time of last station
6	mean total WIP length	mean of all in process levels for the products excluding finished products
7	mean total waiting time	waiting time of all products in the process

In periodic production systems, the main problems with planning are the uncertainties and variations in the manufacturing lead times. These are at the heart of production scheduling. Manufacturing lead times in periodic production systems are often long. Yet the actual processing times can be quite small. Most firms do have an enterprise resource planning (ERP) system with information on the set-up times of machines and (estimated) processing times of jobs at these machines. However, this information is not sufficient to determine the main component of work center throughput time, that is the waiting times. The manufacturing lead times are dominated by the transit times between operations. This is demonstrated by the speed with which urgent orders can be expedited through the system when required. Stommel (1976) showed that about 90% of the total flow time is due to transit times, of which 85% is due to queuing, 3% to quality control and 2% to transportation. Only 10% is due to actual processing operations. This is mostly due to variability in order sizes, the number of transformation processes needed per order and the stochastic inter-arrival times between enquiries and orders. With the widespread efforts to reduce the WIP level throughout the value chain, on-time delivery gains importance (Lödding and Wiendahl, 2003). The problem of determining planning values for manufacturing lead times is mainly a problem of discovering the underlying

factors that influence these inter-operation transit times. At the long-term planning level, lead times are determined by factors like the product structure, the production process and the lay-out of the production facility. At the operational level, the factors that influence inter-operation transit times have been classified by Heinemeyer (1974) into short-term, medium-term and non-quantitative (machine break-downs, missing material, absences etc.). Examples of short-term influence factors are batch quantity, processing time, set-up time, priority rule, due date, etc. Research of Tatsiopoulos and Kingsman (1983) concluded that none of these short-term factors have a significant influence on transit times. The general conclusion is that the medium-term influence factors are by far the most important, these are backlog of work in the shop and capacity planning method among other factors. Riezebos (2010) states that actual throughput times are highly affected by capacity utilization, variation in processing times, batch sizes, work content and capacity control measures. Soman et al. (2004) explain that the main operational issues for MTO companies are capacity planning, order acceptance/rejection and attaining high due date adherence. This exploratory study provides quantitative information from controlled experiments across a range of representative plant environments that is useful in identifying the critical factors for improving performance in a production environment. For representative plant environments, the factors seem to be lot sizes, setup times, yield losses, workforce flexibility, degree of product customization, and product structure. Working with these factors to "shape" a manufacturing environment with more uniform workflows and flexibility to adjust to changing capacity requirements is the key to improving performance (Krajewski et al., 1987). Table 2 gives an overview of the factors that are mentioned in literature involving manufacturing operational performance divided by planning level.

Table 2: Factors involving production operational performance.

Nr.	planning level	factor
1	long term	product structure
2		production process variability
3		degree of product customization
4		lay-out of production facility
5	medium term	capacity utilisation
6		variation in processing times
7		work content
8		capacity control measures
9		backlog of work in the shop
10		capacity planning method
11		order arrival variability
12		workforce availability and flexibility
13	short term	batch sizes
14		processing time
15		setup time
16		transfer time
17		priority rule
18		due date adherence
19	non-quantitative	machine break-down
20		missing material
21		absences

2.7 Lead time reduction and WIP balancing

Soman et al. (2004) explain that the competitive priority is often shorter delivery lead times. Tatsiopoulos and Kingsman (1983) conclude that lead times are determined by both order backlogs, that is input, and by capacity, that is output. A widely known method for keeping WIP on a pre-determined level is Input/output Control (Belt, 1976; Wight, 1974). Figure 19 shows the interdependency between output, lead time and WIP of a production system (Nyhuis, 1991).

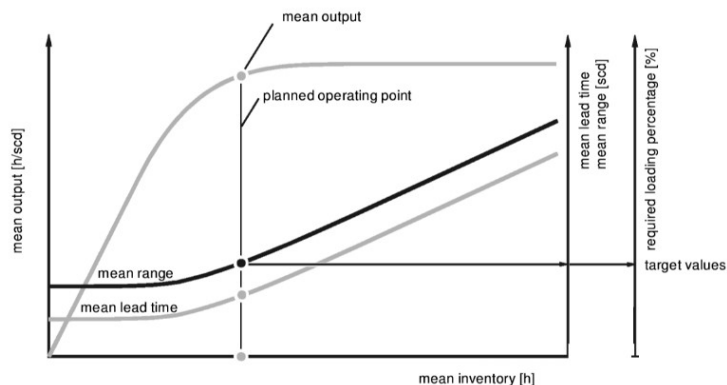


Figure 19: Interdependency between output, lead time and WIP (Nyhuis, 1991).

Actual lead times in a production system can be influenced in many ways, but the impact of the actual workload is clearly dominant. This explains why WLC rules or workload-oriented release rules have become popular. WLC aims at reducing both the average shop time and its variability by releasing orders only when the workload on the relevant machines does not exceed a certain limit. However, the overall lead times of jobs may still vary significantly dependent on the shop workload. The problem is only shifted because a job is waiting within the production process if some bottleneck cannot handle it in time where it increases overall lead times (Zijm and Buitenhok, 1996).

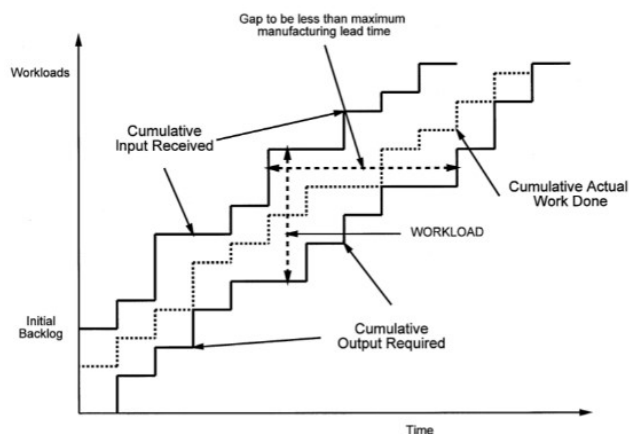


Figure 20: The need to plan work to inputs and outputs rather than work per period.

Fixed lead times can only be maintained by influencing either the required or the available capacity. Order acceptance procedures based on actual workload information offer a natural way to influence demand but are useless if no accurate workload information is available. Altering process plans to shift work from bottleneck to non-bottleneck machines offers another possibility but this requires extremely sophisticated process planning systems. In PPC, output control decisions can dedicate capacity to capacity groups. Capacity changes are generally triggered by large sets of orders, tending to be delivered late. Therefore, output control decisions usually focus on controlling the average lateness of orders. Lateness is defined as the conformity of a schedule to a given due date (Baker, 1974). It is measured by subtracting the promised delivery time from the realised throughput time. Positive lateness (orders are delivered late) and negative lateness (orders are delivered early) can be distinguished. The role of respectively reducing the average and the variance of lateness is illustrated by figure 21. This figure represents a distribution function of lateness. The vertical line indicates zero lateness. Orders right to this line are delivered late and the shaded area represents the percentage of orders delivered late. The percentage of orders delivered late can be decreased by reducing the average lateness (Figure 21b), and/or by reducing the variance of lateness (Figure 21c).

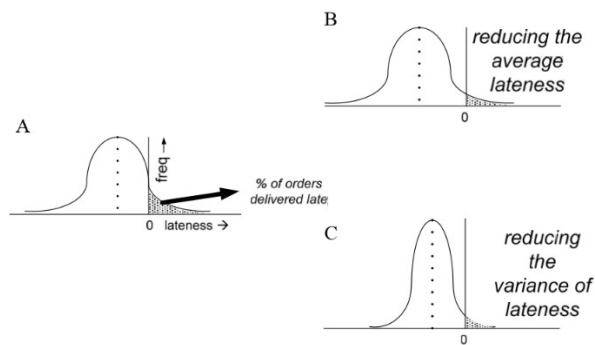


Figure 21: Influence of the average lateness and the variance of lateness.

Input and output control decisions can influence both the average lateness and the variance of lateness. Soepenbergh (2010) proposed a framework within the WLC concept how PPC decisions control the average lateness and the variance of lateness. For each PPC decision the influence on the average lateness and the variance of lateness can be specified.

Table 3: How PPC decisions enable control of the average lateness and the variance of lateness (Soepenbergh, 2010).

PPC decisions	Controlling average lateness	Controlling variance of lateness
Delivery time promising	Promised delivery times based on shop-floor status (e.g., current WIP) of the company	Taking order-related information (e.g., NOP) into account when promising delivery times
Order acceptance	Controlling the number of orders accepted within a certain period	Controlling the number of orders with specific characteristics accepted
Release	Considering those orders that provide capacity groups with good load balance over time	Considering the relative urgency of orders at release
Priority dispatching	Using priority rules that focus on accelerating throughput (e.g., SPT/WINQ)	Using priority rules that focus on reducing variance of lateness (e.g., EDD/ODD)
Output control	Dedicating capacity to those resources where orders are congested	Dedicating capacity to meet the peak requirements of specific orders

Throughput time, and thus lead time, reduction can be a daunting task due to the many factors that influence it and their complex interactions. Johnson (2003) presents a conceptual framework that illustrates these principles. The framework illustrates the factors that influence throughput time, the actions that can be taken to alter each factor, and their interactions. The framework is detailed enough to provide guidance to a practitioner on how to reduce throughput time, while being general enough to apply to most situations. In figure 22 a selection of this framework is given for factors that influence waiting time in a production system as they dominate the total lead time as specified above. The total framework covers all production performance measures found in literature on the different planning levels as proposed in table 2.

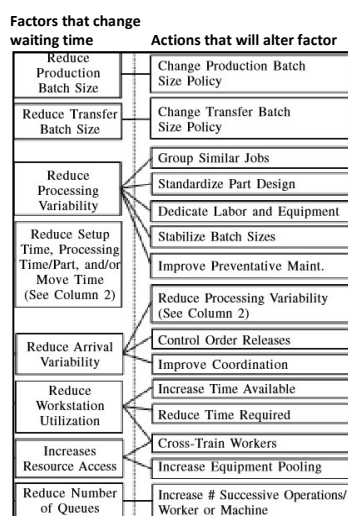


Figure 22: Throughput time reduction framework (Johnson, 2003).

2.8 Applicability of PPC in the case company

The current PPC setup of BaseClear as described in chapter 1 can be classified as a push system. Push systems perform better under demand uncertainty and order size variability, but in pull systems WIP levels are limited and WIP variability is reduced. From a practical standpoint, a pull system is easier to control than a push system. However, pull based systems are often difficult to implement in case of long lead times. Most practical PPC systems consist of both push and pull. Concerning these theoretical findings, it is concluded that the ideal situation for the case company BaseClear would be a hybrid push/pull production system to combine WIP balancing and lead time reduction capabilities.

RBCs produce customised products for each of their customers on a continuing basis, with a regularity of demands. RBCs tend to have a relatively small customer base and compete for the initial order of a continuing supply contract. Products can be customized but may be more than once predictable. Within RBCs there is a medium amount of volume and medium variety of products. BaseClear offers services with a degree of predictability on a continuing basis, but also offers possibilities for customised products for each of its customers. Therefore, the case company BaseClear can be classified as an RBC.

There are reservations regarding the use of MRP-based PPC systems in the MTO industry. Company size has been identified as an important factor for successful implementation. Capital investment and the impact on SMEs of a failed ERP implementation strategy may be an entry barrier for ERP into SME. It may be possible to tailor the design of an MRP system to the needs of a MTO company to some extent, however this would add to the expense. Since the case company BaseClear is a SME in the MTO industry it is concluded that a MRP-based PPC system is not a perfect fit to solve the business problem. TOC is applicable to highly customized industries and able to reduce lead times and improve delivery performance. Literature shows that TOC performs better than MRP within a pure flow shop. In the general flow shop of BaseClear it is likely that bottlenecks will remain relatively stationary and deterministic. Therefore, it is concluded that TOC is not an optimal PPC approach for the case company to solve the business problem. The WLC approach stabilizes the performance of a flow shop and makes it independent of variations in the incoming order stream like in the case company. In general, as variability increases, WLC becomes more applicable and it can lead to the reduction of WIP. WLC reduces the variability of the incoming workload that results from product customization rather than limiting variation in the product mix itself and therefore product customization within the case company can be maintained. WLC is designed for MTO type production environments and can be an effective method of controlling WIP and reducing lead times, accommodating non-repeat production and variable routings like in the case company. Besides these capabilities the simplicity of the concept in practise would be appreciated by the NGS production manager. WLC is likely to be cheaper to implement within a SME than MRP. Therefore, it is concluded that WLC is the most appropriate PPC approach for a general flow shop production RBC company in the MTO sector like BaseClear, that can contribute to solve the business problem. Table 4 summarizes the selection criteria for the preferred PPC concept for the case company.

Table 4: PPC concept selection criteria for the case company BaseClear.

	suitable for push/pull production	suitable for SME RBCs in MTO industry	suitable for optimizing general flow shops	applicable to variability
MRP	+	-	-	+
TOC	+	+	+/-	+/-
WLC	+	+	+	+

Literature shows that the following three factors have the greatest impact on which card-based control system should be chosen for a given context: routing variability, processing time variability and inventory vs order control. Within the case company there is a high routing variability as can be seen in figure 2, high processing time variability as can be seen in figure 3 and order control applies. Besides these three factors also load balancing capabilities are evaluated for each of the four card-based PPC concept that have been reviewed to determine applicability for the business problem within the case company.

Kanban: These systems are widely applied and tested in practice. They are the first choice for controlling confluent product/service flows. They are also a powerful solution for the control of independent product flows if each station is decoupled. However, performance is jeopardised if the flow of individual orders needs to be controlled since Kanban cards represent direct and indirect workload. In general, routing variability should be low as should processing time variability. Kanban control is only a good idea for fast moving parts and Kanban systems suffer from a lack of load balancing capabilities, which hinders their application even to pure flow shops if there is variability. In environments with custom products, changing product mix, infrequent orders, or highly variable demand like in the case company, Kanban is not a reasonable assumption. Much of the available literature addresses one of the main weaknesses of Kanban systems and that is sensitivity to processing time variability. Considering these comments, it is concluded that Kanban is not the most optimal card-based PPC for BaseClear to solve the business problem.

ConWIP: This is a simple, straightforward solution for controlling the flow of individual orders. It is arguably the simplest card-based control system, requiring the fewest parameters to be set. However, it can only be applied in a pure flow shop since it uses a single loop. ConWIP does not apply to shops with high processing time variability since it does not support load balancing. Under ConWIP, some standardization of products is needed because if the number of cards is to regulate the level of WIP, the workload represented by each card will have to be similar. A disadvantage of ConWIP is that WIP levels inside the system are not controlled individually. ConWIP as an approach is of greater applicability to the MTO industry than Kanban. Kanban is most useful for the pure flow shop, while ConWIP may be of more relevance in the general flow shop. However, considering the comments above it is concluded that ConWIP is not the most optimal card-based PPC for BaseClear to solve the business problem.

POLCA: This provides a solution that enhances an existing MRP system. It extends the use of a Kanban-based inventory control system for order control. However, POLCA may introduce blocking if the routing includes feedback loops. POLCA can only be applied when there are simple, directed routings. It also requires an MRP system, and the earliest release date calculated by the MRP system may introduce starvation. Like Kanban and ConWIP, POLCA does not provide support for load balancing, which impedes its use when there is processing time variability like in the case company. POLCA leads to blocking when there is high routing variability. Considering the comments above it is concluded that POLCA is not the most optimal card-based PPC for BaseClear to solve the business problem.

COBACABANA: This is argued to be the first choice for complex (high routing and/or processing time variability) order control problems. The loop structure allows for all possible routing permutations. Moreover, the centralised planning board gives an overview of the current load situation on the shop floor, which supports load balancing. However, it is arguably more complex than the Kanban and ConWIP systems. COBACABANA also provides a means for estimating delivery times. It is specifically suited for order control in high-variety contexts and it allows processing time variability to be accommodated. COBACABANA systems were designed to offer highly customized products to its customers and includes load balancing capabilities. Considering the comments above it is concluded that COBACABANA is the most optimal card-based PPC for BaseClear and could contribute to solve the business problem.

Table 5 summarizes the card-based PPC concept selection criteria for the case company BaseClear.

Table 5: Card-based PPC concept selection criteria for the case company BaseClear.

	high routing variability	high processing time variability	order control	load balancing capabilities
Kanban	-	-	-	-
ConWIP	+/-	-	+	-
POLCA	+/-	-	+	-
COBACABANA	+	+	+	+

2.9 Summary exploration of theory

A literature review has been performed on theories and concepts of PPC to discuss what factors are applicable in the context of the general flow-shop of BaseClear to balance WIP and control lead times. At first, general theories of PPC have been explored and an outline of the difference between pull and push based production systems was given. The review continued with a classification of companies within the MTO industry. The case company BaseClear was classified as a Repeat Business Customizer (RBC) and it was concluded that the most optimal production system for BaseClear should be based on a combination of pull/push production principles to combine WIP balancing and lead time reduction capabilities. Three PPC concepts from the perspective of the MTO industry were reviewed, including Material Requirements Planning, Theory of Constraints and Workload Control. A critical review was performed considering shop configuration, company size, customization and provisions for the customer enquiry, job entry and job release stage. In the MTO situation PPC is complex because of the number of variables involved. There is often a high level of variability with respect to the routings and processing times like in the case company, so it is difficult to predict how the work will be distributed among the various machines at any point in time.

In summary, the following criteria are proposed as the main requirements of a PPC system for the Small and Medium Enterprise general flow shop of BaseClear to balance WIP and control lead times:

1. Inclusion of a customer enquiry stage for delivery date determinations and capacity planning.
2. Inclusion of a job entry and job release stage, focusing on due date adherence.
3. Ability to cope with non-repeat production, i.e. (highly) customized products.
4. Ability to provide PPC for variable shop floor routings.
5. Suitable for push/pull production.
6. Suitable for optimizing general flow shop performance of SME RBC's in the MTO sector.

Based on these criteria it is concluded that a sophisticated PPC approach like WLC is required for the case company that can contribute to better balanced WIP and reduced lead times in the complex production situation of BaseClear.

The literature review continued with an overview of four main card-based production control systems: Kanban, CONWIP, POLCA and COBACABANA. In appendix D a summary and comparison of the four card-based signalling systems is given. One of the key issues in efficient design of production systems with MTO products is the ability to use card-based signals to effectively control the workload in the system. The application of cards within PPC systems is typically restricted to either controlling the release of orders or to control the shop floor. Because of its load balancing capabilities and ability to deal with high processing time variability and high routing variability like in the case company, COBACABANA was classified as the most suitable card-based PPC concept to implement within the case company BaseClear that can contribute to balanced WIP and reduced lead times.

In the last section of the literature review areas of production performance optimization, including load balancing and lead time reduction of general flow-shops were discussed. At the long-term planning level, lead times are in aggregate determined by factors like the product structure, the production process and the lay-out of the production facility. At the operational level factors have been classified into short-term, medium-term and non-quantitative (machine break-downs, missing material, absences etc.). Examples of short-term influence factors are batch quantity, processing time, set-up time, priority rule, due date, etc. The general conclusion is that the medium-term influence factors are by far the most important to solve the business problem, these are among others backlog of work in the shop and capacity planning method. The impact of the actual workload is the most dominant factor. Input and output control decisions can influence both the average lateness and the variance of lateness of orders. A framework how PPC decisions can influence the average lateness and the variance of lateness and a second framework with factors that influence throughput time and the actions that can be taken to alter each factor were proposed. Besides factors that influence lead time seven factors have been found in literature that involve

manufacturing operational performance. Optimisation any of these measures will improve production performance.

The literature research will be finalized with a theoretical model of factors to balance WIP and reduce lead times and an outline of potential suitable solution concepts that can be used in the context of BaseClear which will serve as a basis to solve the business problem. The following two sections will give an answer to the first two sub research questions.

2.9.1 Theoretical model

In this section, an answer will be formulated to sub research question 1 based on the theoretical research performed in chapter 2.

Sub research question 1: What factors of production planning and control theories are applicable in the context of BaseClear to balance WIP and reduce lead times?

To this end a theoretical model is given that is applicable in the context of BaseClear based on the literature review as described in the previous sections:

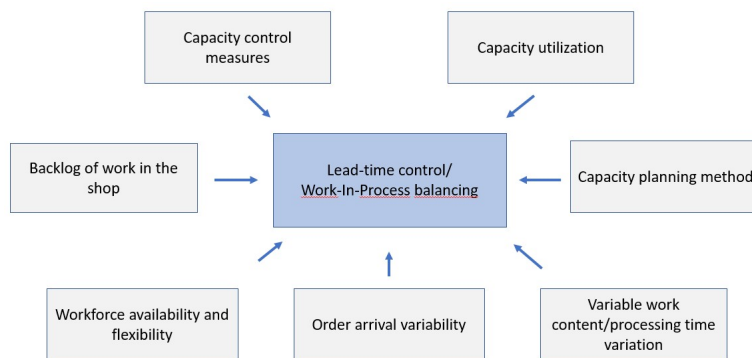


Figure 23: Theoretical model with factors that influence lead time and WIP.

When these factors are projected to the preliminary cause and effect model as represented in figure 4 of chapter 1 it can be concluded that there is overlap with the factors found in practice and the dominant factors found in theory on medium term level. Poor insight in operational performance corresponds to the need of capacity control measures and possibility of backlog of work in the shop. Limited capacity equipment, personnel and space corresponds to the need for controlled capacity utilization, workforce availability and flexibility. Lack of a standardized ERP with feedback relates to the need for a capacity planning method. A complex production layout with custom services and high variability relates to type of work content and processing time variation. And finally, variable workload with high peaks and poor insight in customer enquiries for medium-term planning, relates to order arrival variability.

2.9.2 Formulation of suitable solutions

In this section, an answer will be formulated to sub research question 2 based on the theoretical research performed in chapter 2.

Sub research question 2: What are, according to theory, suitable solutions that BaseClear can introduce to its current production planning and control that can contribute to achieving overall balanced WIP and reduced lead times?

From theoretical perspective, it is concluded that WLC in combination with COBACABANA are suitable PPC concepts for the high-variety and variable context like in the case company BaseClear that can contribute to solve the business problem. To ensure WIP balancing and lead time reduction, total workload must be controlled and should not exceed pre-set maximum limits. Managing lead

times using workload input/output control methods is needed and delivery time allowance can be divided into an allowance for the pre-shop pool waiting time and an allowance for the shop floor throughput time. Considered the factors from section 2.9.1 the solutions that can contribute to accomplish the business goal are summarized underneath:

- Determine optimal and maximum levels of workload for the job pool.
- Determine optimal and maximum levels of WIP within the shop.
- Determine release frequencies for the work orders to keep WIP at the pre-determined level
- Implementation of COBACABANA as a visual workload input/output decision control method by introducing a centralised planning board for an overview of the current workload situation in the job pool and the shop floor. The number of cards should be set equal to 100% of the workload norm and the number of cards in circulation controlled.
- Improve the customer enquiry stage (order acceptance/job entry stage) to control the input of work to the job pool based on levels of WIP within the shop.
- Introduce centralized order release control at the job release stage as the main control point crucial to simplify the remaining planning and control process.

3 RESEARCH METHODOLOGY

The goal of this chapter is to combine the knowledge of the case company and its business problem, as provided in chapter 1, with the literature research performed in chapter 2, to determine the research methodology and strategy by which the research objective can be achieved. The research strategy as given in the following section is based on the objective, method and approach of the research. The chapter concludes with the operational project plan that will be performed.

3.1 Research strategy

A case study has been determined as the most suited strategy for this research which involves an empirical investigation of a contemporary phenomenon within its real-life context using multiple sources of evidence (Robson, 1993; Yin 2003). A case study is a holistic approach to research and when the approach is applied correctly, it becomes a valuable method to develop theory, evaluate programs and develop interventions (Baxter & Jack, 2008). Gerring (2004) defined a case study as an intensive study of a single unit for understanding a larger class of (similar) units. Although case studies are criticized McCutcheon and Meredith (1993) found that case studies can be useful in operations management. Stake (1995) distinguishes three types of case study. An intrinsic case study aimed at a better understanding of the individual case, an instrumental case study using the individual case to develop new theoretical insights and a collective case study using many cases to test an existing hypothesis. This thesis is an intrinsic type of case study, since it aims at a thorough understanding of the individual case. Stake (1995) uses the term intrinsic and suggests that researchers who have a genuine interest in the case should use this approach when the intent is to better understand the case. It is not undertaken primarily because the case represents other cases or because it illustrates a trait or problem, but because in all its particularity and ordinariness, the case itself is of interest. The purpose is not to come to understand some abstract construct or generic phenomenon. The purpose is not to build theory, although that is an option (Stake, 1995).

The formulation of possible improvements to the production planning and control and their outcomes to the operational performance in this research will be guided by discrete event simulation analysis. Simulation is a numerical technique for conducting experiments on a digital computer, which involves logical and mathematical relationships that interact to describe the behaviour and structure of a complex real-world system over extended periods of time. Discrete event simulation is selected to analyse the effect of possible solutions because it is ideally suited for flexible systems which can describe the complex interactions among the resources and activities within the production process. At a discrete event simulation, the state of a system changes only at discrete points in simulated time. Furthermore, using probability distributions to create random arrival and

waiting times makes the model dynamic as well as stochastic because time plays a natural role (Kelton et al., 2014).

The simulation project approach as elaborated by Law (2008) will be used as a guideline for effectively performing the simulation. According to Law (2008) the use of a simulation model is a surrogate for experimentation with the actual system (existing or proposed), which is usually disruptive, not cost-effective, or simply impossible. The advantage of using a simulation approach is that it is easier to explain than mathematical programming models of optimization-based scheduling. Practitioners understand the logic of a simulation model because the simulation is intuitively based upon the behaviour of the actual system. On the other hand, a simulation will not account for randomness and therefore has large discrepancies between its forecast and reality which is a disadvantage of using a simulation approach. Despite its drawbacks, simulations found useful implementations (Hopp and Spearman, 1996). Regarding the design of the possible solutions, Van Aken et al. (2007) underline the need for sufficient data to make rational decisions. A valid model should be made of the future business system and a statement must be made concerning its expected performance. According to Law (2008) validation can be done for all simulation models. In figure 24 an overview of the seven steps of the simulation approach of this project can be found.

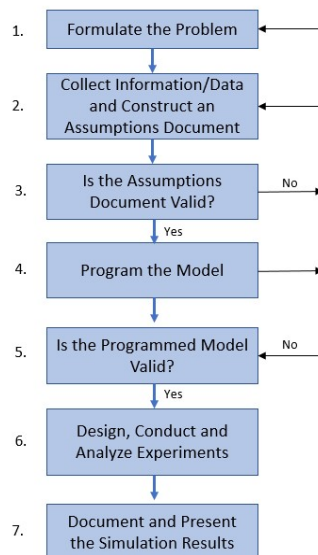


Figure 24: A seven-step approach for conducting a successful simulation study (Law, 2008).

These seven steps partly overlap the five stages of the intervention cycle ++ given in chapter 1. Since the intervention cycle ++ will be used as a guideline for the BPS project and the simulation will only be used to evaluate solutions for the business problem, the different steps of the simulation project approach are subdivided over the three stages that will be covered of the intervention cycle ++. Below the content of the relevant stages of the intervention cycle ++, including the different steps of the simulation project approach, are discussed.

3.1.1 Problem finding (simulation step 1)

During the first stage, the problem and its possible root causes are defined. The first chapter can be considered a deliverable of this stage. Data provided in chapter 1 is based on informal internal interviews with representatives of different departments as well as exploratory historical operational performance measures.

3.1.2 Problem diagnosis (simulation step 2-5)

After defining the problem, a further diagnosis guided by theory is required to empirically validate the business problem and its causes. The literature review in the second chapter makes part of this step. Furthermore, quantitative analyses can contribute to diagnosing the formulated problem.

Concerning the simulation, all required information and data must be collected. A conceptual model, a simplification from reality to something that can be modelled in a computer, should be made (step 2). Once all data is collected, assumptions of the simulation model are discussed with a selected audience of the NGS department and updated where needed to prevent unforeseen problems during the creation process (step 3). The fourth step of the simulation project approach requires the actual creation of the model using simulation software (step 4). Next, a validation of the created simulation model must take place to ensure that it is a good representation of reality (step 5). This includes comparing the results from the model with the expected outcomes. For this purpose, it is important to obtain a (rough) estimate of the main performance indicators outside the simulation software. This can be achieved by quantitative analyses of historical data, but also by doing some manual calculations. There will always be differences between manual estimates and simulation results. If these differences cannot be explained by making additional assumptions, the model should be re-evaluated, i.e. the input data and design of the model should be reconsidered going one step back. The deliverable of this stage is detailed knowledge on the background and nature of the problem and a validation of its causes as formulated in the first chapter. Furthermore, all necessary preparations are made for designing solutions using the simulation model that reflects the current processes. Chapter 2 and 4 of the thesis can be considered a deliverable of this stage. In chapter 4 an answer to sub research question 3 is formulated.

3.1.3 Design of solution (simulation step 6-7)

In this stage a design of solution is formulated. According to Van Aken et al. (2007) designing is the process of determining the required function of an object to be designed, combined with making a model of it. Especially the latter is applicable in this stage, since after the model passed its validation, experiments can be performed by changing certain parameters in the designed model. Changing parameters will create a new model to simulate the effect of possible solutions. Output analysis is about using an existing model correctly to obtain reliable results and should lead to a dominant solution which form the basis for the final recommendations. When significantly aberrant results are obtained while using the same model, reporting the experiments should be reconsidered until the output analysis fully makes sense. After creating a solution design using the simulation models an evaluation must take place to discover the impact on performance. In case of underperformance of a certain solution design, adjustments can be made based on the evaluation outcomes (step 6). The final step in the simulation approach is to analyse and report the simulation results (step 7). The deliverable of this stage is detailed knowledge of possible improvements that can contribute to the operational performance of the NGS department of BaseClear to balance WIP and reduce lead times. Chapter 5 of the thesis can be considered a deliverable of this stage. In chapter 5 an answer to sub research question 4 and 5 is formulated. The main research question is answered in chapter 6.

In table 6 a summary of the research approach and strategy can be found. This table can be used as a guideline for the thesis, briefly providing the goal of each step and methodology used for achieving this goal.

Table 6: Summary of the research strategy.

Intervention stage	Thesis chapter	Goal	Methodology	Objective
Problem finding	1	Find business problem and possible root causes	Informal interviews, exploratory operational performance analysis	Formulate research questions
Problem diagnosis	2	Building a theoretical framework and formulate suitable solutions	Literature research	Answer to sub research question 1 and 2
	4	Thorough operational performance analysis within the case context	Operational performance analysis, informal stake holder interviews	Answer to sub research question 3
		Building a validated simulation model of the current production process	Simulation modelling using historical reference input data	
Design of solution	5	Performing a simulation study to evaluate possible theoretical solutions	Dynamic, Stochastic, Discrete-event simulation study	Answer to sub research question 4 and 5
	6	Design and discuss solutions for the business problem and formulate recommendations for practical implementation		Answer to main research question

4 PROBLEM DIAGNOSIS

In this chapter an empirical validation of the business problem and its causes, guided by theory, is performed to find an answer to sub research question 3. To this end a data analysis is required as a first step towards overcoming the problems occurring in the NGS production process. Therefore, in section 4.1 the current performance of the production process is determined in terms of sample arrival distribution, lead time distribution, WIP distribution, batch scheduling and capacity utilization distribution, forming the basis for improvement. In section 4.2 the results are summarized and an answer to sub research question 3 is formulated. In section 4.3 a simulation model of the current NGS production process is build using Arena software (Rockwell). To this end the NGS production process is mapped and input data for the simulation model collected. Section 4.3 ends with the programming and validation of the simulation model based on the performance measures that are determined in section 4.1.

4.1 Performance analysis current NGS production process

A descriptive analysis of the NGS production process is performed using quantitative data. Historical sample arrival, lead times, Work-In-Process, batch scheduling and capacity utilization measures of the process is analysed. The historical data is accessed via the database of the LIMS that is used within the case company. To obtain valid and reliable results, all NGS samples that have been processed in the year 2016 are analysed and divided into the four different flows in the process that is given in figure 2 (Sequel, MiSeq PE300, HiSeq SR50 and HiSeq PE125). No data of other years was available to analyse seasonal factors. In 2016 a total of 2230 samples have been processed. These 2230 samples are divided over 280 different customer projects and equals 91 unique customers. The raw data can be found in appendix E.

The sample arrival will be determined in section 4.1.1. From table 1 the following performance measures will be determined for the four different process flows since literature shows, as discussed in chapter 2, these measures will give the most suitable information regarding solving the business problem: mean total production lead time, mean total demand satisfaction lead time, mean total WIP and capacity utilization. In section 4.1.2, the mean total production lead time and mean total demand satisfaction lead time is determined. In section 4.1.3, the mean total WIP is determined as the mean total waiting time for each NGS sample. Besides on these measures, the production process batch scheduling throughout the year will be discussed in section 4.1.4 and capacity utilization of the sequencer machines will be determined in section 4.1.5.

4.1.1 Sample arrival distribution

In this section the sample arrival distribution is calculated for the four different flows in the NGS production process. The sample arrival is defined as the mean total number of NGS samples that enter the production process.

In the following table the total number of NGS samples that have been processed in 2016 is given. The samples are divided over the four different process flows and the five different types of sample prep, as these two steps in the process mostly influence the total processing time and sample routing in the NGS production process (as can be seen in figure 2 and 3).

Table 7: Total number of NGS samples processed in 2016.

Sample prep	Sequel	Nextera XT	Amplicon	16S Profiling	TruSeq	Total
Process flow						
MiSeq PE300	0	201	0	771	0	972
HiSeq PE125	0	804	1	0	76	881
HiSeq SR50	0	0	0	0	232	232
Sequel	145	0	0	0	0	145
Total	145	1005	1	771	308	2230

These numbers confirm that there are two dominant flows within the process as discussed in chapter 1, namely Nextera XT sample prep to HiSeq PE125 sequencing (804 samples) and 16S profiling sample prep to MiSeq PE300 sequencing (771 samples).

In the next picture the total number of samples that arrived per month in 2016 is given for each NGS process flow. The samples are divided and coloured per sample prep type, to visualize the variability in sample prep and process flow of the production process. The Nextera XT sample prep is used for MiSeq PE300 as well as HiSeq PE125 sequencing runs and the TruSeq sample prep is used for HiSeq PE125 and HiSeq SR50 sequencing runs and therefore these prep types are visible in both pictures. For the HiSeq SR50 sequencing flow only TruSeq sample prep is performed and for the Sequel sequencing flow only the Sequel sample prep.

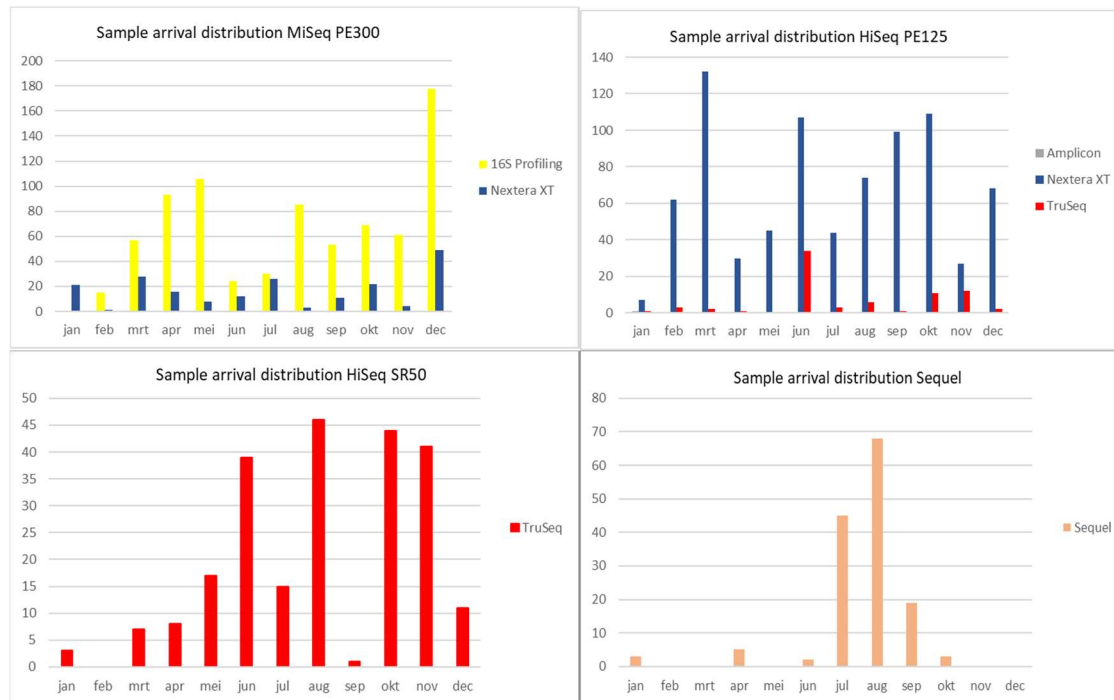


Figure 25: Sample arrival distribution for each NGS process flow divided per sample prep type.

As can be seen in figure 25 the sample arrival of each process flow is not equally distributed over the year, which means that there is a high variability in sample arrival. There seems to be a summer peak for the Sequel flow and the HiSeq SR50 and an end of year peak for the MiSeq PE300. These results have been discussed with the NGS production manager and based on his experience no yearly seasonal effect could be determined when compared to other years. There are no fixed periods of high peaks during the year, although there are peaks with high workload and periods of low sample arrival that sometimes even drop to baseline level for each production flow, randomly divided over the year. In general, a decreased sample arrival variability could be a potential solution for the business problem.

Table 8 shows the results of the mean and maximum sample arrival in days of the 4 different flows in the NGS production process divided per sample prep type. These numbers are used as input parameter for the simulation model that is built in section 4.3.

Table 8: Mean and maximum sample arrival per day of the 4 different flows in the NGS production process.

Sample prep type	Sequel		Nextera XT		Amplicon		16S Profiling		TruSeq	
Process flow	Mean	Max.	Mean	Max.	Mean	Max.	Mean	Max.	Mean	Max.
MiSeq PE300	0	0	1	25	0	0	3	95	0	0
HiSeq PE125	0	0	3	69	1	1	0	0	1	19
HiSeq SR50	0	0	0	0	0	0	0	0	1	25
Sequel	1	16	0	0	0	0	0	0	0	0

4.1.2 Lead time distribution

In this section the lead time distribution of the four different flows in the NGS production process is calculated. Total production lead time is defined as the total number of days between sample registration and data delivery of a NGS sample. Table 9 shows the results of the mean total production lead time of the four different flows in the NGS production process, divided per process step.

Table 9: Mean production lead time of NGS samples divided per process flow.

Flow	MiSeq PE300		HiSeq PE125		HiSeq SR50		Sequel	
	Lead time (days)		Lead time (days)		Lead time (days)		Lead time (days)	
Process step	μ	σ	μ	σ	μ	σ	μ	σ
Administration	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00
Sample QC	1,00	0,00	1,00	0,00	1,00	0,00	1,00	0,00
Sample prep	8,08	6,67	11,15	16,60	10,90	13,46	9,02	5,19
Library QC	4,01	5,40	7,14	10,00	3,99	6,88	3,08	4,27
Sequencing	8,58	9,65	7,17	9,32	6,80	7,83	11,97	13,35
Data analysis	5,00	0,00	5,00	0,00	5,00	0,00	5,00	0,00
Total	26,67	12,12	31,46	23,56	27,69	17,14	30,06	15,12

In figure 26 the lead time distribution of all samples that have been processed in 2016 is given. On the horizontal axis the registration date of each individual sample is given and on the Y axis the corresponding lead time of each sample in days.

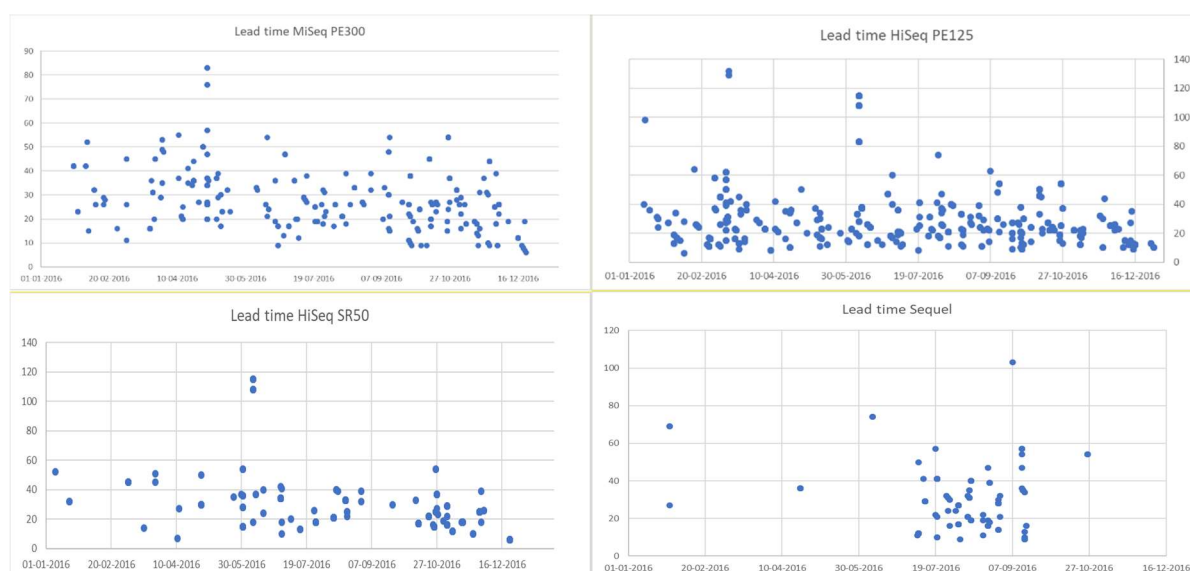


Figure 26: lead time distribution individual NGS samples in 2016.

Based on the data that is visualised in figure 25 and 26 no visual correlation of peaks in sample arrival to exceeding lead times could be determined. Lead time is randomly distributed over the year, although there is a slight negative trend visible towards the end of the year. Certain outliers are visible that influence the mean total lead time for each flow. After inquisition of the NGS production manager, these outliers can be explained by the need of replacements of samples that didn't pass the sample QC step. This customer consultation step introduced significant extra waiting time for some orders and is outside the influence of BaseClear.

Next, the mean total demand satisfaction lead time is measured and is defined as the ratio of samples and orders that are delivered on time to the total delivered number of samples or orders. For standard non-rush NGS sequencing orders a delivery time of 4-6 weeks is offered to customers in 2016, so on time delivery means that data of a sample is delivered within 28 – 42 days. Table 10 shows the results of the mean total demand satisfaction lead time of the four different flows in the NGS production process.

Table 10: Mean total demand satisfaction lead time of the 4 flows in the NGS production process on sample and order level.

		4-week delivery		6-week delivery	
	Samples processed	Samples delivered on-time	Demand satisfaction	Samples delivered on-time	Demand satisfaction
Process flow	#	#	%	#	%
MiSeq PE300	972	625	64,3	887	91,3
HiSeq PE125	881	559	63,5	685	77,8
HiSeq SR50	232	138	59,5	214	92,2
Sequel	145	74	51,0	129	89,0

		4-week delivery		6-week delivery	
	Orders processed	Orders delivered on-time	Demand satisfaction	Orders delivered on-time	Demand satisfaction
Process flow	#	#	%	#	%
MiSeq PE300	127	81	63,8	115	90,6
HiSeq PE125	199	147	73,9	177	88,9
HiSeq SR50	53	30	56,6	48	90,6
Sequel	48	26	54,2	42	87,5

Based on table 10 the promised lead time to customers for the NGS samples that have been processed in 2016 is achieved for about half to two third considering a 4-week delivery time, increasing to 78% until maximum 92% considering a 6-week delivery agreement. These measures confirm the business problem of structural exceeding lead times for the production process.

4.1.3 Work-In-Process distribution

In this section the Work-In-Process distribution of the four different flows in the NGS production process is calculated to gain more insight where in the production process the exceeding lead time arises. Work-In-Process is defined as the mean total waiting time of the NGS samples in the production process and is calculated as the lead time minus the optimal processing time. The optimal processing time is calculated as the total number of days if all processing steps are performed in one successive flow. The optimal processing time for the MiSeq PE300, HiSeq PE125 and HiSeq SR50 flow is 6 days, considering 1 day for the data analysis step. For the Sequel the optimal processing time is 10 days, considering 1 day for the data analysis step. Table 11 shows the results of the mean total waiting time of the four different flows in the NGS production process, divided over the different process steps.

Table 11: Mean production waiting time within the NGS production process.

Flow	MiSeq PE300	HiSeq PE125	HiSeq SR50	Sequel
	Waiting time (days)	Waiting time (days)	Waiting time (days)	Waiting time (days)
Process step	μ	μ	μ	μ
Administration	0,00	0,00	0,00	0,00
Sample QC	0,00	0,00	0,00	0,00
Sample prep	7,08	10,15	9,90	6,02
Library QC	3,01	6,14	2,99	2,08
Sequencing	6,58	5,17	4,80	7,97
Data analysis	4,00	4,00	4,00	4,00
Total	20,66	25,46	21,69	20,06

In figure 27 the processing time distribution of all samples that have been processed in 2016 is visualized in boxplots. On the horizontal axis the different processing steps can be seen and on the Y axis the corresponding processing time distribution in days. The sample registration and sample QC step are not included in the picture since the throughput times of these two process steps is constant.

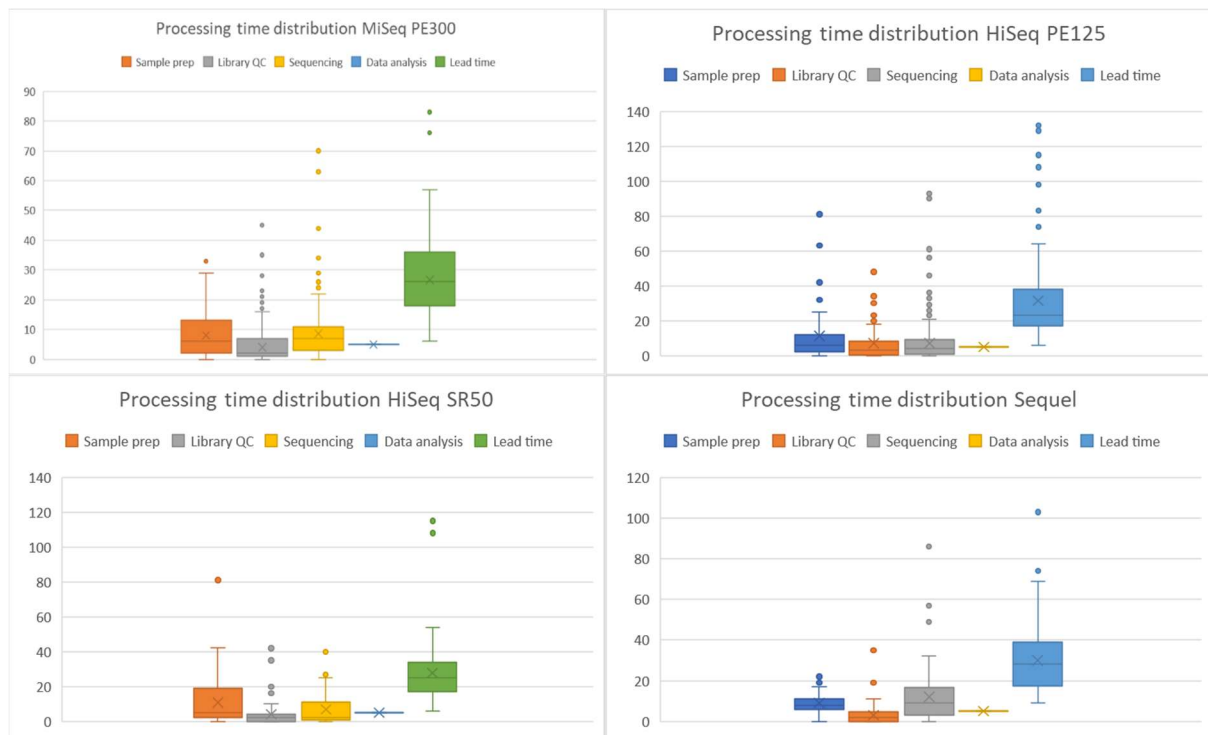


Figure 27: Processing time distribution of the NGS production process.

Based on these figures the waiting time is rather equally distributed over the total NGS production process and several outliers can be distinguished. The sample prep and sequencing step seem to have the most impact on the total waiting time. These figures have been discussed with the NGS production manager and this representation of reality matches his experience. Since sample arrival is highly variable and amount of human workforce limited, the different steps in the process are planned based on availability of personnel and number of samples waiting for each step in a custom weekly work schedule thereby considering due date expiration on individual order level.

4.1.4 Batch scheduling

In figure 28 an overview is given of the number of times a process step is initiated per month for each of flow in the NGS production process in 2016. This data gives more insight how the production is planned and performed over the year. The actual number of samples that are processed each time a process step is performed can vary.

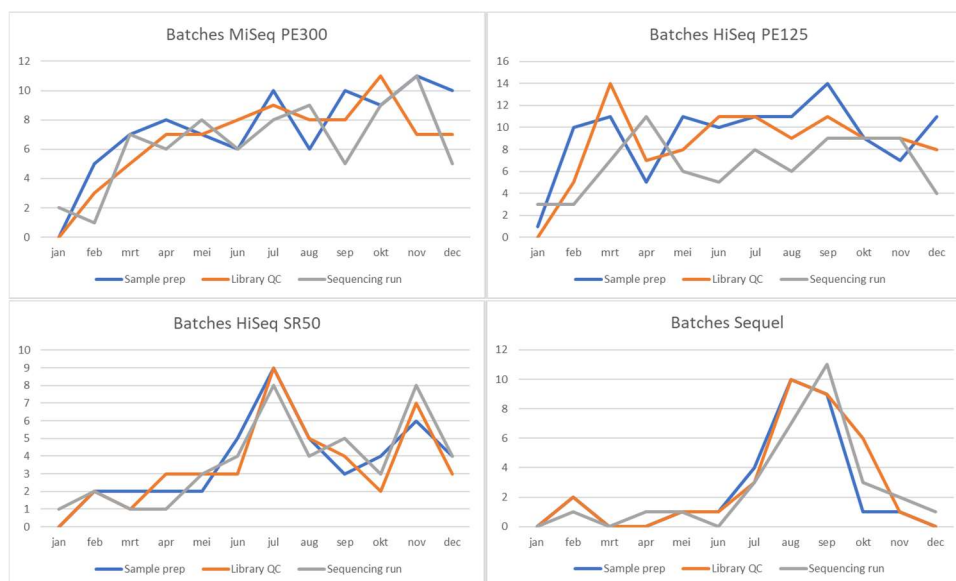


Figure 28: Batch scheduling total NGS production in 2016.

In figure 28 only the sample prep, library QC and sequencing run step are visualized. The sample registration (as starting point of the process) and sample QC step are performed on a daily basis and therefore the throughput times of these process steps is stable. As can be seen in figure 28, production scheduling is performed randomly over the year and there appears to be no fixed production schedule, since there is no stable line visible. These figures have been discussed with the NGS production manager and he explained that work scheduling is mainly based on sample arrival number in combination with amount of data that needs to be generated for each sample, availability of human workforce and equipment per period and lead times that impend to exceed. The peaks in batch scheduling as visualized in figure 28 mainly follow the peaks in sample arrival that is visualized in figure 25 and confirm these finding. Considering the peaks in batch scheduling, the number of batches that can be planned in a certain time frame does not seem to be limited and can be increased if enough resources are available. In general, the number of batches that are scheduled each month varies and could potentially be too low which could cause excessive waiting time during the production process. Increasing the number of batches per month could be a potential solution to the business problem.

4.1.5 Capacity utilization

In this section the capacity utilization of the sequencers in the production process is calculated. For each sequencer the historical utilization, mean and maximum data output per month is calculated based on the production schedule of 2016 as determined in section 4.1.4 (figure 28). In table 12 the mean and maximum data output per month in megabytes (MB) for each sequencer is given.

Table 12: Mean and maximum capacity of the 4 different sequencers per month.

Sequencer	Data output per run (MB)	Mean runs per month (#)	Max. runs per month (#)	Mean data output per month (MB)	Max. data output per month (MB)
MiSeq PE300	9000	6	11	54000	99000
HiSeq PE125	37000	7	11	259000	407000
HiSeq SR50	7500	4	8	30000	60000
Sequel	10000	3	11	30000	110000

In the vertical bars of figure 29 the total input amount of data in megabytes (MB) for each of the four flows the enter the NGS process per month in 2016 is given, divided per sample prep type. This amount of data is the sum of all samples that arrived per month and represents the input of the four flows of the production process per month.

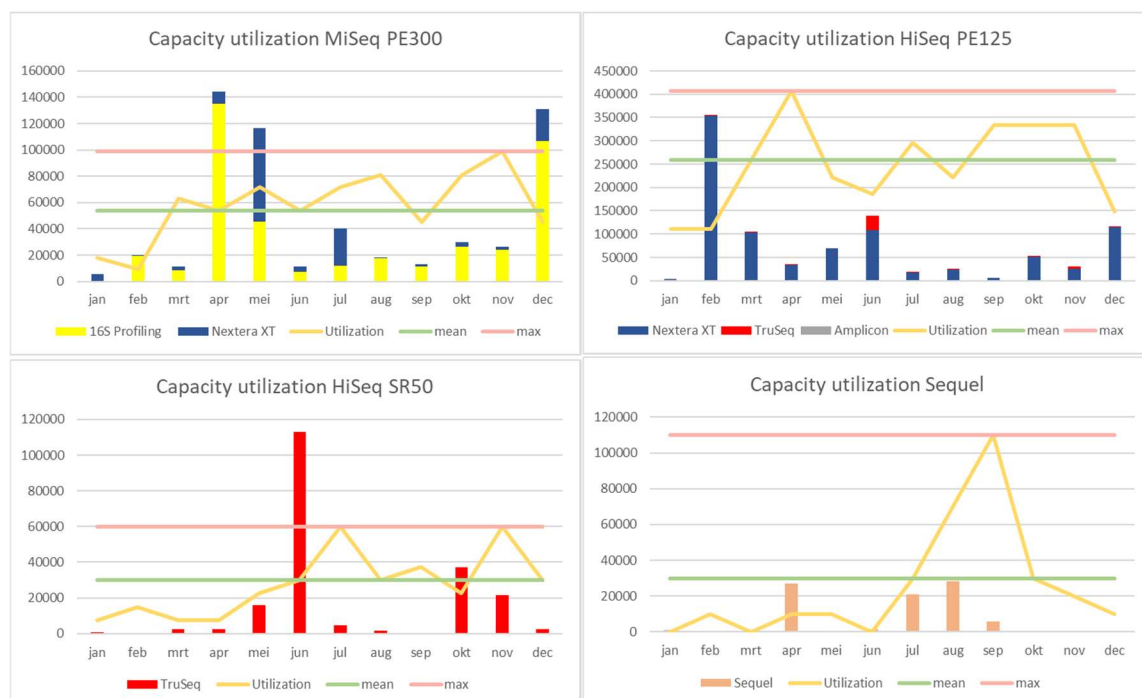


Figure 29: Capacity utilization NGS sequencers in 2016.

The lowest horizontal line in green represents the mean data output in megabytes (MB) per month, and the highest horizontal line in red represents the maximum data output in MB per month based on the sequencing runs that have been scheduled in 2016 (as determined in figure 28 and table 12). The fluctuating horizontal line in orange is the actual data output per month based on the batch schedule of 2016, as determined in figure 28. The actual sequencing capacity utilization is needed at the final stage in the production process and the processing time and waiting time of the previous process steps explain the delay in data output of the sequencers when compared to the sample arrival time, as determined in section 4.1.1.

For each sequencer the total run time lies between 16 and 48 hours. During peaks in workload it is possible to plan more batches in a certain time frame to increase capacity. For all sequencers a factor of, at least, two more batches per month is feasible, which means that for all sequencers the maximum sequencing capacity in the current setup is not a bottleneck. It has been investigated if an eventual backlog of work has an effect on lead time, but based on these measures no effect on lead time could be determined. Exceeding lead times are visible throughout the whole year, also during months when the maximum sequencing capacity is not reached as can be seen in figure 26 and 29.

Particularly for the sequencers, there are economic factors involved. The reagents that are needed to run the sequencers are costly and therefore performing full capacity runs is economically beneficial. The capacity of the other machines in the production process hasn't been investigated in more detail, but this capacity isn't limited as determined in section 4.1.4, less economic factors apply and is mostly influenced by availability of (human) resources.

4.2 Conclusion performance analysis

In this section an answer to sub research question 3 will be formulated based on the operational performance analysis that is performed in section 4.1.

Sub research question 3: How does the current production planning and control of the NGS production process of BaseClear perform in terms of WIP and lead times?

In the NGS production process two dominant flows have been distinguished, the Nextera XT sample prep to HiSeq PE125 sequencing and 16S Profiling sample prep to MiSeq PE300 sequencing. These two flows contribute for about 70% of all samples that have been analysed in 2016. In the four process flows no sample arrival patterns, like seasonal factors, could be determined. A general finding for all process flows is that sample arrival is unequally and randomly distributed over the year. There are periods with random high peaks, but also periods where sample arrival numbers are low or even drop to base line level. Total production is based on a reasonably number of customers and customer demand looks random which makes arrival of work hard to predict and to stabilise. Only long-term trends in increasing or decreasing sample arrival could be determined based on the analysed data. In general, it looks like the variability in sample arrival has an impact on the stability of the production process performance and could be a possible root cause of the business problem.

In terms of the business problem, structurally excessive lead times and unbalanced WIP have been determined for the NGS production process. About 10% of all orders are delivered too late as agreed with customers and there is much variation visible in lead times. A relation of the exceeding lead times to specific process flows could not be determined, this occurs over the complete NGS production process. Based on the data analysis, peaks in workload have no effect on lead times. At least no pattern between increasing sample arrival and exceeding lead times could be determined. Lead times are randomly distributed over the year. WIP is defined as the amount of waiting time of the samples within the production process. There is much waiting time randomly distributed over the total NGS production process and waiting time contributes to 67% - 80% of the total lead time on average, dependent on the process flow. It looks like the waiting time is equally distributed over the total process, although the sample prep and sequencing step seem to differ in a slightly negative manner from the other process steps.

In 2016, production scheduling is mainly based on sample arrival number in combination with amount of data that needs to be generated for each sample, availability of human workforce and equipment per period and lead times that impend to exceed. These figures determine the number of process steps that are scheduled and performed each week. In general, the number of batches that are scheduled each month varies and could potentially be too low which could cause excessive waiting time during the production process. It has been investigated if sequencing capacity has an impact on the poor production performance, but no impact on lead time and WIP could be detected. The sequencing capacity is not limiting and no after-ebony effect on lead time is observed.

The results of the data analysis have been discussed with the NGS production manager. Two potential root causes of the exceeding lead times and unbalanced WIP were brought to light. The variability in sample arrival seems to have an impact on the stability of the production process performance. A potential solution for the business problem could be to stabilize the number of samples that enter the production process. Besides this, a bottleneck could be the number of batches that are scheduled in a certain time frame. Another potential solution for the business problem, based on practical findings and historical data analysis, could be to increase the number of batches of the different process steps that are scheduled each week from sample registration until sequencing, to control throughput times. Since there are economic factors involved in performing sequencing runs, a decision moment for the NGS production manager based on lead time expectation looks of benefit before performing the sequencing step. In chapter 5 alternative scenarios of these two possible solutions for the business problem will be evaluated using adjusted versions of the simulation model that is built and validated in section 4.3.

4.3 Building a simulation model of the current NGS production process

Simulation modelling is considered to be a suitable tool to verify the effect of the anticipated possible solutions to the business problem. In this section a simulation model of the NGS production process is developed and validated using historical data that is analysed in section 4.1. Arena software (Rockwell) will be used to perform the simulation study. Arena is simulation software which has flexible model building capabilities and advanced options for making strategic business decisions. Arena is built on SIMAN simulation language. There are low to high levels of modelling possible in Arena's hierarchical structure. For specialized models with complex algorithms or accessing data from external applications, specific programming based on Visual Basic or C/C++ is possible. For simpler cases, the Basic Process, Advanced Process and Advanced Transfer modules of the Arena software can be used to build complex systems. Generally, Arena provides powerful functions in modelling and enables visualization of the designed operation system under variety conditions and the software has outstanding features for interacting with other applications, like Excel, with its built-in spreadsheet data interface.

Building a simulation model of the NGS production process concerns four steps. The first step is mapping the process, the second step is collection of input data, the third step is programming the simulation model and the final step is validating the model. These steps will be deepened in more detail in the following sections.

4.3.1 Process mapping

In a first step towards building a simulation model, the actual NGS production process as given in figure 2 will be mapped in the simulation software. The model that is build starts with the arrival of NGS samples at the order registration step and ends with the data analysis step. The samples are separated into four different process flows as discussed in section 4.1.

4.3.2 Data collection

After mapping the process, the input data for the simulation model is collected. The performance measures of the current NGS production process, as determined in section 4.1, are used as input data for the model, to give a representation of the real system. Rockwell Arena's Input Analyzer tool is used to determine the best fit of probability distributions of the average waiting times per process step and are discussed in section 4.3.3. All steps provide sufficient data, more than 50 data points, for a theoretical probability distribution. For the actual processing steps (sample registration, sample QC, sample prep, library QC, sequencing and data analysis) fixed throughput times are used, that reflect real-life measures. The historical sample arrival and batch scheduling numbers that are determined in section 4.1 are used as input in the model and total lead time distribution, WIP distribution and total number of samples processed are used as output measures as key performance indicators.

4.3.3 Programming of the simulation model

A dynamic, stochastic and discrete-event simulation model is built using Rockwell Arena Professional software (version 15). The model is dynamic since it accounts for time-dependent changes in the state of the system and stochastic since randomness is present and variable states are not described by unique values, but by probability distributions. Finally, it is a discrete-event model since it operates as a system of discrete sequence of events in time. Each event occurs at a particular instant in time and marks a change of state in the system. The Arena model is built using the Basic Process module. The Basic Process module provides a high level of modelling and is designed to model most systems quickly and easily with a great deal of flexibility (Kelton et al., 2014).

4.3.3.1 Building blocks of the simulation model

A combination of the CREATE, BATCH, PROCESS, SEPARATE, DECIDE, ASSIGN, RECORD and DISPOSE steps of the Basic Process module are used in the simulation. The CREATE blocks are used to determine the arrival of entities. After creation, for each entity attributes can be assigned by the ASSIGN module. The entity enters the model at the BATCH module and continues to a PROCESS module. After being processed, the entity is moved to another PROCESS module or a DECIDE module. The DECIDE module helps determining the entity type or checking the condition before releasing. The RECORD module can record performance information, for instance lead time or WIP. The DISPOSE step removes entities from the model.

4.3.3.2 Parts of the simulation model

Entity: Entities are the dynamic objects in the simulation. They are created, move around for a while and then are disposed as they leave the model. Each entity has a unique active entity number when created to act as its record of existence. These numbers are reused when entities are disposed and new ones are created.

In the simulation model the NGS samples are the entities, or parts to be processed and are visualized as coloured dots. The entities enter the model at the registration process step and the arrival rate is based on the measured sample arrival distribution in section 4.1. In the model there are nine different entity types, one for each sample prep and sequencing run type combination. The random inter-arrival rate is exponentially distributed. The sample arrival pattern is assumed to be uniformly distributed to simulate sample arrival variability.

Batch: This module is intended as the grouping mechanism within the simulation model. Batches of entities can be permanently or temporarily grouped. Temporary batches can be split using the Separate module. Batches may be made with any specified number of entering entities or may be matched together based on an attribute. Entities arriving at the Batch module are placed in a queue until the required number of entities has accumulated or maximum waiting time is reached. Once accumulated, a new representative entity is created.

In the model temporally batches are made before performance of the sample prep, library QC and sequencing step to reflect waiting time in the production process. The probability distributions of these waiting times is determined with Arena's Input Analyzer tool. For all waiting time distributions low square errors were found, but no p -value > 0.05 is found. So all probability distributions do not represent an ideal fit. Erlang probability distribution is considered as the most optimal fit to reflect waiting time within the process before the process step is performed. In appendix F, the Erlang probability distributions used in simulation model are given. The waiting times of three processing steps, sample registration, sample QC and data analysis, the probability distribution is not statistically tested by Arena's Input Analyzer. Since for these processing steps the times are kept constant in the simulation model, the degree of variation in waiting time is negligible.

Separate: This module is used to split a previously batched entity. When splitting existing batches, the temporally representative entity that was formed is disposed and the original entities values that formed the group are retained. The entities proceed sequentially from the module in the same order in which they originally were added to the batch.

Attribute: Attributes are attached to the entities for the purpose of individualization, in which the attached characteristics can differ from one entity to another. The core of attributes are values that are attached to specific entities. The attributes are subject to change by using the ASSIGN module at any time during the simulation run if there is a need in the process. The arrival time (TNOW) are assigned to all entities that enter the model to be able to measure time-persistent statistics.

Variable: A variable or global variable is a piece of information that reflects some characteristic of the model, regardless of how many or what kinds of entities might be around. Many variables are allowed and each is unique. There are variables that are already built inside Arena such as number in queues, current simulation lock time or number of busy machines. However, others can be assigned to track anything that is interesting to collect in the entire system. In the model the following variables are recorded as key performance indicators of which the last three as average, minimal and maximum values.

Table 13: Overview key performance indicators used in the simulation model.

Key Performance Indicator Problem Diagnosis	Key Performance Indicator Arena
Sample arrival	Total entities processed
Time in process	Value added time process steps
WIP	Waiting time in queue
Lead time	Total lead time

Expression: Expressions can be viewed as specialized variables that are defined by a formula instead of storing a specific value.

Resource: Resources represented in the model are employees or machines. An entity seizes (units of) a resource when available and releases it (or them) when finished. A single resource can serve only a specified number of entities at a time, which means that if the machine is busy, other entities wait in a queue. The idle and busy times of the machines can be animated. The resource capacity may be changed in simulations to compare and analyse different scenarios.

In the model the machines that are used within the NGS sequencing production process will be used as resources. The machines have a fixed capacity and are assumed to work without any problems. For running the resources, fixed processing times values are chosen that reflect reality. These process times are constant and therefore deterministic. The utilization of employees is not added to the model.

Queue: There is a queue existing in the model when the entity must wait for a unit of time to be processed.

Statistics: Statistics are recorded during a simulation run and displayed as output performance measures and are classified as tally, time-persistent and counter statistics. Tally statistics or discrete time statistics present the average, minimum or maximum of a list of numbers. Time persistent statistics or continuous-time statistics are time average statistics in simulation. For example, average number in the queue is calculated throughout simulation, or machine utilization in time scheduled. Counter statistics are used to sum of something as accumulating.

The KPI total entities processed is a counter statistic. The other KPI's as given in table 13 are time-persistent statistics.

Event: An event is something that happens at an instant of time that might change attributes, variables or statistical accumulators, like the arrival of new samples that enter the system or finished parts that leave the system.

Simulation Clock and Starting and Stopping: Current value of time in the simulation held in a variable is called the simulation clock. Simulation clock and event calendar are important pieces of any simulation. Starting and stopping conditions should be specified. It is important to think about these conditions and make them consistent in the model.

The simulation model can be used for measuring the performance of the NGS production system based on specific parameters. As the model starts empty at the beginning of the simulation run, while the production process is never empty, results are influenced. Therefore, a warm-up period is required. Data collected during this period is not used for calculating the output statistics. The warm-up period is set to 30 days which equals one production month. To make sure the simulation run provides sufficient data for a valid confidence interval on the output statistics and results are enough to support Arena's assumption of independence between the means each scenario is run for 10 replications. The total simulation run length is set to 395 days with 8 hours a day. So the model represents the production performance of one year, which equals the period for data analysis as used in section 4.1.

The following assumptions have been made for the model in general. All orders are accepted, material and resources are always available and operational, but possibly busy. All necessary information regarding shop floor routings and processing times is known. Since the simulation model is a simplification of reality, the following constraints apply. To prevent the measurements and simulation model from becoming too complex and time consuming, the degree of detail is intentionally kept as limited as possible. The production costs are not included in the model and there is no interchange-ability between work centers. The possibility of rush orders and need of re-work, like samples that do not pass quality control steps, is not included in the model. Randomness in sample arrival is limited due to modelling constraints. The student version of Arena allows only 150 entities within the model at a time. Therefore, the maximum sample arrival for each entity at a time must be limited and was set to three, which equals around factor 20 less maximum samples that could enter the model when compared to reality. The model of the NGS production process that is built in Arena is visualized in figure 30.

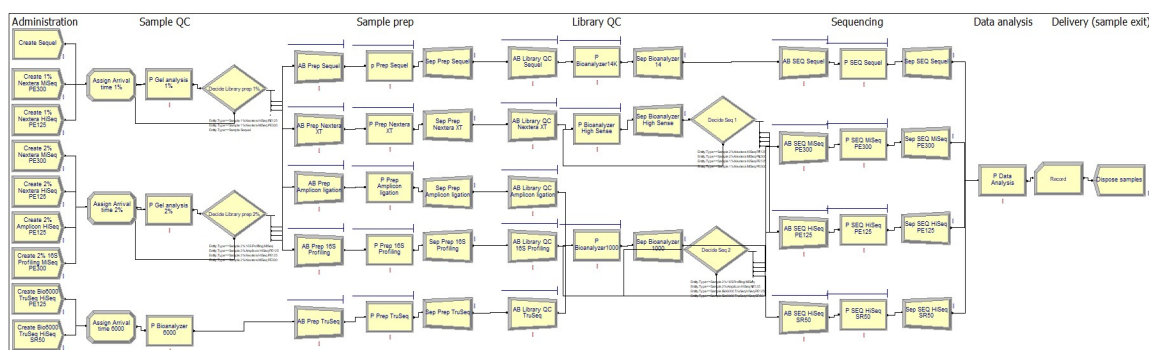


Figure 30: Simulation model of the NGS production process in Arena software (Rockwell).

After running the model with the above-mentioned warm-up period and run length, Arena automatically computes the averages and accompanying half-widths, minimum and maximum values. Based on these measures the confidence interval and significance level are determined. As the measurement occurs only at a single point in time, Arena provides no statistics other than the outcomes of these single measurements. Half widths helps to determine the reliability of the results. The formula used to calculate half width in Arena requires samples to be normally distributed. When sufficient data is collected the half width is automatically calculated and reported. The half width is used to determine the confidence interval and represents the precision of the results. For the confidence interval it is interpreted that, when the simulation experiment is repeated, in 95 per cent of the trials the sample mean will fall within the given range. Smallest confidence intervals are preferred for highest precision. The formulas of these performance measurement output statistics of the simulation models can be found in appendix I. The validity of the simulation model that is build is determined in the following section.

4.3.4 Validation of the simulation model

In this section the simulation model is validated using the historical operational performance reference data from section 4.1. Law (2007) states that validation is the process of determining whether the simulation model is an accurate representation of the system, for the objectives of the study. The idea behind validation is that if the simulation model is conceptually valid, then it can be used to make decisions about the system like those that would be made if it were feasible and cost-effective to experiment with the system itself. Model verification is often defined as ensuring that the computer program of the computerized model and its implementation are correct. Model validation is usually defined to mean substantiation that a computerized model within its domain of applicability possesses a satisfactory range of accuracy consistent with the intended application of the model (Schlesinger et al., 1979). The model is considered valid when for a set of experimental conditions the model's accuracy is within acceptable range. This requires that the accuracy of the model's output variables of interest is specified.

When it comes to analysing the model's performance, the following measurements are key. Lead time distribution and WIP distribution output statistics of the simulation model should match the performance measures that are determined in section 4.1. Processing time is defined as the sum of all value added throughput time in days spent on entity related activities. Value added time relates to the sample registration, sample QC, sample prep, library QC, sequencing and data analysis step. The processing time for the MiSeq PE300 flow is 11 days and for the HiSeq PE125 flow 10 days and is constant during all simulation experiments. WIP is defined as the sum of all non-value added throughput time in days spent on non-entity related activities from sample registration until data delivery. Lead time is defined as the sum of the processing time and WIP from sample registration until data delivery. Average lead time is defined as the average lead time in days of all entities that are processed from sample registration until data delivery for a certain production process flow. The equations for these performance measures can be found in Appendix G. A deviation of 10% in accuracy of the measured average lead time of the model is accepted. Considering the limitations of the simulation, like constrained sample arrival, no specifications are given for the minimum and maximum lead time. To level out variances and come to overall averages, the averaging measurements take place only once at the end of the simulation run. A sensitivity analysis is performed to see which factors have the greatest impact on the performance measures and are tweaked to match the outcomes of the model.

After running the simulation model with the settings described in section 4.3, results were obtained. A total of 84 entities were processed on average per replication run. This entity number reflects a total of 1680 samples in reality (factor 20 higher due to simulation model limitation, as discussed in section 4.3.3.2). Among the 84 processed entities are 40 entities for the HiSeq PE125 flow and 44 entities for the MiSeq PE300 flow. These numbers reflect the 2 dominant flows in the production

process that were found during the problem diagnosis in chapter 4. The total number of samples that are processed fall within the range of 10% deviation when compared with the historical sample number that is processed for both flows in 2016 (which is 1853 samples, as visualized in table 7). No entities were processed for the Sequel and HiSeq SR50 flow, due to the entity entry limitation of the simulation software. In appendix H the raw data of the validation analysis can be found and the output measures of the simulation model are compared with the operational performance measures that were found in chapter 4. The average lead time of the MiSeq PE300 flow fall within the range of 10% deviation that was set as limit specification. The average lead time of the HiSeq PE125 flow exceed the 10% deviation that was set as limit specification. However, as can be seen in figure 26 several outliers are visible that can explain the difference in average lead time of the historical data. It is assumed that, when these outliers are not included in the measurement, the average lead time of the HiSeq PE125 flow fall within the limit specification of 10% as well. After analysing the data and verification of the model, among others by reviewing the outcomes with the NGS production manager, the simulation model is considered to be valid.

Two possible solutions for the business problem that are proposed in section 4.2 are evaluated in simulation experiments that will be conducted in chapter 5.

5 DESIGN OF SOLUTION

The problem diagnosis performed in the previous chapter confirmed the business problem as described in chapter 1 and two possible solutions for the business problem were proposed. In this chapter a solution to the business problem is proposed, guided by a simulation study, to answer sub research question 4 and 5. A discrete event simulation study is performed to evaluate scenarios of the two possible solutions for the business problem. The performance of alternative production planning and control is anticipated. The simulation experiments will be described in section 5.1 and 5.2. The results of the simulation experiments will be analysed, alternative solutions examined and compared to the current situation in section 5.3. The simulation experiments will be summarized in section 5.4 and an answer to sub research question 4 is formulated. In section 5.5 possible solutions for the business problem are proposed to answer sub research question 5.

5.1 Design of the simulation experiments

The validated simulation model representing the current NGS production process as described in section 4.3 will be modified to evaluate scenarios of possible solutions for the business problem, thereby creating new sub models. In chapter 4 two potential root causes of exceeding lead times and unbalanced WIP were brought to light, based on practical findings and historical data analysis. The root causes concern order arrival variability and batch scheduling. A potential solution for the business problem could be to stabilize the number of samples that enter the production process. Another potential solution for the business problem could be to increase the number of batches that are scheduled each week from sample registration until sequencing, to control throughput times of the different processing steps. In the simulation experiment scenarios are evaluated to analyse the effect of these possible solutions on the key performance measures as given in section 4.3.3.2. In each scenario only the two most dominant production process flows (MiSeq PE300 and HiSeq PE125) are analyzed. Since the simulation software only allows 150 entries at a time the Sequel and HiSeq SR50 process flow are not included in the experiments.

5.1.1 Sub model 1: order arrival variability

The first solution that will be evaluated reflects different scenarios for a better-balanced order arrival, to determine the effect on WIP and lead times. This can be accomplished in practice by implementing theoretical factors like a dynamic COBACABANA concept in between the customer enquiry and order release stage. Improving the customer enquiry stage based on actual workload level in the job pool and shop and introduction of a centralized order release control at the job

release stage with standard release frequencies based on capacity control measures. This should have an effect on a better balanced order arrival to the shop floor.

In the initial simulation model, the sample arrival rate was random, with a daily order release interval and number of sample arrivals varied between 0 and 3 entries per day for each of the four flows in the production process. The following modifications will be made to this initial simulation model to evaluate the effect of scenarios on WIP and lead times.

Table 14: Design of simulation experiments sub model 1: order arrival variability.

Experiment	Arrival rate	Order release interval (day)	Entities per arrival
Initial model	Random	1	UNIF(0,3)
Scenario 1	Random	1	1
Scenario 2	Random	2	UNIF(0,3)
Scenario 3	Random	2	1
Scenario 4	Constant	1	UNIF(0,3)
Scenario 5	Constant	1	1
Scenario 6	Constant	2	UNIF(0,3)
Scenario 7	Constant	2	1

The arrival rate is the type of sample arrival stream that will be generated. A random arrival rate uses an exponential distribution and a constant rate uses a constant value, based on the order release interval. The order release interval determines the mean of the exponential distribution (if a random arrival rate is used) or the constant value (if constant is used) for the arrival rate. Both values combined gives a representation of the order arrival frequency in practice. The entities per arrival means the number of entities that will enter the system at a given time with each arrival. The UNIF expression means an uniformly distributed random number in the range mentioned in the table. With these scenarios the effect of a more balanced sample arrival rate, less frequent order release interval and stabilized sample arrival pattern on WIP and lead time can be evaluated. The initial model that was validated in section 4.3 is used as a base reference scenario to compare the results to.

5.1.2 Sub model 2: capacity planning method

The problem diagnosis in chapter 4 revealed that batch scheduling is mainly based on sample arrival number in combination with amount of data that needs to be generated for each sample, availability of human workforce and equipment per period and lead times that impend to exceed, resulting in WIP as waiting time in the process causing excessive lead times. The second solution that will be evaluated reflects the implementation of an increased number of production batches until the sequencing step, to determine the effect on WIP and lead time. A batch size reflect a group of samples that are processed and the number of samples within a batch can vary. In the initial simulation model average batch sizes were used that reflect production batch sizes in the year 2016. The scenarios that will be evaluated are given in table 15.

Table 15: Design of simulation experiments sub model 2: capacity planning method.

Experiment	Average batch size		
	Sample prep	Library QC	Sequencing
Initial model	18	18	18
Scenario 1	12	12	12
Scenario 2	10	10	10
Scenario 3	8	8	8
Scenario 4	7	7	7

The average batch size represents the number of entities to be batched. The initial model that was validated in section 4.3 is used as a base reference scenario to compare the results to.

5.1.3 Sub model 3: combination of solutions

In the final experiment a combination of solutions will be analysed. The one scenario of sub model 1 and the one scenario of sub model 2, that has the most effect on a better balanced WIP and reduced lead times, will be combined into a new sub model to measure the effect of a combination of both scenarios on WIP and lead times. The initial model that was validated in section 4.3 and the one scenario of sub model 1 and the one scenario of sub model 2 that has the most effect on a better balanced WIP and reduced lead times, are used as reference scenarios to compare the results to.

5.2 Conducting the simulation experiments

As the model starts empty at the beginning of the simulation run, while the production process in reality is never empty, results are influenced. Therefore, a warm-up period is required. Data collected during this period is not used for calculating the output statistics. The modified simulation models will be run for the same length as the initial model of section 4.3, including an equal warm-up period. The warm-up period is set to 30 days which equals one production month. To make sure the simulation run provides sufficient data for a valid confidence interval on the output statistics and results are enough to support Arena's assumption of independence between the means, each scenario is run for 10 replications. The total simulation run length is set to 395 days with 8 hours a day. So the model represents the production performance of one year, which equals the period for data analysis as used in section 4.1 and for validating the initial model. This makes the output of all simulation experiments comparable, although some negligible statistical variability may occur due to Arena sequencing its internal operations a little differently (Kelton, 2014).

5.3 Simulation output analysis

In this section, the output of the simulation experiments is analysed. When it comes to analysing the model's performance, the following measurements are key. Processing time is defined as the sum of all value added throughput time in days spent on entity related activities. Value added time relates to the sample registration, sample QC, sample prep, library QC, sequencing and data analysis step. The processing time for the MiSeq PE300 flow is 11 days and for the HiSeq PE125 flow 10 days and is constant during all simulation experiments. WIP is defined as the sum of all non-value added throughput time in days spent on non-entity related activities from sample registration until data delivery. Lead time is defined as the sum of the processing time and WIP from sample registration until data delivery. Average lead time is defined as the average lead time in days of all entities that are processed from sample registration until data delivery for a certain production process flow. The equations for these performance measures can be found in Appendix G.

In order to level out the variances and come to overall averages, the measurements take place only once at the end of the simulation run. As the measurement occurs only at a single point in time, Arena provides no statistics other than the outcomes of these single measurements. Arena automatically computes the averages, accompanying half widths, minimum values and maximum values for the means of all output statistics. Half width helps to determine the reliability of the results. The formula used to calculate half width in Arena requires samples to be normally distributed. When sufficient data is collected the half width is automatically calculated and reported. The half width is used to determine the confidence interval and represents the precision of the results. For the confidence interval it is interpreted that, when the simulation experiment is repeated, in 95 per cent of the trials the sample mean will fall within the given range. Smallest confidence intervals are preferred for highest precision. The sub model performance is measured in a similar way as the initial model, as described in section 4.3.3. The confidence interval and significance level are derived from the provided statistics using formulas that are given in appendix I. The raw data of all simulation experiments can be found in appendix M. After running the model with the above-mentioned warm-up period and run length the outcome is analysed. The outcome of the simulation runs is discussed underneath.

5.3.1 Sub model 1: order arrival variability

After running the 7 scenarios that are given in table 14, results were found that are summarized in table 16. The output measures of the simulation experiments are compared to the measures of the initial model. The statistics as provided by Arena related to the performance measurements can be found in Appendix J.

Table 16: Output analysis simulation sub model 1: order arrival variability.

Scenario	KPI	LEAD TIME						WIP					
	Flow	MiSeq PE300			HiSeq PE125			MiSeq PE300			HiSeq PE125		
	Nr out	Average	Min. Value	Max. Value	Average	Min. Value	Max. Value	Average	Min. Value	Max. Value	Average	Min. Value	Max. Value
Initial model	84	30,89	13,41	49,27	29,94	15,12	48,27	19,89	2,41	38,27	19,94	5,12	38,27
Scenario 1	61	31,27	18,87	44,10	28,02	16,78	40,98	20,27	7,87	33,10	18,02	6,78	30,98
Scenario 2	84	52,97	16,37	75,27	41,15	10,00	64,69	41,97	5,37	64,27	31,15	0,00	54,69
Scenario 3	152	45,00	16,21	82,99	43,10	24,87	71,75	34,00	5,21	71,99	33,10	14,87	61,75
Scenario 4	54	25,05	11,00	45,00	24,09	10,00	36,00	14,05	0,00	34,00	14,09	0,00	26,00
Scenario 5	71	38,17	24,00	42,00	25,00	20,00	30,00	27,17	13,00	31,00	15,00	10,00	20,00
Scenario 6	107	45,70	11,00	78,00	46,61	30,00	60,00	34,70	0,00	67,00	36,61	20,00	50,00
Scenario 7	121	47,91	31,00	72,00	40,00	30,00	50,00	36,91	20,00	61,00	30,00	20,00	40,00

The number out is the number of samples that have been processed from sample registration until data analysis and represents the total output of samples that are processed. The differences in number out for each scenario can be explained by load differences caused by the settings of the scenarios.

The average lead times of both process flows are visualized in figure 31. The legend shows the settings of the validated simulation model and the scenarios that have been tested.

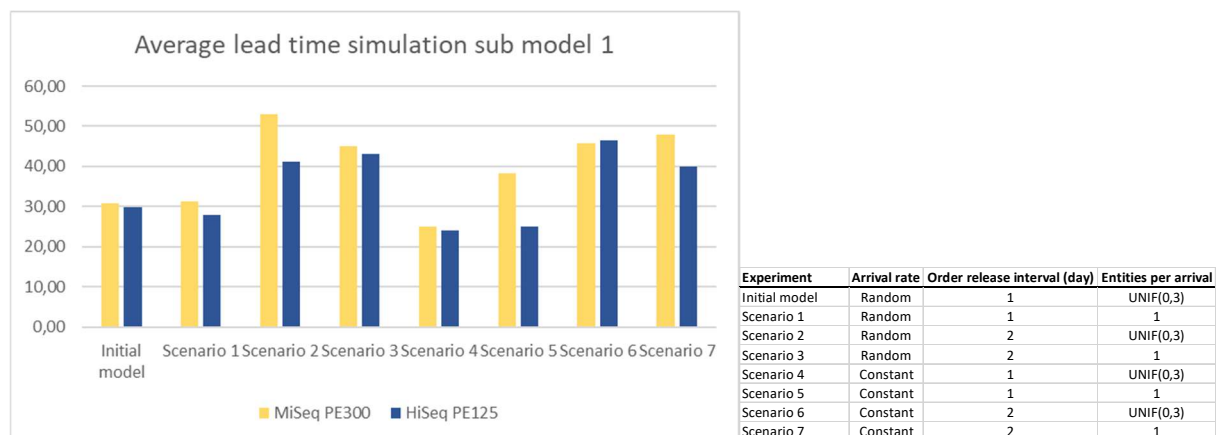


Figure 31: Simulation output sub model 1: average lead time in days.

As can be seen in the above table and figure, changes in order arrival variability has an effect on WIP and lead time. Daily order release with a constant release interval and uniformly distributed sample arrival pattern (scenario 4) has the most effect on lead time reduction. Daily order release with a constant release interval and sample arrival pattern (scenario 5) reduces the average lead time of the HiSeq PE125 flow, but increases the average lead time of the MiSeq PE300 flow. No explanation could be determined for this result. A more stabilized sample arrival pattern when compared to the current situation (scenario 1) also has an effect on lead time reduction, but the effect is limited. Temporally holding samples before releasing them to the shop floor (scenario 2, 3, 6 and 7) increases the average lead time. Therefore, the order release rate should not be set too high in practice, since lead times could increase rapidly. Heaping samples has an effect on the total number of samples that were processed in the simulation model. Unfortunately, due to simulation model limitations the effect of higher numbers of sample arrivals could not be analysed.

In general, although not statistically proven, based on this simulation experiment a more constant and stabilized order arrival rate and pattern, has an effect on WIP balancing and lead time reduction, but the effect is limited. On the other hand, inappropriate order release frequencies and offset in timing and sizing of sample arrival can increase WIP and lead time drastically. These findings confirm the need for optimized order release frequencies based on actual sample arrival numbers and stability in sample arrival in practice.

5.3.2 Sub model 2: capacity planning method

After running the 4 scenarios that are given in table 15, results were found that are summarized in table 17. The output measures of the simulation experiments are compared to the measures of the initial model. The statistics as provided by Arena related to the performance measurements can be found in Appendix K.

Table 17: Output analysis simulation sub model 2: capacity planning method.

Scenario	KPI	LEAD TIME						WIP					
	Flow	MiSeq PE300			HiSeq PE125			MiSeq PE300			HiSeq PE125		
	Nr out	Average	Min. Value	Max. Value	Average	Min. Value	Max. Value	Average	Min. Value	Max. Value	Average	Min. Value	Max. Value
Initial model	84	30,89	13,41	49,27	29,94	15,12	48,27	19,89	2,41	38,27	19,94	5,12	38,27
Scenario 1	85	25,38	14,37	48,41	16,12	10,71	23,14	14,38	3,37	37,41	6,12	0,71	13,14
Scenario 2	88	21,89	11,00	31,72	12,67	10,00	20,42	10,89	0,00	22,72	2,67	0,00	10,42
Scenario 3	96	20,13	11,00	33,28	13,51	10,00	20,14	9,13	0,00	22,28	3,51	0,00	10,14
Scenario 4	104	16,35	11,00	28,48	13,52	10,00	20,50	5,35	0,00	17,48	3,52	0,00	10,50

The number out is the number of samples that have been processed from sample registration until data analysis and represents the total output of samples that are processed. The increasing number of samples until scenario 4 can be explained by the fact that more samples can be processed in a certain time frame due to increased production batch numbers.

The average lead times of both process flows are visualized in figure 32. The legend shows the settings of the validated simulation model and the scenarios that have been evaluated.

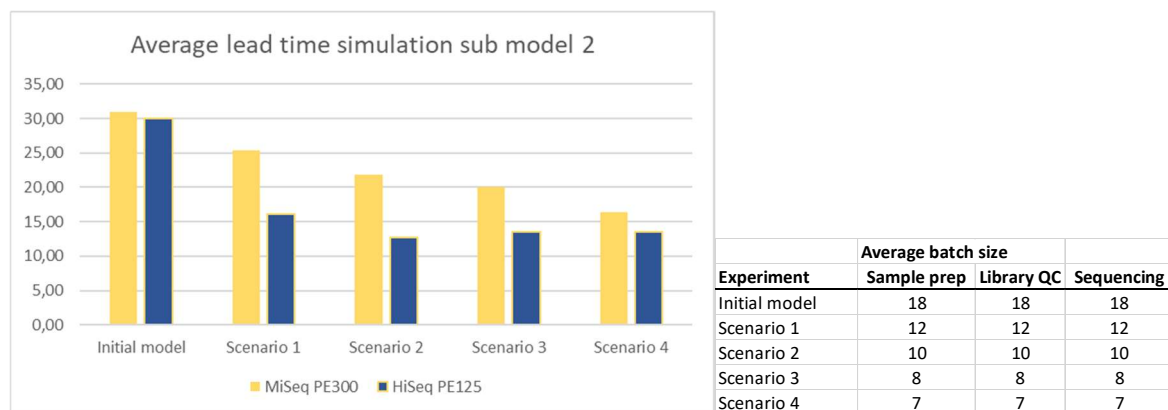


Figure 32: Simulation output sub model 2: average lead time in days.

As can be seen in the above table and figure, changes in the number of batches that are performed for each production step in a certain time frame has an effect on WIP balancing and lead time reduction. The effect of production batches with less samples that are performed more frequently, appears directly. Further, the range and average WIP and lead times decline continuously until the last scenario and number of samples that are processed increases. When compared to the first sub model, the effect of increased batch scheduling on WIP balancing and lead time reduction is stronger, although the maximum number of samples that are processed is more stable. This can be explained by the fact that the total number of samples that enter the process in this sub model is not

adapted so the total load that enters the production process is comparable with the initial model. Based on the data it could not be determined why the MiSeq PE300 flow declines more gradually when compared to the HiSeq PE125 flow.

In general, although not statistically proven, the findings after this simulation experiment confirm that capacity planning methods, like increased batch scheduling, has an effect on WIP balancing and lead times reduction. Inappropriate number of batches that are planned can influence WIP and lead time drastically. These findings confirm the need for optimized batch scheduling based on actual sample arrival numbers. Since the number of batches that are scheduled has a direct effect on resource utilization and therefore production costs, there should be a balance between the number of batches that are scheduled, number of samples that need to be processed and available resources.

5.3.3 Sub model 3: combination of solutions

In the previous sub models it was found that scenario 4 of sub model 1 and scenario 4 of sub model 2 has the most effect on WIP balancing and lead time reduction of the production process. In this final sub model, these two scenarios are combined in sub model 3. After running this scenario, results were found that are summarized in table 18. The output measures are compared with the measures of the initial model and the most optimal scenario of sub model 1 and 2. The statistics as provided by Arena related to the performance measurements can be found in Appendix L.

Table 18: Output analysis simulation sub model 2: combination of solutions.

Scenario	KPI	LEAD TIME						WIP					
	Flow Nr out	MiSeq PE300			HiSeq PE125			MiSeq PE300			HiSeq PE125		
		Average	Min. Value	Max. Value	Average	Min. Value	Max. Value	Average	Min. Value	Max. Value	Average	Min. Value	Max. Value
Initial model	84	30,89	13,41	49,27	29,94	15,12	48,27	19,89	2,41	38,27	19,94	5,12	38,27
Scenario 4 Sub model 1	54	25,05	11,00	45,00	24,09	10,00	36,00	14,05	0,00	34,00	14,09	0,00	26,00
Scenario 4 Sub model 2	104	16,35	11,00	28,48	13,52	10,00	20,50	5,35	0,00	17,48	3,52	0,00	10,50
Scenario 1	68	18,20	11,00	28,00	12,35	10,00	18,00	7,20	0,00	17,00	2,35	0,00	8,00

The average lead times of both process flows are visualized in figure 33.

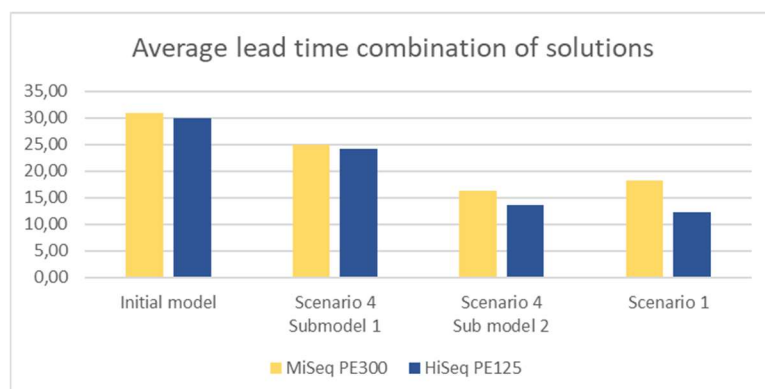


Figure 33: Simulation output sub model 3: average lead time in days.

Scenario 4 of sub model 1 reflects a constant sample arrival rate, with daily release frequency and historical samples arrival pattern that enter the production process when compared with the current situation. Scenario 4 of sub model 2 reflects the introduction of increased production batches which can be achieved in practise by increasing the number of production batches that are scheduled each week. When both scenarios are compared, a suitable capacity planning method like balanced batch scheduling (sub model 2), has a larger effect on average total lead time reduction including WIP

balancing than sub model 1, which represents decreased sample arrival variability, as can be seen in the above table and figure.

When a combination of both scenarios is evaluated, the average lead time of the HiSeq PE125 flow reduces even further to around 17 days, although the average lead time of the MiSeq PE300 flow increases to around 12 days when compared to the results of sub model 2. No explanation could be determined for this result. However, the average and maximum lead time of both flows do not exceed the lead time of 28 days that is agreed to customers. The effect of increased sample throughput of sub model 1 is offset in sub model 3, but for both process flows the minimal lead time of 10 days is achieved.

In general, although not statistically proven, the findings after this simulation experiment show that a combination of both solutions can be introduced in practise to balance WIP and reduce lead times. Increased batch scheduling has the most effect on WIP balancing and lead time reduction. A decreased sample arrival variability can balance WIP and reduce lead times, but the effect is limited. The simulation experiments will be summarized in the following section.

5.4 Summary simulation experiments

In this section, an answer to sub research question 4 is formulated based on the simulation experiments that were performed in the previous three sections.

Sub research question 4: What is the simulated effect of implementing theoretical solutions to the production planning and control on the WIP and lead times of the NGS department?

Simulation modelling was used as an effective tool to evaluate the effect of possible solutions for the business problem. In the simulation study, scenarios in three different sub models were evaluated, to determine the effect on WIP and lead times of the NGS production process.

The first solution that is evaluated reflect scenarios for decreased sample arrival variability. In the initial simulation model, the sample arrival rate was random, with a daily order release interval and volume of sample arrivals varied between 0 and 3 entries per day for each of the four flows in the production process. The effect of a constant sample arrival rate, increased order release interval and stabilized sample arrival pattern was evaluated in 7 different scenarios.

In general, although not statistically proven, based on the simulation experiment, a more constant and stabilized order arrival rate and pattern has an effect on WIP balancing and lead time reduction, but the effect is limited. An average lead time reduction of 5 days was found for both process flows that were analysed. The maximum lead time exceeds the lead time of 28 days that is agreed with customers. On the other hand, inappropriate order release frequencies and offset in timing and sizing of sample arrival can increase WIP and lead time drastically. These findings confirm the need for optimized order release frequencies based on actual sample arrival numbers and stability in sample arrival in practice.

The problem diagnosis in chapter 4 revealed that batch scheduling is mainly based on sample arrival number in combination with amount of data that needs to be generated for each sample, availability of human workforce and equipment per period and lead times that impend to exceed, resulting in WIP as waiting time in the process causing excessive lead times. The second solution that is evaluated reflects the implementation of an increased number of production batches until the sequencing step, to determine the effect of processing more batches in a certain time frame on WIP and lead time. The effect of production batches with less samples that are performed more frequently in a certain time frame on WIP and lead time was evaluated in 4 different scenarios.

In general, although not statistically proven, the findings after the simulation experiment confirm that capacity planning methods, like increased batch scheduling, has an effect on WIP balancing and

lead times reduction and the effect appear directly when more batches are scheduled in a certain timeframe. Inappropriate number of batches that are planned can influence WIP and lead time drastically. An average lead time reduction of around 14 days for the MiSeq PE300 flow and around 16 days for the HiSeq PE125 flow was found. These findings confirm the need for optimized batch scheduling based on actual sample arrival numbers. Since the number of batches that are scheduled has a direct effect on resource utilization and therefore production costs, there should be a balance between the number of batches that are scheduled, number of samples that need to be processed and available resources.

After evaluating scenarios of sub model 1 and sub model 2 it was found that scenario 4 of sub model 1 and scenario 4 of sub model 2 have the most effect on WIP balancing and lead time reduction of the production process. In a final sub model, these two scenarios were combined to evaluate the effect of a combination of solutions on production process performance. The findings after this simulation experiment show that a combination of both solutions can be introduced in practise to balance WIP and reduce lead times. The average lead times and maximum lead time of both process flows that were analysed fall within the agreed delivery time to customers (28 days). Increased batch scheduling has the most effect on WIP balancing and lead time reduction. A decreased sample arrival variability can balance WIP and reduce lead times, but the effect is limited.

5.5 Formulation of solutions

In this section, an answer to sub research question 5 is formulated.

Sub research question 5: What solutions should the NGS department of BaseClear introduce to its production planning and control for possible contributions to better balanced WIP and reduced lead times based on simulated findings?

Based on the simulation experiments performed in the previous sections, the following solutions are proposed to balance WIP and reduce lead time:

- Decrease order arrival variability by realising a constant sample arrival rate.
- Increase production batch scheduling from order registration until the sequencing step.

In the following chapter the main research question is answered, recommendations formulated for management practice regarding implementation of the designed solutions and the research in general is discussed.

6 DISCUSSION

In view of the problem description described in chapter 1, the business problem is: “BaseClear encounters an unbalanced workload regarding its NGS production department which results in variable WIP and exceeding lead times”. In this chapter an enumeration of recommendations for management practise, regarding implementation of potential solutions, is provided and an answer to the main research question formulated by combining the overall conclusions of the sub research questions.

Main research question: How should BaseClear improve the production planning and control of its NGS department to achieve overall balanced Work-in-Process and reduced lead times?

The operational performance of the production planning and control of the core-business process of BaseClear, Next-Generation-Sequencing (NGS), is analysed and possible improvements for decision-making support based on production planning and control theory proposed to balance Work-In-Process and reduce lead times. After a thorough operational performance analysis structural exceeding lead times and unbalanced Work-In-Process have been determined for the NGS production process. About 10% of all orders have been delivered late in 2016 in comparison to

customer agreements and there is variation visible in lead times. Work-In-Process is equally distributed over the NGS production process and waiting time contributes to 67% - 80% of the total lead time on average in 2016.

A general finding for all NGS process flows is that sample arrivals are unequally and randomly distributed over the year. No pattern between increasing sample arrival and exceeding lead times could be determined. Lead times are randomly distributed over the year. In general, the variability in sample arrival has an impact on the stability of the production process performance. In 2016 production scheduling is based on the actual sample arrivals and needed data output per period. These two figures determine the number of process steps that are scheduled and performed each week. No impact of sequencing capacity on lead time and Work-In-Process could be distinguished. The sequencing capacity is not limited and no after-ebony effect on lead time is observed.

After theoretical and empirical research, it can be concluded that there is overlap with the factors found in practice and the dominant factors found in literature on medium term production planning and control level. Poor insight in operational performance corresponds to the need of capacity control measures and possibility of backlog of work in the shop. Limited capacity equipment, personnel and space corresponds to the need for controlled capacity utilization, workforce availability and flexibility. Lack of a standardized ERP with feedback relates to the need for a capacity planning method. A complex production layout with custom services and high variability relates to type of work content and processing time variation. And finally, variable workload with high peaks and poor insight in customer enquiries for medium-term planning, relates to order arrival variability.

After a literature review it has been determined that a balanced order arrival and controlled capacity planning and utilization helps to ensure Work-In-Process balancing and the ability to control and reduce lead times. Total workload must be controlled and should not exceed pre-set maximum limits and a workload input/output control method is needed to manage lead times. It is concluded that workload control in combination with COBACABANA are suitable production planning and control concepts for the high-variety and variable context like in the case company BaseClear. Lead time allowance can be divided into an allowance for the pre-shop pool waiting time and an allowance for the shop floor throughput time.

Based on empirical research, guided by a simulation study, the effect of a better-balanced order arrival and an increased number of production batches until the sequencing step is evaluated. The following solutions are proposed that can possibly contribute to accomplish the business goal:

- Decrease order arrival variability by realising a constant sample arrival rate.
- Increase production batch scheduling from order registration until the sequencing step.

Based on theoretical research, the proposed solutions can be made effective in practise by:

- Improving the customer enquiry stage (order acceptance/job entry stage) to control the input of work to the job pool.
- Determine optimal and maximum levels of WIP for the job pool and shop floor.
- Implementation of a dynamic visual workload input/output decision capacity control method, like COBACABANA, by introducing a centralised planning board for an overview of the current workload situation in the job pool and the shop floor, can help to control order arrival and to maintain a minimal workload level in the shop. The number of cards should be set equal to 100% of the workload norm and the number of cards in circulation should be controlled.
- Determine optimal release frequencies for the work orders to keep Work-In-Process at the pre-determined level in the shop.
- Introduction of the anticipated new lower level NGS service with longer promised lead times can help to stabilize the workload of the job pool and the shop.
- Introduction of centralized order release control at the job release stage as the main control point can simplify the remaining planning and control process.

- Implementation of a standard production schedule with increased number of batches until the sequencing step.
- Sequencing run scheduling based on capacity utilization and due dates expiration measures for lowest operational costs.

The findings resulting from this BPS project are made within the scope set at the beginning of the project. A critical reflection of all methodologic choices that have been made will be outlined to determine if the proposed solutions are based on reliable and valid research with justified academic criteria. The limitations, internal and external validity of the research and the conclusions will be discussed in addition to the assumptions and limitations already discussed in the previous chapters.

Concerning internal validity, the measurement precision, reliability and consistency will be evaluated. The research is mainly based upon averages derived from historical data or obtained from simulation outcomes. Considering the relatively high variability in the production process and since the analysis was based only on one production year, measures could show a large variability. The historical data that is used in the research is filled in manually in the LIMS and can contain errors. Measures, like number of samples for a certain production flow, can change rapidly in time. The construct WIP has been measured by taken the amount of waiting time in the production process as a degree of workload level throughout the production process instead of the actual number of samples within the process.

Besides the limitations that were already discussed in chapter 4, other restrictions to the simulation model apply. Imitating reality, there is a considerable variation in order arrival. Dealing with this variation requires a high degree of flexibility. In practice, this flexibility is achieved by adaptation to the production schedule. In Arena, this flexibility and variability is limited and this can lead to disturbed performance measures. It is good to realise simulation modelling gives no exact answers, but only approximations and estimates. Rush orders are not included in the simulation model as these events are unplanned. Although they disturb the standard process their practical occurrence is limited. Therefore, the impact on the outcome of the research seems to be limited. During the research a student version of the simulation software was used which involved considerable restrictions. The software allowed only a maximum number of 150 entities within the production process. This has a significant effect on the sample arrival variability that could be analysed.

Another limitation of the simulation model is the processing of custom orders that need additional care. This is not included in the model and could influence the measures, since their practical occurrence is significant. The historical data used for the input and performance measurement of the system is just one realisation of the stochastic process. Randomness in the system is unavoidable, because the arrival process is stochastic. Another limitation of the research is that a limited number of solutions has been evaluated in the simulation model. Other possible solutions to the business problem can be evaluated and recommendations are given in chapter 7. Due to simulation model limitations, reality setup could not be imitated identically. Therefore, an ideal situation based on the production measures of 2016 could not be evaluated.

In this paragraph the practical implications of the research will be discussed, by reflecting on the functional specifications of the proposed solutions. The sponsors and the NGS production manager have been consulted to determine if the outcome of the research meets their objectives that were set in the first chapter of the thesis. The solutions should be efficient to use and not to complex. This criterium is met in the sense that COBACABANA is proposed as an easy PPC concept on operational level. Some restrictions of the proposed solutions apply. For instance, it has not been investigated how compliant the proposed PPC concept is with existing software systems that are used within the company. Also the practical design of the COBACABANA concept has not been worked out yet, as well as the maximum and minimum amount of work for the job pool and shop floor. After the proposed solutions are implemented, an effect on a more balanced WIP and reduced lead times is

expected as described in chapter 5. The following risks have been estimated. The impact on production costs hasn't been evaluated. There is a risk that the capacity of the machines are not used at their most. Higher operational costs can be seen after implementing fixed production batch scheduling.

Considering the limitations of the research, in this paragraph the research findings will be generalised to discuss theoretical implications for PPC theory. It reflects how the knowledge of this research in the context of BaseClear contributes to theory of workload control. Hereby considering the external validity of the research. In this thesis the production planning and control system of a Make-to-Order general flow-shop is analysed and solutions proposed for potential improvements. Literature review showed that many studies of the WLC concept have been performed within job-shopping. However, few empirical studies have been done in general flow-shops, like the case company. This research can make a contribution to knowledge how a WLC concept like COBACABANA can contribute to a better PPC of a general flow-shop.

PPC within a general-flow shop, like the case company, can be challenging by variability in order flow, product variety and complexity in production layouts. These factors are present in the case company. There is overlap with the factors found in practice in the general-flow shop of the case company and the dominant factors found in theory on medium term level how WLC can contribute to a better PPC. Poor insight in operational performance corresponds to the need of capacity control measures and possibility of backlog of work in the shop. Limited capacity equipment, personnel and space corresponds to the need for controlled capacity utilization, workforce availability and flexibility. Lack of a standardized ERP with feedback relates to the need for a capacity planning method. A complex production layout with custom services and high variability relates to type of work content and processing time variation. And finally, variable workload with high peaks and poor insight in customer enquiries for medium-term planning, relates to order arrival variability.

In general, it is found that workload balancing, by reducing the order arrival variability to the shop floor, and maintaining a stabilised workload level on the shop floor, by suitable batch scheduling based on available workforce and resource capacity seems key in aiming for the shortest lead times within general-flow shops. When these factors are compared it was found that a suitable capacity planning method has the largest effect on WIP balancing and lead time reduction. The COBACABANA concept can help to maintain a stabilized workload in the pre-shop pool and on the shop floor of a general-flow shop and remain variability in processing times. In order to minimize the number of cards that circulate within a shop a maximum workload norm level for a total process flow could potentially control total workload. However, this should be evaluated in more detail. The design of the proposed solutions seem to be, potentially, wider applicable in general flow-shop settings within the MTO industry to balance WIP and reduce lead times.

Considering the general limitations described above, the outcomes of this research must be dealt with carefully. However, although the limitations described above apply, an effect on operational performance in terms of a better balanced WIP and reduced lead times is expected after implementing the proposed solutions.

7 RECOMMENDATIONS

In this chapter, some interesting aspects and recommendations for further research are provided. The research performed in this thesis can be investigated further. For instance, the problem diagnosis included data of only one production year and therefore the effect of seasonal factors could not be included. Also, there is no focus on production costs and investigating other scenarios like the effect of rush orders on the performance of the production system is an interesting topic for further research. To make a more founded contribution to theory more empirical research is needed.

There is still a lack of insight in problems and barriers that are encountered in the implementation of suitable solutions. Therefore, it is recommended that the actual shape and content of the intervention should be described in an intervention plan before the implementation phase takes

place. This intervention plan should contain recommendations for a change plan, timing of the change plan and actual change process that will be carried out. Further, it is recommended to evaluate the effect of the solutions on the operational performance after the implementation phase.

During the informal interviews that were held potential other subjects were mentioned that could possibly have an effect on the current operational performance. Internal communication and information transfer between the M&S and lab department looks suboptimal. For instance, the quotes that are provided to customers contain errors and uncertainties relating to the work that needs to be performed which could cause delays in the process. Other issues that were observed relate to the decision structure within the company. Multiple employees seem to be involved in managing the production process and project management of custom projects is not structured. Another subject that could have a potential effect on production performance is improvement of the internal laboratory work regulations. Optimising these regulations could prevent the need for replacements or rework that are needed. Also the final step in the production process, data analysis, looks suboptimal. For all orders the standard throughput time is five days, but data pipe-lines should, in theory, be able to process data faster. Looking for back-up capacity and speed up data processing times could possibly also have a contribution to shorter lead times. These subjects can be investigated in more detail to determine their influence on operational performance. Introduction of robotization and automation that can take over manual steps throughout the production process could help to unlock more human workforce that is needed to handle peaks in workload and to stabilize batch scheduling. This is also an interesting topic for further research.

From theoretical perspective, contemporary empirical research on the WLC concept is relatively scarce and many authors regard it as one of the future challenges (Gaalman and Perona, 2002; Stevenson et al., 2005). Future research could elaborate on an integrated card-based production planning and control solution for MTO shops. No studies have been performed on the implementation of COBACABANA in practice to confirm the performance improvements and such is another important direction for future research. Another important avenue for future research is to explore how COBACABANA can enhance production control in shops with multiple production work centers responsible for a product family, which are often created as part of a lean implementation. This may involve, for example, introducing a nested COBACABANA system whereby individual COBACABANA systems are used to control the workload within each cell and another is used to control the workload across work centers.

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APPENDICES

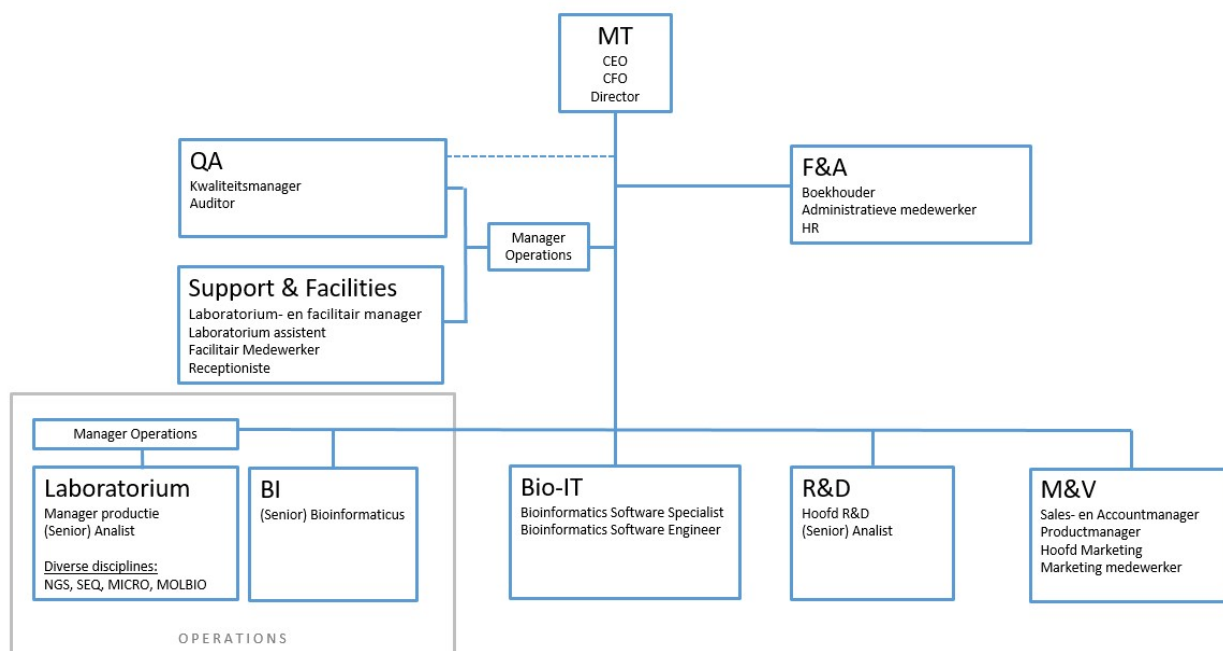
Appendix A

Chronological development of services within the case company BaseClear.

- 1993: Foundation BaseClear, start with LiCor model 400 sequencer
- 1994: Move to ABC building in Leiden
- 1995: Participation in Arabidopsis sequencing project
- 1996: First capillary sequencer
- 1997: New mycoplasma test service
- 1998: New gene synthesis service
- 1999: Introduction Laboratory Information Management System
- 2000: Service package extended (cloning, genotyping and microbiological services)
- 2001: Six sequencers in production
- 2002: Expansion of the robotics
- 2003: Move to the Einsteinweg
New 3730 multicapillary sequencer
- 2004: Participation in ESA-MAP project
- 2005: Start construction extended synthetic gene libraries
- 2006: ISO 17025 accreditation
- 2007: Start ZF-tools project in collaboration with ZF-Screens
- 2008: Start Illumina sequencing services (Illumina GAI)
- Start forensic laboratory
- Official MicroSEQ® service provider
- 2009: Illumina Certified Service provider (CSPPro)
- 2010: Roche Nimblegen Certified Service provider
- 2011: Illumina HiSEQ2000 sequencer
- 2012: VITEK® MS from BioMerieux for MALDI-TOF microbial identifications
- Collaboration with Zymo Research services, offering 5-mC and 5-hmC analysis
- 2013: Upgrade Illumina HiSEQ2000 to Illumina HiSEQ2500
- Offering PacBio RS sequencing services
- 2015: Start with Oxford Nanopore sequencing (MinION)
- Dedicated R&D department for custom project
- 2016: Purchase of PacBio Sequel system

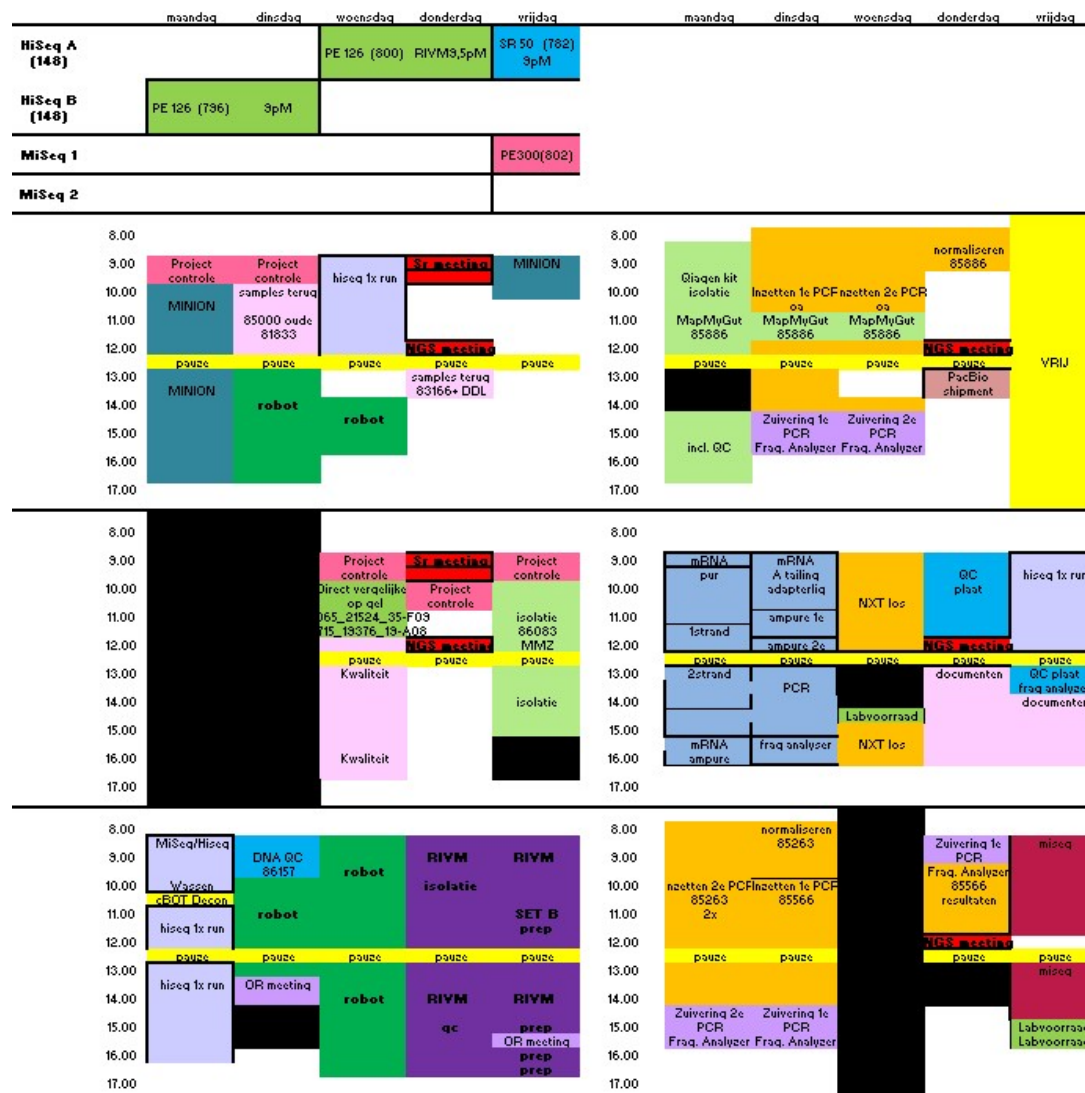
Appendix B

Chart of BaseClear in 2017.



Appendix C

Example of a weekly production schedule of the NGS department at BaseClear.



Appendix D

Summary and comparison of the four card-based signalling systems.

Table 19: The loop structure of the (common) Kanban, ConWIP, POLCA and COBACABANA systems.

	Common Kanban	ConWIP	POLCA	COBACABANA
Where established?	Between two stations	Between entry and exit stations	Between two stations	Between stations and a central release function that precedes the shop floor
Relation to the routing	Needs to be established for each possible routing step	One single loop must contain all possible routings	Needs to be established for each possible routing step.	Routing independent (i.e. not related to the routing)
Contains (operations per Order)	One operation	All operations	Two operations (an operation forms part of two loops for all except the first and last operations)	One operation
WIP-Cap (Limit on work in the loop)	Per station	On the shop floor load (the load at a single station is not limited)	Per station	Per station

Table 20: Consequences for the applicability of the loop structure.

	Common Kanban	ConWIP	POLCA	COBACABANA
Consequences: routing variability	Only allows for simple, directed routings	Only allows for the Pure flow shop, i.e. where all work visits all stations in the same order	Only allows for simple, directed routings. Leads to blocking if the loop structure is undirected	Allows for all possible routing characteristics
Consequences: processing time variability	Individual loops keep processing time information local. Does not allow for load balancing across stations	General loop does not provide processing time information. Does not allow for load balancing across stations	Individual loops keep processing time information local. Does not allow for load balancing across stations	Centralised information provides a global view of the shop floor, which facilitates load balancing across stations
Consequences: inventory vs. order control	Creates a problem of card propagation in the order control problem since information has to be transmitted for each routing step. This creates direct/indirect load in each loop and prohibits control in an order control problem	Does not allow for controlling the work-in-process at each station, so should not be applied to an inventory control problem	Similar structure to Kanban but problems resolved by card properties. Allows for inventory and order control problems	Uses a centralised release function to control the mix of orders released to the shop floor. Designed for the order control problem

Table 21: Card properties of the common Kanban, ConWIP, POLCA and COBACABANA systems.

	Common Kanban	ConWIP	POLCA	COBACABANA
What does it say?	A part/product was or will be used	We finished one of the jobs in the system, release another job	We finished one of the jobs you sent us; you can send us another	The operation belonging to this part/product at this station has been completed
Card type(s)	Originally, three (in the internal supply chain): Withdrawal Kanbans; work-in-process Kanbans (was used) and production Kanbans (will be used); for shop floor control, often reduced to one common Kanban	Only one	Only one	Two (which appear in pairs): A release card for load balancing calculations and an operation card for feedback
Information transmitted	Which part/product was or will be used and should thus be produced. This may include information on the processing time, due date, etc.	That the shop floor has capacity to work on another job	That the next station in the routing of the job has future capacity availability	For the operation card: which job has been completed at which station. For the operation/release cards: the processing time of this operation (given by the size of the cards)

Table 22: The consequences of card properties for applicability.

	Common Kanban	ConWIP	POLCA	COBACABANA
Consequences: routing variability	None	None	Prohibits feedback loops due to the risk of blocking	None
Consequences: processing time variability	Only gives information on jobs that were or will be used at a station. Does not allow for load balancing	Only gives information on jobs completed by the system. Does not allow for load balancing	Only gives information on jobs completed at a station. Does not allow for load balancing	Release cards allow for visualising the current load situation and job progress on the shop floor. Allows for load balancing. Load balancing calculations are facilitated by the planning board and the release cards
Consequences: inventory vs. order control	If cards are bound to a specific order (order control problem), they have to wait at a station until all preceding operations have been completed (indirect load). This prohibits Kanban's use for order control problems	Jobs are not prioritised since cards are job-anonymous. Requires higher level IT support for creating an appropriate sequence in which jobs are released to the shop floor	Cards are job-anonymous, which avoids the problems of Kanbans. Requires an MRP system for prioritising jobs according to urgency (an earliest release date for each operation)	The centralised release function avoids the problems of Kanban and ensures prioritising of jobs

Appendix E

Raw data problem diagnosis

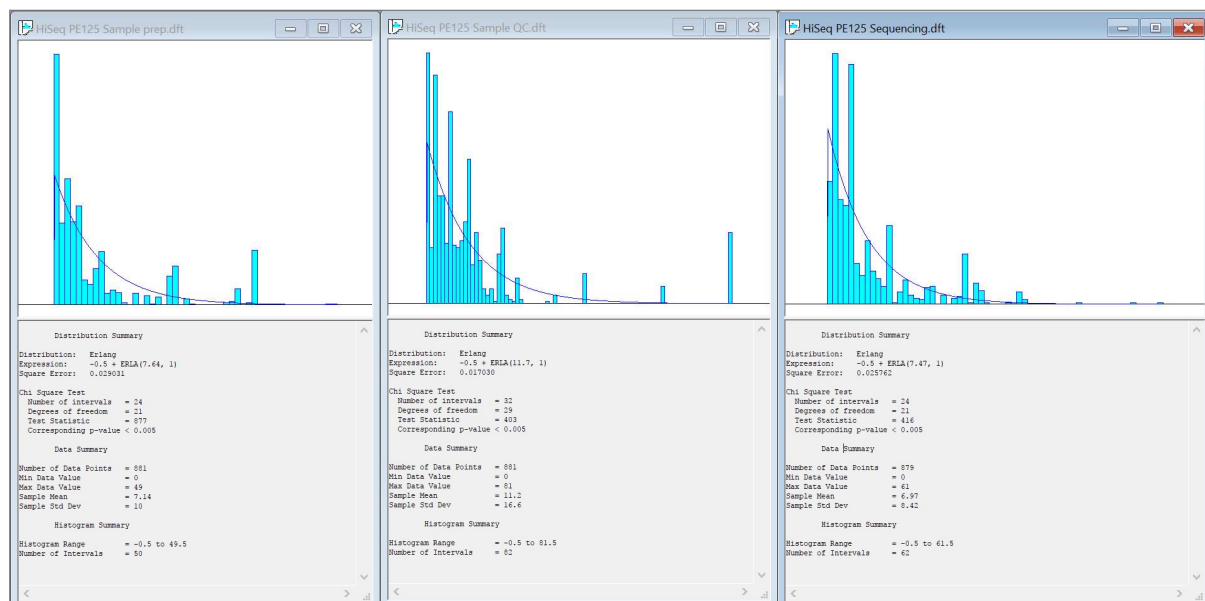
Sample code	Order code	Amount of data (MB)	Sample prep type	Sequencing type	Administration entry date	Sample QC Date	Sample prep date	Library QC date	Sequencing date	Data delivery date	Delivery date
15530	75568	420	TruSeq	HiSeq SR50	08-01-2016	09-01-2016	17-02-2016	22-02-2016	24-02-2016	29-02-2016	07-03-2016
15627	75590	420	Nextera XT	HiSeq PE125	11-01-2016	12-01-2016	02-02-2016	09-02-2016	15-02-2016	20-02-2016	18-02-2016
15634	75608	420	Nextera XT	HiSeq PE125	12-01-2016	13-01-2016	02-02-2016	21-03-2016	14-04-2016	19-04-2016	26-04-2016
15772	75694	250	Nextera XT	HiSeq PE125	15-01-2016	16-01-2016	02-02-2016	04-02-2016	15-02-2016	20-02-2016	02-03-2016
15789	75749	250	TruSeq	HiSeq SR50	19-01-2016	20-01-2016	08-02-2016	09-02-2016	15-02-2016	20-02-2016	17-02-2016
15790	75749	250	TruSeq	HiSeq SR50	19-01-2016	20-01-2016	08-02-2016	09-02-2016	15-02-2016	20-02-2016	17-02-2016
15800	75782	250	Nextera XT	HiSeq PE125	20-01-2016	21-01-2016	08-02-2016	09-02-2016	15-02-2016	20-02-2016	17-02-2016
15802	75638	250	Nextera XT	HiSeq PE125	21-01-2016	22-01-2016	04-02-2016	04-02-2016	09-02-2016	14-02-2016	26-02-2016
15804	75825	250	TruSeq	HiSeq PE125	21-01-2016	22-01-2016	28-01-2016	04-02-2016	15-02-2016	20-02-2016	17-02-2016
15805	75825	250	Amplicon	HiSeq PE125	21-01-2016	22-01-2016	28-01-2016	04-02-2016	15-02-2016	20-02-2016	17-02-2016
16029	75881	500	Nextera XT	HiSeq PE300	25-01-2016	26-01-2016	08-02-2016	09-02-2016	02-03-2016	07-03-2016	07-03-2016
16030	75881	500	Nextera XT	HiSeq PE300	25-01-2016	26-01-2016	08-02-2016	09-02-2016	02-03-2016	07-03-2016	07-03-2016
16031	75881	250	Nextera XT	HiSeq PE300	25-01-2016	26-01-2016	08-02-2016	09-02-2016	02-03-2016	07-03-2016	07-03-2016
16032	75881	250	Nextera XT	HiSeq PE300	25-01-2016	26-01-2016	08-02-2016	09-02-2016	02-03-2016	07-03-2016	07-03-2016
16033	75881	250	Nextera XT	HiSeq PE300	25-01-2016	26-01-2016	08-02-2016	09-02-2016	02-03-2016	07-03-2016	07-03-2016
16034	75881	250	Nextera XT	HiSeq PE300	25-01-2016	26-01-2016	08-02-2016	09-02-2016	02-03-2016	07-03-2016	07-03-2016
16035	75881	250	Nextera XT	HiSeq PE300	25-01-2016	26-01-2016	08-02-2016	09-02-2016	02-03-2016	07-03-2016	07-03-2016
16036	75881	250	Nextera XT	HiSeq PE300	25-01-2016	26-01-2016	08-02-2016	09-02-2016	02-03-2016	07-03-2016	07-03-2016
16037	75881	250	Nextera XT	HiSeq PE300	25-01-2016	26-01-2016	08-02-2016	09-02-2016	02-03-2016	07-03-2016	07-03-2016
16038	75881	250	Nextera XT	HiSeq PE300	25-01-2016	26-01-2016	08-02-2016	09-02-2016	02-03-2016	07-03-2016	07-03-2016
16039	75881	250	Nextera XT	HiSeq PE300	25-01-2016	26-01-2016	08-02-2016	09-02-2016	02-03-2016	07-03-2016	07-03-2016
16040	75881	250	Nextera XT	HiSeq PE300	25-01-2016	26-01-2016	08-02-2016	09-02-2016	02-03-2016	07-03-2016	07-03-2016
16041	75881	250	Nextera XT	HiSeq PE300	25-01-2016	26-01-2016	08-02-2016	09-02-2016	02-03-2016	07-03-2016	07-03-2016
16042	75881	250	Nextera XT	HiSeq PE300	25-01-2016	26-01-2016	08-02-2016	09-02-2016	02-03-2016	07-03-2016	07-03-2016
16043	75881	250	Nextera XT	HiSeq PE300	25-01-2016	26-01-2016	09-02-2016	09-02-2016	02-03-2016	07-03-2016	07-03-2016
16044	75881	250	Nextera XT	HiSeq PE300	25-01-2016	26-01-2016	09-02-2016	09-02-2016	02-03-2016	07-03-2016	07-03-2016
16045	75881	250	Nextera XT	HiSeq PE300	25-01-2016	26-01-2016	09-02-2016	09-02-2016	02-03-2016	07-03-2016	07-03-2016
16046	75881	250	Nextera XT	HiSeq PE300	25-01-2016	26-01-2016	09-02-2016	09-02-2016	02-03-2016	07-03-2016	07-03-2016
16067	75954	250	Nextera XT	HiSeq PE300	28-01-2016	29-01-2016	02-02-2016	04-02-2016	15-02-2016	20-02-2016	11-04-2016
16068	75954	250	Nextera XT	HiSeq PE300	28-01-2016	29-01-2016	02-02-2016	04-02-2016	15-02-2016	20-02-2016	11-04-2016
16069	75954	250	Nextera XT	HiSeq PE300	28-01-2016	29-01-2016	02-02-2016	04-02-2016	15-02-2016	20-02-2016	11-04-2016
16070	75954	250	Sequel	Sequel	28-01-2016	29-01-2016	04-02-2016	04-02-2016	01-04-2016	06-04-2016	11-04-2016
16071	75954	250	Sequel	Sequel	28-01-2016	29-01-2016	04-02-2016	04-02-2016	01-04-2016	06-04-2016	11-04-2016
16084	75955	250	Sequel	Sequel	28-01-2016	29-01-2016	17-02-2016	18-02-2016	19-02-2016	24-02-2016	29-03-2016
16085	75955	250	Nextera XT	HiSeq PE125	28-01-2016	29-01-2016	17-02-2016	18-02-2016	19-02-2016	24-02-2016	29-03-2016
16086	75955	500	Nextera XT	HiSeq PE125	28-01-2016	29-01-2016	17-02-2016	18-02-2016	19-02-2016	24-02-2016	29-03-2016
16135	75954	500	TruSeq	HiSeq PE125	01-02-2016	02-02-2016	02-02-2016	04-02-2016	15-02-2016	20-02-2016	11-04-2016
16136	75954	500	TruSeq	HiSeq PE125	01-02-2016	02-02-2016	02-02-2016	04-02-2016	15-02-2016	20-02-2016	11-04-2016
16137	75994	500	TruSeq	HiSeq PE125	01-02-2016	02-02-2016	02-02-2016	04-02-2016	09-02-2016	14-02-2016	03-03-2016
16233	76013	500	Nextera XT	HiSeq PE125	01-02-2016	02-02-2016	04-02-2016	04-02-2016	09-02-2016	14-02-2016	13-03-2016
16234	76013	500	Nextera XT	HiSeq PE125	01-02-2016	02-02-2016	04-02-2016	04-02-2016	09-02-2016	14-02-2016	13-03-2016
16236	76013	500	Nextera XT	HiSeq PE125	02-02-2016	03-02-2016	23-02-2016	26-02-2016	02-03-2016	07-03-2016	13-03-2016
16237	75855	500	Nextera XT	HiSeq PE125	02-02-2016	03-02-2016	18-02-2016	18-02-2016	02-03-2016	07-03-2016	13-03-2016
16286	76063	500	Nextera XT	HiSeq PE125	03-02-2016	04-02-2016	08-02-2016	09-02-2016	15-02-2016	20-02-2016	25-02-2016
16287	76063	250	Nextera XT	HiSeq PE125	03-02-2016	04-02-2016	08-02-2016	09-02-2016	15-02-2016	20-02-2016	25-02-2016
16288	76066	250	16S Profiling	HiSeq PE300	03-02-2016	04-02-2016	08-02-2016	03-03-2016	11-03-2016	16-03-2016	29-03-2016
16289	76066	250	16S Profiling	HiSeq PE300	03-02-2016	04-02-2016	08-02-2016	03-03-2016	11-03-2016	16-03-2016	29-03-2016
16290	76066	250	16S Profiling	HiSeq PE300	03-02-2016	04-02-2016	08-02-2016	03-03-2016	11-03-2016	16-03-2016	29-03-2016
16291	76066	250	16S Profiling	HiSeq PE300	03-02-2016	04-02-2016	08-02-2016	03-03-2016	11-03-2016	16-03-2016	29-03-2016
16295	75955	500	16S Profiling	HiSeq PE300	04-02-2016	05-02-2016	15-02-2016	03-03-2016	22-03-2016	27-03-2016	29-03-2016
16296	75955	500	16S Profiling	HiSeq PE300	04-02-2016	05-02-2016	15-02-2016	03-03-2016	22-03-2016	27-03-2016	29-03-2016
16320	76111	250	Nextera XT	HiSeq PE300	05-02-2016	06-02-2016	08-02-2016	09-02-2016	15-02-2016	20-02-2016	18-02-2016
16321	75637	250	Nextera XT	HiSeq PE125	05-02-2016	06-02-2016	08-02-2016	09-02-2016	15-02-2016	20-02-2016	13-04-2016
16328	75568	250	Nextera XT	HiSeq PE125	08-02-2016	09-02-2016	09-02-2016	09-02-2016	14-02-2016	14-02-2016	07-03-2016
16329	75568	250	Nextera XT	HiSeq PE125	08-02-2016	09-02-2016	17-02-2016	23-02-2016	02-03-2016	07-03-2016	07-03-2016
16350	76165	250	16S Profiling	HiSeq PE300	09-02-2016	10-02-2016	03-03-2016	03-03-2016	07-03-2016	12-03-2016	11-03-2016
16351	76165	250	16S Profiling	HiSeq PE300	09-02-2016	10-02-2016	03-03-2016	03-03-2016	07-03-2016	12-03-2016	11-03-2016
16352	76202	250	16S Profiling	HiSeq PE300	09-02-2016	10-02-2016	03-03-2016	03-03-2016	07-03-2016	12-03-2016	29-03-2016
16353	76203	250	16S Profiling	HiSeq PE300	10-02-2016	11-02-2016	17-02-2016	18-02-2016	02-03-2016	07-03-2016	26-04-2016
16354	76203	250	16S Profiling	HiSeq PE300	10-02-2016	11-02-2016	17-02-2016	18-02-2016	02-03-2016	07-03-2016	26-04-2016
16475	76203	30	Nextera XT	HiSeq PE125	15-02-2016	16-02-2016	16-02-2016	18-02-2016	14-04-2016	19-04-2016	26-04-2016
16526	76319	30	16S Profiling	HiSeq PE300	16-02-2016	17-02-2016	01-03-2016	03-03-2016	08-03-2016	13-03-2016	04-04-2016
16527	76319	30	Nextera XT	HiSeq PE125	16-02-2016	17-02-2016	01-03-2016	03-03-2016	08-03-2016	13-03-2016	04-04-2016
16529	76319	1000	Nextera XT	HiSeq PE125	16-02-2016	17-02-2016	01-03-2016	03-03-2016	08-03-2016	13-03-2016	04-04-2016
16530	76320	1000	16S Profiling	HiSeq PE300	16-02-2016	17-02-2016	01-03-2016	03-03-2016	11-03-2016	16-03-2016	29-03-2016
16532	76227	15000	16S Profiling	HiSeq PE300	17-02-2016	18-02-2016	01-03-2016	03-03-2016	11-03-2016	16-03-2016	13-03-2016

[illegible]

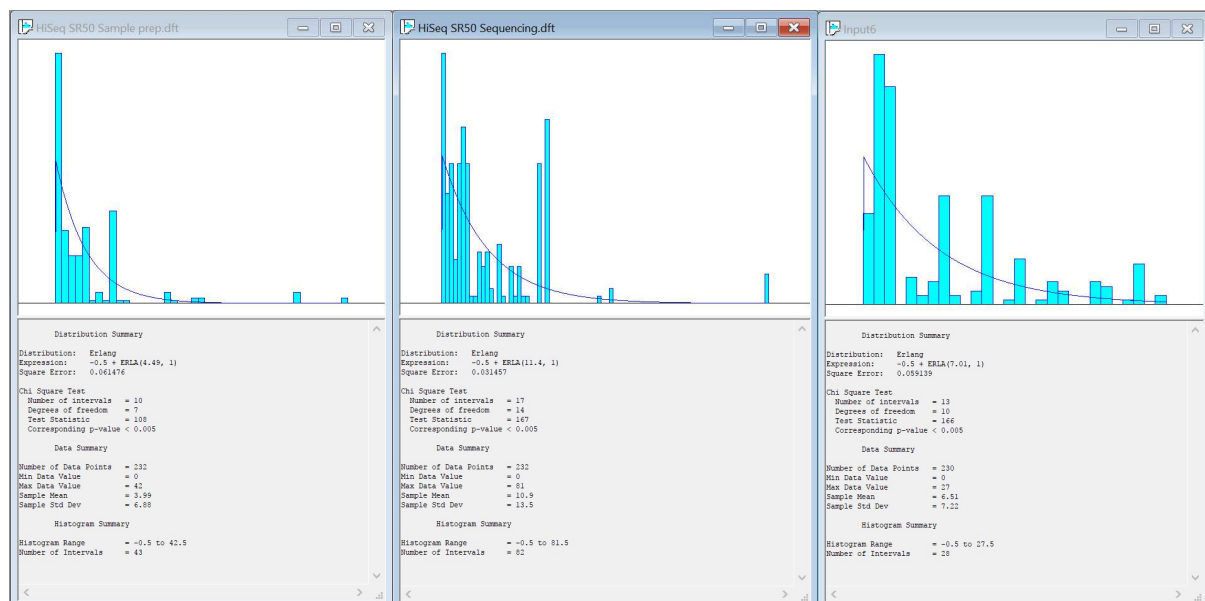
Appendix F

Erlang probability distributions used in simulation model

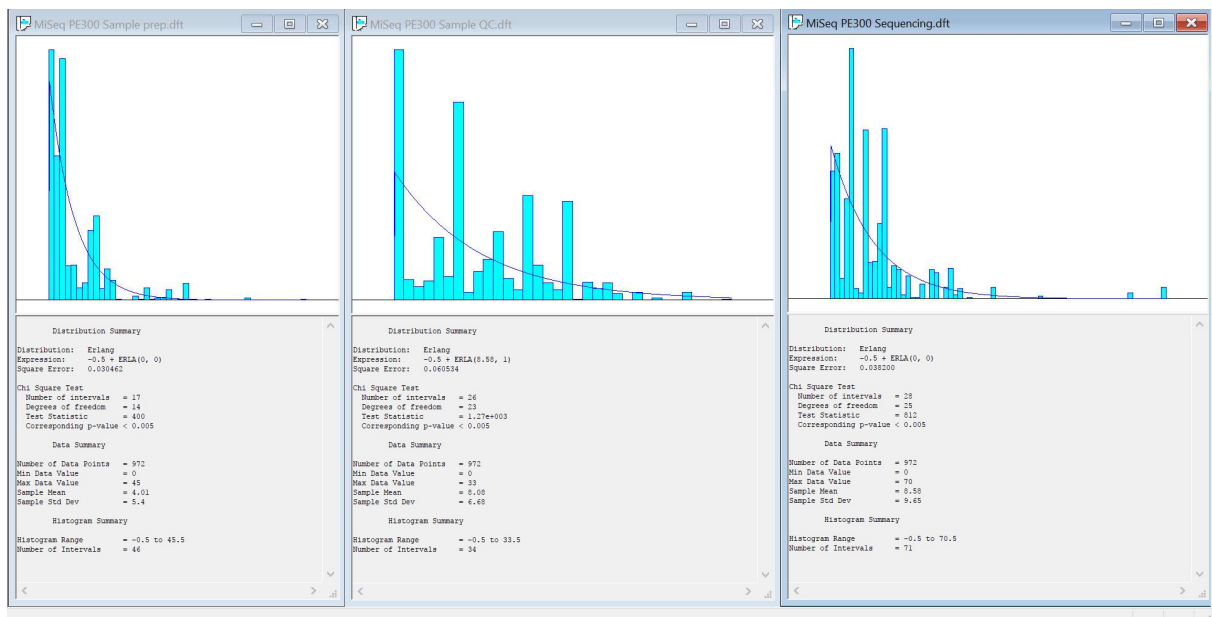
HiSeq PE125



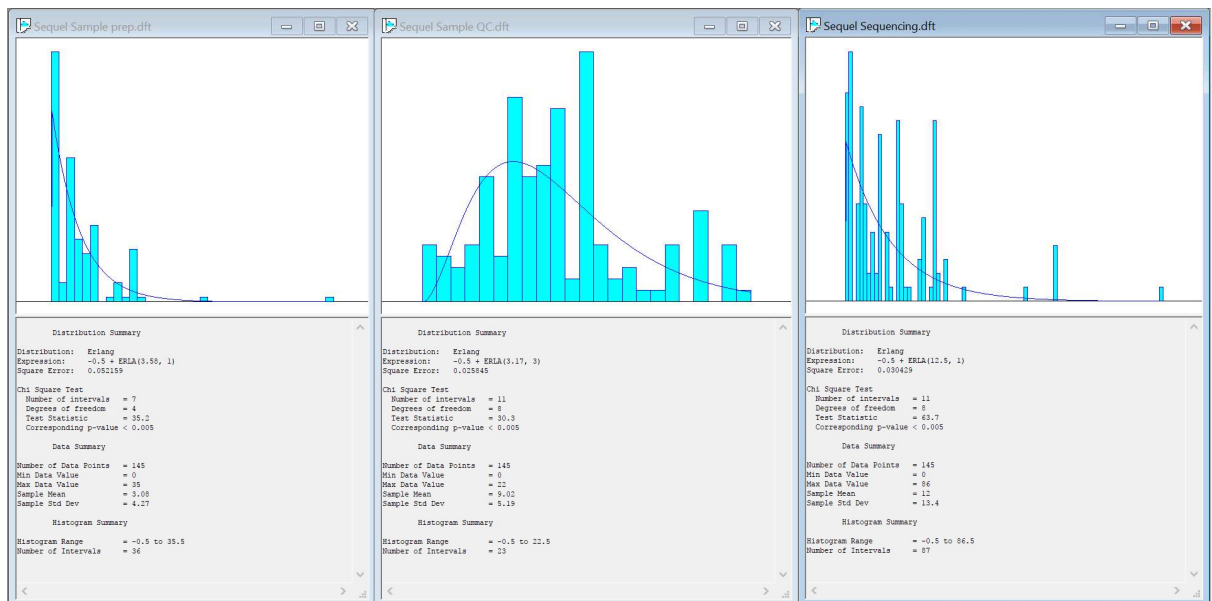
HiSeq SR50



MiSeq PE300



Sequel



Appendix G

Mathematical foundations of performance measures

Processing time

= value-added time in days spent on entity related activities

= (Sample registration + Sample QC + Sample prep + Library QC + Sequencing + Data analysis)

Where:

Sample registration = 1 day

Sample QC = 1 day

Sample prep = 1 day (HiSeq PE125) or 2 days (MiSeq PE300)

Library QC = 1 day

Sequencing = 1 days

Data analysis = 5 days

WIP

= non-value added time (NAT) in days spent on non-entity related activities in between 2 processing steps

= (NAT Sample registration/Sample QC + NAT Sample QC/Sample prep + NAT Sample prep/Library QC + NAT Library QC/Sequencing + NAT Sequencing/Data analysis)

Lead time

= Processing time + WIP

Average lead time

= average lead time in days of each entity per production process flow

= (total lead time for each process flow / total number of entities processed for each process flow)

Appendix H

Simulation model validation data

Table 23: Simulation model validation output compared with data from problem diagnosis.

KPI	Flow	MiSeq PE300						HiSeq PE125					
	Tool	Average	Half width	Min. Value	Max. Value	Confidence interval	Significance level (%)	Average	Half width	Min. Value	Max. Value	Confidence interval	Significance level (%)
Lead time	Arena	30,89	2,86	13,41	49,27	(28,22;33,94)	90,74	29,94	2,38	15,12	48,27	(27,56;32,32)	92,05
	Problem diagnosis	31,70	NA	11,00	88,00	NA	NA	35,50	NA	10,00	136,00	NA	NA
WIP	Arena	19,89	2,86	2,41	38,27	(17,22;22,94)	85,62	19,94	2,38	5,12	38,27	(17,56;22,32)	88,06
	Problem diagnosis	20,70	NA	0,00	77,00	NA	NA	25,50	NA	0,00	126,00	NA	NA

Simulation model validation raw output data Arena

Replications: 12 Time Units: Days

Key Performance Indicators

System		Average				
Number Out		65				
Wait Time		Average	Half Width	Minimum Average	Maximum Average	Minimum Value
Sample 1% Nextera HiSeq PE125		19.8496	2,56	14.1817	27.8520	5.8842
Sample 1% Nextera MiSeq PE300		20.9908	7,24	0.00	37.8841	0.00
Sample 2% 16S Profiling MiSeq		15.3123	2,67	7.9211	21.7158	2.4156
Sample 2% Nextera HiSeq PE125		20.0355	2,19	15.7854	25.9774	5.1173
Sample 2% Nextera MiSeq PE300		24.8480	3,06	20.3363	36.4147	18.9968
Sample Sequel		10.0666	5,03	0.00	19.2970	0.00
Total Time		Average	Half Width	Minimum Average	Maximum Average	Minimum Value
Sample 1% Nextera HiSeq PE125		29.8496	2,56	24.1817	37.8520	15.8842
Sample 1% Nextera MiSeq PE300		29.3241	9,46	0.00	47.8841	0.00
Sample 2% 16S Profiling MiSeq		26.3123	2,67	18.9211	32.7158	13.4156
Sample 2% Nextera HiSeq PE125		30.0355	2,19	25.7854	35.9774	15.1173
Sample 2% Nextera MiSeq PE300		34.8480	3,06	30.3363	46.4147	28.9968
Sample Sequel		17.4000	8,34	0.00	30.2970	0.00

Appendix I

Formulas performance measurement output statistics of simulation models

Confidence interval

= average \pm half width

Significance level

= 100% - half width / average

Appendix J

Performance measurement output statistics of sub model 1: order arrival variability

	KPI												
	Flow	MiSeq PE300						HiSeq PE125					
Scenario	Nr out	Average	Half width	Min. Value	Max. Value	Confidence interval	Significance level (%)	Average	Half width	Min. Value	Max. Value	Confidence interval	Significance level (%)
Initial model	84	30,89	2,86	13,41	49,27	(28,22;33,94)	90,74	29,94	2,38	15,12	48,27	(27,56;32,32)	92,05
Scenario 1	61	31,27	2,02	18,87	44,10	(29,25;33,29)	93,54	28,02	3,07	16,78	40,98	(24,95;31,09)	89,04
Scenario 2	84	52,97	8,32	16,37	75,27	(44,65;61,29)	84,29	41,15	8,95	10,00	64,69	(32,20;50,10)	78,25
Scenario 3	152	45,00	5,50	16,21	82,99	(39,50;50,50)	87,78	43,10	3,47	24,87	71,75	(39,63;46,57)	91,95
Scenario 4	54	25,05	7,19	11,00	45,00	(17,86;32,24)	71,30	24,09	5,56	10,00	36,00	(18,53;29,65)	76,92
Scenario 5	71	38,17	0,00	24,00	42,00	(38,17;38,17)	100,00	25,00	0,00	20,00	30,00	(25,00;25,00)	100,00
Scenario 6	107	45,70	6,94	11,00	78,00	(38,76;52,64)	84,81	46,61	3,52	30,00	60,00	(43,09;50,13)	92,45
Scenario 7	121	47,91	0,00	31,00	72,00	(47,91;47,91)	100,00	40,00	0,00	30,00	50,00	(40,00;40,00)	100,00

	KPI												
	Flow	MiSeq PE300						HiSeq PE125					
Scenario	Nr out	Average	Half width	Min. Value	Max. Value	Confidence interval	Significance level (%)	Average	Half width	Min. Value	Max. Value	Confidence interval	Significance level (%)
Initial model	84	19,89	2,86	2,41	38,27	(17,22;22,94)	85,62	19,94	2,38	5,12	38,27	(17,56;22,32)	88,06
Scenario 1	61	20,27	2,02	7,87	33,10	(18,25;22,29)	90,03	18,02	3,07	6,78	30,98	(14,95;21,09)	82,96
Scenario 2	84	41,97	8,32	5,37	64,27	(33,65;50,29)	80,18	31,15	8,95	0,00	54,69	(22,20;40,10)	71,27
Scenario 3	152	34,00	5,50	5,21	71,99	(28,50;39,50)	83,82	33,10	3,47	14,87	61,75	(29,63;36,57)	89,52
Scenario 4	54	14,05	7,19	0,00	34,00	(6,86;21,24)	48,83	14,09	5,56	0,00	26,00	(8,53;19,65)	60,54
Scenario 5	71	27,17	0,00	13,00	31,00	(27,17;27,17)	100,00	15,00	0,00	10,00	20,00	(15,00;15,00)	100,00
Scenario 6	107	34,70	6,94	0,00	67,00	(27,76;41,64)	80,00	36,61	3,52	20,00	50,00	(33,09;40,13)	90,39
Scenario 7	121	36,91	0,00	20,00	61,00	(36,91;36,91)	100,00	30,00	0,00	20,00	40,00	(30,00;30,00)	100,00

Appendix K

Performance measurement output statistics of sub model 2: capacity planning method

	KPI						LEAD TIME						
	Flow	MiSeq PE300						HiSeq PE125					
Scenario	Nr out	Average	Half width	Min. Value	Max. Value	Confidence interval	Significance level (%)	Average	Half width	Min. Value	Max. Value	Confidence interval	Significance level (%)
Initial model	84	30,89	2,86	13,41	49,27	(28,22;33,94)	90,74	29,94	2,38	15,12	48,27	(27,56;32,32)	92,05
Scenario 1	85	25,38	3,45	14,37	48,41	(21,93;28,83)	86,41	16,12	1,15	10,71	23,14	(14,97;17,27)	92,87
Scenario 2	88	21,89	2,08	11,00	31,72	(19,81;23,97)	90,50	12,67	0,83	10,00	20,42	(11,84;13,50)	93,45
Scenario 3	96	20,13	2,41	11,00	33,28	(17,72;22,54)	88,03	13,51	0,89	10,00	20,14	(12,62;14,40)	93,41
Scenario 4	104	16,35	1,47	11,00	28,48	(14,88;17,82)	91,01	13,52	1,33	10,00	20,50	(12,19;14,85)	90,16

	KPI						WIP						
	Flow	MiSeq PE300						HiSeq PE125					
Scenario	Nr out	Average	Half width	Min. Value	Max. Value	Confidence interval	Significance level (%)	Average	Half width	Min. Value	Max. Value	Confidence interval	Significance level (%)
Initial model	84	19,89	2,86	2,41	38,27	(17,22;22,94)	85,62	19,94	2,38	5,12	38,27	(17,56;22,32)	88,06
Scenario 1	85	14,38	3,45	3,37	37,41	(10,93;17,83)	76,01	6,12	1,15	0,71	13,14	(4,97;7,27)	81,21
Scenario 2	88	10,89	2,08	0,00	22,72	(8,81;12,97)	80,90	2,67	0,83	0,00	10,42	(1,84;3,50)	68,91
Scenario 3	96	9,13	2,41	0,00	22,28	(6,72;11,54)	73,60	3,51	0,89	0,00	10,14	(2,62;4,40)	74,64
Scenario 4	104	5,35	1,47	0,00	17,48	(3,88;6,82)	72,52	3,52	1,33	0,00	10,50	(2,19;4,85)	62,22

Appendix L

Performance measurement output statistics of sub model 3: combination of solutions

	KPI						LEAD TIME							
	Flow	MiSeq PE300						HiSeq PE125						
Scenario	Nr out	Average	Half width	Min. Value	Max. Value	Confidence interval	Significance level (%)	Average	Half width	Min. Value	Max. Value	Confidence interval	Significance level (%)	
Initial model	84	30,89	2,86	13,41	49,27	(28,22;33,94)	90,74	29,94	2,38	15,12	48,27	(27,56;32,32)	92,05	
Scenario 4 Submodel 1	54	25,05	7,19	11,00	45,00	(17,86;32,24)	71,30	24,09	5,56	10,00	36,00	(18,53;29,65)	76,92	
Scenario 4 Sub model 2	104	16,35	1,47	11,00	28,48	(14,88;17,82)	91,01	13,52	1,33	10,00	20,50	(12,19;14,85)	90,16	
Scenario 1	68	18,20	2,55	11,00	28,00	(15,65;20,75)	85,99	12,35	0,77	10,00	18,00	(11,58;13,12)	93,77	

	KPI							WIP						
	Flow	MiSeq PE300							HiSeq PE125					
Scenario	Nr out	Average	Half width	Min. Value	Max. Value	Confidence interval	Significance level (%)		Average	Half width	Min. Value	Max. Value	Confidence interval	Significance level (%)
Initial model	84	19,89	2,86	2,41	38,27	(17,22;22,94)	85,62		19,94	2,38	5,12	38,27	(17,56;22,32)	88,06
Scenario 4 Sub model 1	54	14,05	7,19	0,00	34,00	(6,86;21,24)	48,83		14,09	5,56	0,00	26,00	(8,53;19,65)	60,54
Scenario 4 Sub model 2	104	5,35	1,47	0,00	17,48	(3,88;6,82)	72,52		3,52	1,33	0,00	10,50	(2,19;4,85)	62,22
Scenario 1	68	7,20	2,55	0,00	17,00	(3,88;9,75)	64,58		2,35	0,77	0,00	8,00	(1,58;3,12)	67,23

Appendix M

Simulation experiments raw output data Arena

Sub model 1: order arrival variability

Scenario 1

Replications: 10 Time Units: Days

Key Performance Indicators

System		Average				
Number Out		55				
Wait Time		Average	Half Width	Minimum Average	Maximum Average	Minimum Value
						Maximum Value
Sample 1% Nextera HiSeq PE125		17.6943	3,07	11.6974	23.2256	6.9852
Sample 1% Nextera MiSeq PE300		13.2690	8,50	0.00	30.8477	0.00
Sample 2% 16S Profiling MiSeq		20.2770	2,02	13.8352	22.6932	7.8736
Sample 2% Nextera HiSeq PE125		18.3621	3,07	10.5448	23.3454	6.7836
Sample 2% Nextera MiSeq PE300		15.8642	8,16	0.00	29.8880	0.00
Total Time		Average	Half Width	Minimum Average	Maximum Average	Minimum Value
						Maximum Value
Sample 1% Nextera HiSeq PE125		27.6943	3,07	21.6974	33.2256	16.9852
Sample 1% Nextera MiSeq PE300		19.2690	12,09	0.00	40.8477	0.00
Sample 2% 16S Profiling MiSeq		31.2770	2,02	24.8352	33.6932	18.8736
Sample 2% Nextera HiSeq PE125		28.3621	3,07	20.5448	33.3454	16.7836
Sample 2% Nextera MiSeq PE300		22.8642	11,52	0.00	39.8880	0.00

Scenario 2

Replications: 10 Time Units: Days

Key Performance Indicators

System		Average				
Number Out		52				
Wait Time		Average	Half Width	Minimum Average	Maximum Average	Minimum Value
						Maximum Value
Sample 1% Nextera HiSeq PE125		31.3888	8,66	0.00	43.8792	0.00
Sample 1% Nextera MiSeq PE300		45.2085	8,38	27.0367	61.3985	15.7420
Sample 2% 16S Profiling MiSeq		35.4989	7,50	20.2799	50.0469	5.3727
Sample 2% Nextera HiSeq PE125		30.8549	9,23	0.00	47.3328	0.00
Sample 2% Nextera MiSeq PE300		45.2259	9,10	21.3665	57.7453	17.3187
Sample Sequel		1.4598	3,30	0.00	14.5979	0.00
Total Time		Average	Half Width	Minimum Average	Maximum Average	Minimum Value
						Maximum Value
Sample 1% Nextera HiSeq PE125		40.3888	10,76	0.00	53.8792	0.00
Sample 1% Nextera MiSeq PE300		55.2085	8,38	37.0367	71.3985	25.7420
Sample 2% 16S Profiling MiSeq		46.4989	7,50	31.2799	61.0469	16.3727
Sample 2% Nextera HiSeq PE125		39.8549	11,20	0.00	57.3328	0.00
Sample 2% Nextera MiSeq PE300		55.2259	9,10	31.3665	67.7453	27.3187
Sample Sequel		2.5598	5,79	0.00	25.5979	0.00

Scenario 3

Replications: 10 Time Units: Days

Key Performance Indicators

System		Average				
Number Out		87				
Wait Time	Average	Half Width	Minimum Average	Maximum Average	Minimum Value	Maximum Value
Sample 1% Nextera HiSeq PE125	33.0651	3,61	26.1319	44.3209	14.8742	61.7563
Sample 1% Nextera MiSeq PE300	36.8128	6,49	23.3793	50.8261	12.0452	71.9971
Sample 2% 16S Profiling MiSeq	35.0640	5,10	22.1093	46.8128	5.2196	70.1410
Sample 2% Nextera HiSeq PE125	33.1599	3,33	24.5084	38.7113	15.1352	60.8881
Sample 2% Nextera MiSeq PE300	30.1657	4,91	21.0289	44.7953	14.4872	53.1516
Sample Sequel	16.5401	2,74	11.9212	24.9489	4.2908	35.1416
Total Time	Average	Half Width	Minimum Average	Maximum Average	Minimum Value	Maximum Value
Sample 1% Nextera HiSeq PE125	43.0651	3,61	36.1319	54.3209	24.8742	71.7563
Sample 1% Nextera MiSeq PE300	46.8128	6,49	33.3793	60.8261	22.0452	81.9971
Sample 2% 16S Profiling MiSeq	46.0640	5,10	33.1093	57.8128	16.2196	81.1410
Sample 2% Nextera HiSeq PE125	43.1599	3,33	34.5084	48.7113	25.1352	70.8881
Sample 2% Nextera MiSeq PE300	40.1657	4,91	31.0289	54.7953	24.4872	63.1516
Sample Sequel	27.5401	2,74	22.9212	35.9489	15.2908	46.1416

Scenario 4

Replications: 10 Time Units: Days

Key Performance Indicators

System		Average				
Number Out		42				
Wait Time	Average	Half Width	Minimum Average	Maximum Average	Minimum Value	Maximum Value
Sample 1% Nextera HiSeq PE125	13.9914	5,49	0.00	20.2000	0.00	26.0000
Sample 1% Nextera MiSeq PE300	18.0833	9,75	0.00	34.0000	0.00	34.0000
Sample 2% 16S Profiling MiSeq	14.2485	2,25	6.8571	17.3750	2.0000	27.0000
Sample 2% Nextera HiSeq PE125	14.1952	5,63	0.00	21.8000	0.00	26.0000
Sample 2% Nextera MiSeq PE300	9.8500	9,59	0.00	34.0000	0.00	34.0000
Sample Sequel	1.3714	3,10	0.00	13.7143	0.00	19.0000
Total Time	Average	Half Width	Minimum Average	Maximum Average	Minimum Value	Maximum Value
Sample 1% Nextera HiSeq PE125	21.9914	8,43	0.00	30.2000	0.00	36.0000
Sample 1% Nextera MiSeq PE300	25.0833	12,99	0.00	44.0000	0.00	44.0000
Sample 2% 16S Profiling MiSeq	25.2485	2,25	17.8571	28.3750	13.0000	38.0000
Sample 2% Nextera HiSeq PE125	22.1952	8,55	0.00	31.8000	0.00	36.0000
Sample 2% Nextera MiSeq PE300	13.8500	13,15	0.00	44.0000	0.00	44.0000
Sample Sequel	2.4714	5,59	0.00	24.7143	0.00	30.0000

Scenario 5

Replications: 10 Time Units: Days

Key Performance Indicators

System		Average				
Number Out		58				
Wait Time		Average	Half Width	Minimum Average	Maximum Average	Minimum Value
						Maximum Value
Sample 1% Nextera HiSeq PE125		15.0000	0,00	15.0000	15.0000	10.0000
Sample 1% Nextera MiSeq PE300		30.5000	0,00	30.5000	30.5000	31.0000
Sample 2% 16S Profiling MiSeq		20.0000	0,00	20.0000	20.0000	13.0000
Sample 2% Nextera HiSeq PE125		15.0000	0,00	15.0000	15.0000	10.0000
Sample 2% Nextera MiSeq PE300		31.0000	0,00	31.0000	31.0000	31.0000
Total Time		Average	Half Width	Minimum Average	Maximum Average	Minimum Value
						Maximum Value
Sample 1% Nextera HiSeq PE125		25.0000	0,00	25.0000	25.0000	20.0000
Sample 1% Nextera MiSeq PE300		40.5000	0,00	40.5000	40.5000	41.0000
Sample 2% 16S Profiling MiSeq		31.0000	0,00	31.0000	31.0000	24.0000
Sample 2% Nextera HiSeq PE125		25.0000	0,00	25.0000	25.0000	30.0000
Sample 2% Nextera MiSeq PE300		41.0000	0,00	41.0000	41.0000	41.0000

Scenario 6

Replications: 10 Time Units: Days

Key Performance Indicators

System		Average				
Number Out		62				
Wait Time		Average	Half Width	Minimum Average	Maximum Average	Minimum Value
						Maximum Value
Sample 1% Nextera HiSeq PE125		36.8711	3,43	29.3333	44.2500	20.0000
Sample 1% Nextera MiSeq PE300		40.1333	7,79	26.0000	59.0000	19.0000
Sample 2% 16S Profiling MiSeq		25.4371	3,89	16.4667	33.6154	0.00
Sample 2% Nextera HiSeq PE125		36.3612	3,62	28.0000	42.6667	20.0000
Sample 2% Nextera MiSeq PE300		38.5633	9,14	22.0000	60.3333	17.0000
Total Time		Average	Half Width	Minimum Average	Maximum Average	Minimum Value
						Maximum Value
Sample 1% Nextera HiSeq PE125		46.8711	3,43	39.3333	54.2500	30.0000
Sample 1% Nextera MiSeq PE300		50.1333	7,79	36.0000	69.0000	29.0000
Sample 2% 16S Profiling MiSeq		36.4371	3,89	27.4667	44.6154	11.0000
Sample 2% Nextera HiSeq PE125		46.3612	3,62	38.0000	52.6667	30.0000
Sample 2% Nextera MiSeq PE300		48.5633	9,14	32.0000	70.3333	27.0000

Scenario 7

Replications: 10 Time Units: Days

Key Performance Indicators

System	Average					
Number Out	90					
Wait Time	Average	Half Width	Minimum Average	Maximum Average	Minimum Value	Maximum Value
Sample 1% Nextera HiSeq PE125	30.0000	0,00	30.0000	30.0000	20.0000	40.0000
Sample 1% Nextera MiSeq PE300	39.2857	0,00	39.2857	39.2857	27.0000	61.0000
Sample 2% 16S Profiling MiSeq	35.4783	0,00	35.4783	35.4783	20.0000	54.0000
Sample 2% Nextera HiSeq PE125	30.0000	0,00	30.0000	30.0000	20.0000	40.0000
Sample 2% Nextera MiSeq PE300	36.0000	0,00	36.0000	36.0000	27.0000	61.0000
Sample Sequel	15.0000	0,00	15.0000	15.0000	8.0000	22.0000
Total Time	Average	Half Width	Minimum Average	Maximum Average	Minimum Value	Maximum Value
Sample 1% Nextera HiSeq PE125	40.0000	0,00	40.0000	40.0000	30.0000	50.0000
Sample 1% Nextera MiSeq PE300	49.2857	0,00	49.2857	49.2857	37.0000	71.0000
Sample 2% 16S Profiling MiSeq	46.4783	0,00	46.4783	46.4783	31.0000	65.0000
Sample 2% Nextera HiSeq PE125	40.0000	0,00	40.0000	40.0000	30.0000	50.0000
Sample 2% Nextera MiSeq PE300	46.0000	0,00	46.0000	46.0000	37.0000	71.0000
Sample Sequel	26.0000	0,00	26.0000	26.0000	19.0000	33.0000

Sub model 2: capacity planning method

Scenario 1

Replications: 10 Time Units: Days

Key Performance Indicators

System		Average				
Number Out		54				
Wait Time						
	Average	Half Width	Minimum Average	Maximum Average	Minimum Value	Maximum Value
Sample 1% Nextera HiSeq PE125	6.0526	1,08	3.6909	8.6058	0.7108	13.1465
Sample 1% Nextera MiSeq PE300	4.6472	5,74	0.00	22.0459	0.00	22.0459
Sample 2% 16S Profiling MiSeq	14.3870	3,45	8.1784	25.0694	3.3716	37.4113
Sample 2% Nextera HiSeq PE125	6.1845	1,21	3.8753	9.7911	1.0018	12.1461
Sample 2% Nextera MiSeq PE300	1.7241	3,90	0.00	17.2405	0.00	17.2405
Total Time						
	Average	Half Width	Minimum Average	Maximum Average	Minimum Value	Maximum Value
Sample 1% Nextera HiSeq PE125	16.0526	1,08	13.6909	18.6058	10.7108	23.1465
Sample 1% Nextera MiSeq PE300	7.6472	9,05	0.00	32.0459	0.00	32.0459
Sample 2% 16S Profiling MiSeq	25.3870	3,45	19.1784	36.0694	14.3716	48.4113
Sample 2% Nextera HiSeq PE125	16.1845	1,21	13.8753	19.7911	11.0018	22.1461
Sample 2% Nextera MiSeq PE300	2.7241	6,16	0.00	27.2405	0.00	27.2405

Scenario 2

Replications: 10 Time Units: Days

Key Performance Indicators

System		Average					
Number Out		53					
Wait Time		Average	Half Width	Minimum Average	Maximum Average	Minimum Value	Maximum Value
	Sample 1% Nextera HiSeq PE125	3.8569	0,67	1.9145	5.2603	0.00	10.4210
	Sample 1% Nextera MiSeq PE300	1.6827	3,81	0.00	16.8265	0.00	17.0244
	Sample 2% 16S Profiling MiSeq	10.8981	2,08	4.5005	14.4925	0.00	22.7276
	Sample 2% Nextera HiSeq PE125	4.1563	0,98	2.7194	6.7156	0.1618	10.6912
Total Time		Average	Half Width	Minimum Average	Maximum Average	Minimum Value	Maximum Value
	Sample 1% Nextera HiSeq PE125	13.8569	0,67	11.9145	15.2603	10.0000	20.4210
	Sample 1% Nextera MiSeq PE300	2.6827	6,07	0.00	26.8265	0.00	27.0244
	Sample 2% 16S Profiling MiSeq	21.8981	2,08	15.5005	25.4925	11.0000	33.7276
	Sample 2% Nextera HiSeq PE125	14.1563	0,98	12.7194	16.7156	10.1618	20.6912

Scenario 3

Replications: 10 Time Units: Days

Key Performance Indicators

System		Average				
Number Out		54				
Wait Time	Average	Half Width	Minimum Average	Maximum Average	Minimum Value	Maximum Value
Sample 1% Nextera HiSeq PE125	3.6855	0,79	1.5311	5.5752	0.3005	9.2348
Sample 1% Nextera MiSeq PE300	3.7777	4,35	0.00	13.1342	0.00	13.3584
Sample 2% 16S Profiling MiSeq	9.1315	2,41	4.4707	13.5616	0.00	22.2810
Sample 2% Nextera HiSeq PE125	3.3500	0,98	1.4389	5.3721	0.00	10.1472
Total Time	Average	Half Width	Minimum Average	Maximum Average	Minimum Value	Maximum Value
Sample 1% Nextera HiSeq PE125	13.6855	0,79	11.5311	15.5752	10.3005	19.2348
Sample 1% Nextera MiSeq PE300	6.7777	7,81	0.00	23.1342	0.00	23.3584
Sample 2% 16S Profiling MiSeq	20.1315	2,41	15.4707	24.5616	11.0000	33.2810
Sample 2% Nextera HiSeq PE125	13.3500	0,98	11.4389	15.3721	10.0000	20.1472

Scenario 4

Replications: 10 Time Units: Days

Key Performance Indicators

System		Average				
Number Out		56				
Wait Time	Average	Half Width	Minimum Average	Maximum Average	Minimum Value	Maximum Value
Sample 1% Nextera HiSeq PE125	3.3356	1,02	1.1600	6.0718	0.00	9.5561
Sample 1% Nextera MiSeq PE300	1.0682	2,42	0.00	10.6822	0.00	11.8546
Sample 2% 16S Profiling MiSeq	5.3559	1,47	2.9347	9.0785	0.00	17.4824
Sample 2% Nextera HiSeq PE125	3.7230	1,65	0.9814	8.6486	0.00	10.5031
Total Time	Average	Half Width	Minimum Average	Maximum Average	Minimum Value	Maximum Value
Sample 1% Nextera HiSeq PE125	13.3356	1,02	11.1600	16.0718	10.0000	19.5561
Sample 1% Nextera MiSeq PE300	2.0682	4,68	0.00	20.6822	0.00	21.8546
Sample 2% 16S Profiling MiSeq	16.3559	1,47	13.9347	20.0785	11.0000	28.4824
Sample 2% Nextera HiSeq PE125	13.7230	1,65	10.9814	18.6486	10.0000	20.5031

Sub model 3: combination of solutions

Scenario 1

Replications: 10 Time Units: Days

Key Performance Indicators

System		Average				
Number Out		41				
Wait Time		Average	Half Width	Minimum Average	Maximum Average	Minimum Value
						Maximum Value
Sample 1% Nextera HiSeq PE125		2.4214	0,78	1.0909	4.5000	0.00
Sample 2% 16S Profiling MiSeq		7.2048	2,55	2.7857	13.7143	0.00
Sample 2% Nextera HiSeq PE125		2.2900	0,76	1.5000	5.0000	0.00
Sample Sequel		0.4571	1,03	0.00	4.5714	0.00
Total Time		Average	Half Width	Minimum Average	Maximum Average	Minimum Value
						Maximum Value
Sample 1% Nextera HiSeq PE125		12.4214	0,78	11.0909	14.5000	10.0000
Sample 2% 16S Profiling MiSeq		18.2048	2,55	13.7857	24.7143	11.0000
Sample 2% Nextera HiSeq PE125		12.2900	0,76	11.5000	15.0000	10.0000
Sample Sequel		1.5571	3,52	0.00	15.5714	0.00