MASTER

A comparison of production planning strategies
a product vs. a capacity oriented approach

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A comparison of production planning strategies:

A product vs. a capacity oriented approach

- An application in a pharmaceutical company -

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Abstract

A multi-product single-machine production planning problem has been studied by a discrete-event rolling-horizon simulation model. It has been computed what the best planning strategy at the level of material coordination is for the Tablets Production Department at Organon Oss. The best planning strategy, the product oriented strategy, has been implemented in an operational tool to support the planner in his decision which production order(s) to release.

Preface

This report presents the results of my 9-month graduation project, carried out at the Production Planning Department of Organon in Oss from February 2006 to November 2006. The graduation project is the last part of the Master's degree program Industrial Engineering and Management Science at the Technische Universiteit Eindhoven (TU/e).

I would like to thank some persons for helping and supporting me in carrying out this project. First, I would like to thank my supervisors of the TU/e, Jan Fransoo and Simme Douwe Flapper, and my supervisors at Organon, Wenny Raaymakers, Sjoerd Buddingh' and Gert Bosch for their help, their valuable and critical remarks, and their continuous support. Second, I would like to thank my colleagues of PPO, CSD, and SCO for providing me with excellent data, valuable remarks, and helpful ideas.

Moreover, I would like to thank my colleagues I shared the room with for the great time I had. They gave me a completely different view on statistics.

Finally, I would like to thank Rosemarijn van Andel, my family and my friends for their continuous interest in my work, and for supporting me all the time.

Anton Hennink
Eindhoven, November 2006

Management summary

Introduction
NV Organon is a pharmaceutical company that creates, manufactures, and markets prescriptive medicines. Its largest production site is located in Oss, where this research project has taken place. Pharmaceutical Operations Oss (POO) is the department responsible for the production, packaging and quality control of the medicines in Oss. One of the main concerns of POO is delivery reliability of its products. This report deals with production and inventory control at POO. The goal of this research project is to increase the logistical performance of POO by improving the logistical control structure.

Some characteristics of bulk tablets (production)
The production process of Organon consists of three main steps: the production of Active Pharmaceutical Ingredients (API's) from raw materials, the production of bulk from API's, and country specific packaging of bulk. After the production of API's and after the production of bulk, the products are quality controlled. In this report, the focus is on the production of bulk tablets at the Tablets Production Department (TPD). On the long term, the production of bulk tablets is controlled by an advanced planning (AP) system that considers the full supply chain and all international production sites. On the short term, a Material Requirements Planning (MRP) system controls the production activities of POO.

Some interesting characteristics of bulk tablets (production) are given below.

- Production is done in batches. A processing step of a batch usually takes xx or xx days.
- Demand for bulk tablets is quite variable and uncertain.
- Operators are highly utilized (xx% < ρ < xx%), while the utilization rate of machines is low to moderate (ρ < xx%). A machine can not work without a trained operator.
- The norm lead time of bulk tablets production is xx weeks, the norm lead time of the quality process is xx weeks. The actual lead time is quite variable and on average longer than xx weeks.
- There is a small probability (around xx%) that a full bulk batch is rejected by the Quality Department after bulk production.

The following hypotheses have been formulated for this research project.

Hypothesis 1
A planning strategy that determines which production orders to open[1] after the review period, and that makes a production plan for future periods, outperforms the current production planning strategy on inventory costs and availability of released bulk tablets.

Because there currently is no formal method for planning at the level of material coordination, hypothesis 1 states that a planning strategy that decides which production orders to open and that makes a production plan for future periods outperforms the current way of working. Planning strategies at the level of material coordination are for example given by Bemelmans (1985).

Hypothesis 2
A planning strategy for the Tablets Production Department in which a buffer stock is created to deal with limited availability of operator capacity, and with uncertainty in demand, operator capacity availability, lead times, and quality rejections outperforms the current production planning strategy on inventory costs and availability of released bulk tablets.

According to Silver et al. (1998, pg. 247, pg. 280) buffer stocks should be based on uncertainties during the replenishment lead time and on variability in the lead time itself. Furthermore, according to Sox et al. (1999) safety stocks should form a buffer to deal with scheduling conflicts caused by stochastic demand of other products that need to be produced with the same resource that only has a limited availability.

[1] At POO the term 'open' is used instead of 'released'. In the remainder of this text we will also use the term 'open' for two reasons. First, because releasing a production order should not be confused with the approval of bulk tablets by the Quality Department, which is called 'releasing' too. Second, because the production planner at POO is not only responsible for releasing production orders; he is also responsible for detailed scheduling of the production activities and for opening the production orders in the MRP system.

Research assignment
These two hypotheses lead to the following research assignment:

1. *Develop a planning strategy for production and inventory control at the level of material coordination for the Tablets Production Department, and determine the control parameters of the planning strategy such that a target service rate is obtained.*

   This planning strategy should be able to deal with:
   - *Limited availability of operator capacity at the TPD.*
   - *Uncertainty and variability in demand for bulk tablets.*
   - *Uncertainty and variability in operator capacity availability at the TPD.*
   - *Uncertainty and variability in lead times of the production and quality control process.*
   - *Uncertainty about quality rejections of bulk batches.*

2. *Develop and implement a tool that advices the planner which production orders to open. Furthermore, the tool should make a production plan including future production order releases.*

This research assignment is at the level of 'material coordination'. Typical tasks that belong to material coordination are setting internal due dates for orders, ensuring material being available, and controlling the inventories. Moreover, material coordination has to provide for the timing of orders (Bemelmans, 1985, pg. 18, pg. 30). Only the determination of the control parameters (critical inventory positions like safety stocks) falls beyond the scope of material coordination.

Three alternative solutions
To solve the research assignment, we introduced three planning methods at the level of material coordination. These planning methods are the product oriented strategy (POS), the capacity oriented strategy (COS), and the hybrid control strategy (HCS) (Bemelmans, 1985). In the POS, the decision to start a production order depends solely on the inventory position of an individual product, while in the COS, the status of individual products is ignored, and a production decision is based on an aggregate inventory position that reflects how much capacity is stored in all inventories. In the HCS fastmovers are controlled by the COS, while slowmovers are controlled by the POS.

The simulation experiments
For the three planning strategies (POS, COS, and HCS) we have built three multi-product single-machine discrete-event rolling-horizon simulation models in MS Excel to study which of the three planning strategies is the best for the specific situation at POO. Because of the complexity of many products with different demand patterns, stochastic lead times, quality rejections, and the interference on the single finite capacity (operator capacity), an analytical approach was not possible, which determined the need for simulation.

In these simulation models all make-to-stock (MTS) products are modeled as single products, and all make-to-order (MTO) products are modeled as one product that has non-preemptive priority on the capacity. In each week it is decided for which product(s) a production order is opened, based on the planning strategy. In the HCS, slowmovers have non-preemptive priority on the fastmovers. Furthermore, a finite availability of operator capacity is considered, and if more products compete for the same capacity, run out times of individual products are used to decide which production orders to open.

The goal of a simulation experiment is to obtain a target service rate for the availability of released bulk tablets. The critical inventory level (e.g. safety stock in the POS model) will be adjusted until the target service level is reached. The three planning strategies are compared on the criteria below. The first criterion is the most important.
- The total inventory investment
- The percentage of periods that the end inventory is outside target
- Nervousness of the production plan
- Variability in production quantities per period
- Ease of implementation

For each strategy, we have made simulation experiments under six different settings in which the desired service rate (xx% or xx%) and the utilization rate (ρ = xx%, ρ = xx%, ρ = xx%, ρ = xx%) were adjusted. We had to vary these two parameters, because historical data could not provide us an exact value for these two.

Some interesting aspects of the simulation model are described below.

- Demand and interarrival times have been stochastic. For most products, they have been modeled by an exponential distribution.
- We have made a model to create a dependency in the demand forecast, because the demand forecast for week *t* is autocorrelated.
- All produced batches can be rejected by the Quality Department with a probability of x%. For Product xx, this probability has been x%.
- The lead time between opening a production order and releasing the bulk tablets has been stochastic, and has been somewhere between x weeks and x weeks (excluding x weeks review time).
- Operator capacity has been finite, stochastic, and modeled as a 'single-machine'. Machine capacity has not been considered, because machine utilization is not high.
- All demand that is not satisfied directly from the shelf is backordered.

The results of the simulation experiments

From the simulation experiments, it can be concluded that the POS and the COS have been almost equal in their inventory investment needed to obtain a target service rate. However, in two of the six cases, the POS has been significantly better:

- If ρ = xx% and the target service rate is xx%, the inventory investment for the POS is significantly lower than for the COS.
- If ρ = xx% and the target service rate is xx%, the inventory investment for the POS is significantly lower than for the COS.

The HCS performs much worse than the POS and the COS under high operator utilization rates (ρ = xx% and ρ = xx%), because under high utilization rates very large inventory investments are needed in the fastmovers to obtain the target service level. These large inventory investments are needed, because a lot of capacity inventory needs to be placed in the fastmovers to deal with the congestion effects caused by the limited operator capacity under high utilization rates. Because the HCS performs much worse than the POS and the COS on inventory investment, it has not been tested on the other four criteria.

The percentage of periods that the inventory has been outside target in the POS has been on average xx%. The COS could not be tested on this criterion, because target inventory levels can not be set at an individual product level. To test the nervousness of the production plan and the variability in production quantities per period, we have measured the coefficient of variation in inter production times. This is the time between opening two production orders of the same product. For the POS, this coefficient of variation has been on average xx, for the COS it has been slightly higher; on average xx. In our opinion, this coefficient of variation is pretty large.

We expect that the POS is easier to implement than the COS, because the concept behind the POS comes close to a MRP approach, which is the approach used at this moment at the TPD. Therefore, it is much easier to implement the POS in the current information systems, and in the current organizational structure. Moreover, it is easier to understand for the people that need to work with this planning method.

Conclusion which planning strategy outperforms the others

It has been decided that the POS outperforms the COS and the HCS as a planning strategy for production and inventory control at the level of material coordination for the Tablets Production Department for the following reasons. First, the POS needed significantly lower inventory investments to obtain the target service rate than the POS in two of the six simulation experiments. Second, the POS makes the production plan slightly more stable than the COS. Third, the POS is easier to implement in the current information systems and the current organizational structure, and it is also easier to understand for the people that need to work with this planning strategy.

Conclusion of our results compared to Bemelmans (1985)
In contrast to Bemelmans (1985) we conclude that the POS needs lower inventory investments than the COS. Even under high utilization rates up to xx%, we can not prove that the COS performs significantly better. The main reason that we obtained other results than Bemelmans (1985) is that we considered more product related uncertainties, and to protect the inventory of a product against product related uncertainties, it is best to have buffer stocks in individual products. Another reason that we obtained other results is that we allowed capacity stock in the POS. This capacity stock and the safety stock needed to protect against product related uncertainties can complement each other; safety stock can also be used to buffer against capacity limitations, and capacity stock can be used to buffer against product related uncertainties. Moreover, the increase in performance is larger for the POS than for the COS if autocorrelation is introduced in the demand forecast, as we have done. However, a significant difference can not be found.

Proof of hypothesis 1
To show that hypothesis 1 is correct, we need to prove that the POS outperforms the current planning method. Unfortunately, it is not possible to model the current planning method, because the decision to open a production order in the current planning method is not made in a straightforward way. Furthermore, it is not possible to compare the results of the simulation models with the results obtained in reality, because it is not possible to model reality completely.

However, in our POS simulation experiments the outside inventory target rate has been xx% against xx% in reality. In addition, in our POS simulation experiments with current safety stocks we obtained a higher service rate than in reality: xx% in reality vs. xx% if ρ = xx%, and xx% if ρ = xx%. Moreover, Bemelmans (1985) shows that the performance of the POS and the COS have been close to the overall optimal solution. In contrast, we think that the coefficient of variation in inter production times is pretty large in the simulation experiments, what shows us that the production plan is not very stable.

Altogether, it is reasonable that we suggest in hypothesis 1 that a planning strategy that determines which production orders to open after the review period, and that makes a production plan for future periods, outperforms the current production planning strategy on inventory costs and availability of released bulk tablets. However, the hypothesis can not be completely founded.

New safety stock settings
Safety stocks, as the control parameter in the POS, have been proposed for all MTS products. The new safety stock settings need the same monetary investment as the current safety stocks, but they are distributed differently over the products. Once the target service level is reached, safety stocks can be lowered by a factor of the standard deviation of average weekly demand. All MTO products have no safety stock. Because MTO products have no safety stock, and therefore no buffer to protect them against uncertainties, they have non-preemptive priority on MTS products in the production plan.

Proof of hypothesis 2
To show that hypothesis 2 is correct, simulation experiments have been performed with current safety stock settings and with the new safety stock settings. We have to conclude that the results under the new and under the current safety stocks are similar on service rate and inventory investment. However, the service rates of the products are more equal to each other under the new safety stock settings.

Implementation
To carry out the second part of the research assignment, an operational tool has been developed that supports the planner to make the decision which production order(s) to open. In this tool all bulk tablets have been modeled. Based on the POS, the operational tool computes a production plan. In this production plan, week *t* and week *t+xx* are fixed. The decision for week *t+xx* needs to be implemented, and a plan for week *t+xx* to week *t+xx* is made. Each week, the operational tool needs to be run with the latest data from Apollo, what makes it a discrete-event rolling-horizon production plan. It is interesting to note that the production planners already worked with the operational tool and they agreed on the production plan made by it.

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1: Introduction

The goal of this chapter is to give the reader a short introduction about the context of this research project. Therefore, the background of the research project, including some key figures of Organon, is given in section 1.1, and an initial demarcation can be found in section 1.2. The structure of this report is given in section 1.3.

1.1 Background

NV Organon has been founded in 1923, and it is a business unit of Akzo Nobel. However, it will be separated as Organon BioSciences N.V. in the short future. It is the largest international Dutch pharmaceutical company, and it has a strong commitment to health care. Organon creates, manufactures and markets innovative prescription medicines that improve the health and quality of human life. The company concentrates its efforts in four core therapeutic fields: fertility, gynecology, anesthesia and neuroscience, although research is also conducted in immunology and oncology. Organon products are sold in over 100 countries worldwide, and in more than 60 countries a subsidiary, which is called a Local Company, has been founded. The key product brands of Organon are given in table A.1 in Appendix A.

Sales of Organon in 2005 were 2,425 million euro, and Organon has about 14,000 employees. Organon has 11 production sites of which the production site Oss (Pharmaceutical Operations Oss (POO)) is the largest, because it produces about 50% of the total production volume. POO is one of the three international production sites, the two other sites are found in Ireland and France. Production, as well as packaging, takes place at the production sites. Moreover, some production or packaging activities are outsourced.

Since a few years Organon has been improving the performance of its supply chains. Several tools have been developed to increase sales forecast accuracy and to support the production sites in production planning. Currently, there are some initiatives to further increase the performance of the supply chain. One of them is to decrease the total lead time. In April 2006 the lead time of most packaging activities was decreased from xx to xx weeks. This makes the availability of bulk products (intermediates as tablets, ampoules, etc) more important, because slack is reduced at the Packaging Department. Furthermore, management considers delivery reliability in general to be more important at all stages in the supply chain.

The goal of this research project is to increase the logistical performance of POO by improving the logistical control structure. Directly at the start of the project, an initial scope has been determined to make the project feasible within the available timeframe.

1.2 Initial scope

This report deals with production planning / production and inventory control at POO. "Production planning is the process of determining a tentative plan for how much production will occur in the next several time periods, during an interval of time called the planning horizon. Production planning also determines expected inventory levels, as well as the workforce and other resources necessary to implement the production plans. Production planning is done using an aggregate view of the production facility, the demand for products, and even of time (using monthly time periods, for example)." (Thomas and McClain, 1993). Next to determining a production plan, the actual release of production orders to fulfill the plan, is part of this report too.

Logistical point of view
The research project is carried out from a logistical point of view, which means that the focus will not be on improving aspect of the production process. "Production planning is affected by higher level decisions that constrain production. Fixed resources limit production. Fixed resources may include plant, equipment, and workforce." (Thomas and McClain, 1993). Furthermore, aspects like marketing, accounting, etc are considered to be outside the scope.

Product group: tablets
Organon produces 3 types of products: tablets, parenterals, and special products. It has been decided to focus on only one of the product groups, namely tablets. This decision has been made because most products in the tablets group are in a stable phase of their life cycle, and there had been no material shortages for tablets.

Production site: Oss
As stated before, Organon has 11 production sites over the world. Furthermore, manufacturing and packaging activities are outsourced to many suppliers. In this research project, the focus will be only on products that are produced and/or packed at the production site in Oss.

1.3 Structure of the report

The report is structured in the following way. In chapter 2, the current situation at POO, and its position in the supply chain, is described. The goal of this chapter is to introduce the main characteristics and to show the logistical performance of POO to the reader. In chapter 3, the hypotheses and the research assignment are given. The main goal of the remainder of this report is to test the hypotheses and to carry out the research assignment, which makes chapter 3 the cornerstone of this report. Moreover, the problem area is demarcated in more detail in this chapter, and the research approach is given.

In chapter 4, three logistical strategies that change the current logistical control structure are proposed. To test the logistical performance of these strategies, a simulation model has been built. Chapter 5 describes the design, the assumptions and the results of the simulation study, and it will conclude by selecting the best strategy. The best strategy needs to be implemented in the logistical control structure, which will be the topic of chapter 6. The most important part of this chapter is the description of the operational tool that has been built to support the planner. In this operational tool, the best strategy from chapter 5 is implemented. Finally, conclusions and recommendations are found in chapter 7.

We would also like to direct your attention at the lists of abbreviations, definitions, and variables, which are given at page 54 to 58.

2: Description of POO and its position in the supply chain

In this chapter, a description of the current situation at Pharmaceutical Operations Oss and its position in the supply chain is given. The goal of this chapter is to introduce the main characteristics of POO to the reader. The main responsibilities of POO are the production, packaging, and quality control of prescribed medicines at the production site in Oss, the Netherlands. The PCIO-model (Bemelmans, 1988) is used to support a structured analysis. According to this model, first the primary process (P) is described in section 2.1, then the logistical control structure (C) is described in section 2.2 and the information systems (I) are given in section 2.3. Last, the organizational structure (O) is discussed in section 2.4. In section 2.5, two developments in the supply chain are described, and in section 2.6, the logistical performance of the current structure is found. A conclusion is drawn in section 2.7[2]

2.1 Primary process

In short, the production process of Organon in Oss consists of three steps: the production of Active Pharmaceutical Ingredients (API) from raw materials (RM), the production of bulk products, and country-specific packaging of the bulk products into finished products (FP), as given in figure 2.1. Some products, like tablets, have another stockpoint between bulk and finished product, namely semi-finished product. This is an intermediate product in the packaging process, and it is not given in figure 2.1. Generally, finished products are shipped from the production site (PS) to Local Companies (LC), but also to agents or tender customers. Local Companies are local sales offices of Organon and they sell the finished products to wholesalers, hospitals, and pharmacists. Agents usually are persons or companies that operate in smaller countries, which are not attractive enough for Organon to set up a Local Company. Tender orders are large orders placed by organizations like the United Nations or the World Health Organization. Often, more than one supplier subscribes for the tender order, and usually, the manufacturer that offers the lowest price will get the order.

Next to demand for finished products, there also is exogenous demand for API's, bulk products or semi-finished products, like blisters. For bulk products and semi-finished products, exogenous demand mainly comes from other production sites of Organon.

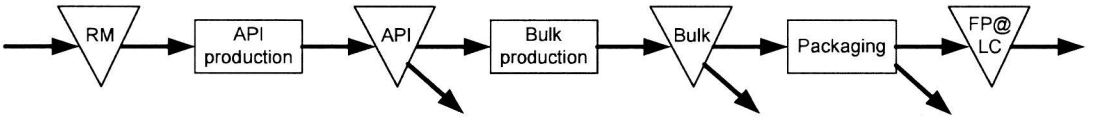

Figure 2.1: Primary process

Figure 2.1 is the cornerstone for section 2.1. In section 2.1.1, we will deal with the production of bulk tablets, and in section 2.1.2, the packaging process is explained. In section 2.1.3, processes that are not given in figure 2.1 are described. Furthermore, in Appendix B, the production process of API's is described.

2.1.1 Bulk production

Bulk production is the name for the production of large amounts of medicines, like tablets or injection fluids. It can be split in three types of processes: tablets production, parenterals production and special products production. In this report, the focus is on tablets production. Bulk products are produced in (large) batches and are generally suitable for a number of customers or product presentations. After the bulk products are manufactured, they are tested on their quality. As long as the Quality Department has not released the batches, it is not allowed to transfer them to the Local Companies or to other customers, and sometimes it is not allowed to pack them either. The production process of bulk tablets is described below. In appendix C, the production process of parenterals and special products is given. The quality testing process is described later, in section 2.1.3.

[2] Most data in this section has been gathered by interviews with many employees at different positions in the organization. A summary was made of every interview, which was offered for correction to the interviewees. If data appeared to be controversial, the interviewees were confronted with this, and they were asked for a reaction. Finally, the description of the current situation has been reviewed by the most important stakeholders.

Before continuing to the description of the production processes of tablets, we will first discuss some of the similarities of the three production processes and the three types of bulk products.

- The demand for bulk products is quite variable and quite uncertain. This aspect will be studied in more detail in section J.1.1.
- Production is done in batches, and usually it takes xx day to xx or xx days to produce one batch. Often, a few batches are combined for yield and/or efficiency reasons. Producing more than one batch in a row is called a campaign.
- Most production steps are carried out shortly after each other, and the intermediate products will not leave the production floor. It usually happens that an intermediate product waits a few days before it will continue to the next production step.
- Machines and operators are not always available for production because of tests, maintenance work, and development work. These kind of activities need to be announced at least two months in advance.
- The storage life of bulk products is, dependent on the bulk product and the country specific registration, on average between xx and xx years.

The production process of bulk products is typically a batch/mix process (Fransoo and Rutten, 1994).

Tablets production

At POO, about two billion tablets a year are produced for 44 different bulk products out of 19 API's[3]. In appendix D a Pareto analysis is found of the production volumes per product. Production is done in two shifts. The production process consists of a maximum of four sequential steps: granulating, tableting, coating, and printing. The first two steps need to be executed for all products. Some products also pass through the third and/or the fourth step. To manufacture the tablets, 11 granulating machines are available, in which excipients are added to the API's to create a homogeneous mixture, which often is milled and mixed too. Furthermore, 12 tablet compressing machines are available, in which the granulate is compressed into tablets. There are two coating machines, and there is one printing machine that currently is in its test-phase. The products can be manufactured by only one granulating machine, tableting is often possible on more than one tablet compressing machine, just like coating is often possible on both machines. The total lead time (including planning time, waiting time, etc.) of tablets production is approximately xx weeks. Setups take about xx to xx hours, depending on the kind of products where is switched between. Figure 2.2 gives a visualization of the production process of tablets.

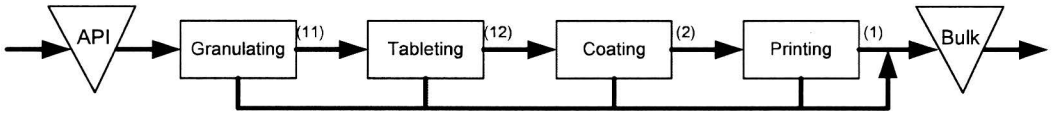

Figure 2.2: Production process of tablets

The utilization rates of the machines are low to moderate. There is only one machine, the 'Snelkneder', which had ρ > xx% in 2005, namely ρ = xx %. In appendix E, the utilization rates of all machines are found. It is harder to give a utilization rate of operators, because it is unknown how much time an operator could have worked on an order, but did not because there was no order. However, operators make a registration of their hours; it is registered how much time they have spend on a machine for production, cleaning, and changeover, and it is registered how much time they were not available for production. Comparing these two leads to ρ = xx% for operators. Table 2.1 gives a summary. There are some complicating factors that could change the utilization rate of operators as well as machines. For example, what is the influence of operator flexibility? Some overtime work can be done, or a day off can be shifted to another day. And what is done and registered if an order is finished about an hour before the working day is over? Usually, a new order will not be started. Answers to these questions can not be given, and therefore, the utilization rates should be seen as estimates. Availability of operators is important, because a machine can not work without a trained operator.

[3] Source: Budget 2006

Utilization rate of operators[4]	
Labor capacity (hours)	xx
Not available for production (hours)	xx -
Available for production (hours)	xx
Actual on machine (hours)	xx
Utilization rate	xx%

Table 2.1: Utilization rate of operators in 2005

It should also be noted that availability of operators varies per month, due to holidays, trainings, illness, etc. In Appendix E in figure E.1, average monthly operator capacity can be found. The goal of this chart is to show that there is a seasonal effect in operator capacity, and that operator capacity varies per month. If we eliminate the seasonal effect, the coefficient of variation is xx. The coefficient of variation is computed by dividing the standard deviation of a data set by its average.

2.1.2 Packaging

After the bulk products have been produced, the next step is to pack them according to customer specification. Packaging is generally country specific and therefore the 90 to 100 different bulk products lead to about 1700 different finished products. Tablets need to be blistered and some blistered products are placed in a sachet too (sacheting), because these tablets are sensitive to humid conditions. Then, the products are packed in a carton package and an information leaflet is added, which is called cartoning. There are 5 thermoforming machines available for blistering, 4 machines for sacheting, and 4 machines for cartoning. The products are linked to a specific machine, although there is a back-up machine available for most products. If a machine is setup for a product with another size, setup takes about xx hours. If a machine only needs to be cleaned, it takes less than xx hours. Next to the machines described above, there are some dedicated lines or machines for specialized packaging processes. An overview of the packaging process is given in figure 2.3. The total lead time (including planning time, waiting time, etc.) of the packaging process is approximately xx weeks.

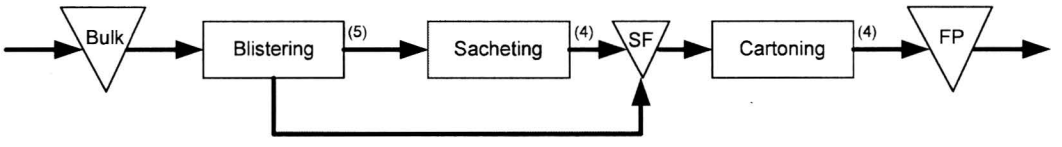

Figure 2.3: Packaging process

Operators are interchangeable within some limits. Similar to the production of bulk products, operator availability is the main bottleneck for the packaging process too. After packaging, the finished products are stored for a short time, because some documents, like a certificate of analysis, need to be made or collected. If the product is ready, as well as the documents, the order can be shipped to a Local Company or another customer.

2.1.3 Other processes

Next to the production processes and the packaging process, there are three other processes, which play a role in, or influence the primary process. These are the outsourcing process, the quality process, and the material handling process

For some products, parts of the production process are outsourced. This is done in many forms, e.g. the bulk production is outsourced, packaging is outsourced, both are outsourced, etc. Processes are outsourced to third parties, as well as other production sites of Organon. About xx to xx% of the added value of the primary process of POO is outsourced.

Because of strict regulations and laws related to pharmaceutical products, quality is one of the key factors in production. Therefore, every batch of API or bulk product needs to be tested on quality, and there is always a risk that a full batch is rejected on quality by the Quality Department. In 2005 and the start of 2006, the capacity of analysts at one of the labs has been the main bottleneck in the quality process, and therefore waiting times have been quite large. On average, the tests take about xx

[4] Source: Productie Stuur Informatie

weeks, but the total lead time is about xx to xx weeks, and there is a large variance in the lead time. In section J.1.4 we will study the lead time of the release process in more detail.

The final process mentioned is the material handling process, because the people that are responsible for this process realize the physical flow of goods from warehouse to production or packaging, and vice versa. One of their key tasks is to deliver the exact amount of Active Pharmaceutical Ingredients and excipients to the Production Departments at the right time. The material handling process is responsible for a substantial amount (up to xx weeks) of the total lead time in the supply chain.

2.2 Supply chain control structure

A general control structure of the supply chain of Organon is given in figure 2.4. At first sight, this figure may seem quite difficult. Therefore, it will be explained in the following steps. The red squares in figure 2.4 show which activities are described in which section.

- At the bottom of the figure, the stockpoints and production processes are given, as explained in section 2.1. The stockpoint Bulk is the customer order decoupling point (CODP) for most products. Downstream of this stockpoint production is driven by customer orders; upstream of this stockpoint production is driven by forecasts.

- In the top right of the figure we find Demand Planning (DP). In DP a sales forecast for the Local Company is made. Furthermore, a replenishment order forecast for the Local Company is found in this system. The role of DP is explained in section 2.2.1.

- In the top middle of the figure, we find Advanced Planning (AP). In AP plans are made for the medium and the long term (xx months to xx years ahead). These plans are, among other things, based on the forecasts in DP, and used to plan the production of bulk products, the production of API's, the need for products made by subcontractors, the need for products that are purchased, and the transfers between the production sites. Furthermore, AP checks the capacity for API production, bulk production, and packaging. Section 2.2.2 describes the role of AP in more detail.

- Material coordination is responsible for the short term planning (xx to xx months horizon) of packaging (section 2.2.3), bulk production (section 2.2.4), purchasing of excipients, packaging materials, and other additional materials (section 2.2.5), and for API production (Appendix F). All materials are allocated to production orders based on the FEFO-rule (first expired first out).

Additional to section 2.2.1 to 2.2.5, which are directly linked to the supply chain control structure in figure 2.4, we will also discuss the exceptions to the general structure in section 2.2.6, and describe how safety stocks are determined in section 2.2.7. Furthermore, in section 2.2.8, the supply chain control structure of Organon is linked with the literature.

2.2.1 Activities supported by DP

Sales forecast for Local Companies, replenishment forecast of orders that the Local Companies place at the production sites, and future inventory levels of products at Local Companies are found in DP. It works in monthly buckets. The sales forecast is automatically computed by a statistical model at the beginning of a month, based on historical sales data. This sales forecast can be adjusted by the Local Companies, because they have extra market knowledge. At the end of the month this leads to a resultant forecast. This resultant forecast is imported by AP at the beginning of the next month. Based on the resultant forecast, inventory levels at Local Companies, and other information, AP computes, among other things, a replenishment advice up to month *t+xx*. (See section 2.2.2). The replenishment advice for the first xx months is exported to DP again. If a Local Company disagrees with the replenishment advice, it can adjust this advice, which results in a replenishment order forecast. The replenishment order forecast is manually entered in the information system of the production site. It is used to order packaging materials, and for the short term planning of bulk production.

Organon has developed an order frequency procedure based on a trade-off between inventory holding costs and order costs. A finished product can be in the category high, medium, or low, what respectively means that a replenishment order can be placed each month, each quarter or each half-year.

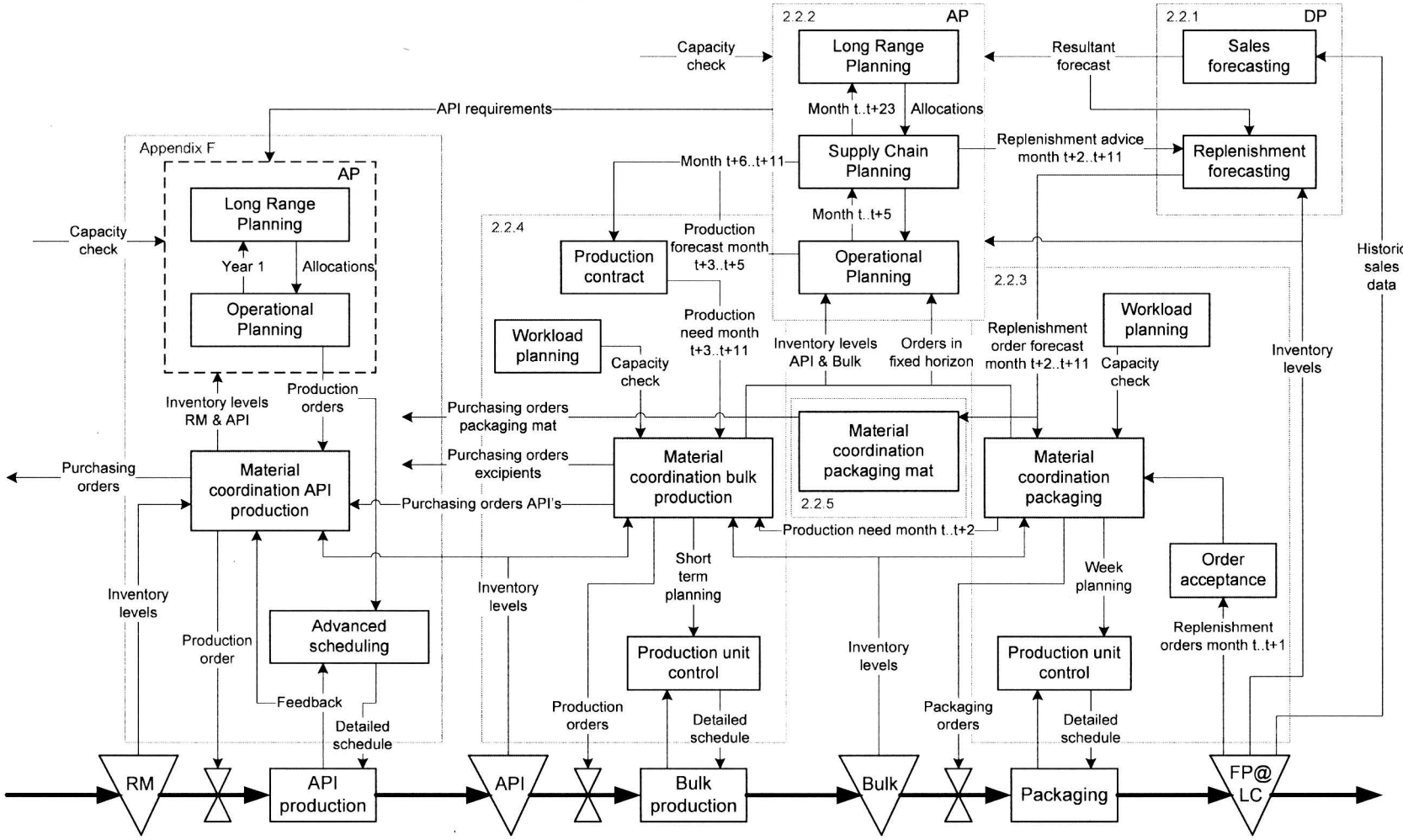

Figure 2.4: The supply chain control structure

2.2.2 Activities supported by AP

With the help of an advanced planning system, a replenishment advice for replenishment orders that Local Companies place at the production sites, and a production forecast for the production of bulk products and API's are computed. Furthermore, plans are made for subcontracting, transfers between production sites, and purchasing. Three plans are made; a long range plan (LRP), a supply chain plan (SCP), and an operational plan (OP). The long range plan is used to allocate production to production sites, to control the raw materials for API production, and to balance capacity to aggregate demand. The goal of the supply chain plan is to balance demand and capacity over time for all production sites, to determine transfers and allocations, and to determine the production need for API's. The operational plan is used to forecast the need for bulk products, purchased products, and subcontracted products and it is leading in the operations. In figure 2.5, it can be seen how the 3 plans and the Material Requirements Planning (MRP) system 'work together'. Part of the lower level plan is always fixed input for the higher level plan.

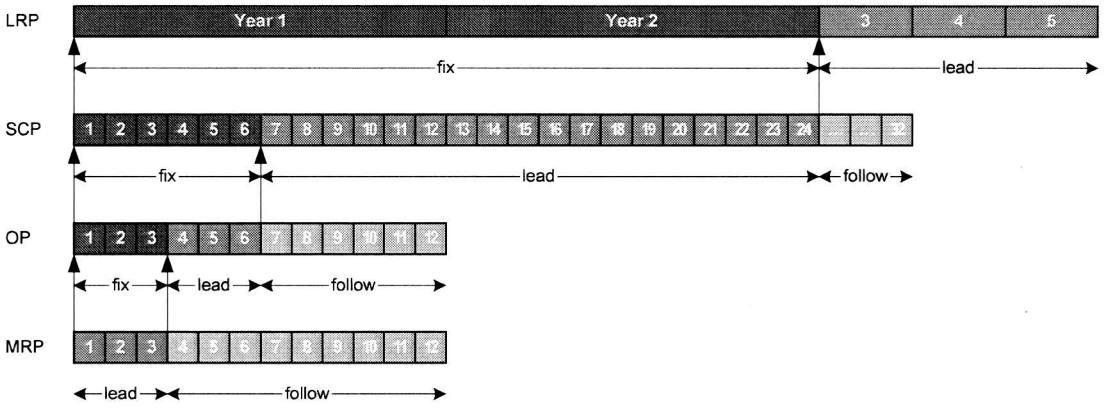

Figure 2.5: Links between the plans

Inputs for AP are the inventory levels from API to finished product at the Local Company[5]. Also the resultant forecasts and the placed replenishment orders from DP are imported into AP, and the orders in the MRP systems that are placed in the fixed horizon. Furthermore, numerous parameters are set, like safety stock levels, lead times, penalty points, and capacity restrictions. Capacities for the bottleneck machines are available and defined as hard constraints, but operator capacity is not defined, or only defined as a soft constraint.

The size of a replenishment order computed by AP is such that at the end of the month in which the order should arrive at the Local Company, the expected inventory approximately equals the safety stock. For finished products that are not ordered every month, the size is such that the expected inventory three or six month after arrival of the order approximately equals the safety stock. The size of production orders is determined in a similar way, but batch sizes or capacities can make a difference.

AP is a system based on mixed integer linear programming (MILP) and its objective is to minimize penalty points. Penalty points are given for inventory holding, below safety stock inventory levels, and out-of-stocks.

2.2.3 Material coordination packaging

The objective of the material coordination for packaging is to control the packaging process and to deliver the replenishment orders on time at the Local Company. The key control parameter is due date adherence. First, a capacity plan is made each month for month *t+xx*. Based on the replenishment order forecast and work-on-hand, it is determined how much capacity is needed on each machine. If a certain amount of available capacity is assigned, the machines can be planned up to the assigned capacity. By assigning capacity, a percentage for machine breakdowns etc is taken into account. The three different product groups, tablets, parenterals, and special products, all have their own packaging lines and therefore they are planned separately.

[5] Please note that API's are stocked at API OPS and the production site; therefore the stockpoint API can be split in two controlled stockpoints.

The packaging process is fully driven by replenishment orders. A replenishment order must be in a xx%-range with its last forecast. After a replenishment order is accepted by the production site, the availability of (released) bulk product, packaging material and capacity is checked. If a replenishment order is placed that is outside the xx%-range, this check should be done before acceptance too. Based on assigned capacity and materials, the packaging orders are planned in a week bucket and finally, at a more detailed level, the packaging orders are leveled over the week, based on more detailed knowledge of machine workloads and operator availability. The goal of the detailed planning is to minimize cleaning and setup costs. On a daily basis it is checked whether the weekly schedule can be realized or that some small changes need to be made.

Moreover, material coordination for packaging will create a production need for bulk products based on placed packaging orders and on replenishment order forecasts. This production need for bulk products can be different from the production need that is determined in OP and in the production contract.

2.2.4 Production contract and material coordination bulk production

The objective of the material coordination for bulk production is to control the production process, and to keep inventory of bulk products, API's, and excipients at agreed levels. The key control parameters are bulk availability and efficiency. Coordination of bulk production is done a little different for the three product groups. In this section we will describe the material coordination of bulk tablets, in appendix G, the material coordination of bulk parenterals and special products will be given.

Production contract and material coordination tablets production

In the first place, the production need for bulk products is determined by the operational plan. With the outcomes of the operational plan and the supply chain plan, a production contract is made for the next year, of which month *t+xx* is the most important month. The production contract can be seen as an agreement between the Planning Department, the Production Department, and the Quality Control Department on the production volumes of month *t+xx*. But the planner bases the production contract not only on the operational plan and the supply chain plan, but also on a MRP explosion. Based on replenishment order(s) (forecasts), and packaging order(s) (forecasts), the MRP system computes demand for bulk products. Taking this demand, current inventory levels of bulk products, and already opened production orders into account, a production plan can be computed too.

In the operational plan capacity of all machines is considered at an aggregated level; the plan should be realizable in a month. In the production contract, operator capacity is considered too, at the same aggregated level. An important reason to make the production contract is to determine the need for operators in month *t+xx*. The operational plan may be changed if it turns out to be unrealizable when operator capacity is taken into account. The production need from the production contract of month *t+xx* is placed in the MRP system as firm planned production orders. Because MRP cannot create a planned production order prior to a firm planned production order, no planned orders are created up to month *t+xx*.

Once the production contract is made, the firm planned production orders are scheduled over the month. As time goes by, all kind of variations have occurred. In inventory projections that the MRP system makes, it can be seen which product is expected to fall below safety stock or to go out-of-stock first. With the help of these inventory projections, the planner may reschedule the firm planned production orders.

If materials and capacity are available, and if a firm planned production order is ready to be released, this production order is opened[6]. The planner makes a detailed production plan for all opened production orders and all production orders that will be opened in the coming three weeks. In this detailed production plan, operator and machine availability are considered at a daily level, and each production step is planned separately. Norm times are used for planning the different production steps, and it is tried to increase efficiency by producing more than one batch in a row, because this increases yield and decreases cleaning times. This fixed campaign size is determined every year. Every day,

[6] At POO the term 'open' is used instead of 'release'. In the remainder of this text we will also use the term 'open' for two reasons. First, because releasing a production order should not be confused with the approval of bulk tablets by the Quality Department, which is called 'releasing' too. Second, because the production planner at POO is not only responsible for releasing production orders; he is also responsible for detailed scheduling of the production activities and for opening the production orders in the MRP system.

there is a meeting between the planner and the Production Department to discuss the plan, and to make adjustments if needed.

API's are ordered based on the production contract, and current inventory levels of API's. The procedure is that an order for an API must be within a xx% range compared to the one month ahead forecast. Purchasing orders of excipients and other additional materials are based on an MRP explosion of the firm planned production orders. Each day, purchasing lists are created by the MRP system, and based on these lists the planner places the purchasing orders.

We would like to note two shortcomings at the level of material coordination for bulk tablets. First, it is unclear on which information the decision to open a certain production order is based; there is no formal method to decide which production order should be opened first. Second, it is unclear how firm planned production orders are scheduled; there is no formal method to make a production plan to set the time at which firm planned production orders are planned to be opened. The difference between these two shortcomings is that the first one is about the decision to open a production order; the second one is about making a plan for future production order releases.

Lead time – decision structure
In figure 2.6 the lead time – decision structure can be found. This figure shows the latest moment at which a logistical decision needs to be made to adhere to the production order due date. On average, additional materials need to be ordered xx weeks before the order is opened, while API's can be ordered xx weeks before the order is opened. Currently, because of some problems, the tablets planner orders API's just after the production contract is made. Some flexible workforce can be arranged within a week, but usually there is a meeting every month to discuss this aspect for the next (few) month(s). Every week, a forecast is made for the Materials Handling Department (MHD). In this forecast it can be found which orders will be opened in the first week to come. Detailed scheduling of the production floor takes place every day. This schedule is very detailed one month in advance, and less detailed for two or even three months in advance.

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Figure 2.6: Lead time – decision structure

In figure 2.6 it is also found when the OP is solved and when the production contract is made. The OP is solved around the xx^{th} of month *t* for month *t+xx*, and the production contract is made around the xx^{th}. Because the OP / production contract is made only once a month, while orders can be opened every day, we have given the time between making the OP / production contract and opening the first order for month *t* and opening the last order for month *t*. For example, it can be seen that the time between making the production contract and opening the first order is xx to xx weeks.

2.2.5 Material coordination packaging materials
Packaging materials are ordered based on replenishment order forecasts; otherwise the lead time of the packaging process would be too long, because the lead time of ordering packaging materials is about xx weeks for most products. Packaging materials are for example cartons and foils, but also information leaflets. Based on inventory levels of packaging materials, forecasted replenishment orders, and defined lead times, a purchasing order for packaging materials will be placed. The size of the purchasing order will cover demand for a few months, and usually, a little more than needed is ordered, to be sure that there will not be a shortage if the replenishment order is more than forecasted, or if some packaging materials are rejected.

2.2.6 Exceptions to the general structure
The general control structure that was given in figure 2.4 is applicable in most situations, but several exceptions to this structure exist. First, exogenous demand or outsourced production is not given. Therefore, no incoming or outgoing streams are given in the control structure caused by outsourced activities or demand at the level of API's, bulk products, or semi-finished products. Second, only the supply chain of the added value stream is given; from the production of Active Pharmaceutical Ingredients to finished products. The flow of excipients and other additional materials is only partly given. Third, only the 'full DP' situation is given. At this moment, the largest Local Companies, responsible for xx% of the sales volume, are fully connected to DP. For the smaller Local Companies and for agents, responsible for xx% of the sales volume, there is a light version of DP, in which no sales forecasts are found, only replenishment order(s) (forecasts). The last xx% of sales volume comes from tender orders, and these are not modeled in DP.

2.2.7 Safety stocks

The Local Companies are autonomous in determining their safety stock levels for finished products, since they are the owners of their inventories and they are responsible for managing them. They receive a safety stock advice, but they do not have to follow that advice. The advised safety stock level actually is an inventory cover, and it is based on the sales forecast error, the replenishment lead time + review time, and a customer service level. Currently, a single-echelon model is used to compute the safety stock.

POO has a safety stock for most bulk products and for API's. These safety stocks are based on demand variations. A model originally developed by Arthur D. Little (ADL) is used to compute the safety stocks. In this model, first the forecasted demand in period t is determined by equation 2.1.

$$\hat{D}_t = \frac{1}{L_{norm} + R} \cdot \sum_{t=-(L_{norm}+R)}^{-1} D_t \qquad (2.1)$$

where,

$\hat{D}_t$	:	Forecasted demand in period t
D_t	:	Actual demand in period t
L_{norm}	:	Norm (production) lead time
R	:	Review time

Second, by equation 2.2, the forecast error (ε_t) is determined for period t. Third, the standard deviation of the forecast error (σ_ε) is determined by equation 2.3, where T usually is xx to xx periods. Fourth, the safety stock level (ss) is determined by equation 2.4, where k is the inverse of the standard normal cumulative distribution.

$$\varepsilon_t = D_t - \hat{D}_t \qquad (2.2)$$

$$\sigma_\varepsilon = \sigma\{\varepsilon_{t-T}, \ldots, \varepsilon_t\} \qquad (2.3)$$

$$ss = k \cdot \sigma_\varepsilon \cdot \sqrt{L_{norm}} \qquad (2.4)$$

The safety stock that is determined with the equations above is adjusted for some products because of restrictions caused by storage life, or extra knowledge about changing market conditions, like demand growth or decline, etc. Furthermore, some bulk products are made-to-order, and therefore, they do not have a safety stock.

Please note that the safety stock is based on variation in monthly demand for bulk tablets, and not on uncertainties during the lead time. There are several uncertainties during the lead time, like uncertainty in demand, uncertainty in the availability of operator capacity, uncertainty about quality rejections, and uncertainty in the lead time itself. Moreover, it is uncertain whether a production order can be opened at all, because of the limited availability of operator capacity.

API Operations (API OPS) has a safety stock for API's too, but this safety stock is a strategic inventory with the purpose to be able to supply the market (e.g. the production sites) even if there is a large step in demand, or if supply is stopped for some reason. API OPS also has some safety stocks at the intermediate and raw material levels. It is not known how the safety stock levels are determined.

2.2.8 Link with the literature

Section 2.2.1 to 2.2.7 focused strongly on the situation at POO. In this section, we try to link the supply chain control practices at POO with the available literature. Clearly, a hierarchical control structure is used. This kind of control structure is preferred by many authors, such as Meal (1984), Bertrand (1990), and Fransoo (1993), because it reduces the complexity of the control problem, and it places the control decisions at the right place in the organization. The control structure for the production of bulk products at Organon knows three hierarchical levels. At the highest hierarchical level, decisions are made to allocate production to production sites and to invest in capacity. Then, at the medium level, it is decided how much of which product to produce in which bucket. A rolling horizon is used for

this problem, and the decision made in the first 'open bucket' (usually month *t+xx*) is implemented. At the lowest level, the production orders within the bucket are sequenced and scheduled, where resources are allocated to production orders. The main factor by which is aggregated is time. At the lowest level, the used time bucket is a day, while at the other two levels data is aggregated to months or years.

A clear distinction between the literature on hierarchical control structures and the control structure at POO is in the way POO makes its short term plans. At the lowest hierarchical level, a MRP system supports the production planner, and the information in the MRP system can change the decision that was made at the medium control level. One of the first authors that has written about MRP was Orlicky (1975), and many researchers continued on his work. But the MRP concept has some drawbacks, which are discussed in appendix H.

MRP is a logistical control method at the level of material coordination. "The task of material coordination is to coordinate the activities of the production units in order to realize the commitments that have been made at the tactical level with respect to customer service rate, inventory budget and workforce levels. So, material coordination is not involved in the trade-off between different performance criteria, but has to take necessary actions to reach the given performance targets. Typical tasks that belong to material coordination are setting internal due dates for orders, ensuring material being available, and controlling the inventories. Moreover, material coordination has to provide for the timing of orders." (Bemelmans, 1985, pg. 18, pg. 30).

Bemelmans (1985) shows that there are other strategies to control production and inventories at the level of material coordination than MRP only. He introduces the product oriented strategy (POS), the capacity oriented strategy (COS), and the hybrid control strategy (HCS). In the POS, the decision to start a production run depends solely on the inventory position of an individual product, while in the COS, the status of individual products is ignored, and a production decision is based on an aggregate inventory position that reflects how much capacity is stored in all inventories. In the HCS some products are controlled by the COS, while other products are controlled by the POS.

Bertrand et al. (1998) propose a framework in which it is shown that material coordination is separated from production order release and detailed scheduling (including resource planning) of production activities. At POO, all these planning activities are performed by the same production planner or the same production planning team. Moreover, the production planner also starts the production order by opening it in the MRP system. As a result, the different planning activities are intertwined at POO.

The control of packaging at POO is quite different to the control of bulk production. The highest level is the same, but for packaging, the medium hierarchical level is already driven by replenishment orders of the Local Companies. With a MRP approach it is decided what packaging activity to perform in the first open bucket (usually week *t+xx* or *t+xx*). Then, at the lowest level, the packaging orders within the bucket are sequenced and scheduled, where resources are allocated to packaging orders.

A specific part of the control structure at Organon is the way in which sales and sales forecast information downstream in the supply chain are used to control the processes upstream in the supply chain. This approach is for example advocated by Lee et al. (1997) and the main advantage is that changing market conditions can be reacted on in an earlier stage, and the bullwhip effect[7] can be reduced. Croson and Donohue (2003) showed that even in stable industries where the demand distribution is commonly known, point-of-sale data reduces variability upstream in the supply chain, by reducing order oscillation of upstream members.

2.3 Information systems

To support the control processes, four key information systems are used: Demand Planning (DP), Advanced Planning (AP), Apollo (MRP), and MS Excel (spreadsheets). In figure 2.4 it could already be seen which activities are supported by these information systems, except for MS Excel. MS Excel is often used next to Apollo, mainly to consider capacities, and to schedule production and packaging orders, because these activities are not supported by Apollo.

[7] With the bullwhip effect we generally mean the increase of variation upstream in the supply chain.

Demand Planning is a web-based tool, and it is the IT link between Local Company and production site. Advanced Planning is a planning system that supports several planning activities in the supply chain. Both are connected to the Aggregation Database (ADB), in which data is stored about production sites, Local Companies, products, sales, inventory and safety stock levels, replenishment orders and forecasts, etc. Once new data is available, the old data will be overwritten, and therefore it is hard to find the changes made in the past.

2.4 Organization

This section gives an overview of the way the people are organized to make the primary process possible. In appendix I, figure I.1 an organization chart with all the departments that have a role in the primary process can be found. To support the text below, in appendix I, figure I.2 it is found which department is responsible for which part of the process in the control structure.

The Local Companies (LC) are responsible for their own inventory and safety stock levels, for reliable sales and replenishment forecasts, and for placing replenishment orders. Customer Relations (CR) accepts the replenishment orders, advises the Local Companies in replenishment forecasting, makes the week planning for packaging, and orders the packaging materials. The Packaging Department (PD) makes a detailed planning for the packaging process, and they physically pack the products. Coordination & Documentation (C&D) makes and collects the documents needed before shipment is possible. Furthermore, they decide when which replenishment order is shipped, and they coordinate the process after the customer order decoupling point for non-standard replenishment orders. Transport & Shipping (T&S) is responsible for (physically) preparing the transport out of the production site.

Production Planning Oss (PPO) is responsible for planning the production of bulk products. There are subdepartments for planning the production of tablets, parenterals, and special products. They make the operational plan and the production contract. Furthermore, they make a detailed plan for the Production Departments for a period of a few weeks to two months, and they actually open the production orders in Apollo. PPO also is responsible for the stockpoint Bulk, and they place purchasing orders for API's, excipients and other additional materials. Another department within Logistics is the Outsourcing Department, which is responsible for coordinating all outsourced activities, from bulk production to packaging. The Production Departments (XPD) manufacture the bulk products. There are departments for the production of tablets (TPD), parenterals (PPD), and special products (SPD). The Production Departments approve the schedules of PPO, and they make a planning for the operators. API OPS is responsible for the planning and the execution of their own production process, and for keeping the inventory of API's at safety stock targets, which are set by Supply Chain Operations (SCO).

SCO is responsible for the IT model and the logistical model behind AP and DP. They also make the supply chain plan and the long range plan, and they are responsible for allocating API's to production sites in case of scarcity. Furthermore, they have a role in developing new logistical models and in educating production sites and Local Companies. Two other departments, Quality Assurance (QA) and Materials Handling (MHD), are not given in figure I.2, but their roles are also important. QA tests the quality of raw materials, API's, bulk products, and finished products. MHD takes care of all physical movements of products in the factory and the warehouse. In addition, they deliver the exact amount of API's and excipients to the Production Departments.

Within POO there are 6 mini Business Units (MBU), in which several departments have a seat. The MBU's have a more process oriented view. The three product groups, tablets, parenterals and special products have their own MBU which integrate the Planning Department (PPO), the Production Department (XPD), and QA. The MBU Customer Order Process represents the Customer Service Department (CSD), the Packaging Department (PD) and QA. Furthermore, there are MBU's for purchasing and outsourcing. The MBU's are responsible for the operation results of their process.

2.5 Developments in the supply chain

There are two interesting developments we would like to mention. First, in 2005, Vendor Managed Inventory (VMI) has been introduced for six Local Companies. Currently, in November 2006, xx Local

Companies are on VMI. This means that the inventories at these Local Companies are controlled by the Customer Service Department. In this way, the CSD can better level the workload at the Packaging Department, and in times of shortage, they can better allocate the products. As a result of VMI, the CODP moves from bulk products to finished products at Local Companies.

Second, at the end of 2006, two extra interfaces are introduced between AP / DP and Apollo. In the first interface, the operational plan and the supply chain plan for bulk production are placed in Apollo as firm planned orders. Apollo will not compute a bulk production plan anymore. In the second interface, replenishment order forecasts are placed in Apollo. All replenishment order forecasts are placed at the first of the month, and based on these forecasts, Apollo will compute a packaging plan.

2.6 Performance of the supply chain

In this section, the performance of the supply chain is given. In section 2.6.1, the focus will be on the availability of products. In section 2.6.2, a more detailed overview of the performance of bulk tablets production at POO is found.

2.6.1 Availability of products

Availability of (released) bulk products and delivery reliability are seen as the most important logistical performance indicators at Organon. At three levels there is a measurement: availability of released bulk products, delivery performance of the production site (POO) to the Local Companies, and non stock-out probabilities at Local Companies. The availability of released bulk products at POO is the percentage of replenishment orders for which released bulk product is available at the latest possible moment a packaging order has to be opened according to the standard lead times defined in MRP. Figure 2.7 gives the availability of released bulk products for the period of May 2005 to September 2006. Average availability in this period was xx%. The target availability for 2006 is xx%; this target is also given in the figure. Based on this figure it is concluded that availability of released bulk tablets has been too low.

The delivery performance of POO is determined by comparing the actual shipment date with the order request date. The percentage of orders that are shipped in the week of the order request date is the delivery reliability of POO. Figure 2.8 gives the results of from May 2005 to September 2006. The target delivery reliability for 2006 is xx%, this target is also given in the figure. Unfortunately, this data is only available for all product groups, not for tablets only. Based on this figure, it is concluded that the delivery reliability of POO has been too low.

An out-of-stock at a Local Company is reported if the inventory of a product is zero for two weeks, while there was a sales forecast for that product in that month, and there was a sale in the last three months. Unfortunately, this data is only available for full-DP Local Companies and for all product groups. Figure 2.9 gives the non stock-outs in 2005.

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Figure 2.7: Released bulk tablets availability

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Figure 2.8: Delivery reliability of POO

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Figure 2.9: Non stock-outs of Full DP LC's in 2005

2.6.2 Performance of bulk tablets production at POO

In this section, three extra performance measures are given at the level of bulk production at POO. We will focus on inventory levels of bulk tablets, nervousness in the production plan, and variation in monthly production quantities. In appendix J an extensive analysis of POO and its supply chains is found. In this appendix it will be shown why we focus at bulk production. Furthermore, these three performance measures are discussed in more detail in this appendix, and it is shown why we have selected these performance measures.

Inventory levels of bulk tablets[8]

Inventories of bulk tablets have been outside target in xx% of the periods we studied. The inventory targets are defined by a lower and an upper bound. The lower inventory bound of a product is its safety stock. The upper inventory bound of a product is its safety stock + its batch size * its campaign size. In appendix J, section J.1.3 a detailed analysis on inventory levels of bulk tablets can be found.

In figure 2.10, the aggregated physical released stock is compared to the aggregated lower bound and the aggregated upper bound. Aggregation has been done over all make-to-stock (MTS) bulk tablets. 'Released' means that the bulk tablets are approved by the Quality Department. 'Physical stock' is the inventory that is physically in the warehouse, also called the on hand stock. It can be seen that the aggregated physical released stock has been too low. If we even consider the leveling stock[9] of approximately xx million tablets, the aggregated physical released stock falls below xx, because the leveling stock needs to be subtracted from the physical stock!

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Figure 2.10: Aggregated physical released stock of bulk tablets

Nervousness in the production plan[10]

To stabilize the production plan, it is tried to implement the production contract (see section 2.2.4) as much as possible. We have analyzed the production contract of TPD from January 2005 to March 2006. It appears that, on average, each month xx% of the batches that have been produced were not forecasted, and xx% of the batches that were forecasted, have not been produced. Appendix K, section K.2 gives a detailed view of the quality of the production contract.

In figure 2.11, a more detailed view is given about the way that the production forecast develops over time. The results for Marvelon Z.ME are given, but similar results are found for other products. These results are given in Appendix L. From these figures we conclude that the production plan for bulk tablets is nervous and instable over time.

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Figure 2.11: Development of bulk production forecast of Marvelon Z.ME

Variation in monthly production quantities[11]

In table 2.2, average bulk production for the period of January 2005 to March 2006 is found. Moreover, the standard deviation and the coefficient of variation are given. The underlying data can be found in appendix O. From table 2.2 we may conclude that the variation coefficient of monthly production quantities is high.

Actual monthly bulk production			
(*1000 tab)	Average	St. dev.	Coef. of var.
Marvelon			
Remeron 30			
Cerazette			
Orgametril			

Table 2.2: Actual monthly bulk production

2.7 Conclusion

In this chapter, we have described POO and its position in the supply chain. We have shown that the logistical performance of bulk tablets production has been too low, considering availability of released bulk tablets, inventory targets, nervousness in the production plan, and variation in monthly production quantities. During this chapter, we already gave three causes that lead to these problems, namely:

[8] Source: Monthly inventory report (VRDyyyymmdd_MBU.xls)

[9] Because the demand for bulk tablets of the Packaging Department is planned before the actual usage (safety time), there is some extra stock, called leveling stock. The result is that the physical stock should be higher than you would expect based on safety stocks, batch sizes, and campaign sizes. The safety time is approximately xx weeks, what is equal to approximately xx million tablets leveling stock.

[10] Source: Production contracts TPD

[11] Source: Production contracts TPD

1. There is no formal method to decide which production order to open first.
2. There is no formal method to make a production plan to set the time at which firm planned production orders are planned to be opened.
3. The current safety stock is not based on uncertainties during the total lead time, but on demand variation.

In appendix J an extensive analysis is found of POO and its supply chains. Among others, in this appendix we will show that the basic causes given above lead to a lower logistical performance, and we will show that these basic causes are the most interesting to tackle.

3: Project definition

Now that the reader is familiar with the main characteristics of POO and its position in the supply chain, we will further define this research project. In section 3.1, two hypotheses have been formulated to improve the logistical performance of POO. The research assignment is based on these hypotheses, and it is also found in this section. Then, in section 3.2, a detailed scope of this research project is given. Finally, the research approach is described in section 3.3.

3.1 Research assignment

In chapter 1, a small introduction on the background of this research project could be found. It was already given that the management of POO considers delivery performance in general to be very important. In section 2.6, it could be seen that the availability of released bulk tablets has been below the target of xx%, namely xx%. Furthermore, it could be seen that inventories have been outside target in xx% of the studied periods, the production plan has been nervous, and monthly production quantities have been variable. Three causes that lead to these problems have been selected:

1. There is no formal method to decide which production order to open first.
2. There is no formal method to make a production plan to set the time at which firm planned production orders are planned to be opened.
3. The current safety stock is not based on uncertainties during the total lead time, but on demand variation.

Based on these three causes, two hypotheses have been formulated to improve the logistical performance of POO. The hypotheses are given below.

Hypothesis 1
A planning strategy that determines which production orders to open after the review period, and that makes a production plan for future periods, outperforms the current production planning strategy on inventory costs and availability of released bulk tablets.

Hypothesis 1 is based on cause 1 and 2. Because there currently is no formal method for planning at the level of material coordination, hypothesis 1 states that a planning strategy that decides which production orders to open and that makes a production plan for future periods outperforms the current way of working. Planning strategies at the level of material coordination are for example given by Bemelmans (1985).

Hypothesis 2
A planning strategy for the Tablets Production Department in which a buffer stock is created to deal with limited availability of operator capacity, and with uncertainty in demand, operator capacity availability, lead times, and quality rejections outperforms the current production planning strategy on inventory costs and availability of released bulk tablets.

Hypothesis 2 is based on cause 3. According to Silver et al. (1998, pg. 247, pg. 280) buffer stocks should be based on uncertainties during the replenishment lead time and on variability in the lead time itself. Furthermore, according to Sox et al. (1999) safety stocks should form a buffer to deal with scheduling conflicts caused by stochastic demand of other products that need to be produced with the same resource that only has a limited availability.

Research assignment
These two hypotheses lead to the following research assignment:

1. *Develop a planning strategy for production and inventory control at the level of material coordination for the Tablets Production Department, and determine the control parameters of the planning strategy such that a target service rate is obtained.*

   This planning strategy should be able to deal with:
   - *Limited availability of operator capacity at the TPD.*
   - *Uncertainty and variability in demand for bulk tablets.*
   - *Uncertainty and variability in operator capacity availability at the TPD.*
   - *Uncertainty and variability in lead times of the production and quality control process.*
   - *Uncertainty about quality rejections of bulk batches.*

2. *Develop and implement a tool that advices the planner which production orders to open. Furthermore, the tool should make a production plan including future production order releases.*

In appendix J, an extensive analysis of POO and its supply chains is found. It is shown that the demarcation of the research assignment (focusing on bulk tablets production planning) is correct, the considered uncertainties and variables are correct, and it is shown that the research assignment is relevant. In short, the research assignment is relevant, because the stock investment of bulk tablets is about € xx million[12] if we consider safety stock and batch sizing stock.

3.2 Scope of the research project

Before we will continue solving the research assignment, we will first explicitly state what will be and what will not be considered in this project. In other words, the scope of the research project will be determined. The main reasons to focus has to do with the limited time available for this research project. Moreover, we want to concentrate the research project on the most relevant aspects only.

Material coordination
In general, it can be stated that this research assignment is at the level of 'material coordination', as defined in section 2.2.8. It should be noted that the determination of the control parameters of the planning strategy falls beyond the scope of material coordination, but will be part of this research project.

Production planning bulk tablets
In this project we will focus on the production planning of bulk tablets only. We will come back at this point in appendix J, where we will prove that this demarcation is correct and relevant. The Packaging Department, API OPS, Local Company strategies, or replenishment order acceptance are not redesigned in any way. This is reasonable, because there is a CODP in front of and after bulk production.

Short term planning
The new planning method will only focus on short term planning, because the activities of material coordination take place at the short term level. With 'short term' we mean the first few future months in which the AP system makes no calculations; in figure 2.6, we already showed that the logistical decisions for bulk production are made within a timeframe of xx weeks. We do not want to make adjustments to the mid term or long term planning procedure, because the current procedure of an operational plan and a supply chain plan performs well. The AP system takes all relevant aspects, like demand, capacity, lead times etc into account in the correct detail for mid term and long term planning.

[12] Source: Safety stock proposal (Voorstel veiligheidsvoorraad 2006_2.xls)

Released bulk tablets only
Inventory of bulk tablets can be released or unreleased. In this thesis, we only consider released bulk tablets. So, we assume that inventory only comes available once it is approved by the Quality Department. This decision has been made in accordance with Organon, because availability of released bulk tablets has been too low, while availability of unreleased bulk tablets has been close to target. Moreover, there is a financial risk when bulk products are packed unreleased.

Operator capacity only
Because operators are highly utilized (xx%-xx%), machine utilization is low to moderate (<xx%), and a machine can only work when a trained operator is with the machine, it has been decided only to consider operator capacity in this research project.

Batch sizes
In the pharmaceutical industry, many aspects are subject to laws and regulations. Once there is a registration for a specific batch size, lots of effort and money need to be invested to change the batch size. Therefore we will assume the batch size to be fixed. Next to batch sizes, for some products we also have campaign sizes, in which several batches of the same product are produced in a row. Also campaign sizes are considered to be fixed, because the computations for the optimal campaign size fall beyond the scope of material coordination. "On the level of material coordination, batch sizes are fixed. Therefore, set-up time is just part of the processing time." (Bemelmans, 1985, pg. 31). Furthermore, the influence of limited capacity not considered, current campaign sizes are already (economically) optimal.

Information systems and organizational structure
One of the strongest aspects of the PCIO-model, given in chapter 2, is that it shows that a change in one of the areas has an effect on the other areas too. At the start of this report, we stated that the production process (P) will not be changed, but the control structure (C) will be. This will have an effect on the information systems (I) and the organizational structure (O). It is our intention to minimize the needed change on information systems and on the organizational structure, because a large change is probably not accepted by senior management and will be a danger for a successful implementation.

Uncertainties
In the research assignment we already stated that we explicitly consider uncertainties in demand, operator capacity availability, lead times, and quality rejections. But there are also some uncertainties that will not be considered in this research project.

1. *Yield:* The yield of the production process is stable, easy to predict, and therefore assumed to be deterministic. Please note that 'yield' is not equal to a 'quality rejection', because a quality rejection means that a full batch is disapproved by the Quality Department after the production process has taken place.
2. *Supply uncertainties:* At the Tablets Production Department problems with the availability of materials have been rare, and therefore supply uncertainties will not be considered. There have been no supply problems for API's, and for additional materials, enough buffer stocks are held.
3. *Record errors:* Obviously it can happen that a mistake is made by entering an order in the MRP system. But it is not known that this aspect ever led to an incorrect decision, and therefore, we will not consider this aspect.
4. *Machine breakdowns:* At the Tablets Production Department, machine breakdowns are rare and usually easy to solve, according to the production officer. Furthermore, if a machine has a serious breakdown, another machine can be used for production, because most machines are interchangeable.
5. *Shelf life:* Most products have a shelf life of xx to xx years, and therefore this aspect is irrelevant for our research project. However, Product xx has a shelf life of only xx months, and for this product, we will take shelf life into account. In chapter 5, we will return to this aspect.

3.3 Research approach

This research project has been approached in the following way. The first step of this research project is to identify production planning strategies at the level of material coordination. In chapter 4, we will identify three alternatives (Bemelmans, 1985):

- Product oriented strategy (POS)
- Capacity oriented strategy (COS)
- Hybrid control strategy (HCS), which is a combination of the POS and the COS

The second step of this research project is to determine which planning strategy performs best for the specific situation at POO, considering the elements and uncertainties given in the research assignment. Because the situation at POO differs considerably from the situation in the simulation models of Bemelmans (1985), we have decided to perform new simulations. Chapter 5 describes all the aspects related to the simulation study.

For each planning strategy, a simulation model is built, and several simulations experiments are done. Because we can not identify an exact value for the utilization rate of operators and the target service rate, we have to perform six simulation experiments for each planning strategy. It is determined which critical inventory levels (control parameters) are needed to obtain a certain delivery performance under a given utilization rate. The planning strategies are compared on criteria that are developed in chapter 5 too, and based on these criteria, the best planning strategy is selected.

To show that hypothesis 1 is correct, we need to prove that the planning strategy selected in chapter 5 outperforms the current planning method. Unfortunately, it is not possible to compare the results of the simulation models with the results obtained in reality, because it is not possible to model reality completely. Furthermore, it is not possible to model the current planning method, because the decision to open a production order in the current planning method is not made in a straightforward way. Therefore, it is only possible to qualitatively show that hypothesis 1 is correct.

The third step is to decide at which value the control parameters need to be set when the best strategy is implemented at POO. Because the six different simulation experiments advised different settings for the control parameters, it has been decided to start by implementing an aggregated safety stock that needs the same monetary investment as the current safety stock. However, individual safety stocks are distributed over the products in a different way, based on the results of the simulation experiments. By comparing the performance obtained with the new safety stocks with the performance obtained with the old safety stocks, we can show whether hypothesis 2 is correct. Setting the control parameters is part of chapter 6.

The last step is to implement the best production planning strategy, including its control parameters in the organization. Therefore, an operational tool will be developed in MS Excel. This tool will support the planner in making his short term production planning decisions. In chapter 6, this operational tool is described. Furthermore, we will show how the operational tool needs to be used.

4: Introduction of three alternative solutions

In the research assignment it has been stated that a new planning strategy at the level of material coordination needs to be developed for the Tablets Production Department. In this section three planning strategies to solve the research assignment are introduced. The three planning strategies are called the product oriented strategy, the capacity oriented strategy, and the hybrid control strategy.

Whybark and Williams (1976) have shown that the control of buffer stocks should be adjusted to the sources of uncertainty. Fundamentally, there are two sources of uncertainty. First, there is uncertainty due to the behavior of individual products, like demand uncertainty, or uncertainty caused by quality rejections. Second, there is uncertainty due to the behavior of resources, like operator availability.

Consequently, according to Bemelmans (1985), at the level of material coordination, there are two fundamentally different strategies for production and inventory control; the product oriented strategy (POS), and the capacity oriented strategy (COS). In the POS, the decision to start a production run depends solely on the inventory position of an individual product, while in the COS, the status of individual products is ignored, and a production decision is based on an aggregate inventory position that reflects how much capacity is stored in all inventories. Bemelmans (1985) also identifies a combination of these two strategies, the hybrid control strategy (HCS). In the HCS fastmovers are controlled by the COS, while slowmovers are controlled by the POS.

Probably, choosing one of the three strategies will not lead to the overall optimal strategy, but to be able to find a solution at all, we need to reduce the control complexity by taking away some decision freedom. Control complexity comes from a variety of sources. "There are many products in various stages of progress, complex relationships between resource restrictions and much uncertainty with respect to the availability of these resources." (Bemelmans, 1985, pg. 9).

We will now discuss the POS and the COS in more detail, including their performance under different simulation settings. Then, the HCS is discussed in more detail.

Product Oriented Strategy
The POS and the COS are characterized by the aggregation – decomposition approach to reduce the control complexity. For the POS, decomposition is used. If we have *N* products, we consider *N* models (a model for each single product) in which the interference of all products on the capacity is ignored. A production run is started if the inventory position falls below a predefined critical level; the safety stock. Since it is possible that there are more products for which a production run is required, we need to develop a single rule to choose which product has priority. Because in our study, products are not identical with respect to their demand distribution, we have decided not to use individual inventory positions, but the run-out time to set priorities. The run-out time is the number of periods until the inventory of a product expects to fall below zero.

Capacity Oriented Strategy
For the COS a technique called aggregation is used. The decision to produce or not is based on an aggregate inventory position. Because in our study, products are not identical with respect to their capacity usage, we first multiply the inventory positions with their capacity usage, and based on the amount of capacity stored in the inventories, it is decided to start a production run. Once it is decided to start a production run, a disaggregation step is made to decide for which product a production run needs to start. Because products are not identical with respect to their demand distribution, we cannot use the individual inventory positions for this decision, therefore the run-out time is used again.

Performance of the POS and the COS
In a simple simulation model, Bemelmans (1985) shows that the POS and the COS perform different in several situations. The simple simulation model is characterized by the following elements:

- Products are made to stock by a single production unit.
- All products are identical.
- The demand size equals one at each demand instant. The interarrival time between demand instants is negative exponentially distributed with mean one.
- All unsatisfied demand is backordered.
- Inventory holding costs and stock-out costs are linear with positive or negative inventory. These costs are also used to compare the strategies on.

- The interarrival time between successive production opportunities is negative exponentially distributed. The mean of the interarrival time determines the utilization rate.

It is shown that the POS performs best under a low utilization rate (ρ = 0.25), and it performs slightly better with many products (N = 20). The COS performs best under moderate and high utilization rates (ρ = 0.84 and ρ = 0.90) and with few products (N = 5 and N = 2). Changing other parameters, like inventory and backordering costs, production lead times, and batch sizes influences total costs, but not the decision which strategy is best. Furthermore, for the case that N = 2, it is shown that the simple strategies are close to the overall optimal solution. For larger N it has not been possible to compute the overall optimal solution because of numerical difficulties.

Because Bemelmans (1985) shows that the performance of the POS and the COS have been close to the overall optimal solution, it is reasonable that we suggest in hypothesis 2 that a planning strategy that determines which production orders to open after the review period, and that makes a production plan for future periods, outperforms the current production planning strategy on inventory costs and availability of released bulk tablets.

It seems reasonable that the COS performs best under high utilization rates, because the COS explicitly considers finite capacity in the case of limited, stochastically available capacity where the queuing phenomenon leads to large delays. Moreover, it seems reasonable that the POS performs best when N = 20, because an aggregate inventory position becomes a worse measure for the state of the system as individual inventories tend to get out of balance.

Hybrid Control Strategy

In the HCS, the POS and the COS are combined to better control non-identical products. Products are placed in the slowmover or fastmover category based on their demand pattern and claim on capacity. Slowmovers have non-preemptive priority[13] on the capacity and are controlled by the POS. This seems reasonable, because if slowmovers have priority, they will not experience a high utilization rate. In contrast, fastmovers see a high utilization rate, and therefore, they can be controlled best by the COS. As a result, fastmovers hold some extra inventory (capacity inventory) to deal with tight capacity restrictions. Tentatively, it seems logical to place capacity inventory in the fastmovers only, because these products have high demand patterns and their inventory will be used in the short run. In contrast, the inventory of a slowmover will be used in the long run, but in the short run, it is completely inefficient. It is unknown how the HCS performs compared to the POS and the COS in different simulation settings.

Final remarks

Please note that the POS, the COS, and the HCS are control strategies at the level of material coordination. At the tactical planning level, the control parameters, like safety stocks and batch sizes have already been set, and they are inputs for material coordination. Many authors have studied the trade-offs made at the tactical level. Silver et al. (1998) give a good overview of several (traditional) methods to compute the control parameters. In most of these methods, limited capacity is not an issue. Capacity oriented methods are discussed by Elmaghraby (1978) and Sox et al. (1999). Rajagopalan (2002), Soman (2005), and Williams (1984) discuss methods to set the control parameters if some products are made to stock, and others are made to order, which is similar to the fastmover / slowmover approach we make in the HCS. In this study, we will determine one control parameter at the tactical planning level, and that is the critical inventory position (e.g. safety stock) at which a production order needs to be created.

It must be noted that there are other alternative solutions too that we did not consider in this chapter, because those solutions are expected to perform worse for the situation at POO. In appendix Q we will discuss those solutions.

In the remainder of this report, we will study which of the three planning methods given above performs best considering the specific situation of POO. This will be done in a simulation study, which will be discussed in the next chapter.

[13] A production run of a product with non-preemptive priority will be started immediately after the current production run is finished. This means that the current production run will not be interrupted. This seems reasonable, because the reason to use batches in the first place is to control setup times and costs.

5: Simulation study: a comparison of three planning strategies

The goal of this chapter is to determine which of the three planning strategies introduced in chapter 4 is best for the specific situation of POO, and to compute the optimal control parameters for each strategy under different simulation settings. Simulation models will be used to determine the best strategy and its control parameters. In section 5.1, the assumptions and other decisions we had to make to build the simulation models, are discussed. In section 5.2, the focus is on the simulation models themselves. Some preparations before the simulation models can actually be run are discussed in section 5.3. In this section, aspects like the warm up period and the simulation plan are given. Then, in section 5.4, the results of all simulation experiments are given and discussed. The conclusion can be found in section 5.5.

For the three planning strategies (POS, COS, and HCS) we have built three multi-product single-machine discrete-event rolling-horizon simulation models in MS Excel. We had to build separate models for the three strategies, because the strategies differ in the way the production decision is made. MS Excel has been chosen above other software packages, because it is very common software, which enables Organon to reproduce the simulations if needed, and to adapt the model if needed.

Before the modeling assumptions are discussed in section 5.1, we will examine two aspects in more detail below. First it is argued why simulation was needed. Second, the criteria where the planning strategies are compared on are given.

Need for simulation
Because of the complexity of many products with different demand patterns, stochastic lead times, quality rejections, and the interference on the single finite capacity (operator capacity), an analytical approach was not possible, which determined the need for simulation. Moreover, because the situation at POO differs considerably from the situation in the simulation models of Bemelmans (1985), we could not blindly apply his results. This aspect is discussed in more detail at the end of section 5.1, because all modeling assumptions need to be discussed first.

Criteria to compare planning strategies on
In a simulation experiment[14], all variables are set at specific values. Only the critical inventory level will be adjusted so a certain service rate can be obtained. The most important criterion to compare the POS, the COS and the HCS is the inventory investment needed to obtain a target service rate. The service rate is defined as the percentage of periods in which the inventory level is positive. Only periods in which demand is found are considered. This service rate definition has been chosen because it is similar to the method currently used to measure bulk availability, and because it is preferred by the authors. Please note that we do not consider other costs, like operator costs. This decision has been made, because operator costs do not influence the decision which strategy is best. In each comparison between the strategies, the utilization rate is equal, and therefore, operator costs are equal.

Other criteria to compare the three planning strategies on are not cost-related, and are given below. The first three criteria are the same as the performance measures given in section 2.6.

- The percentage of periods that the end inventory is outside target.
- Nervousness of the production plan.
- Variability in production quantities per period.
- Ease of implementation.

5.1 Modeling assumptions

In this section we will discuss the assumptions, choices and decisions we had to make to build and run the simulation models. We will also discuss the difference between our simulation study and the simulation study of Bemelmans (1985). Moreover, we will give the variables that can be adjusted in the models and their initial values are given.

[14] A simulation experiment is a simulation of more than one run (usually 25 runs) with the same settings.

Released bulk tablets
Although the production and the quality release process are separate processes, we have decided to model these processes as a single process. We have made this decision because we focus on released bulk tablets only. Modeling these two processes separately will only lead to a more complex simulation without any extra output.

Week buckets
It has been decided to model in week buckets, because a week bucket provides us the wanted level of detail for material coordination. The following characteristics led to the decision for weekly buckets: the total lead time is approximately xx weeks (norm lead time excluding review time); about xx orders a week are opened; MRP inventory projections are made once a week; available operator capacity at the short term is considered once a week; and most meetings for material coordination are once a week. Moreover, modeling in day buckets is too detailed for material coordination at POO, and modeling in month buckets is too rough for material coordination at POO. Because the variables only change at discrete points in time (once a week), the simulation models are discrete-event models.

MTS and MTO products
All MTS bulk tablets that are produced at POO and that currently have a safety stock are modeled. In total, 26 bulk tablets are modeled explicitly. In Appendix R, table R.1 a list of these MTS products is found. The other bulk tablets are modeled as a single make-to-order (MTO) product that only claims capacity. This is allowed, because MTO products have no buffer stock and need to be made if there is demand for the product. A list of the MTO products is found in appendix AC. It is assumed that this single MTO product has non-preemptive priority on the capacity, because then the MTO product can be made in time to fulfill demand. In the following sections we will give demand patterns and other aspects related specifically to MTS and MTO products.

Demand pattern MTS products
To determine the demand pattern and the demand forecast pattern for the 26 MTS bulk tablets, weekly demand (forecast) data has been analyzed. Because the data for actual weekly bulk usage was not readily available, we determined it by considering weekly inventory changes[15] and bulk production[16]. The problem of this method is that (de)blocking or rejecting bulk tablets changes the inventory while there has been no demand. This effect could be filtered out for the largest part with the help of the senior planner. Only for Product xx and Product yy this was not possible, and therefore it has been decided to use the budget of 2007 to determine average weekly demand for these products.

For all 26 products a demand distribution that was most suitable has been fit by a goodness-of-fit test. For most products the size of a demand instant has been modeled by a negative exponential distribution. Also, interarrival times are negative exponentially distributed. For some bulk tablets, a normal or gamma distribution has been used to model the size of a demand instant. It must be noted that sometimes the chosen demand distribution is just the best fit, but statistically it could be proven that the choice had been incorrect. However, based on a visual check, we decided to fit the exponential distribution in these cases. Product xx and Product yy are also modeled by an exponential distribution. In Appendix R, table R.1 the demand model for the 26 modeled bulk tablets is found.

A disadvantage of the exponential and gamma distribution is their long tails. For example, once every 10.000 periods a demand of at least 9.2 times the average demand is computed. This situation will not occur at POO. From our historical demand data, we could see that it only happened once that demand was xx times as large as the average demand for that product. Therefore, we maximized the output of the exponential and gamma distribution at xx times the average demand. Moreover, we analyzed whether demand has been autocorrelated over time. On average, the lag-1 autocorrelation (Chatfield, 2004, pg. 23) has been xx, and therefore we decided not to consider autocorrelation in demand.

An important aspect is that the *demand forecast* has autocorrelation. The size of this autocorrelation is on average xx. This is reasonable, because the forecast of bulk usage for period $t+\tau$ in period t is probably the same as the forecast for period $t+\tau$ in period $t-1$. To model this aspect, we need to introduce an autoregressive or moving average process, but the problem of these models is that the coefficient of variation increases over time (Chatfield, 2004, pg. 38), and this is not the case for the

[15] Source: Weekly inventory mutations (Mutaties in bulk_MRP_avail_yyyy_ww.xls). Period: wk 24/2005 – wk 23/2006
[16] Source: Apollo

demand forecast of bulk tablets, which is approximately stable. To our knowledge there is no literature that describes autocorrelated demand forecast models in which the coefficient of variation stays stable, and therefore, we have decided to develop our own model.

In our demand forecast model, there are 3 options in each period:

1. The demand forecast does not change.
2. There is a small change in the demand forecast.
3. There is a large change in the demand forecast.

Based on the available historical data it has been determined for each product how often the demand forecast changes. We made the assumption that half of these forecast changes are small, and half of these forecast changes are large. The half with the small forecast changes has been analyzed to determine a good model for the size of these forecast changes. Often, it was not possible to fit a probability distribution[17], but based on a visual inspection, it has been decided to model the forecast changes by a gamma distribution. A large forecast change is modeled like the forecast size is reconsidered; the model to determine actual demand is used again. The result is some kind of 'reset option' to keep the coefficient of variation stable.

The demand forecast model is as follows:

$$\hat{D}_{j,t,t-\tau} = \begin{cases} \hat{D}_{j,t,t-\tau-1} & ; \text{ with probability } P\alpha \quad (5.1) \\ \hat{D}_{j,t,t-\tau-1} \pm SC_{j,t} & ; \text{ with probability } P\beta \quad (5.2) \\ \hat{D}_{j,t,t-\tau}\ (new) & ; \text{ with probability } P\varphi \quad (5.3) \end{cases}$$

$$0 \le P\alpha \le 1$$

$$0 \le P\beta \le 1$$

$$0 \le P\varphi \le 1$$

$$P\alpha + P\beta + P\varphi = 1$$

where;

$\hat{D}_{j,t,t-\tau}$	:	Demand forecast of product *j* for period *t* in period *t-τ*
$SC_{j,t}$	:	Size of a small change of the demand forecast of product *j* for period *t*
$\hat{D}_{j,t,t-\tau}$ *(new)*	:	Completely new demand forecast of product *j* for period *t* (large change)
$P\alpha$	:	Probability of no change in the demand forecast
$P\beta$	:	Probability of a small change in the demand forecast
$P\varphi$	:	Probability of a large change in the demand forecast

The model for demand and demand forecast is validated by comparing the results of the model with the available historical data. The first three moments; average, standard deviation, and autocorrelation, are approximately the same in the model compared to historical data. Therefore we conclude that our model is good. In Appendix R, table R.2 the demand forecast model for the 26 modeled bulk tablets is found. Moreover, the autocorrelation in demand forecast of the actual data is compared to the autocorrelation in demand forecast of the simulated data. It can be seen that these two are close to each other.

Demand pattern MTO products

Weekly bulk usage could be computed by considering weekly inventory changes and bulk production. Unfortunately, this is not possible for MTO products, because this data is not available for most MTO products. Therefore, we used data of monthly bulk usage[18]. Assuming that there is only one demand instant per month for a single MTO product, we randomly placed this demand in one week of that

[17] If a lot of data are available a goodness of fit test will probably reject all candidate probability distributions (Liman et al., 2004, pg. 108). This is a good reason that we could not fit any distribution to model the small forecast changes.

[18] Source: Usage history report (USGHST_ddmmyy.xls). Period: June 2005 – May 2006.

month. This is reasonable, because demand for MTO products is small, there are only a few demand instants a year, and usually, there is only one customer.

In the simulation model, MTO products are only modeled as capacity users, because a MTO product does not hold inventory. It is only produced if there is demand for it. For that reason, we converted the demand for MTO products to hours of operator work, and we fitted an exponential distribution on the size of it. The interarrival times have been modeled by an exponential distribution too. The results are found in table R.1 in appendix R.

Lead times

In our simulation model, lead times are rounded to weeks. Based on historical data of May 2005 to May 2006, the following lead time distribution, excluding review time, has been found for the total process of production and quality control:

Lead time distribution						
Lead time (in weeks)						
Probability						

Table 5.1: Lead time distribution

We have decided that the total lead time can not be larger than xx weeks, although in the historical data lead times of more than xx weeks can be found. We have made this decision, because if a product is expected to go out-of-stock, it will be prioritized, and it should always be possible to finish all activities within xx weeks. In the simulation experiments, the same lead time distribution is used for all bulk tablets.

The norm lead time of the total process is set at xx weeks, because that is its current value. Because all decisions at the level of material coordination are based on forecasts after the norm lead time, we have to look almost xx months ahead in time.

Review period

A production order can not be opened immediately after all data is downloaded into a decision tool. Usually, a data download takes place at Monday, and then a production plan needs to be made before Thursday, because at Thursday, a forecast for the next week must be sent to MHD. At some day in the second week, the production order will be opened and MHD will deliver the exact amount of materials to the Production Department. This leads to a review period of on average xx weeks, hence, we rounded the review period to xx weeks. The review period is added to the lead time in the simulation study.

Quality rejections

Because the probability that a batch is disapproved by the Quality Department is small, there is few historical data available, and therefore, it is not possible to determine quality rejection probabilities on historical data. Based on a proposal of the senior planner and the head of TPD, we have set the probability of rejection at xx% for all products, except for Product xx. For this product, the probability of rejection has been set at xx%. If a product is produced in a campaign, each batch has a probability of rejection of xx%, so usually not the complete campaign is rejected. For MTO products it is assumed that the weekly production is fully disapproved. The rejection probabilities are mutually independent.

Capacity

In section 2.1.1, we have analyzed the availability of operator capacity. This monthly data has been converted to weekly data by multiplying average and variance with 12/52. This is reasonable, because monthly data has been shown to be normally distributed by a goodness-of-fit test. In section 2.1.1, it was already raised that it is hard to give a clear utilization rate of operators. Therefore, we have made simulation runs under different utilization rates. With ρ = xx%, and normal quality rejection probabilities, average capacity is xx operator hours a week, and the standard deviation is xx operator hours a week.

Only operator capacity has been considered, because machine utilization rates are low to moderate (ρ < xx%), and because a machine can not work without a trained operator. In the simulation models, operator capacity is modeled as a 'single machine', and therefore our study can be placed under the multi-product single-machine problems in the literature. It is reasonable to model operators as a 'single machine', because operators are interchangeable. Furthermore, the simulation model is at the level of

material coordination and weekly buckets are used, and therefore, a detailed model of operator capacity is not needed.

Another modeling assumption concerning capacity is how we modeled 'rest capacity'. It has been decided that the simulation models may open as many production orders until available rest capacity falls below zero. The production order that makes available rest capacity fall below zero can be opened too in this period. In the next period, we will subtract the amount of negative capacity in this period from the available capacity. This modeling assumption has been made, because otherwise rest capacity will be lost, while it was needed.

Trend
For all aspects, we assumed that there is no trend over time. So, there is no trend in the available capacity, no trend in demand patterns, and no trend in the demand forecast. This last assumption is not completely true, because on average, the demand forecast declines a little if the demand instant comes closer. However, large differences are found between the products, and it would dramatically increase the complexity of the simulation model if we model a demand forecast with trend.

Seasonal effects
In our simulation model, seasonal effects are not considered. Therefore, we had to correct our historical data to eliminate the seasonal effect. For the availability of operators, the seasonal effect was eliminated, as was already discussed in section 2.1.1. For historical bulk usage it was more difficult to eliminate seasonal effects. In appendix S, it can be seen that monthly demand for Marvelon and Cerazette was lower during the holiday periods, but for the other products no effect could be found over the studied period of four years[19]. Furthermore, in the historical weekly demand data used to model weekly demand, no seasonal effect for any product could be found. However, it was remarkable that for the four largest products (Marvelon Z.ME, Cerazette, Remeron 30MG CTO NB, and Livial 2,5MG NS) weekly demand was only zero during the holidays. To compensate for this effect, we decided to consider the zero demand instances in the average size of a demand instant, and we set the arrival probability at 1.

Safety time of the Packaging Department
To work more efficiently, the Packaging Department has the option to reschedule packaging orders up to xx weeks forward. This 'safety time' causes the Ready-for-release (RR) date to be xx weeks before the planned date to open a packaging order. Therefore, bulk tablets need to be available xx weeks earlier than they will be used. The performance measure of (released) bulk availability is also based on the RR-date. Actually, it is based on the calculated RR-date, which is computed by subtracting the norm lead times of the Packaging Department from the replenishment order date. Historical data[20] showed us that the difference between calculated RR-date and actual open date of a packaging order has been on average xx weeks. Because the MRP system plans all packaging orders with the RR-date in or before the current week as demand for bulk tablets in the current week, a demand forecast for bulk tablets in the current week of xx times the average size[21] is found in the MRP system, as shown in section J.1.1.

In our simulation model we assume that the Packaging Department uses the bulk at the RR-date, because POO wants to give some decision freedom to the packaging planners, and because that is the moment where the performance measure of POO is based on. That bulk tablets will stay on average xx weeks on the production floor of the Packaging Department without being used is not the scope of this project. Because of this assumption, there is just a normal demand forecast for the current week, instead of one that is xx times its normal size. It must be noted that in reality, there still is a large demand forecast for the current week. But this is no problem, because the current inventory is also larger than it was planned to be, because the demand forecast of last week was also much larger than the actual demand in that week. This extra inventory is the leveling stock of the Packaging Department.

[19] Source: Usage history report (USGHST_ddmmyy.xls). Period: June 2002 – May 2006
[20] Source: Order niet C-vrij en beschikbaar yyyy_mm.xls. Period August 2005 – July 2006.
[21] Source: Weekly inventory mutations (Mutaties in bulk_MRP_avail_yyyy_ww.xls). Period: wk 24/2005 – wk 23/2006

Shelf life
Restrictions caused by a limited shelf life are not taken into account, because for most bulk tablets the shelf life is xx to xx years, which is long enough to avoid problems. Only for Product xx, shelf life forms an important constraint. Product xx must be packed within xx months after the production order is opened. For this reason it is not accepted that the safety stock of Product xx is larger than one batch size, whatever the consequences are concerning released bulk availability[22].

Inventory costs
For all bulk tablets, we have taken the current cost price to compute the inventory investment[23]. This is not completely correct; ideally, only the added value may be used. According to Silver et al. (1998, pg. 44), the value of an item should ideally measure the actual amount of money (variable cost) that has been spent on the SKU (stock keeping unit) to make it available for usage. Because this information was not readily available, and because the current cost price is also used at the moment to compute the performance of POO, we decided to use the current cost price in our simulation models. In Appendix R, table R.1 the cost price of the 26 modeled bulk tablets is found.

Only physical inventory levels, also called on hand stock, of released bulk tablets have been considered in the simulation models. This means that we will not consider work-in-process (WIP) inventories of the Production Department and the Quality Department. This decision can be made, because the same lead time distribution has been used in the simulation experiments, and therefore, WIP inventory costs are the same in all experiments. Furthermore, as already discussed under the heading 'safety time of the Packaging Department' leveling stock has not been considered in the simulation models too.

Sequence dependent setup times
There are some restrictions with respect to the sequence of some activities at the Tablets Production Department caused by sequence dependent setup times. But in accordance with the production planner, it has been decided to ignore these restrictions, because the norm lead time of the production activities is long enough to make a detailed schedule in which sequence dependent setups can be considered while the norm lead time is not exceeded.

Backorders
All demand that can not be satisfied directly from the shelf is backordered. This is reasonable, because demand comes from the Packaging Department, and their demand comes from the Local Company, and both are part of Organon.

Stock-out
A stock-out is registered if the inventory of a product is below zero, and if there is demand in that week. To compute an out-of-stock rate, only weeks wherein demand is found, are considered. All weeks without demand are neglected, independent of the inventory level. This way to compute the performance is similar to the current way to compute the (released) bulk availability.

Starting inventory
The starting inventory is computed by equation 5.4 for the POS simulation model:

$$I_{start,j,POS} = \theta \cdot ss_j + rand() \cdot BS_j \cdot CS_j + xx \cdot \overline{D}w_j \qquad (5.4)$$

where;

$I_{start,j,POS}$	:	Starting inventory of product *j* in the POS simulation model
θ	:	A value that is computed to make the starting inventory representative
ss_j	:	Safety stock of product *j*
rand()	:	A random value between 0 and 1
BS_j	:	Batch size of product *j*
CS_j	:	Campaign size of product *j*
$\overline{D}w_j$	:	Average weekly demand for product *j*

[22] Actually, we can not guarantee that the inventory of Product xx stays below a certain level in the COS simulation model.
[23] Source: Apollo

The starting inventory consists of (a part of) the batch size * campaign size, and (a part of) the safety stock. In simulations under high utilization rates, θ has been given a value below 1, because part of the safety stock is capacity stock in that case. The value of θ has been determined manually by comparing the inventory position in week 1 with average inventory levels during the simulation. Furthermore, because there are no production orders yet at the start of the simulation, and because the norm production lead time + the review time is xx weeks, we have added xx weeks of average weekly demand to the starting inventory. Altogether, this results in an inventory level that is representative from the start of the simulation.

For the COS, the starting inventory is computed in a different way, because there is no individual safety stock for individual products in the COS. Equation 5.5 gives the starting inventory for the COS.

$$I_{start,j,COS} = rand() \cdot BS_j \cdot CS_j + \psi \cdot \overline{D}w_j \qquad (5.5)$$

where;

$I_{start,j,COS}$	:	Starting inventory of product *j* in the COS simulation model
ψ	:	A value that is computed to make the starting inventory representative

In the HCS, the starting inventory of fastmovers is computed by equation 5.5, while for slowmovers, it is computed by equation 5.4.

Demand forecast period

Although material coordination does not want to make decisions at the long term, we still look forward until week *t+xx*. We need to know the demand forecast until this period, because otherwise, under high utilization rates in the COS or the HCS simulation model, it can happen that no inventory expects to fall below zero in the considered period. If this happens, a random product will be selected for production, and if this is a slowmover, capacity stock is placed in the wrong product. Because the simulation models do not look further than week *t+xx*, they can be classified as rolling-horizon models.

Fastmovers in HCS

In the HCS, the following four products are modeled as fastmovers: Marvelon Z.ME, Cerazette, Remeron 30MG CTO NB, and Livial 2,5MG NS. These products have demand in almost every week, claim approximately xx% of available operator capacity, and have a long shelf life. Therefore, they are ideal to place capacity inventory in.

Comparison with the simulation study of Bemelmans (1985)

Our simulation study differs considerably from the simulation study of Bemelmans (1985). The major dissimilarities are given below.

1. In our simulation study an autocorrelated demand forecast model is considered, which is not considered by Bemelmans (1985).
2. In our simulation study more variabilities and uncertainties are considered. Bemelmans (1985) does not consider uncertainties in the lead time, uncertainties caused by quality rejections, and uncertainties in the availability of capacity.
3. In our simulation study products are not identical on many aspects.
4. We modeled MTO products that have non-preemptive priority on the capacity. Bemelmans (1985) does not consider MTO products.
5. Bemelmans (1985) defined stock-out costs, while we defined a target service rate.

Variables

Altogether, the variables below can be adjusted in the simulation models. In Appendix R the initial values of most of these variables are given for all 26 modeled bulk tablets.

- D_j : Demand size for product *j* in 1000 tablets ($\overline{D}_j$ and σ_{D_j})
- Pa_j : Probability of an arrival of product *j*
- SC_j : Size of a small change of the demand forecast of product *j* in 1000 tablets. ($\overline{SC}_j$ and σ_{SC_j})
- $P\alpha$: Probability of no change in the demand forecast
- $P\beta$: Probability of a small change in the demand forecast
- $P\varphi$: Probability of a large change in the demand forecast
- ss_j : Safety stock of product *j* in 1000 tablets (POS-model)

- CL : Critical level in hours of operator capacity (COS-model)
- BS_j : Batch size of product j in 1000 tablets
- CS_j : Campaign size of product j
- LTD : Lead time distribution
- L_{norm} : Norm lead time in weeks (not easy to adjust)
- Pqr_j : Probability of a quality rejection of product j
- C : Available operator capacity in hours ($\overline{C}$ and σ_C)
  -> By adjusting this parameter, ρ can be changed
- cp_j : Cost price of product j in euros
- cu_j : Capacity usage in hours to produce 1000 tablets of product j
- Demand (forecast) model (not easy to adjust)

Now that all the assumptions have been discussed, and all the decisions we had to make are given, we will describe the simulation models themselves in the next section.

5.2 Architecture of the simulation models

For each of the three strategies (POS, COS and HCS) a discrete-event rolling-horizon simulation model has been built. These three models only differ in the way that the production decision is made. In this section, we will summarize the architecture of the simulation models. A detailed description can be found in appendix T.

The models contain three important components, and these components will be discussed below:
- Input and performance sheet (section 5.2.1 and appendix T.1)
- Product sheets (section 5.2.2 and appendix T.2)
- Capacity sheet (section 5.2.3 and appendix T.3)

5.2.1 Input and performance sheet

In this sheet, the user can set all variables, like safety stocks, lead times, and probability of quality rejections. Only demand characteristics can not be adjusted in this sheet. They need to be set in the product sheets. If all variables are set, and a simulation is run, the performance of all products is also found in this sheet. The two most important performance indicators are the out-of-stock rate and the inventory investment needed to obtain the desired out-of-stock rate. The out-of-stock rate is 1 – service rate. For more information on the input and performance sheet, the reader is referred to appendix T.1.

5.2.2 Product sheets

Each product has its own sheet in the simulation models, which means that there are 26 product sheets. In this sheet, all computations related to a specific product can be found. For each simulated week the following elements are found:
- Actual demand in week t
- A demand forecast for week t to week $t+xx$
- Production in week t
- (Physical) end inventory in week t
- Projected inventory levels after the norm lead time; the inventory position in week t
- Run out times in week t

In the product sheet, it is also found what the lead time is of a specific production order, when it will be released by the Quality Department, or whether it will be disapproved by the Quality Department. In contrast to the MTS products, all MTO products are modeled as one product and are given in one product sheet. Only their claim on capacity and their probability to get disapproved by the Quality Department are given in this sheet.

In section 5.1, we already showed how demand and demand forecasts are modeled. Below, we will describe how production orders, end inventories, inventory positions, and run out times are computed. The inventory position is used to base the production decision on, because this is the first moment that a production decision can influence inventory levels. The inventory position is computed by equation 5.6.

$$Ipos_{j,t} = I_{j,t-1} - \sum_{\tau=0}^{\tau=L_{norm}} \hat{D}_{j,t+\tau,t} + OPO_{j,t} \quad (5.6)$$

where;
$Ipos_{j,t}$: Inventory Position of product j in period t
$I_{j,t}$: End inventory of product j in period t
$OPO_{j,t}$: Opened Production Orders for product j in period t

The end inventory is computed by equation 5.7.

$$I_{j,t} = I_{j,t-1} + FPO_{j,t} - D_{j,t} \quad (5.7)$$

where;
$FPO_{j,t}$: Finished Production Order of product j in period t

Actual production orders are not computed in the product sheets, but in the capacity sheet, which will be discussed in section 5.2.3, because in the capacity sheet, capacity is considered, and it can be decided for which product a production order needs to be released. Run out times are used to prioritize between products if capacity is insufficient to open all production orders. The run out time is the smallest τ_1 for which equation 5.8 is below zero.

$$RO_{j,t} = \min \tau_1 \text{ for which } I_{j,t-1} - \sum_{\tau=0}^{\tau_1} \hat{D}_{j,t+\tau,t} + OPO_{j,t} < 0 \quad (5.8)$$

where;
$RO_{j,t}$: Run out time of product j in period t

For more information on the product sheets, the reader is referred to appendix T.2.

5.2.3 Capacity sheet

The capacity sheet is the 'brain' of the simulation model, because in this sheet the actual production decisions are made. This sheet is also different for the three strategies, which is the main reason that we had to build three simulation models. Below, we will summarize how the production decision is made for the three strategies.

Production decision in the POS simulation model

The decision for which products a production run should be started, considering a limited availability of capacity, is made in the following way in the POS simulation model:

- By comparing the inventory position with the safety stock level, it is determined whether there is a production need for product j in period t ($PN_{j,t}$). The production need is zero if the inventory position is above safety stock, otherwise it is PS_j, which is the batch size * the campaign size. This is done for all products. See equation 5.9.

  If $Ipos_{j,t} < ss_j$, then $PN_{j,t} = PS_j = BS_j * CS_j$, otherwise $PN_{j,t} = 0$ (5.9)

- Based on the run out time computed by equation 5.8, products receive a rank. The product that expects its inventory level to fall below zero first gets the highest rank (rank 1). If more than one product has the same run out time, a random factor will determine their rank. See equation 5.10.

  $$RO_{1,t} \leq RO_{2,t} \leq ... \leq RO_{26,t} \quad (5.10)$$

- If the available capacity in period t minus the capacity needed to produce the MTO products is larger than zero, the production need of the product with rank 1 is loaded. If available capacity is still positive, the production need of the product with rank 2 is loaded. This will be repeated until available capacity becomes negative, or until all products are considered. The amount of

negative capacity is subtracted from available capacity in the next week. $Cneg_0$ is set at 0. The procedure can be found in equation 5.11 to 5.16.

$$i = 0$$

$$Cneg_{t-1} = min\left(C_{i,t-1}, 0\right) \quad (5.11)$$

$$C_{i,t} = C_t - CN_{MTO,t} + Cneg_{t-1} \quad (5.12)$$

$$i = i + 1 \quad (5.13)$$

If $C_{i-1,t} > 0$, then load $PN_{j,t}$ of product j with $RO_{i,t}$, otherwise stop. (5.14)

$$CN_{i,t} = PN_{j,t} \cdot cu_j \text{ for product } j \text{ with } RO_{i,t} \quad (5.15)$$

$$C_{i,t} = C_{i-1,t} - CN_{i,t} \quad (5.16)$$

Return to equation 5.13

where;

C_t	:	Available capacity in period t
$Cneg_t$	:	Negative rest capacity in period t
$C_{i,t}$	:	Available rest capacity in period t after product j with $RO_{i,t}$ is loaded
$CN_{i,t}$	:	The capacity need for product j with $RO_{i,t}$ in period t to produce $PN_{j,t}$

- For the products that are loaded a production order ($PO_{j,t}$) of size $PN_{j,t}$ is opened.
- This cycle is repeated every week.

More information on the capacity sheet of the POS simulation model can be found in appendix T.3.1.

Production decision in the COS simulation model

The decision for which products a production run should be started, considering a limited availability of capacity, is made in the following way in the COS simulation model:

- The inventory positions in period t for all products are converted to hours of operator work and accumulated, as shown in equation 5.17. The total amount of capacity that is stored in the inventories after the norm lead time (CSI_t) is compared to a predefined critical level (CL). The difference between these two determines the total production need (TPN_t). See equation 5.18.

$$CSI_t = \sum_j Ipos_{j,t} \cdot cu_j \quad (5.17)$$

$$TPN_{0,t} = max\ (0;\ CL - CSI_t) \quad (5.18)$$

- Based on the run out time, products receive a rank. The product that expects its inventory level to fall below zero first gets the highest rank (rank 1). If more than one product has the same run out time, a random factor will determine their rank. See equation 5.10.
- If the available capacity in period t minus the capacity needed to produce the MTO products is larger than zero, the production need of the product with rank 1 is loaded. If available capacity is still positive, the production need of the product with rank 2 is loaded. This will be repeated until available capacity becomes negative, or until all products are considered. The amount of negative capacity is subtracted from available capacity in the next week. $Cneg_0$ is set at 0. *However*, we will not produce more than the total production need ($TPN_{0,t}$) determined in equation 5.18. The procedure can be found below.

$i = 0$

$Cneg_{t-1} = min(C_{i,t-1}, 0)$ *(5.11)*

$C_{i,t} = C_t - CN_{MTO,t} + Cneg_{t-1}$ *(5.12)*

$i = i + 1$ *(5.13)*

If $C_{i-1,t} > 0$ and $TPN_{i-1,t} > 0$, then load PS_j of product j with $RO_{i,t}$, otherwise stop. *(5.19)*

$CN_{i,t} = PS_j \cdot cu_j$ for product j with $RO_{i,t}$ *(5.20)*

$C_{i,t} = C_{i-1,t} - CN_{i,t}$ and $TPN_{i,t} = TPN_{i-1,t} - CN_{i,t}$ *(5.16) & (5.21)*

Return to equation 5.13

where;
$TPN_{i,t}$: Total rest production need in period t after product j with $RO_{i,t}$ is loaded

- For the products that are loaded a production order ($PO_{j,t}$) of size PS_j is opened.
- This cycle is repeated every week.

More information on the capacity sheet of the COS simulation model can be found in appendix T.3.2.

Production decision in the HCS simulation model
In the HCS simulation model, the production decisions are made in the same way as above. Fastmovers and slowmovers have been split. First, the procedure for slowmovers is followed. If there is any capacity left, the procedure for fastmovers is followed. More information on the capacity sheet of the HCS simulation model can be found in appendix T.3.3.

5.3 Simulation preparations

In this section, some aspects related to the execution of the simulation are discussed. We will show how we determined the warm up period, the run length, and the number of replications for the simulations in section 5.3.1. Then, we will give the simulation plan in section 5.3.2. In the simulation plan it is described at which values the variables are set, and which variables are changed to study which of the three planning strategies is best. In this section, attention will be paid to the model error as well.

5.3.1 Warm up period, run length and number of replications

The warm up period is set at 100 weeks for all simulation experiments, based on the Welch graphical method (Liman et al., 2004). In appendix U it is found how we determined this warm up period. The run length of one simulation run is 880 weeks. This value is based on the fact that we had to constrain the model to 1000 weeks (because otherwise the MS Excel file would grow above 100MB), and 120 weeks are not considered: 100 weeks as warm-up period, and 20 weeks as 'cooling down' period. This cooling down period is needed because from week 981 the run out times are not fully reliable anymore, because there is no demand forecast after week 1000.

The number of replications is set at 25, because in that case, the 95% confidence interval of the service rate is average service rate +/- 1% in most simulation experiments. It must be noted that the utilization rate affects the width of the confidence interval. For the POS simulation model, if ρ = xx% the width is +/- 0.4%, while it is +/- 0.8% if ρ = xx%. When ρ increased to xx%, we even had to make 50 runs to decrease the confidence interval width to +/- 2.0%. Because of the time it takes to run one simulation experiment of 25 runs (approximately 15 minutes), available time did not allow us to extend

a simulation experiment to, for example, 100 runs. In Visual Basic, a macro has been developed to execute 25 runs in a row. This macro is also given in appendix U.

5.3.2 Simulation plan

Mentioned previously, the main goal of the simulation experiments is to determine which of the three strategies is best. A fair comparison between the three strategies is made as follows. Under exactly the same settings, we keep on adjusting the safety stock / critical level until a given service rate is obtained, e.g. xx%. This is done for all three simulation models. Then, the three planning strategies can be compared with each other on the five performance criteria. To compare these strategies in a structured way, a simulation plan is made, because we want to check the performance of the three strategies under different simulation settings. However, to determine which strategy is best, there are two problems that need to be overcome:

1. What is exactly the utilization rate of operators?
2. What is the service rate we need to model to reach a service rate of xx% in reality?

1. Utilization rate

In section 2.1.1, we already estimated the utilization rate of operators to be xx%, but an exact figure can not be given. We also noted that there is some flexibility in operator capacity, due to for example overwork, but this flexibility will not be modeled. To overcome the problem that we can not exactly determine the utilization rate of operators and the influence of flexibility in operator capacity, we decided to make simulation experiments under different utilization rates, namely: ρ = xx%, ρ = xx%, ρ = xx%, and ρ = xx%. The lower and upper bound in utilization rate have been chosen at these values, because we are sure that the real utilization rate of operators is somewhere in this region. Furthermore, varying the utilization rate of operators gives us insight in the relation between utilization rate and inventory investment.

2. Service rate

The goal of POO is to achieve a service rate of xx% on released bulk products. But our model is not exactly equal to reality, and therefore, an xx% service rate in the model does not have to lead to an xx% service rate in reality. This is called the model error. To determine the service rate we need to model to reach an xx% service rate in reality, a study is done to determine the model error. The results are found in appendix V. Our conclusion is that we need to model a xx% service rate to obtain an xx% service rate in reality. However, as explained in appendix V, we will also make some simulation experiments under a service rate of xx%.

The plan

We would like to make 18 simulation experiments: For each strategy, four simulation experiments are conducted with the goal to obtain a service rate of xx%, and two simulation experiments are conducted with the goal to obtain a service rate of xx%. See table 5.2.

Simulation experiments				
Service rate	Utilization rate			
		1. POS, 2. COS & 3. HCS	4. POS, 5. COS & 6. HCS	
	7. POS, 8. COS & 9. HCS	10. POS, 11. COS & 12. HCS	13. POS, 14. COS & 15. HCS	16. POS, 17. COS & 18. HCS

Table 5.2: List of simulation experiments

The simulation experiments are conducted in the following way. For all three strategies, rejection rates, lead times, cost prices, demand models, batch and campaign sizes, and capacity usage are set at their current values, as given in appendix R, and section 5.1. Then, the following step-by-step plan is executed for the three strategies.

1. **Product Oriented Strategy**
   - Determine initial safety stock levels for all products under infinite capacity with the goal to obtain the given service level of xx% (or xx%) for each individual product. The initial safety stock can not be under 0 tablets, and the safety stock of Product xx is maximal the size of 1 batch.
   - Adjust the available capacity to set the utilization rate at the preferred level.

- Adjust the initial safety stock of each product with a factor of the standard deviation of average weekly demand until the total service level is xx% (or xx%). The safety stock of Product xx still is maximal the size of 1 batch.
- Register the total inventory investment.

In appendix AA, initial safety stocks and standard deviations of average weekly demand can be found.

The way of working described above is chosen because the POS assumes that there are no congestion effects between products on the capacity. However, under high utilization rates these congestion effects will arise, and the safety stock of each product needs to be adjusted in the same way to create some capacity stock. Because under high utilization rates it will happen that some production orders are opened too late, it seems logical that the variation in demand is used as the factor to base extra safety stocks on.

It must be noted that utilization rate and lead time are related. Under high utilization rates, waiting times will increase, and therefore, the lead time will increase. Under infinite capacity, there will be no waiting times, only processing times. Still, we assumed the same lead time distribution for all simulation experiments. In appendix W, it will be explained why this assumption is valid for our simulation models.

2. **Capacity Oriented Strategy**
   - Adjust the available capacity to set the utilization rate at the preferred level.
   - Adjust the critical level to obtain a total service level of xx% (or xx%).
   - Register the total inventory investment.

3. **Hybrid Control Strategy**
   - Adjust the available capacity to set the utilization rate at the preferred level.
   - For slowmovers, the initial safety stock of the POS is used too in the HCS, and it is adjusted in the same way until the total service level of slowmovers is xx% (or xx%).
   - Adjust the critical level to obtain a total service level of xx% (or xx%) for the fastmovers.
   - Register the total inventory investment.

5.4 The results of the simulation experiments

In this section, we will show the results of the simulation experiments to determine which strategy is best. Five criteria have been selected at the start of this chapter to compare the three planning strategies on. In section 5.4.1, the focus is on the performance of the three planning strategies on inventory investment, because this is the most important criterion. In section 5.4.2, the planning strategies are compared on the four other criteria. Our simulation results are compared with the simulation results of Bemelmans (1985) in section 5.4.3. Furthermore, the effect on the performance of the 'uncertainty aspects' given in the research assignment is studied in section 5.4.4.

5.4.1 Criterion 1: the inventory investment

In this section we will compare the three strategies on the inventory investment needed to obtain a certain service rate. In figure 5.1, the total inventory investment needed to obtain an average service rate of xx% under the four utilization rates of operators is given for the three planning strategies. In figure 5.2 the same figure is found, only we have zoomed in to be able to compare the strategies better. The total inventory investment needed to obtain an average service rate of xx% can be found in figure 5.3. Without any statistical analysis, it can already be seen that the HCS performs worse than the POS and the COS under high utilization rates of operators, and the performance of the POS and the COS are approximately the same.

The HCS performs much worse than the POS and the COS under high operator utilization rates, because under high utilization rates very large inventory investments are needed in the fastmovers to obtain the target service level. These large inventory investments are needed, because a lot of capacity inventory needs to be placed in the fastmovers to deal with the congestion effects caused by the limited operator capacity under high utilization rates. Because the HCS performs obviously worse than the POS and the COS, the focus of the remainder of this section will be on comparing the POS and the COS.

 # Deleted
Figure 5.1: Total inventory investment needed to obtain an average service rate of xx%

Figure 5.2 is the same as figure 5.1, only we have zoomed in to be able to compare the strategies better.

 # Deleted
Figure 5.2: Total inventory investment needed to obtain an average service rate of xx%; figure 5.1 zoomed in

 # Deleted
Figure 5.3: Total inventory investment needed to obtain an average service rate of xx%

In appendix X, table X.1 to X.6, the exact values of the simulation results are found; simulated service levels, simulated utilization rates, inventory investments, and 95% confidence intervals are given. Furthermore, it is studied whether there are any significant differences[24] between the simulation experiments. As an example, we have given the table of ρ = xx% and the target service rate is xx% below in table 5.3. In appendix X, table X.7, the safety stocks and critical inventory levels needed to obtain the results are given, among other information.

Simulation experiments 13 to 15				
Goal:	**Service level**	**xx%**	**Utilization rate**	**xx%**
	Strategy	*Service level*	*Utilization rate*	*Inventory investment*
Average **LB - UB**	POS			
Average **LB - UB**	COS			
Average **LB - UB**	Hybrid			

Table 5.3: Simulation experiment 13 to 15. Goal: Service level = xx%, ρ = xx%

From the simulation experiments, it can be concluded that the product oriented strategy and the capacity oriented strategy are almost equal in their inventory investment needed to obtain a certain service rate. However, in two cases, the POS is significantly better:

- If ρ = xx% and the target service rate is xx%, the inventory investment for the POS is significantly lower than for the COS.
- If ρ = xx% and the target service rate is xx%, the inventory investment for the POS is significantly lower than for the COS.

In contrast to Bemelmans (1985) we can not conclude that the COS needs lower inventory investments than the POS under high utilization rates. In contrast, we can even conclude that the POS needs lower inventory investment under ρ = xx% (and a target service rate of xx%). To understand the performance difference, we have analyzed what the variation is over the service rates per product in the POS and in the COS, and we have analyzed how inventories are distributed over the products in the POS and in the COS.

Variation over the service rate per product
From the results of the simulation experiments, we see that in all situations the standard deviation over the service rates per product is larger in the COS than in the POS. These results are found in table 5.4. A poor service rate of one product needs to be compensated by a good service rate of another product. Because inventory investments increase non-linearly when the service rate increases, more inventory investments have been needed in the COS compared to the POS.

[24] Two samples are significantly different if we are more than 95% confident that one of the samples performs better. This definition for 'significant' will also be used in the remainder of this report.

Variation over the service rate per product			
Service rate	Utilization rate	POS	COS
Low	Low	4.49%	6.85%
Low	High	5.02%	6.87%
High	Very low	0.67%	4.72%
High	Low	1.12%	4.52%
High	High	1.83%	4.35%
High	Very high	2.45%	4.12%

Table 5.4: Standard deviation over the service rate per product: POS vs. COS

Distribution of inventory over the products

In table X.7 in appendix X, it is shown how inventories are distributed over the products in the various simulation experiments. For each product and each simulation experiment, it is shown which percentage of the total inventory is stored in that product (relative inventory). For each product we have compared the relative inventory of that product in the POS with the relative inventory of that product in the COS. If the difference between these two is more than 15%, the cell turns red or green.

In table 5.5 the relative inventory of a product averaged over the six COS simulation experiments is divided by the relative inventory of a product averaged over the six POS simulation experiments. If the difference between these two is more than 15%, the value is red or green. This table gives a good overview of the way that inventories are distributed over the products by the COS and by the POS.

Average inventory in COS vs. average inventory in POS		
Product name	Product ID	Average inventory in COS / POS
CERAZETTE		109%
LIVIAL 2,5MG NS		119%
MARVELON Z.ME		104%
REMERON 30MG CTO NB		116%
DESO/EE-50/35 PS CT		90%
DESO/EE-100/30 PS CT		91%
EXLUTON		100%
MARVELON Z.ME CT		100%
MARVELON Z.ME ZO		88%
MERCILON		66%
MINISTAT		83%
ORADEXON 0,5MG		69%
ORADEXON 1,5MG		81%
ORGAMETRIL		103%
OVESTIN 1MG 6MM		99%
OVESTIN 1MG ZO		91%
OVESTIN 2MG		103%
OVESTIN 2MG ZO		90%
PLACEBO CT		87%
PLACEBO WIT ZO		98%
REMERON 15MG CTO NB		78%
THYRAX 0,025MG DT ZO		140%
THYRAX 0,1MG DT ZO		128%
TOLVON 10MG CT		101%
TOLVON 30MG CTO		113%
TOLVON 60MG CTO		85%

Table 5.5: Average relative inventory in the POS vs. average relative inventory in the COS

It can be seen that in the COS more inventory has been placed in the fastmovers (Livial 2,5MG NS and Remeron 30MG CTO NB) and in Thyrax 0,025 MG DT ZO and 0,1MG DT ZO. In the POS more stock has been placed in many slowmovers (Mercilon, Ministat, Oradexon 0,5MG and 1,5MG, Placebo CT, Remeron 15MG CTO NB, and Tolvon 60MG CTO). Considering shelf life, it is questionable whether it is advisable to have more stock in slowmovers. Therefore, we have compared safety stocks with average yearly demand for all products. The most extreme case we found is the safety stock for Ministat in the simulation experiment with ρ = xx% and a target service rate of xx%. In this case, the safety stock was xx% of average yearly demand. Because the shelf life usually is xx to xx years, even the most extreme case is not risky considering shelf life.

From table 5.4 and table 5.5 it can be concluded that the COS underestimates the production need for slowmovers. Therefore, slowmovers perform worse on service rate in the COS compared to the POS. The COS compensates the lower service rate of slowmovers by extra inventory investments in the fastmovers. Because inventory investments increase non-linearly with the service rate, the total inventory investment in the COS is higher than in the POS.

5.4.2 Criteria 2 to 5

In this section we will compare the POS and the COS on the criteria given below. The HCS is not considered in this section, because of its poor performance on inventory investment under high utilization rates.

- The percentage of periods that the end inventory is outside target.
- Nervousness of the production plan.
- Variability in production quantities per period.
- Ease of implementation.

The percentage of periods that the end inventory is outside target

Under the POS, we made four simulation experiments under four different settings. The percentage of periods that the end inventory has been outside target is given in table 5.6 for the four simulation experiments. The target is defined by a lower bound and an upper bound. The lower bound is defined by the safety stock of a product minus its capacity inventory, and the upper bound is defined by the safety stock of a product plus its batch size * campaign size. In appendix Y, table Y.1 the outside inventory target rate can be found for the individual products.

Unfortunately, we can not give an outside inventory target rate under the COS, because there are no individual safety stocks or other individual target stocks. It is not possible to define an outside inventory target rate for the COS that can be compared fairly with the POS.

Outside inventory target rate (POS)		
Service rate	Utilization rate	

Table 5.6: The percentage of periods that inventories are outside target

Nervousness of the production plan and variability in production quantities per period

It is more difficult to show nervousness in the production plan in the POS or the COS, because in the simulation study, we do not make a production plan each week for many weeks in the future, we only make a production decision in a certain week. It would also be technically unfeasible to include a production plan option; the Excel file would probably grow to a size of 1 GB, and one simulation experiment would probably take many hours.

In addition, it is hard to show variability in monthly production quantities in the POS or the COS, because the simulation tool works in weekly buckets, instead of monthly buckets. Moreover, it is assumed that each production order is a full campaign, while in reality the batches of a campaign are not finished in the same week.

To overcome these two problems, we have taken another measure of stability. It is studied what the time is between opening two production orders of the same product. The standard deviation of this inter production time is divided by the average inter production time, which gives us the coefficient of variation in inter production times. A summary of the results for the same four simulation experiments

as described above is given in table 5.7 for the POS, and in table 5.8 for the COS. In appendix Y, the coefficient of variation in inter production times can be found for the individual products. It can be seen that the POS performs slightly better than the COS on this aspect; the production plan is more stable in the POS.

Coefficient of variation in inter production time (POS)		
Service rate	Utilization rate	

Table 5.7: Coefficient of variation in inter production time in the POS

Coefficient of variation in inter production time (COS)		
Service rate	Utilization rate	

Table 5.8: Coefficient of variation in inter production time in the COS

The results show that the coefficient of variation in inter production times is very stable between the simulation experiments. However, we think that this coefficient of variation is pretty large. Moreover, the variation over the products is pretty large too. The coefficient of variation in inter production times is related to the size of an average demand instant compared to the batch size * the campaign size. For example, the average demand size of Mercilon is high (xx% of the batch size), and as a result, the coefficient of variation in inter production times is large too (approximately 1.1).

It is surprising that the COS has a higher coefficient of variation in inter production times than the POS, because a characteristic of capacity oriented production planning methods in general often is a stable production plan. In our simulations, every product scores a little higher in the COS, thus an explanation can not be found in product related characteristics. Unfortunately, we can not give a good explanation for the difference in the score of the POS and the COS on the coefficient of variation in inter production times.

Ease of implementation
The concept behind the POS comes close to a MRP approach, which is the approach used at this moment at the TPD. Therefore, it is much easier to implement the POS in the current information systems, and in the current organizational structure. Moreover, it is easier to understand for the people that need to work with this planning method.

5.4.3 Comparison with the results of Bemelmans (1985)
In the simulation study of Bemelmans (1985) it is proven that the COS has lower inventory holding costs and stock-out costs than the POS under high utilization rates (ρ = 84% or ρ = 90%). However, in our study we even can not prove that the COS needs significantly lower inventory investments under a utilization rate of xx%. Furthermore we can prove that the POS needs significantly lower inventory investments if ρ = xx% (and the target service rate is xx%) and if ρ = xx% (and the target service rate is xx%). In section 5.1 we showed that our simulation study is different on some aspects compared to Bemelmans (1985), and three of those aspects can explain why we obtained other results.

1. Uncertainties and variabilities
In our simulation study, we considered more variabilities and uncertainties than demand variability and limited capacity. We also modeled lead time uncertainty, uncertainty caused by quality rejections, and uncertainty in the availability of operator capacity. The first two uncertainties we modeled are product related, and it is best to buffer against those uncertainties with safety stock in individual products. Only the last uncertainty is not product related. We have used the POS simulation model to study the effect of the uncertainty aspects. The results of this study are found in section 5.4.4. In that section it is shown that the product related uncertainties have a larger effect on the performance than the capacity related uncertainties. Therefore, the POS performs better than the COS.

2. Capacity stock in the POS

In the POS simulation model, we also included capacity stock to buffer against limited operator capacity, while Bemelmans (1985) does not allow capacity stock in the POS. This capacity stock is probably not optimally distributed over the products, but because there already is safety stock to buffer against product related uncertainties, those two types of buffer stock can complement each other; safety stock can also be used to buffer against capacity limitations, and capacity stock can be used to buffer against product related uncertainties.

Moreover, it has been observed that under high utilization rates the safety stocks in the POS become quite high and the inventory position of most products has been under its safety stock most of the time. Consequently, the production decision in the POS is often based on the run out time of products, which is very similar to the way that the production decision in the COS is made. In other words, the POS becomes like the COS under high utilization rates and high safety stocks.

3. Autocorrelation in the demand forecast

In our simulation study an autocorrelated demand forecast model has been considered. To study the effect of this demand forecast model, two extra simulation experiments have been performed. Under ρ = xx% and a target service rate of xx%, we have run the POS and the COS simulation models *without* autocorrelated demand forecasts[25]. Actually, each demand forecast has been based on the demand model itself, not on other demand forecasts ($P\varphi$ = 1 in equation 5.3). A summary of the results of these two simulation experiments is given in table 5.9. The results of the simulation experiments *with* the autocorrelated demand forecast could already be found in table 5.3.

From the simulation results, we conclude the following.

- There has been no significant difference on inventory investment between the POS and COS, *with* and *without* an autocorrelated demand forecast.
- The inventory investment has been significantly lower if the demand forecast is autocorrelated for the POS and the COS.
- The increase in performance is larger for the POS than for the COS if autocorrelation is introduced in the demand forecast. However, a significant difference can not be found.

Simulation experiments without autocorrelated demand forecasts				
Goal:	**Service level**	**xx%**	**Utilization rate**	**xx%**
	Strategy	*Service level*	*Utilization rate*	*Inventory investment*
Average **LB – UB**	POS (N=50)			
Average **LB – UB**	COS (N=25)			

Table 5.9: Simulation experiments without autocorrelated demand forecasts

5.4.4 Effect of the uncertainty aspects

To gain more insight in the effect of the 'uncertainty aspects' on the inventory investment needed to obtain a target service rate, we also made simulation experiments without one of the 'uncertainty aspects'. Under ρ = xx% and a desired service rate of xx%, we used the POS simulation model to study the effect of

- no uncertainty in the lead time,
- no uncertainty in the capacity availability of operators,
- no quality rejections, and
- unlimited capacity.

Below, in table 5.10, the results are given. It can be seen that, if one of the uncertainty aspects is taken away, that a significantly lower inventory investment is needed to obtain the same service level of xx%. The largest profit is made if lead times would be exactly the norm lead time, or if available capacity is unlimited. If lead times would be exactly the norm lead time, also WIP inventories would decrease. If available capacity would be unlimited, many more investments in operators will be needed to increase capacity. The smallest profit is made if available operator capacity would be deterministic.

[25] For the POS simulation experiment we had to compute initial safety stocks (under ρ = 0%) again, because the service rate is related to the demand forecast model.

The effect of stochastic aspects on the needed inventory investment in the POS				
Goal:	**Service level**	**xx%**	**Utilization rate**	**xx%**
	Strategy	*Service level*	*Utilization rate*	*Inventory investment*
Average **LB - UB**	POS All uncertainties			
Average **LB - UB**	POS Norm lead times			
Average **LB - UB**	POS Deterministic capacity			
Average **LB - UB**	POS No rejections[26]			
Average **LB - UB**	POS Unlimited capacity[27]			

Table 5.10: The effect of stochastic aspects on the needed inventory investment in the POS

5.5 Conclusion

In this chapter, we gave an extensive description of the simulation models and simulation experiments. In this section we will give three types of conclusions. First, we will conclude which planning strategy outperforms the others for the specific situation at POO. Second, we will conclude on our results compared to the results of Bemelmans (1985). Third, the first hypothesis of chapter 3 is answered.

5.5.1 Conclusion which planning strategy outperforms the others

We showed that the performance on inventory investment of the HCS is not good under high utilization rates, and that the POS and the COS perform almost equally well in most situations, although in some simulation experiments we could show that the POS needed significantly lower inventory investments to obtain the target service rate. Furthermore, the POS makes the production plan slightly more stable than the COS, and the POS is easier to implement in the current information systems and the current organizational structure, because the concept behind the POS is close to a MRP approach. This makes it also easier to understand for the people that need to work with this planning strategy. For these reasons it has been decided that the POS outperforms the COS and the HCS as a planning strategy for production and inventory control at the level of material coordination for the Tablets Production Department.

5.5.2 Conclusion of our results compared to Bemelmans (1985)

In contrast to Bemelmans (1985) we conclude that the POS needs lower inventory investments than the COS. Even under high utilization rates up to xx%, we can not prove that the COS performs significantly better. The main reason that we obtained other results than Bemelmans (1985) is that we considered more product related uncertainties, and to protect the inventory of a product against product related uncertainties, it is best to have buffer stocks in individual products. Another reason that we obtained other results is that we allowed capacity stock in the POS. This capacity stock and the safety stock needed to protect against product related uncertainties can complement each other; safety stock can also be used to buffer against capacity limitations, and capacity stock can be used to buffer against product related uncertainties. Moreover, the increase in performance is larger for the POS than for the COS if autocorrelation is introduced in the demand forecast, as we have done. However, a significant difference can not be found on this aspect.

5.5.3 Proof of hypothesis 1

To show that hypothesis 1 is correct, we need to prove that the POS outperforms the current planning method. Unfortunately, it is not possible to model the current planning method, because the decision to open a production order in the current planning method is not made in a straightforward way.

[26] We had to change the available capacity in the simulation experiment without quality rejections to get ρ = xx% to study the effect of uncertainty caused by quality rejections only, and not to study the effect of a change on the utilization rate.

[27] In the simulation experiment with unlimited capacity, we did not obtain a service level of xx%. This is caused by the fact that one batch safety stock is not enough for Product xx to obtain the xx% service rate.

Furthermore, it is not possible to compare the results of the simulation models with the results obtained in reality, because it is not possible to model reality completely.

However, in our POS simulation experiments the outside inventory target rate has been xx% against xx% in reality. In addition, in our POS simulation experiments with current safety stocks we obtained a higher service rate than in reality: xx% in reality vs. xx% if ρ = xx%, and xx% if ρ = xx%. Moreover, Bemelmans (1985) shows that the performance of the POS and the COS have been close to the overall optimal solution. In contrast, we think that the coefficient of variation in inter production times is pretty large in the simulation experiments, what shows us that the production plan is not very stable.

Altogether, it is reasonable that we suggest in hypothesis 1 that a planning strategy that determines which production orders to open after the review period, and that makes a production plan for future periods, outperforms the current production planning strategy on inventory costs and availability of released bulk tablets. However, the hypothesis can not be completely founded.

6: Implementation

In this chapter, we will show how the product oriented strategy needs to be implemented in the Production Planning Department (PPO). In section 6.1, it will be shown how the safety stock levels that will be implemented have been computed from the safety stock levels under the different settings in the simulation experiments. Then, in section 6.2, the second part of the research assignment is performed; the operational tool, that will be used as a decision support tool by the planners of PPO to decide which production orders need to be released, will be described. In section 6.3, it is given how the planners need to work with the operational tool. The chapter finishes with some extra notes in section 6.4.

6.1 Safety stock settings

In chapter 5, we concluded that the product oriented strategy is the best planning strategy at the level of material coordination for the Tablets Production Department. Under different utilization rates and service levels, the POS performed best. However, we did not give the levels at which safety stocks need to be set. Setting safety stocks will be the goal of this section. According to the PCIO-model (Bemelmans, 1988), this is a change at the level of the control structure.

Two problems have been discussed already in section 5.3.2. How to model the service rate and how to model the utilization rate? Because it was not easy to answer these two questions, we made simulation experiments under six different settings in chapter 5, with the result that different safety stocks had been advised in the different simulation experiments. To determine the safety stocks that need to be implemented, we decided to follow the strategy below. The results can be found in appendix Z.

- First, for each simulation experiment performed in chapter 5, we compute the investment in safety stock of each product.
- Second, for each simulation experiment, we compute the relative investment of each product by comparing the investment in the safety stock of product *j* with the total investment in safety stock.
- Third, we compute the average relative investment of each product by averaging over the simulation experiments.
- Last, for each product, the average relative investment is multiplied with the current total investment in safety stock, resulting in a safety stock level of each product that will be implemented.

The result is that we have the same investment in safety stocks as we currently have, but the safety stock is distributed over the products in another way. Furthermore, under the new settings, part of the safety stock investment is capacity inventory. In the old situation, production orders were scheduled forward sometimes in case of capacity shortages to prevent that a product went below safety stock. In the new situation, this is not needed anymore, because part of each safety stock is capacity inventory. The result is that in the old situation some extra inventory investments were needed to deal with capacity shortages, while this is not needed anymore in the new situation.

Once that the new safety stocks are implemented and the service levels are on target or even above target, PPO may start to reduce all safety stocks with a factor of the standard deviation of average weekly demand of every product. In appendix AA, these standard deviations are found.

6.1.1 Proof of hypothesis 2

To show that hypothesis 2, given in chapter 3, is correct, we have made extra simulation experiments. Under ρ = xx% and under ρ = xx% simulation experiments have been performed with current safety stock settings and with the new safety stock settings. A summary of the results can be found in table 6.1 and 6.2. It can be seen that the results under the new and under the current safety stocks are similar. However, as can be seen in table 6.3, the standard deviation over the service rate per product is lower under the new safety stocks. This means that the service rates of the products are more equal to each other.

Performance current safety stock vs. new safety stock (ρ = xx%)				
Goal:		Utilization rate	xx%	
	Strategy	*Service level*	*Utilization rate*	*Inventory investment*
Average	POS			
LB - UB	Current safety stock			
Average	POS			
LB - UB	New safety stock			

Table 6.1: Performance current safety stock vs. new safety stock if ρ = xx%

Performance current safety stock vs. new safety stock (ρ = xx%)				
Goal:		Utilization rate	xx%	
	Strategy	*Service level*	*Utilization rate*	*Inventory investment*
Average	POS			
LB - UB	Current safety stock			
Average	POS			
LB - UB	New safety stock			

Table 6.2: Performance current safety stock vs. new safety stock if ρ = xx%

Variation over the service rate per product			
Service rate	**Utilization rate**	**Current safety stock**	**New safety stock**
		5.26%	2.19%
		6.09%	4.39%

Table 6.3: standard deviation over the service rate per product: current safety stock vs. new safety stock

6.2 The operational tool

The operational tool is a spreadsheet model built in MS Excel that supports the planners of PPO in the decision making process. According to the PCIO-model (Bemelmans, 1988), this is a change at the level of the information systems. The outcomes of the operational tool are an advice on the production orders to open in the week after the review period of two weeks, and on the plan for future periods. The outcomes are based on the POS. In this section, we will give the architecture of the operational tool, in section 6.3, it will be described how the tool needs to be used.

The operational tool has been built in almost the same way as the POS simulation model: there is a product sheet for each product (also for MTO products), there is a capacity sheet to compute which production order will be opened at which moment, and there is an input sheet to set safety stocks, batch sizes, etc. Moreover, there is production plan sheet, in which the production plan is given and in which the production plan can be manually adjusted, there is an inventory evaluation sheet in which inventory projections are given in tablets, hours of operator work, and monetary value, and there are two data sheets in which the data download from Apollo can be found. Below, these sheets will be described. In addition, there is a front page sheet with links to the other sheets, but we will not describe that sheet into more detail in this report.

6.2.1 Input sheet

The following parameters can be set in the input sheet for all products (MTS and MTO):

- Safety stock
- Batch size
- Yield %
- Campaign size
- Capacity usage
- Cost price

Furthermore, the amount of available operator capacity per week can be set in the input sheet. Available operator capacity is needed up to week *t+xx*, because we want to compute a production plan up to this week. In section 6.2.2 it is explained why we want a production plan up to week *t+xx*. In week *t* and week *t+xx* no capacity availability levels need to be set, because the production plan is

already fixed in this period. In week *t+xx* a negative capacity level can be set if too much capacity has been used when the production plan was made a week before ($Cneg_{t-1}$). The architecture of the input sheet can be found in section AB.1 in appendix AB. The input levels of safety stock, batch size, yield %, campaign size, capacity usage and cost price of MTO products are given in Appendix AC.

6.2.2 Product sheets

Each product (MTS and MTO) has its own product sheet. In these sheets information on demand forecasts, opened production orders, and current inventory levels are found. They are downloaded from Apollo. Production orders that are scheduled to be opened in xx are fixed orders (The review time of xx weeks).

If the inventory position of a certain bulk product falls below safety stock, a production need is created. For MTS products, the capacity sheet is used to compute when a production order will be opened to fulfil the production need. For MTO products, the decision to open a production order is computed in the product sheet itself: if the inventory position falls below zero, a production order is created. This means that a production order for MTO products does not consider the situation of other products. We have made this decision, because MTO products have non-pre-emptive priority on MTS products, and therefore, they are produced immediately if there is a production need. The production planner can manually adjust the production plan computed by the operational tool. This is done in the production plan sheet, and the results can be found in the product sheets too.

Moreover, in the product sheet, inventory positions, end inventory levels and run out times are computed, based on expected demand and the production plan. This will give us a projection of future inventory levels. Just like in the simulation study, inventory positions, end inventory levels, and run out times are computed by respectively equation 5.6, 5.7 and 5.8. In addition, in the product sheets it is computed when a production order needs to be opened, but there is not enough capacity available, with the result that the production order needs to wait. In section AB.2, appendix AB the product sheet is described in more detail.

A production plan is made up to xx weeks in advance (week *t+xx*). This means that we can influence inventory levels up to week *t+xx*, because the norm lead time for production and quality control is xx weeks. From more than xx weeks forward, the operational tool will not be used anymore, because the AP system is responsible for making plans at that term. It must be noted that we need demand forecasts up to week *t+xx* to determine a good production plan, because we need to compute run out times up to xx weeks after the norm lead time.

6.2.3 Capacity sheet

In the capacity sheet it is computed which production orders for MTS products to open from week *t+xx* to week *t+xx*. The capacity sheet of the operational tool has been built in almost the same way as the capacity sheet of the POS simulation model described in section 5.2.3 and Appendix T.3.1. There are three differences:

- The production orders of all MTO products are given separately, in stead of one large order.
- The capacity need for MTO products ($CN_{MTO,t}$) is computed by summing the capacity need of all individual production orders for MTO products. This capacity need is subtracted from available operator capacity (C_t) to produce MTS products.
- Available operator capacity in week *t* (C_t) is taken from the input sheet.

Furthermore, there are two differences between the capacity sheet of the POS simulation model and the capacity sheet of the operational tool to give the production planner the ability to manually adjust the production plan. If the planner wants to avoid that a production order is opened, if he wants to change the size of a production order, or if he wants to open a production order of another product, he can adjust the production plan in the production plan sheet, and the capacity sheet will give priority to the changes made by the production planner. In appendix AB, section AB.3 the equations that have been changed compared to the POS simulation model can be found.

6.2.4 Production plan sheet

In this sheet, an overview is found of which production orders will be opened from week *t* to week *t+xx*. The production orders that will be opened in week *t* and week *t+xx* are orders in the fixed period and downloaded from Apollo. The production plan of week *t+xx* to week *t+xx* is computed by the operational tool.

In this sheet, the production planner has the possibility to manually adjust the production plan for all products if that is needed, e.g. if materials are not available to start a production run. Based on these adjustments, a new production plan will be computed.

Furthermore, in the production plan sheet it can be found which production orders for MTS products are waiting to be produced, but can not start a production run because there is not enough operator capacity available. We have also added the run out times of all MTS products in this sheet, so the production planner can see immediately which products expect to go out-of-stock first.

An overview of the production plan sheet is found in section AB.4, appendix AB. In this sheet, we only refer to other sheets, no new computations are made. Therefore, no equations are given in section AB.4.

6.2.5 Inventory evaluation sheet

In the inventory evaluation sheet inventory projections are given up to week *t+14*. These inventory projections are just the end inventories from the product sheets. The projections are given in tablets, in hours of operator work, and in euros. In section AB.5, appendix AB the inventory projection in tablets is given.

6.2.6 Data sheets

There are two data input sheets; the production input sheet and the demand input sheet. In these sheets, the data download from Apollo is given. In weekly buckets we can find when production is scheduled to be approved by the Quality Department, and when demand for bulk products is expected to take place. Based on the product ID other sheets take data from these sheets. See for example the HLOOKUP function in equation AB.2.

6.3 Future way of working

The introduction of the product oriented strategy as the planning method at the level of material coordination, and the introduction of the operational tool will change the current way of working for the planners of PPO. The new way of working to decide which production orders will be opened is described below. A user manual will be developed for the operational tool. According to the PCIO-model (Bemelmans, 1988), this is a change at the level of the control structure.

- On Monday, a data download is automatically made from Apollo. Inventory levels, demand forecasts, and opened production orders are found in this download.
- The data download is imported into the operational tool. A Visual Basic macro is developed to execute the data import automatically. This macro is found in appendix AD.
- Weekly operator capacity availability is inserted in the operational tool by the production planner. $Cneg_{t-1}$ is copied by the macro of appendix AD based on the production plan made in week *t-1*.
- The operational tool will make a production plan for week *t+xx* to week *t+xx*.
- The production plan of the first open bucket, week *t+xx*, is implemented. The plan for week *t+xx* to week *t+xx* is taken for granted.
- Of course, the production planner may change the production plan if this is needed. For example, if he has knowledge not known by the operational tool, like problems with the availability of certain machines or problems with the availability of API's. If the production planner needs to change the plan for some products, the operational tool will compute a new plan with this new information.
- The new production plan of week *t+xx* to week *t+xx* will be returned to Apollo, and production orders are placed in Apollo as firm planned production orders. This needs to be done manually by the production planner.

Because the operational tool is loaded with new data once a week, and because only the production decision for week *t*+xx is implemented, it creates a discrete-event rolling-horizon production plan.

It is interesting to note that the 'weekly download link' has already been established, because every week inventory projections are made in a similar way as the operational tool. Furthermore, the production planners already worked with the operational tool and they agreed on the production plan

made by it. Furthermore, in their opinion the operational tool provided a good overview of the total inventory situation, and they agreed that the operational tool was user friendly.

6.4 Extra notes

We would like to make some extra notes related to the implementation of the product oriented strategy and the operational tool.

Seasonal effects
In section 5.1, we already discussed seasonal effects in demand for bulk tablets. During the summer holidays demand has been below average, and before the summer holidays demand has been above average. In our simulations, we eliminated seasonal effects. But in reality, they will be there, and to cope with these seasonal effects, safety stocks for bulk tablets, especially for the fastmovers, need to be increased before the summer holidays.

Flexibility in safety stock settings
At the level of material coordination, the trade-off between different performance criteria (service rate, machine efficiency, inventory costs, etc.) has already been made, with the result that control parameters like safety stocks are set. However, sometimes it is better not to follow these safety stocks directly, e.g. if we have external market knowledge about tender orders or sudden declines / increases in sales. In these cases it is best to (temporarily) change the safety stock level of the particular product to control its inventory.

Apollo interface
At the end of 2006, the interface between Apollo and AP will start to run. This means that all replenishment order forecasts of Local Companies will be placed at the first day of the month. This will influence demand forecasts at the level of bulk tablets, and it needs to be studied what the effect is, and what the best way is to deal with this new situation.

Current information systems
The new safety stock levels proposed in section 6.1 need to be implemented in the current information systems as Apollo and Advanced Planning.

Simulation model reruns
If the situation at the TPD changes, it can be worthwhile to rerun the simulation model. For example, campaign sizes or demand sizes may change considerably. It is no problem to rerun the simulation model, but results (e.g. safety stock levels) should be interpreted with care, because the desired service rate and utilization rate have a large influence on the results of the simulation study. It is best to run several experiments under different settings, just like we did in our simulation study.

7: Conclusions and recommendations

The conclusions of this research project are given in section 7.1. In this section, we will return to the hypotheses and the research assignment. In section 7.2, some recommendations are given.

7.1 Conclusions

We formulated the following hypotheses and research assignment for this research project:

Hypothesis 1
A planning strategy that determines which production orders to open after the review period, and that makes a production plan for future periods, outperforms the current production planning strategy on inventory costs and availability of released bulk tablets.

Hypothesis 2
A planning strategy for the Tablets Production Department in which a buffer stock is created to deal with limited availability of operator capacity, and with uncertainty in demand, operator capacity availability, lead times, and quality rejections outperforms the current production planning strategy on inventory costs and availability of released bulk tablets.

Research assignment

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1. *Develop a planning strategy for production and inventory control at the level of material coordination for the Tablets Production Department, and determine the control parameters of the planning strategy such that a target service rate is obtained.*

   This planning strategy should be able to deal with:
   - *Limited availability of operator capacity at the TPD.*
   - *Uncertainty and variability in demand for bulk tablets.*
   - *Uncertainty and variability in operator capacity availability at the TPD.*
   - *Uncertainty and variability in lead times of the production and quality control process.*
   - *Uncertainty about quality rejections of bulk batches.*

2. *Develop and implement a tool that advices the planner which production orders to open. Furthermore, the tool should make a production plan including future production order releases.*

Three planning strategies (the product oriented strategy, the capacity oriented strategy, and the hybrid control strategy) have been tested on their performance by a multi-product single-machine discrete-event rolling-horizon simulation, considering the specific situation of the Tablets Production Department.

Conclusion which planning strategy outperforms the others
We showed that the performance on inventory investment of the HCS is not good under high utilization rates, and that the POS and the COS perform almost equally well in most situations, although in some simulation experiments we could show that the POS needed significantly lower inventory investments to obtain the target service rate. Furthermore, the POS makes the production plan slightly more stable than the COS, and the POS is easier to implement in the current information systems and the current organizational structure, because the concept behind the POS is close to a MRP approach. This makes it also easier to understand for the people that need to work with this planning strategy. For these reasons it has been decided that the POS outperforms the COS and the HCS as a planning strategy for production and inventory control at the level of material coordination for the Tablets Production Department.

Conclusion of our results compared to Bemelmans (1985)
In contrast to Bemelmans (1985) we conclude that the POS needs lower inventory investments than the COS. Even under high utilization rates up to xx%, we can not prove that the COS performs significantly better. The main reason that we obtained other results than Bemelmans (1985) is that we considered more product related uncertainties, and to protect the inventory of a product against product related uncertainties, it is best to have buffer stocks in individual products. Another reason that we obtained other results is that we allowed capacity stock in the POS. This capacity stock and the safety stock needed to protect against product related uncertainties can complement each other; safety stock can also be used to buffer against capacity limitations, and capacity stock can be used to buffer against product related uncertainties. Moreover, the increase in performance is larger for the POS than for the COS if autocorrelation is introduced in the demand forecast, as we have done. However, a significant difference can not be found on this aspect.

Proof of hypothesis 1
To show that hypothesis 1 is correct, we need to prove that the POS outperforms the current planning method. Unfortunately, it is not possible to model the current planning method, because the decision to open a production order in the current planning method is not made in a straightforward way. Furthermore, it is not possible to compare the results of the simulation models with the results obtained in reality, because it is not possible to model reality completely.

However, in our POS simulation experiments the outside inventory target rate has been xx% against xx% in reality. In addition, in our POS simulation experiments with current safety stocks we obtained a higher service rate than in reality: xx% in reality vs. xx% if ρ = xx%, and xx% if ρ = xx%. Moreover, Bemelmans (1985) shows that the performance of the POS and the COS have been close to the overall optimal solution. In contrast, we think that the coefficient of variation in inter production times is pretty large in the simulation experiments, what shows us that the production plan is not very stable.

Altogether, it is reasonable that we suggest in hypothesis 1 that a planning strategy that determines which production orders to open after the review period, and that makes a production plan for future periods, outperforms the current production planning strategy on inventory costs and availability of released bulk tablets. However, the hypothesis can not be completely founded.

Proof of hypothesis 2
Safety stocks, as the control parameter in the POS, have been proposed for all MTS products. The new safety stock settings need the same monetary investment as the current safety stocks, but they are distributed differently over the products. Once the target service level is reached, safety stocks can be lowered by a factor of the standard deviation of average weekly demand. All MTO products have no safety stock. Because MTO products have no safety stock, and therefore no buffer to protect them against uncertainties, they have non-preemptive priority on MTS products in the production plan.

To show that hypothesis 2 is correct, simulation experiments have been performed with current safety stock settings and with the new safety stock settings. We have to conclude that the results under the new and under the current safety stocks are similar on service rate and inventory investment. However, the service rates of the products are more equal to each other under the new safety stock settings.

Operational tool
To carry out the second part of the research assignment, an operational tool has been developed that supports the planner to make the decision which production order(s) to open. In this tool all bulk tablets have been modeled. Based on the POS, the operational tool computes a production plan. In this production plan, week *t* and week *t+xx* are fixed. The decision for week *t+xx* needs to be implemented, and a plan for week *t+xx* to week *t+xx* is made. Each week, the operational tool needs to be run with the latest data from Apollo, what makes it a discrete-event rolling-horizon production plan. It is interesting to note that the production planners already worked with the operational tool and they agreed on the production plan made by it.

Altogether, we conclude that the two hypotheses have been tested, and that the research assignment has been performed.

7.2 Recommendations

Our main recommendation is to use the operational tool for planning the production of bulk tablets. The decision which production orders to open should be based on the production plan computed by the operational tool. The current inventory projections of bulk tablets do not have to be used anymore, because inventory projections are also given in the operational tool.

According to the budget of 2006, it is allowed to have an average stock investment of € xx million in released bulk tablets, considering safety stock, batch sizing stock, and leveling stock. At this moment, week 44 in 2006, the stock investment is below target, namely € xx million. This means that we first need to recover lost ground. The advantage of the operational tool is that it is good in setting priorities and can therefore make the best production decision. Furthermore, it can be found how many production orders are waiting to be produced, which gives insight in the backlog of the Production Department.

In the POS simulation tool, we based the capacity inventory for MTS products on the standard deviation of average weekly demand of each individual product. This simple rule has been effective, but is probably not optimal, because some products reached higher service rates than others. With a trial and error method, safety stocks can be adjusted, and it can be tried to equalize the service rates of all products. This will lead to lower inventory investments, as the relation between inventory investments and service rate is non-linear. Another approach is to obtain lower service rates for expensive products, and higher service rates for inexpensive products.

One of the main goals of (senior) management should be to reduce all kind of uncertainties during the lead time or to reduce the lead time itself, because large profits can be made in this case. For example, we showed that the total inventory investment can be reduced with xx% if lead times would be deterministic and equal to the norm lead time. Moreover, it should be tried to reduce the fixed period in the production plan from xx weeks to xx week for the same reason.

A main issue within POO is head count. In our simulation studies we have shown that a decrease in utilization rate from ρ = xx% to ρ = xx% leads to a decrease in inventory investment of € xx, under a target service rate of xx%. This decrease in utilization rate can be accomplished approximately by hiring one full time operator. The decrease in inventory investment does not justify the extra operator.

It needs to be studied whether it is possible to implement the operational tool too at the Parenterals and the Specials Production Departments. An obstacle can be that the capacity complexity is different at these departments, because machine utilization rates are much higher.

To be able to control production and inventories with a MRP system, the parameters like yield and lead times, should be complete, consistent, up-to-date, and according to reality (Bertrand et al., 1998, pg. 54). For example, we have shown that the lead time of the quality control process has been xx days, while the norm lead time is only xx days. If the actual lead time deviates from the norm lead time set in the MRP system, the norm lead time needs to be adjusted. An argument that the norm lead time in the MRP system should be equal to the target lead time is not valid. Moreover, at POO, the lead time starts running when the production order is opened. Actually, the lead time should start from the moment that a production order should be opened; the moment at which the inventory position falls below safety stock. This would give a better insight in the way that the process is under control.

We have shown that, even when replenishment orders are already placed, there still are many changes in the timing or the size of replenishment orders. Customer Relations should try not to accept changes after a replenishment order has been accepted already, because this only leads to extra and unnecessary nervousness in the supply chain.

Since 2005, the production site in Oss made a first start with VMI. The first goal was to gain trust of the Local Companies. Now, it is advisable to study how the logistical concept can be improved to really gain from the advantages of VMI. Moreover, it should be studied what the effect of VMI is on controlling production and inventories of bulk products.

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List of abbreviations

ADB	:	Aggregation Database
ADL	:	Arthur D. Little
AP	:	Advanced Planning
API	:	Active Pharmaceutical Ingredient
API OPS	:	API Operations
av.	:	average
C&D	:	Coordination & Documentation
CODP	:	Customer Order Decoupling Point
COS	:	Capacity Oriented Strategy
CR	:	Customer Relations
CSD	:	Customer Service Department
DP	:	Demand Planning
ELSP	:	Economic Lot Scheduling Problem
eq.	:	equation
FEFO	:	First Expired First Out
FP	:	Finished Products
h	:	hours
HCS	:	Hybrid Control Strategy
KPI	:	Key Performance Indicator
LB	:	Lower Bound
LC	:	Local Company
LRP	:	Long Range Plan(ning) (AP)
MBU	:	Mini Business Unit
MHD	:	Materials Handling Department
MILP	:	Mixed Integer Linear Programming
MPS	:	Master Production Schedule
MRP	:	Material Requirements Planning (Apollo)
MTO	:	Make-to-order: in this report all bulk tablets without safety stock
MTS	:	Make-to-stock
OP	:	Operational Plan(ning) (AP)
PCIO	:	Process / Control / Information Systems / Organizational Structure
PD	:	Packaging Department
POO	:	Pharmaceutical Operations Oss
POS	:	Product Oriented Strategy
PPD	:	Parenterals Production Department
PPO	:	Production Planning Oss
PS	:	Production Site
QA	:	Quality Assurance
RM	:	Raw Material
R.O.	:	Run Out
RR	:	Ready for Release
SC	:	Supply Chain
SCO	:	Supply Chain Operations
SCP	:	Supply Chain Plan(ning) (AP)
SELSP	:	Stochastic Economic Lot Scheduling Problem
SKU	:	Stock Keeping Unit
SPD	:	Special Products Department
st. dev.	:	standard deviation
T&S	:	Transport & Shipping
tab	:	tablets
TPD	:	Tablets Production Department
UB	:	Upper Bound
VMI	:	Vendor Managed Inventory
WIP	:	Work-in-process
XPD	:	PPD, SPD, TPD

List of definitions

Additional materials
These are for instance the primary and secondary packaging materials, like vials, ampoules, blisters, cartons, information leaflets.

Apollo
This is the name used for the MRP system at POO.

Availability of released bulk products at POO (Organon KPI)
The availability of released bulk products at POO is the percentage of replenishment orders for which released bulk product is available at the latest possible moment a packaging order has to be opened according to the standard lead times defined in MRP.

Batch sizing stock
To reduce setup and cleaning times, production runs are done in batches. As a result, there is inventory caused by the size of the batch, called batch sizing stock.

Bulk usage
Demand for bulk tablets.

Calculated RR-date
The calculated RR-date is computed by subtracting the norm lead times of the Packaging Department from the replenishment order date.

Campaign
The production of more than one batch in a row.

Capacity inventory / stock
This is 'safety stock' used to cope with the uncertainty that comes from the limited availability of (operator) capacity. Because it is not always possible to start all production runs under high utilization rates, some extra inventory is needed.

Coefficient of variation
The coefficient of variation is computed by dividing the standard deviation of a data set by its average.

Delivery performance of POO (Organon KPI)
The delivery performance of POO is determined by comparing the actual shipment date with the order request date. The percentage of orders that are shipped in the week of the order request date is the delivery reliability of POO.

End inventory
The end inventory is the inventory that is physically in the warehouse at the end of a period.

Excipients
These are the additive materials used by the production process, like lactose.

Fastmovers
Marvelon Z.ME, Cerazette, Remeron 30MG CTO NB, and Livial 2,5MG NS

Inter production time
The number of weeks between opening two production orders of the same product.

Inventory position
The inventory position is the expected inventory level after the norm lead time.

Leveling stock
Bulk products need to be available xx weeks before it will be used, so the Packaging Department can level its orders. The inventory needed for this aspect is called leveling stock.

Non-preemptive priority
A production run of a product with non-preemptive priority will be started immediately after the current production run is finished. This means that the current production run will not be interrupted.

Out-of-stock at a Local Company (Organon KPI)
An out-of-stock at a Local Company is reported if the inventory of a product is zero for two weeks, while there was a sales forecast for that product in that month, and there was a sale in the last three months.

Out-of-stock rate
This is 1 – service rate.

Production contract
This is a contract between the Planning Department (PPO), the Production Department (XPD), and QA on the production volumes of month *t+xx*.

Quality rejection
A quality rejection means that a full batch is disapproved by the Quality Department after the production process has taken place.

Released bulk
This is bulk that has been approved and released by the Quality Department.

Run out time
The run out time is the number of periods until the inventory of a product expects to fall below zero.

Service rate / level
The service rate is defined as the percentage of periods in which the inventory level is positive. Only periods in which demand is found are considered.

Simulation experiment
This is a simulation of more than one run (usually 25 runs) with the same settings.

Simulation run
This is a simulation of one run of 880 weeks.

List of variables

i	:	Index for run out time
j	:	Product index
t	:	Period index
τ	:	Period index

BS_j	:	Batch size of product j
C_t	:	Available operator capacity in period t
$C_{i,t}$	:	Available rest capacity in period t after product j with $RO_{i,t}$ is loaded
$CCSF_t$	:	Cumulated change in sales forecast in period t
CL	:	Critical level (COS-model)
$CN_{i,t}$	:	The capacity need for product j with $RO_{i,t}$ in period t to produce $PN_{j,t}$
$Cneg_t$	:	Negative rest capacity in period t
cp_j	:	Cost price of product j
CS_j	:	Campaign size of product j
CSI_t	:	Total amount of capacity stored in the inventories after L_{norm} in period t
cu_j	:	Capacity usage to produce 1000 tablets of product j
$D_{j,t}$	:	Demand size for product j in period t
$\hat{D}_{j,t,t-\tau}$ *(new)*	:	Completely new demand forecast of product j for period t (large change).
$\overline{D}w_j$	:	Average weekly demand for product j ($\overline{D}_j \cdot Pa_j$)
$FPO_{j,t}$	:	Finished Production Order of product j in period t
$I_{j,t}$	:	End inventory of product j in period t
$I_{start,j,COS}$	:	Starting inventory of product j in the COS simulation model
$I_{start,j,POS}$	:	Starting inventory of product j in the POS simulation model
$Ipos_{j,t}$	:	Inventory Position of product j in period t
$Irel_j$	:	Relative inventory of product j (compared to total inventory)
k	:	Inverse of the standard normal cumulative distribution
L_{norm}	:	Norm lead time
$L_{POj,t}$	:	Lead time of the production order of product j opened in period t
LTD	:	Lead time distribution
N	:	Number of simulation runs
$OPO_{j,t}$	:	Opened Production Orders for product j in period t
Pa_j	:	Probability of an arrival of product j
Pqr_j	:	Probability of a quality rejection of product j
$P\alpha$	:	Probability of no change in the demand forecast
$P\beta$	:	Probability of a small change in the demand forecast
$P\varphi$	:	Probability of a large change in the demand forecast
$PN_{j,t}$	:	Production need for product j in period t
$PO_{j,t}$	:	Production order of product j opened in period t
PS_j	:	Production size of product j (BS_j * CS_j)
R	:	Review time
rand()	:	A random value between 0 and 1
RO_i	:	Run out time of the product with rank i.
$RO_{j,t}$	:	Run out time of product j in period t
S_t	:	Sales at Local Company in period t
$SC_{j,t}$	:	Size of a small change of the demand forecast of product j for period t
ss_j	:	Safety stock of product j (POS-model)
$ss_{inv,j}$	:	Monetary investment in safety stock of product j
$ss_{rel.inv,j}$	:	Relative monetary investment in safety stock of product j
$t_{v,\alpha/2}$	:	A value from the Student t-distribution
TPN_t	:	Total production need in period t (COS-model)
$TPN_{i,t}$	:	Total rest production need in period t after product j with $RO_{i,t}$ is loaded
v	:	Degrees of freedom

α	:	Level of significance
ε_t	:	Forecast error in period t
θ	:	A value that is computed to make the POS starting inventory representative
ρ	:	Utilization rate
ψ	:	A value that is computed to make the COS starting inventory representative

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$\overline{x}$	:	Average of variable x
σ_x	:	Standard deviation of variable x
$\hat{x}_{t,t-\tau}$	:	Forecast of variable x for period t in period t-τ

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Appendix A: Product assortment of Organon

Product assortment of Organon[28]								
Gynecology: Contraception	Cerazette	Desogen (US)	Gracial	Implanon	Laurina	Marvelon	Mercilon	NuvaRing
Gynecology: Hormone Therapy	Andriol	Livial	Ovestin	Riselle				
Anesthesia	Zemuron (US)	TOF-watch	Esmeron	Norcuron	Orgaran			
Fertility	Follistim (US/Japan)	Orgalutran	Pregnyl	Puregon				
Neuroscience	Remeron SolTab	Remeron						
Urology	OncoTice / Tice BCG							

Table A.1: Product assortment of Organon

[28] Source: www.organon.nl

Appendix B: API production

The production process of Active Pharmaceutical Ingredients takes place at API Operations, which main production site is located in Oss. There are two main types of API's: biochemicals and chemicals. Both have their own production facilities. The equipment at Biochemicals is mostly dedicated to a single product; the equipment at Chemicals is usually multi-purpose. The total lead time of the production process is usually xx and can consist of xx production steps. As a rule-of-thumb, the total lead time of a production step is xx or xx. In the beginning of the process, the products are still quite generic, but at a certain moment, a split is taking place, and then the products become a specific API. After the API's have been produced, about half of the volume is stocked at the stockpoint API to be available for bulk production at POO or one of the other international production sites of Organon; the other half is sold to third parties.

In total, API OPS produces 160 API's, of which 55 are further processed at Organon. API's are very important to Organon, as they form the key ingredient for the medicines. Furthermore, there often is no alternative supplier for an API, which makes API OPS a crucial link in the supply chain. Therefore, scarcity of API's is a main issue for the performance of Organon.

Appendix C: Production process parenterals and special products

Parenterals production

Considering parenterals production in Oss, about 50 million ampoules and vials per year are produced, for 39 different bulk products out of 23 API's[29]. Parenterals are the name for injection fluids in the pharmaceutical industry. Production takes place in only one shift. The production process consists of three or four steps. First, at the preparation section the injection fluids are made from the API's and excipients in batches from xx to xx liters. Then, at the filling section the vials and ampoules are filled. Furthermore, at the filling section, a number of products are freeze-dried. Finally, the products are visually inspected at the inspection section on contents and appearance. Ten machines are available for producing the injection fluids, three of them are for oil based fluids, seven for water based fluids. The machines differ mainly in size, and most injection fluids can be made on two or three machines. Three production lines are available for filling, and four freeze-driers are available to make readily soluble powders of the fluids. At the filling section, each product is linked to a single production line, but the freeze-driers are interchangeable. Visual inspection is done manually, or by a machine, depending on the product. There is a buffer of work-in-process in front of the inspection section to control its workload. Figure C.1 gives an overview of the production process for parenterals.

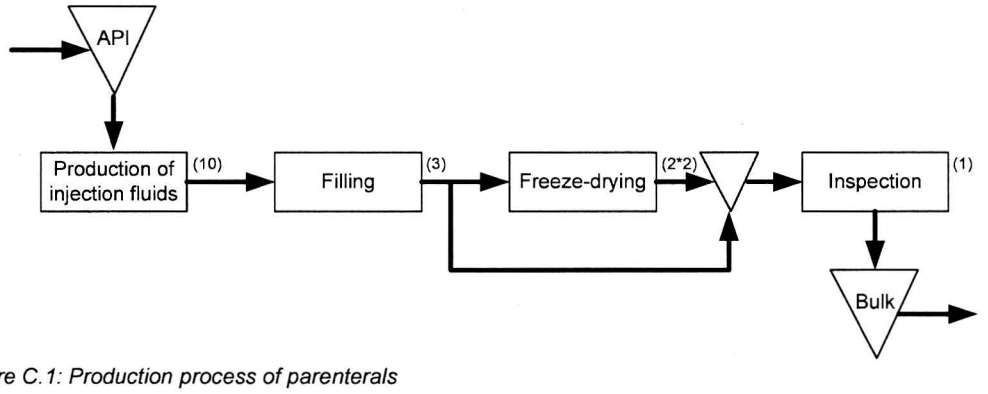

Figure C.1: Production process of parenterals

After a batch is produced, a machine needs to be cleaned, which takes about xx hour. But if a filling machine is setup for ampoules or vials of another size, setup takes about xx hours. Currently, one filling machine for vials forms a bottleneck for the production of parenterals. Furthermore, operator utilization is high at the Parenterals Production Department too.

Special products production

Three different special products are made in Oss: Nuvaring, Implanon, and Multiload granulate, using two API's[30]. Nuvaring and Implanon are polymers that contain hormones that are absorbed by the human body. The demand for Nuvaring is currently growing, and the growth in demand for Implanon is for a large part dependent on tender orders and the upcoming introduction in the USA. Production is done in three shifts, and the production process of special products differs considerably from the production processes of tablets and parenterals. Figure C.2 shows the production process of Implanon. Because there are many similarities in the production of Nuvaring, Implanon, and Multiload, figure C.2 is quite representative for the production of special products.

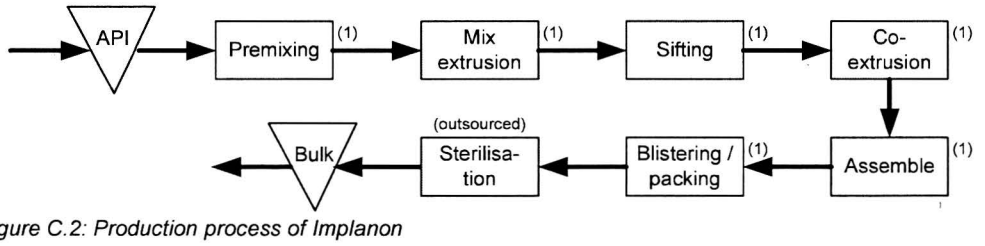

Figure C.2: Production process of Implanon

[29] Source: Budget 2006
[30] Source: Budget 2006

Most of the machines for the production of special products are dedicated, although two production steps of Multiload need to be done on machines for Implanon / Nuvaring. After the production of three batches at the extruders, xx days are needed to clean the machines. The total throughput time for the special products is about xx, because some steps, like co-extrusion can take xx, and many steps have to be taken. Moreover, production needs to be done in large batches, and batches need to be combined, to optimize the efficiency of a line and to maximize the yield of the production.

Appendix D: Pareto analysis of tablets production[31]

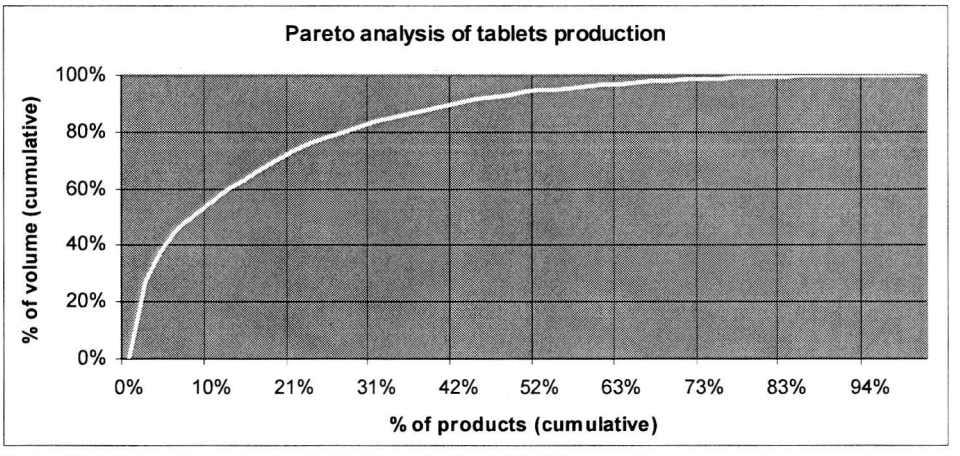

Figure D.1: A Pareto analysis of tablets production at POO

[31] Source: Budget 2006

Pareto analysis		
	% of products (cumulative)	% of volume (cumulative)

Table D.1: A Pareto analysis of all tablets produced at POO

Appendix E: Utilization rates

Utilization rates of granulating machines in 2005					
Machine name	Available hours per machine	# of machines	Total available hours[32]	Actual hours busy[33]	Utilization rate
HM					
OG					
QC					
RM					
MI01					
T2					
MI017					
WSG1					
WSG2					
SK					
MI012					

Table E.1: The utilization rates of the machines at the granulating section in 2005

Utilization rates of tableting and coating machines in 2005					
Machine name	Available hours per machine	# of machines	Total available hours	Actual hours busy	Utilization rate
GC					
AC					
DM					
CA					
FP2					
FP3					
FP4					
FP6					
FP7					
FP8					
FP9					
FP10					

Table E.2: The utilization rates of the machines at the tableting section in 2005

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Figure E.1: Average monthly operator capacity[34]

[32] Source: Calculatiegegevens T.P.D. 2005
[33] Source: Productie Stuur Informatie (Development activities are included in busy hours)
[34] Source: Productie Stuur Informatie. Period January 2003 – August 2006

Appendix F: Control API production

From July 2006, API production is controlled by an AP system too. A long range plan with a horizon of xx years and buckets of three months is made to resolve capacity problems in the long term by reallocations, make or buy decisions etc. An operational plan with a horizon of xx year and week buckets is made each week to determine the production need for week *t* to week *t+xx*, where week *t* to *t+xx* are fixed. The production plan is imported in the MRP system, and based on current inventory levels, lead times, and production need, purchasing orders are placed for chemicals and other excipients. Note that the MRP system is only used to plan purchasing orders of non-critical materials. The plans from AP are used to purchase raw materials and other critical materials, which usually have long lead times. Based on the operational plan of week *t* to *t+xx* an advanced scheduling tool is used to make a detailed production plan for all resources.

The demand forecast for API's comes from the supply chain plan and the long range plan of the international production sites and international subcontractors of Organon. But this is only 50% of the demand for API's. The other 50% of the demand comes from third parties, Process Development, local production sites and local subcontractors of Organon, and from API OPS local production sites. The future requirements of these customers are found in DP. Based on forecasted demand, current inventory levels of raw materials and API's, and defined parameters, like safety stocks, capacities, and lead times, the production plan is made in AP. Actual replenishment orders still need to placed by the 'customers' of API OPS, and if an actual replenishment order deviates too much from the forecast, it could be that API OPS is not able to deliver the full order.

Actually, the situation is more complex than described above, because every stockpoint in the API production process is controlled by the AP system. Because the production process can have up to xx production steps, the model is quite complex. But it is outside the scope of this document to discuss this AP model in more detail.

Appendix G: Material coordination parenterals and special products

Material coordination parenterals production

For parenterals, the production need for month *t+xx* to *t+xx* is usually given by the production contract. The production need for month *t* to *t+xx* is leveled in buckets of a month, and the monthly need is then assigned to week buckets. By assigning production need to week buckets, current inventory levels of bulk products, and expected 'demand' (replenishment orders and forecasts that lead to packaging orders and demand for bulk products) are considered, and if it is needed, the production need can be increased or decreased. It is tried to reduce setup times by producing more than one batch with the same vial / ampoule size in one week. Of course, availability of API's, excipients, additional materials, and capacity is considered at all levels. Next, a daily planning is made together with the production floor, and operator capacity is allocated to production orders. At least, the planning for the xx should be fixed, and it is tried to fix the schedule up to xx weeks, but operational problems can always lead to a schedule that needs to be adjusted. Planning and scheduling is fully done on the bottleneck, the filling machines. This automatically leads to a production need for the other machines, based on the lead times of the production steps.

Material coordination special products production

Planning the special products is different, because of three reasons. First, most of the machines are dedicated to a single product. Second, at this moment, all capacity is needed to fulfill demand, and third, lead times of production are about xx, much more than the lead times to produce tablets or parenterals. Therefore, at this moment, the bottleneck machines, which are the assembly machines, are planned at full capacity, and the other machines are planned in such a way that the bottleneck machines can work at all time, with complying to the restrictions in the production process and the availability of API's, excipients, and additional materials. In the short term, capacity will be increased, and then the operational plan or the production contract will be leading to plan and schedule the production of special products. Also for the special products, information from the production floor, like machine break-downs or operator unavailability, can change the schedule.

Appendix H: Drawbacks of MRP

According to Bertrand et al. (1990, 1998), and adapted to the situation at POO, we would like to note the following drawbacks of MRP:

- MRP does not distinguish between organizational decision functions and decision support systems. Management at the various organizational positions should have insight in the situation in a way that is relevant for them, as in the hierarchical control approach. At this moment, a lot of adapted Excel files are needed to create management reports.
- MRP is of no use for performance evaluation, which is a necessary step in the design of a production control system. Once data is changed, the old data cannot be retrieved anymore.
- Production – Sales coordination is difficult to use, because MRP is too restrictive. At the Master Production Schedule (MPS) level, short term flexibility is not taken into account.
- MRP is deterministic. It does not take demand uncertainties and production yield into account. Safety stocks can help, but they can be quite ineffective.
- Production Departments cannot be modeled adequately in MRP. Especially, MRP assumes that throughput times are constant, but it has no control mechanism to keep them constant. Extra control mechanisms are needed to control the Production Department, like the planning sheets of TPD.
- The primary goal for MRP is to create production needs, but it has difficulties to plan across a customer order decoupling point or to plan in case of unknown production yield. Both are present at POO.
- MRP has difficulties to plan efficiently in case of high utilization rates.

Appendix I: Organizational structure of POO

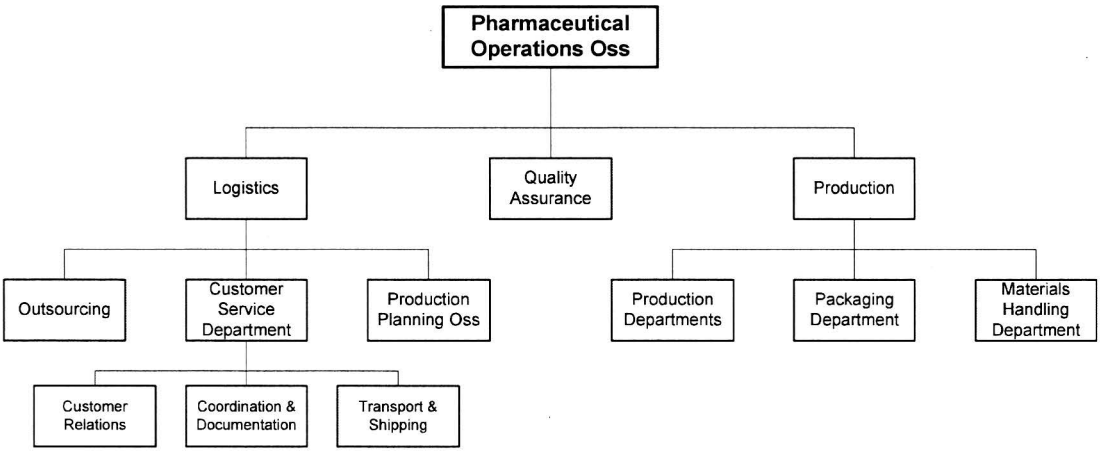

Figure I.1: Organizational structure of POO

In figure I.1 two departments that have a role in the primary process are not found: Supply Chain Operations and API Operations. These departments are not part of POO. Furthermore, there are some departments within POO that are not in the figure, because they are outside the scope of this research project.

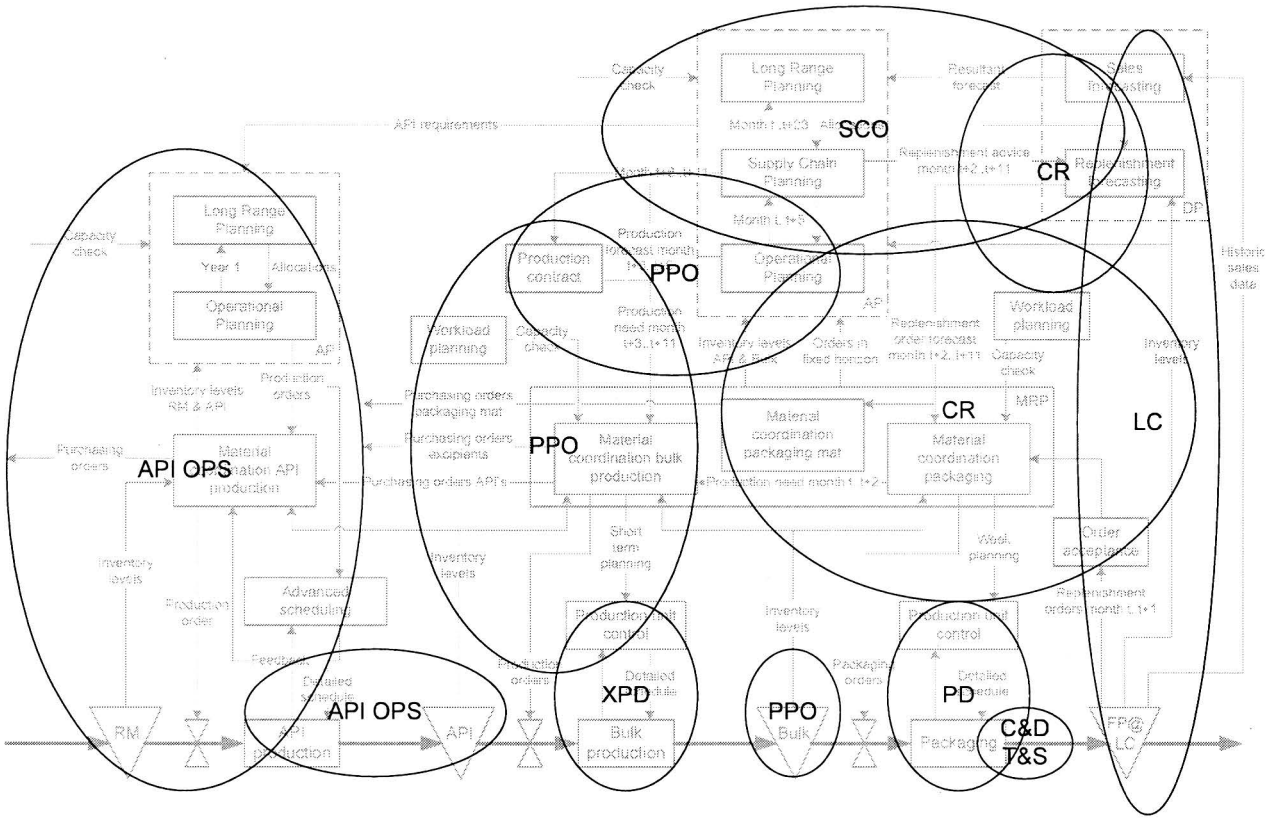

Figure I.2: Responsibilities of the departments

Appendix J: Analysis of POO and its supply chains

The goal of this appendix is to show that the demarcation of the research assignment is correct, and that the research assignment is relevant. During this chapter, we will also show which uncertainties and variations are most important. This will be done in two steps. The first step is to make a quantitative analysis of several important logistical aspects in the supply chain. This step is found in section J.1. The focus is broader than POO only, because the logistical performance of POO, like delivery reliability, is related to the performance of other stages in the supply chain. The result of the first step is the identification of three main problems related to the control of bulk tablets production.

The second step is found in section J.2, and it is a cause and effect analysis of the three main problems. The goal of this analysis is twofold. First, we would like to determine the relevance of the selected problem areas by estimating their effect on the (financial) performance of POO. Second, we would like to get a better understanding of the basic causes that lead to the problem areas we identified. We will show that the three main problems can be solved best by improving the planning method for planning the production of bulk tablets.

J.1 Identification of the three main problems

In this section, we will give an extensive analysis of the performance of several aspects of the supply chains of Organon. A summary of all the studied aspects is given in figure J.1. The aspects related to bulk production will be discussed in this appendix. The other aspects can be found in Appendix N. The goal of this section is to identify the three main problems at the level of bulk production.

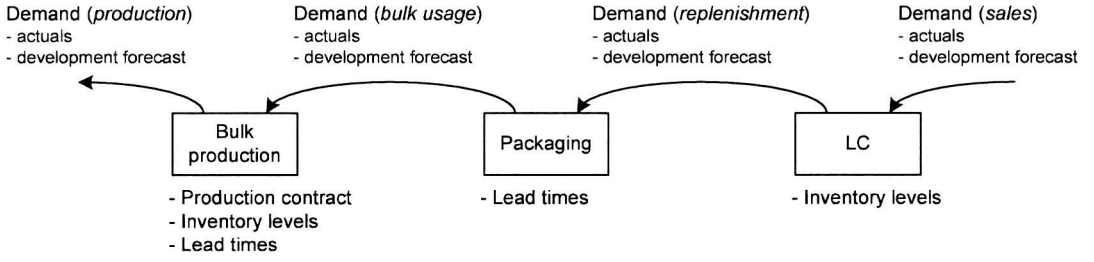

Figure J.1: Aspects in the supply chain to be studied

The supply chains of four products have been studied in detail. These products are given below. Between brackets is the name that will be used in the remainder of this chapter. These products have been chosen in accordance with Organon, because they give a representative view of all products.

- Marvelon Z.ME (Marvelon)
- Remeron 30MG CTO NB (Remeron 30)
- Cerazette (Cerazette)
- Orgametril (Orgametril)

We would like to make a last point before we continue to the results. We used several sources of information to obtain data, with the result that the data periods differ in size and in timing. Usually data has been available for a period of only one year, sometimes even less. Conclusions have been drawn with precaution, caused by the limited amount of information.

J.1.1 Bulk usage

This section can be split in two parts. Actual bulk usage is given first, and then the way the forecast of bulk usage develops over time is given, because this shows the reliability of the bulk usage forecast.

Actual bulk usage[35]

In table J.1, average bulk usage for the period of January 2005 to March 2006 is found. Moreover, the standard deviation and the coefficient of variation are given. The underlying data can be found in appendix O.

[35] Source: Usage history report (USGHST_ddmmyy.xls)

Actual monthly bulk usage			
(*1000 tab)	Average	St. dev.	Coef. of var.
Marvelon			
Remeron 30			
Cerazette			
Orgametril			

Table J.1: Actual monthly bulk usage

Development of bulk usage forecast over time[36]

A very important aspect related to controlling inventories is the reliability of the demand forecast. If the demand forecast changes a lot, more buffer stocks are needed to deal with this uncertainty. In figure J.2, we find the development of the bulk usage forecast over time of Marvelon. This figure must be read in the following way. Each line represents the bulk usage forecast for a specific month, month *t*. The most left point of a line, is the actual bulk usage in month *t*. If we follow the line to the right, we see the bulk usage forecast for month *t* at month *t-τ*.

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Figure J.2: Development of bulk usage forecast over time of Marvelon

Similar results are found for Remeron 30, Cerazette, and Orgametril. These results are given in Appendix K, section K.1. A remarkable aspect is that the one-month ahead bulk usage forecast is on average almost xx as large as the other forecasts and the actual usage. This has the following two reasons.

1. A safety time is present in the MRP system. If the Packaging Department plans to use bulk tablets in week *t*, the demand for bulk tablets is usually projected in week *t-xx*.
2. All backorders of the Packaging Department are assumed to take place in the current week.

Combining table J.1, figure J.2, and the figures in Appendix K, section K.1, we conclude that the variability in bulk usage over the month is quite large, and that there is an uncertainty in the forecast. Therefore, variability and uncertainty in demand for bulk products is part of the research assignment.

J.1.2 Bulk production

This section is structured in the same way as section J.1.1. First, we will give the actual production quantities, then we will give the development of the production forecast over time.

Actual bulk production[37]

In table J.2, average bulk production for the period of January 2005 to March 2006 is found. Moreover, the standard deviation and the coefficient of variation are given. The underlying data can be found in appendix O. From table J.2 we may conclude that the variation coefficient of monthly production quantities is high.

Actual monthly bulk production			
(*1000 tab)	Average	St. dev.	Coef. of var.
Marvelon			
Remeron 30			
Cerazette			
Orgametril			

Table J.2: Actual monthly bulk production

Development of bulk production forecast over time[38]

An important element within POO is the monthly production contract (see section 2.2.4). To stabilize the production plan, it is tried to implement the production contract as much as possible. We have analyzed the production contract of TPD from January 2005 to March 2006. It appears that, on average, each month xx% of the batches that have been produced were not forecasted, and xx% of the batches that were forecasted, have not been produced. In total, xx% more than forecasted is produced in the period we studied. About xx% of the production orders could not be forecasted,

[36] Source: OP plans tablets
[37] Source: Production contracts TPD
[38] Source: Production contracts TPD

because of a quality rejection, or because these are MTO products without forecasts. Appendix K, section K.2 gives a detailed view of the quality of the production contract.

In figure J.3, a more detailed view is given about the way that the production forecast develops over time. The results for Marvelon are given, but similar results are found for the other products. These results are given in Appendix L. From these figures we conclude that the production plan for bulk tablets is nervous and instable over time.

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Figure J.3: Development of bulk production forecast over time of Marvelon

J.1.3 Inventory levels of bulk tablets[39]

Inventory levels of bulk tablets are of great importance for the logistical performance of POO. If inventory levels are too low, the risk of an out-of-stock is high. If inventory levels are too high, inventory costs will be too high. POO has set safety stocks, batch sizes and campaign sizes to keep inventories at comfortable levels. It is tried to keep inventory above safety stock and below a maximum stock, which is safety stock + batch size * campaign size. Safety stocks, batch sizes, and campaign sizes also are the main control parameters for the planning systems (AP and MRP).

In figure J.4, the aggregated physical released stock of bulk tablets is given. 'Released' means that the bulk tablets are approved by the Quality Department. 'Physical stock' is the inventory that is physically in the warehouse, also called the on hand stock. MTO products are not considered in this figure.

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Figure J.4: Aggregated physical stock of bulk tablets

Because the demand for bulk tablets of the Packaging Department is planned before the actual usage (safety time), there is some extra stock, called leveling stock. The result is that the physical stock should be higher than you would expect based on safety stocks, batch sizes, and campaign sizes. The safety time is approximately xx weeks, what is equal to approximately xx million tablets leveling stock. Considering this, the physical released stock falls below xx!

One of the reasons that inventory levels are too low is that the Quality Department had capacity problems in the studied period, and therefore, they were not able to finish their activities within the norm lead time of xx weeks. Therefore, we also analyzed what the stock levels would have been if the quality process would have taken exactly xx weeks. The results are also given in figure J.4 by the dotted black line. It can be seen that aggregated inventories would have been higher, but considering the leveling stock again of xx million tablets, they were still too low.

A more detailed analysis is made in appendix M. In this appendix, the inventory levels of the 4 bulk products we studied are found. Also one extra product, Thyrax 0.1MG is given. It can be seen that, even if we do not consider leveling stock, inventories are outside target in xx of the xx studied periods. If we also assume that the release process would have taken exactly xx weeks, we still see that inventories are outside target in xx of the xx studied periods. Therefore we conclude that inventories of bulk tablets are not sufficiently under control.

J.1.4 Lead times of bulk production and quality control

The lead time of producing a bulk product consists of two parts: the production lead time and the quality control lead time. These lead times are of great importance for the inventory levels of bulk products. The production lead time is the time between opening an order in Apollo and closing it again. The quality control lead time is the time between the arrival of a sample to the approval of the sample. Usually, a sample arrives at the Quality Department a day after the production order is closed in Apollo. The lead times have been measured for all approvals of tablets from May 2005 to May 2006. The results are given in table J.3. It can be seen that the production lead time is below the norm, but the quality process lead time is almost xx the norm. Because the total lead time is much larger than the norm lead time, and because of the variation in the lead time, we considered variability and uncertainty in lead times in our research assignment.

[39] Source: Monthly inventory report (VRDyyyymmdd_MBU.xls)

Lead times						
	Total		Production		Quality control	
(in days)	Average	St. dev.	Average	St. dev.	Average	St. dev.
Actual lead time						
Norm lead time						
Overdue						

Table J.3: Lead times of tablets production and quality control

J.1.5 Performance of other aspects in the supply chain

In Appendix N, an analysis of all aspects from figure J.1 we did not discuss yet can be found. The final conclusion from appendix N is that there are some logistical problems at the level of Local Companies, but in accordance with Organon it has been decided not to focus the remainder of this research project on those aspects. The most important reason not to focus on the level of Local Companies comes from the fact the supervisors of Organon do not have decision power at the Local Companies.

J.1.6 Conclusion of section J.1

In section J.1 we showed that there are three main problems. These problems are at the level of bulk production. Although we also found some problems at other levels in the supply chain, it has been decided not to focus on those problems in the remainder of this report. The three main problems are given below.

1. Inventory levels of bulk tablets have not been sufficiently under control. Inventory levels of released bulk tablets have been outside target in xx of the xx studied periods. Furthermore, in section 2.6 we already showed that availability of released bulk tablets has been on average xx%, while the target availability is xx%.
2. The production plan for bulk tablets is nervous and instable over time. It changes every month.
3. The variation coefficient of monthly production quantities of bulk tablets is high, varying from xx for Cerazette to xx for Orgametril.

J.2 Cause and effect analysis of the three main problems

In section J.1, we have found three main problems at the level of bulk production, but we did not show yet that these problems can be solved best by changing the current planning method. Furthermore, we did not show yet that solving these problems leads to a better logistical performance. In this section, we will give the basic causes of the three main problems to show that we need to change the planning method. Furthermore, we will determine the (financial) effects of the three main problems, because that determines the relevance of the research assignment.

In figure J.5 a cause and effect diagram (Aken, 2005, pg. 46) is found, in which causes, problems, and effects are grouped by gray 'clouds'. It can be seen that all kind of variations and uncertainties in demand for bulk tablets, supply of bulk tablets, lead times of the production process and the release process are causes of the problem areas. Furthermore, capacity restrictions of operators at the Production Department and the current planning method are causes too. Please note that in this diagram the causes are not worked out into detail yet; only categories of causes are given. In section J.2.2, we will describe the causes in more detail.

Six effects have been identified in figure J.5. Three are caused by inventories that are insufficient under control, and three are caused by the nervous production plan, and by the variation in monthly production quantities of bulk tablets. We will describe the (financial) effects of the problem areas in more detail in section J.2.1. Also, the impact of the three main problems on the logistical performance of POO is given. Please note that we will focus on the effects of the problem areas first and then on the causes, because it needs to be determined first whether it is interesting at all to solve the problems.

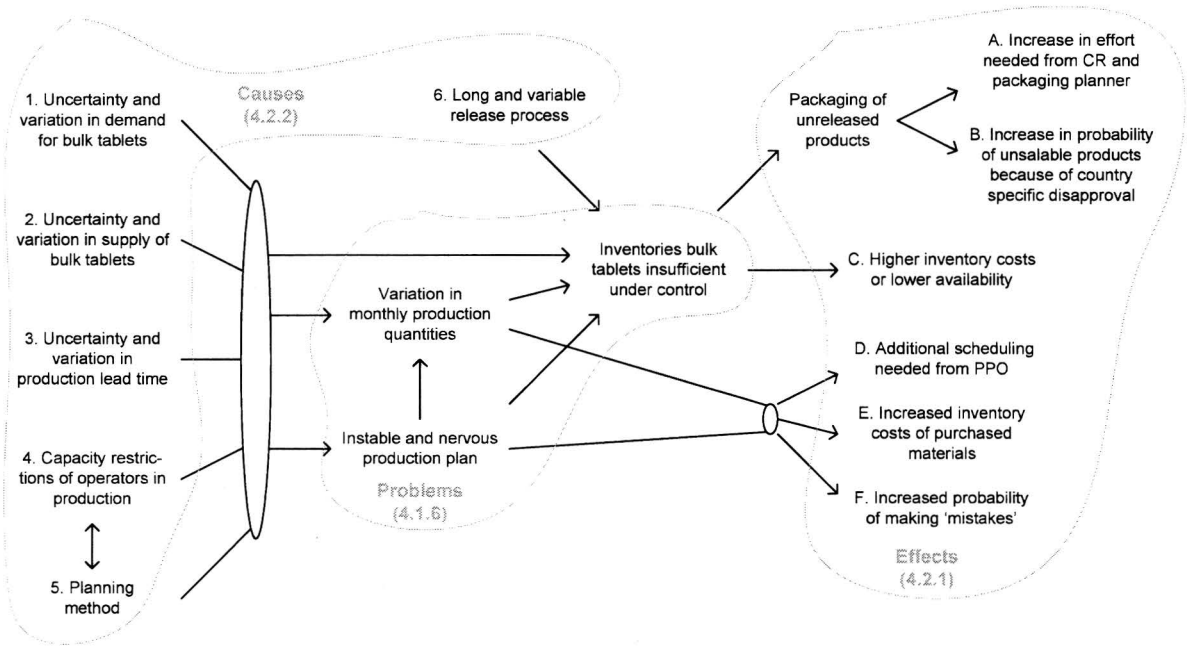

Figure J.5: Cause and effect diagram

J.2.1 Relevance of the problem areas

After discussions with the planners of TPD and CR, and after a literature review (Carlson et al., 1979; Blackburn et al., 1985; Blackburn et al., 1986; Kazan et al., 2000), six main effects were identified, which are specific for the situation at Organon. These effects show the impact of the three main problems on the performance of POO, and they are given at the right side of figure J.5.

A. If inventories are insufficiently under control, the probability increases that bulk tablets need to be packed unreleased to adhere to the due date. The effect of unreleased packaging is that more effort of CR (packaging planners) is needed. For example, each replenishment order that is packed while the bulk tablets are still unreleased, takes about xx more time of the packaging planner. If the bulk tablets are still unreleased when the product needs to be shipped to meet the due date, several people can spend xx to organize that the product is released and shipped on time.

B. Furthermore, if unreleased bulk tablets are packed, the probability increases that a product is packed for a specific country, while later the bulk product is not approved for that country. If this happens, large amounts of tablets need to be destroyed. In 2004 and 2005 it happened xx times that an unreleased bulk product was packed, but disapproved later for the specific country it was packed for. The total costs of taking the risk of unreleased packaging of bulk products were around € xx[40].

C. Because inventories are insufficiently under control, the availability of (released) bulk tablets will decrease, or safety stocks need to be increased to keep availability at the same level. The stock investment of bulk tablets is about € xx[41] if we consider safety stock and batch sizing stock. Reducing inventories will lead to lower cost in the future, and also some capital will become available for investments.

D. A fourth negative effect of a variable and instable production plan is that more planning effort is needed from the planners of PPO. The cost of one full-time planner is about € xx per year and PPO has xx planners, of which xx are working for planning bulk tablets. If the workload caused by re-planning can be reduced with xx%, xx PPO-planner could do other value added work which should at least compensate its costs of € xx.

[40] Source: FOV database
[41] Source: Safety stock proposal (Voorstel veiligheidsvoorraad 2006_2.xls)

E. Almost all excipients, additional materials, and other purchased materials are ordered on 'the safe side'; a safety factor is applied on quantity and lead time, to ensure that these materials are always available when a production order needs to be opened. An instable production plan will lead to purchase orders that are placed earlier, just to be sure, but of course, this will increase inventory costs. The current stock investment in additional materials for bulk tablets is € xx[42].

F. The last negative effect of a variable and instable production plan is more 'soft'. It is expected that a stable plan will reduce the probability of making all kind of mistakes, but it is hard to quantify this aspect. However, in the pharmaceutical industry a mistake can be very costly.

Altogether, the effects, as described above, clearly determine the relevance of the identified problem areas, and thereby determine the relevance of the research assignment. Mainly, profits can be made if inventories of bulk tablets can be reduced, while at least the same service level is achieved. Because the relevance of the problem areas has been defined, we will continue with describing the causes in the next section.

J.2.2 Causes of the problem areas

In the left side of figure J.5 it could be seen that the causes of the three problems can be placed under six categories:

1. Uncertainty and variation in demand for bulk tablets,
2. Uncertainty and variation in supply of bulk tablets
3. Uncertainty and variation in the production lead time of bulk tablets
4. Capacity restrictions of operators in production
5. The current planning method
6. Uncertainty and variation in the release process

In this section the focus will be on these 6 categories. The categories are identified by open brainstorm sessions with the planners and managers, and by considering Heisig (2002). The planners and managers could also give feedback on my ideas. Please note, that we will discuss the planning method and capacity restrictions in one section, because we think that they are intertwined too much to discuss separately.

1) Uncertainty and variation in demand for bulk tablets

In figure J.6 the reasons for variation and uncertainty in demand for bulk tablets are given. We will not describe all the causes in detail, because for the largest part the figure is clear. Uncertainty and variation in demand is often a result of uncertainty and variation in packaging and replenishment orders, which are caused by the fact that all kind of unforecasted orders are accepted, probably for good reasons. Variation in demand for bulk tablets is also caused by batching and clustering effects to improve efficiency.

[42] Source: Project additional materials (Optimale bestelhoeveelheid_v31.xls)
It should be noted that currently a project is going on to reduce the costs of ordering and holding additional materials, which will make it hard to identify the reason of reduced inventory costs of additional materials at the end of the project

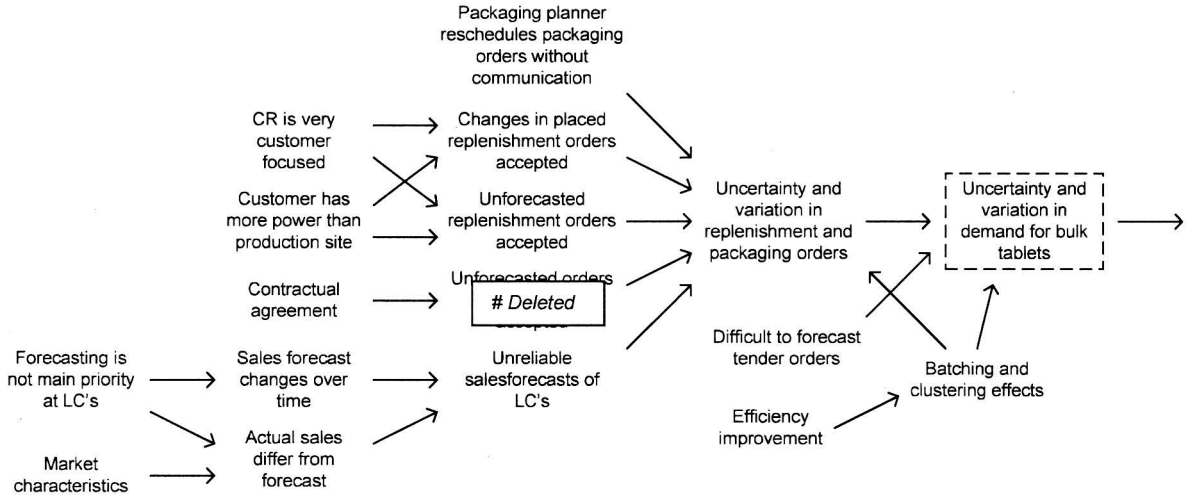

Figure J.6: The reasons for uncertainty and variation in demand for bulk tablets

2) Uncertainty and variation in supply of bulk tablets

In figure J.7 the reasons for variation and uncertainty in the supply of bulk tablets are given. We can distinguish three main reasons for supply uncertainty and variation. First, it may happen that a production order can not start, because there are no materials available. Second, there may be problems during production, like yield problems or machine breakdowns. Third, after production, bulk tablets can be disapproved by the Quality Department, or they need to be destroyed because their shelf life is expired. According to the production planners, the problems from the first two categories are minor. Therefore, we did not include them in our research assignment. However, quality rejections are a main issue, and therefore included in the research assignment. Because the figure is clear for the largest part, we will not discuss it in more detail.

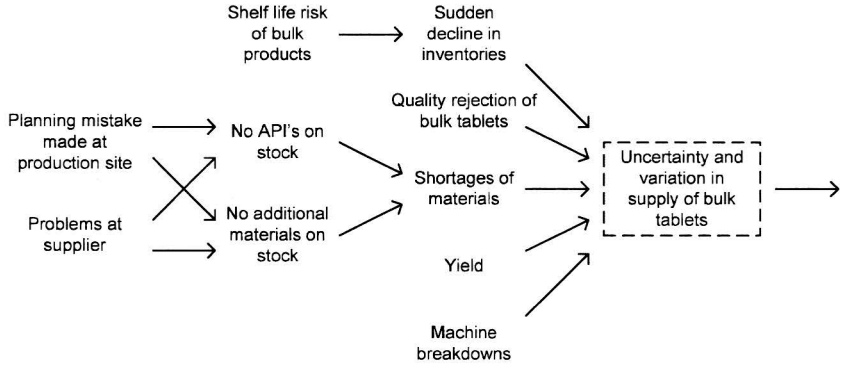

Figure J.7: The reasons for uncertainty and variation in supply of bulk tablets

3) Uncertainty and variation in the production lead time of bulk tablets

Production lead time consists of two parts: processing time and waiting time. In section J.1.4 it was shown that there is some variation in the lead time of production. Because processing times are under control[43], variation comes from waiting times. As shown in figure J.8, waiting times at the production floor are caused by operators that are highly utilized, and by the fact that the workload is not constant. Because machine utilization is low to moderate (see appendix E), it only has a minor influence on production lead times, and therefore it is not given in figure J.8, and not included in the research assignment.

[43] Source: Productie Stuur Informatie (A software program that registers KPI's, like processing times for production)

However, as shown in section J.1.4, the average production lead time is below the norm, and the variation coefficient in the production lead time is only xx, which shows us that the workload at TPD is controlled pretty well.

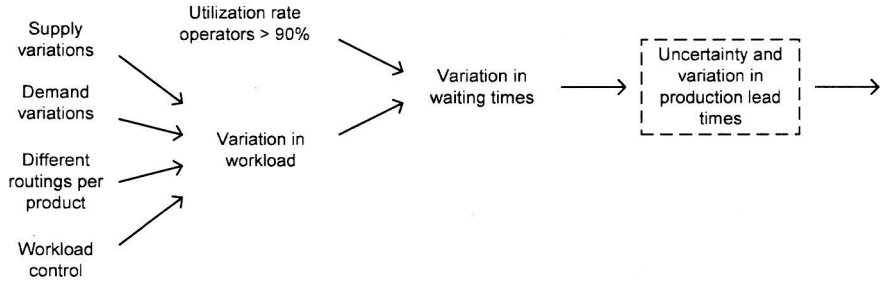

Figure J.8: The reasons for uncertainty and variation in the production lead time of bulk tablets

4&5) Planning method and capacity restrictions of operators in production
In section 2.2.4 we have described the current method of planning production and inventories of bulk tablets at the short term (up to month *t+xx*). It was described that an operational plan and a production contract are made for month *t+xx*, but as time goes by and the date of opening a production order comes closer, the situation has changed. Although the planner tries to stick to the old plan, sometimes the production plan needs to be changed. The planner uses MRP inventory projections as his main source of information to reschedule firm planned production orders, but it is unclear which criteria are used by the planner to actually make a rescheduling decision; there is no formal method to make a production plan to set the time at which firm planned production orders are planned to be opened. It is probably clear that rescheduling firm planned production orders will lead to a more nervous production plan.

There comes a moment in time that a scheduled firm planned production order needs to be opened. The decision to actually open a production order is primarily based on the workload of the Production Department. However, there is no formal method to decide which production order should be opened first. Therefore it is reasonable to conclude that there is a large probability that not always the optimal decision is made, which causes inventories of bulk tablets to be outside target. Furthermore, monthly production quantities will be more variable too.

In addition, the quality of the MRP inventory projections is questioned, because MRP can not model uncertainties in demand, supply, and lead times. The planner has no insight in the uncertainty of a projected inventory in a certain week, which may make it difficult to make a good rescheduling decision. Moreover, in the MRP inventory projections it is assumed that all backorders of the packaging activities are fulfilled in the current week, which is impossible. Besides, because of the safety time at the Packaging Department, demand for bulk tablets is projected two weeks earlier than actual demand will take place.

Another drawback of the current planning method is related to the high utilization rate of operators. In section 2.1.1 we already discussed the utilization rate of operators. Because of variations and uncertainties in demand, supply, and lead times, combined with the high utilization rate of operators, there is a large probability that several products compete for the same resource at the same time. If available operator capacity is too small for a certain time period, some firm planned production orders need to be rescheduled. Often it is not possible to reschedule them forward in time, which means that a production order will be opened too late. The result is that the probability increases that the inventory of that product will fall below safety stock, or the product will go out-of-stock. Furthermore, rescheduling firm planned production orders will lead to a more nervous production plan, and more variation in production quantities too.

Please note that it is not stated that in the current planning method capacity restrictions are neglected. As already described in section 2.2.4, operator capacity is considered at an aggregate level in the operational plan and the production contract, and at a detailed level for the coming three weeks. When the planner considers the need for operator capacity, he may conclude that he can not open all firm planned production orders at the time he wants, and rescheduling is needed. But because it is often

not possible to reschedule a firm planned production order forward in time, the result is that the production order is opened too late.

To deal with uncertainties, safety stock is held for most products. But this safety stock is based on variation in demand, while it should be based on all kind of uncertainties that can happen during the lead time of production and the release process. These uncertainties are for example demand uncertainty, uncertainty in the availability of operator capacity, and uncertainty about quality rejections, but also uncertainty in the lead time itself should be considered. Moreover, there should be a safety stock to buffer against rescheduling caused by the limited availability of operator capacity.

There are some other aspects too which can lead to more variation, nervousness, or insufficient controlled inventories. First, there can be record errors in the planning systems, which can lead to incorrect rescheduling decisions, but is unknown how often record errors happen at Organon. Second, AP and MRP compute a plan from scratch each time. Every change in any parameter (like safety stock, penalty points or lead times) or any value (like demand or supply) can lead to a plan that changes. For example, a small change in a replenishment order can lead to scheduling in or out a complete campaign at the level of bulk production. But in the MRP system, planned production orders can only be generated after firm planned production orders. Therefore, this will result to changes at the mid term only.

In figure J.9, a visual representation is made of the causes and problems identified above.

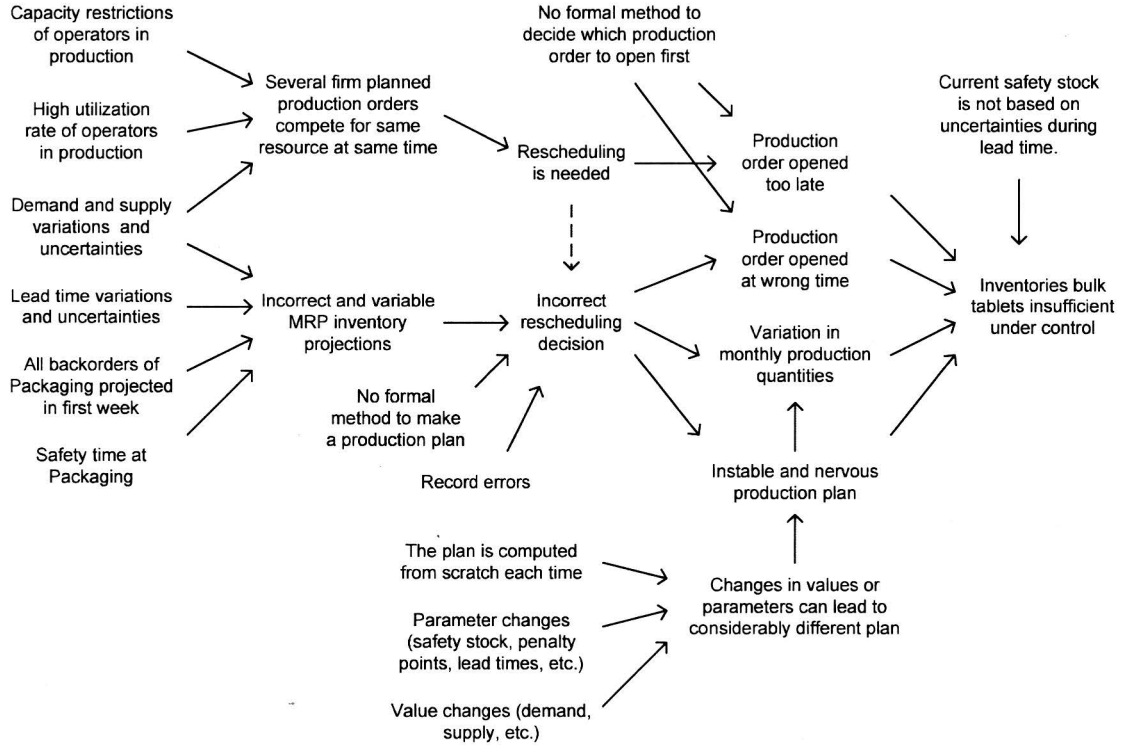

Figure J.9: The planning method and capacity restrictions as a cause of the problem areas

6) Uncertainty and variation in the release process

As shown in section J.1.4, the lead time of the release process has been almost xx its norm. In figure J.10 the reasons for this long and variable release process are given. A high utilization rate of analysts and pharmacists cause the waiting times of release activities to be long, and because PPO sets the priorities for release activities, extra variation is introduced in the system. Because the release process comes after the production process, its length and variability have no influence on nervousness in the production plan, but it is a reason that inventories of released bulk tablets are insufficient under control, as could be seen in figure J.5. It must be noted, that during 2006, more analysts and pharmacists were hired, and from approximately September 2006, the lead time of the release process reduced.

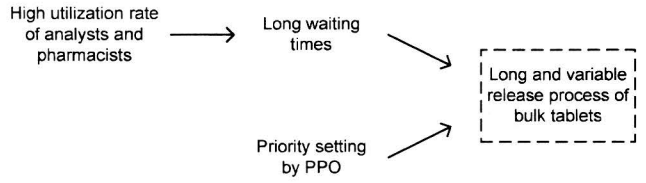

Figure J.10: The reasons for the variable and uncertain release process of bulk tablets

Evaluation of the basic causes

Above, we have described various basic causes that lead to inventories that are insufficiently under control, a production plan that is nervous and instable over time, and production quantities of bulk tablets that are variable. Taking away or reducing the effect of a basic cause is a good way to solve the identified problems. It should be noted that most of the basic causes are variations and uncertainties that are outside the control of the people involved in this research project. Therefore, we have analyzed all the basic causes in a simple way. First, we have determined whether it is possible to take away the basic cause at all considering our position in Organon. Second, for the basic causes we can take away, it is evaluated what the expected increase in performance can be on the six aspects given in section J.2.1. An overview is found in appendix P.

It can be seen in appendix P that most of the basic causes, which can be addressed in this research project, are in the category 'planning method and capacity restrictions of operators in production'. We have selected the following three basic causes, because they received the highest rating. These three causes are related to the planning method of bulk tablets production.

1. There is no formal method to decide which production order to open first.
2. There is no formal method to make a production plan to set the time at which firm planned production orders are planned to be opened.
3. The current safety stock is not based on uncertainties during the total lead time, but on demand variation.

In figure J.9 it has already been shown how these basic causes are related to the three main problems.

J.2.3 Conclusion of section J.2

In section J.2.1 it has been shown that the research assignment is relevant, because the (financial) effects of the three main problems are large. Then, in section J.2.2 it has been shown that the three main problems can be solved best by improving the planning method of bulk production. The three selected basic causes are directly linked to the two hypotheses.

J.3 Conclusion

The main goal of this chapter was to show that the demarcation of the research assignment has been correct, and that the research assignment is relevant. First we showed that there are some areas for improvement at the level of bulk production, by selecting three main problems. Then we showed that the basic causes of these main problems can be found in the planning method. Furthermore, we showed that the research assignment is relevant by determining the (financial) effects of the three main problems.

Moreover, during this chapter, we also showed which uncertainties and variations are important for the specific situation of POO, and which are not. Therefore, it had been decided to include the following aspects in the research assignment.

- Limited availability of operator capacity at the TPD.
- Uncertainty and variability in demand for bulk tablets.
- Uncertainty and variability in operator capacity availability at the TPD.
- Uncertainty and variability in lead times of the production and quality control process.
- Uncertainty about quality rejections of bulk tablet batches.

Appendix K: Development of bulk usage forecast over time and quality monthly production contract

K.1 Development of bulk usage forecast over time

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Figure K.1: Development of bulk usage forecast over time of Remeron 30

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Figure K.2: Development of bulk usage forecast over time of Cerazette

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Figure K.2: Development of bulk usage forecast over time of Orgametril

K.2 Quality monthly production contract[44]

Quality monthly production contract										
	Monthly average	15 months total	2005 Jan	Feb	Mar	Apr	May	Jun	Jul	Aug
# batches forecasted # batches produced										
difference										
# batches unforecasted # batches not produced										

Quality monthly production contract (continued)							
	Sep	Oct	Nov	Dec	2006 Jan	Feb	Mar
# batches forecasted # batches produced							
difference							
# batches unforecasted # batches not produced							

Table K.1: Quality of the monthly production contract

Legend table K.1:

# batches unforecasted :	This are the batches of product *j* which have been produced but which have not been forecasted in the production contract.
# batches not produced :	This are the batches of product *j* which have been forecasted in the production contract, but which not have been produced.

[44] Source: Production contracts TPD

Appendix L: Development of bulk production forecast over time

 # Deleted
Figure L.1: Development of bulk production forecast over time of Remeron 30

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Figure L.2: Development of bulk production forecast over time of Cerazette

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Figure L.3: Development of bulk production forecast over time of Orgametril

Appendix M: Physically released stock of bulk tablets

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Figure M.1: Physically released stock of Marvelon

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Figure M.2: Physically released stock of Remeron 30

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Figure M.3: Physically released stock of Cerazette

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Figure M.4: Physically released stock of Orgametril

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Figure M.5: Physically released stock of Thyrax 0.1

Appendix N: Logistical performance of Local Companies

In this appendix, the focus is on logistical aspects related to the Local Company, and on the bullwhip effect. We will look at the sales of Local Companies in section N.1. In section N.2, the focus is on the replenishment orders that Local Companies place at the production site in Oss. In section N.3, we will give an overview of the inventory levels of finished products at the Local Companies. In section N.4, the bullwhip effect in the supply chain will be discussed. Last, in section N.5, a conclusion is given.

N.1 Sales at Local Companies

One of the goals of the AP system is to compute a production plan for bulk tablets. This production plan is related to the sales and sales forecasts at Local Companies. Therefore, a reliable sales forecast is important for the control of the complete supply chain. Just like in section J.1 we will give actual sales and the sales forecast development in this section.

Actual sales[45]

Table N.1 to N.4 show the actual sales of Marvelon, Remeron 30, and Cerazette. For the period of January 2005 to March 2006, total sales are given in table N.1. (The underlying data can be found in appendix O.) Because there is only sales data available for full DP Local Companies, we could only give this data in table N.1. Sales of some specific finished products at Local Companies are given in table N.2 to N.4. For bulk production, total sales are most important. It is remarkable that variability is very small, which can be seen by the coefficients of variation.

Actual aggregated monthly sales (full DP LC's)			
(*1000 tab)	**Average**	**St. dev.**	**Coef. of var.**
Marvelon			
Remeron 30			
Cerazette			
Orgametril			

Table N.1: Actual aggregated monthly sales

Actual sales Marvelon					
in tablets (*1000)	**Total**	**Portugal 3*21**	**China 1*21**	**Netherlands 3*21**	**Italy 1*21**
Mar-06					
Feb-06					
Jan-06					
Dec-05					
Nov-05					
Average					
St. dev.					
Coef. of var.					

Table N.2: Actual sales of Marvelon

Actual sales Remeron 30					
in tablets (*1000)	**Total**	**Switzerland 3*10**	**China 1*10**	**Greece 3*10**	**Spain 3*10**
Mar-06					
Feb-06					
Jan-06					
Dec-05					
Nov-05					
Average					
St. dev.					
Coef. of var.					

Table N.3: Actual sales of Remeron 30

[45] Source: ADB

Actual sales Cerazette					
in tablets (*1000)	Total	France 3*28	Argentina 1*28	Poland 1*28	Norway 3*28
Mar-06					
Feb-06					
Jan-06					
Dec-05					
Nov-05					
Average					
St. dev.					
Coef. of var.					

Table N.4: Actual sales of Cerazette

Development of sales forecast over time[46]

The reliability of the sales forecast, and the way the sales forecast develops over time is probably more important than the variation in sales, because large changes in sales forecasts at the short term cannot be reacted on by the production site, because of the lead times in the supply chain. Figure N.1 to N.3 give an overview about the way that sales forecasts develop over time. In these figures, the sales forecasts of the same bulk product are aggregated over the Local Companies. It can be seen that the sales forecasts are quite stable over time, considering that the total change in sales forecast is usually xx% of the safety stock of the bulk product. However, it is hard to give a comprehensive conclusion.

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Figure N.1: Development of aggregated sales forecast over time of Marvelon

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Figure N.2: Development of aggregated sales forecast over time of Remeron 30

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Figure N.3: Development of aggregated sales forecast over time of Cerazette

We already stated that sales and sales forecast finally determine the operational plan. Because of the fact that the operational plan is made for month *t+xx*, and because of the lead times in the supply chain, each change in the sales forecasts from month *t* to at least month *t+xx*, changes the production plan of the fixed period. Therefore, we also looked at the 'cumulated change in sales forecast' ($CCSF_t$). The $CCSF_t$ is computed by equation N.1. The results are given in table N.5. It can be seen that the cumulated sales forecast change for Marvelon, but also for Remeron 30 is large. The large changes for Marvelon are partly caused by a tender order.

$$CCSF_t = \sum_{\tau=0}^{xx} \hat{S}_{t+\tau,t-1} - \sum_{\tau=0}^{xx} \hat{S}_{t+\tau,t-2} \qquad (N.1)$$

$\hat{S}_{t,t-1}$: Expected sales in month *t*, forecasted at the end of month *t-1*.

[46] Source: OP plans

Cumulated change in sales forecast			
(*1000 tab)	Marvelon	Remeron 30	Cerazette
Plan of Apr-06			
Mar-06			
Feb-06			
Jan-06			
Dec-05			
Average			
St. dev.			
Coef. of var.			

Table N.5: Cumulated change in sales forecast

For example, the value xx in the upper left cell of table N.5 means the following. In the plan of April 2006, the sales forecast for the period of xx 2006 to xx 2006 was increased with xx tablets compared to the sales forecast of that period in the plan of xx 2006.

If we look at the level of individual finished products at the Local Companies approximately the same can be seen as in the figures and tables presented above. A common figure is that once in a few months, the sales forecasts for the coming year are changed. Sometimes they are increased, and sometimes, they are decreased.

N.2 Replenishment orders of Local Companies

The replenishment orders that the Local Companies place at the production site, determine directly the activities of the Packaging Department, and thereby, the demand for bulk tablets. To optimize the supply chain, the AP system computes replenishment advices, and the replenishment orders should be close to the replenishment advice. Once that a replenishment order is placed, it should not change anymore. Just like in the other sections, we will give actual replenishment orders and replenishment order forecast development in this section.

Actual replenishment orders[47]

Actual replenishment orders for the period of January 2005 to March 2006 are given in table N.6. (The underlying data can be found in appendix O.) We have made an aggregation over all finished products of the same bulk product. It can be seen that the coefficient of variation is not very large, but it is larger than for the actual sales only. There are several reasons for this observation.

1. Not all finished products are ordered each month. Some are ordered only two or four times a year.
2. All orders are included in this analysis, while we could only include full DP Local Companies to determine sales variability. Variability is larger for replenishment orders of light DP Local Companies and for tender orders.
3. The size of a replenishment order is not always what it should be.

Actual aggregated monthly replenishment orders			
(*1000 tab)	Average	St. dev.	Coef. of var.
Marvelon			
Remeron 30			
Cerazette			
Orgametril			

Table N.6: Actual aggregated monthly replenishment orders

Development of replenishment order forecast over time[48]

In figure N.4 to N.6 it can be seen how replenishment order forecasts develop over time. Again, we have aggregated over the finished products that contain the same bulk product. The figures can be split in three parts:

- Actual: This is the size of the actual replenishment order at the requested delivery date
- Forecast of 1 to xx months ahead: In this period the replenishment order is already placed at the production site.

[47] Source: Apollo
[48] Source: OP Plans and Apollo

- Forecast of xx to xx months ahead: In this period, the replenishment advices of the AP system are given. These advices are the replenishment order forecasts. Ultimately, the replenishment advice for xx months ahead, should be the replenishment order a month later for xx months ahead.

From figure N.4 to N.6, we see two remarkable results. First, even when a replenishment order is already placed, there still are a lot of changes. Orders are rescheduled to be shipped in another month, or the size of the replenishment order is changed. The second remarkable result is that the xx-month ahead replenishment advice is larger than the xx-month ahead replenishment order in xx of the xx studied periods. This means that Local Companies order less than was advised and expected by the AP system, which should have a positive effect on the delivery reliability of POO.

Please note that the above is based on a lead time of the packaging activities of xx months, because that was the situation in the data collection period. Currently, the lead time of the packaging activities is reduced to xx months.

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Figure N.4: Development of aggregated replenishment order forecast over time of Marvelon

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Figure N.5: Development of aggregated replenishment order forecast over time of Remeron 30

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Figure N.6: Development of aggregated replenishment order forecast over time of Cerazette

N.3 Inventory levels of finished products at Local Companies[49]

One of the assumptions that AP plans on is that Local Companies steer their inventory levels towards safety stock. In the case that a Local Company has too much inventory, AP will create a low replenishment advice at the first possible moment, and the production need will be decreased. However, if a Local Company is more comfortable with an inventory level above safety stock, it will place a replenishment order that was not expected, or larger than expected. The result is that there is a higher probability that there is no bulk available. But, in this section we will show that Local Companies control their inventories pretty good, and there should be no negative effect on the performance of POO caused by the inventory strategy of Local Companies.

Figure N.7 gives the aggregated end inventory of all tablet packages at all Local Companies for March 2006. Furthermore, projected end inventories for future months are given, just like safety stock levels. It can be seen that the difference between the current inventory level and the safety stock in March 2006 is about the same as for the future months, for which AP decides about the inventory level. The same can be seen if we compare the end inventory of December 2005, January 2006, and February 2006 with future projections. In October and November 2005, inventory levels were too high, but this problem seems to be solved.

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Figure N.7: Aggregated (projected) end inventory of all tablet packages compared to safety stock targets

> *The reason that the end inventory is not at safety stock levels is because of the fact that not all products are ordered each month by the Local Companies. For a product that is ordered only twice or four times a year, the average end inventory level is, of course, above safety stock level.*
> *There is a small inventory dip in July, because some Local Companies close for a month during summer.*
> *The inventory levels of the last four months are a little lower, because for some finished products there is no sales forecast data available for more than xx or xx months ahead.*

At the level of finished products, aggregated over all Local Companies there are no astonishing results, but it can be seen that inventory levels for Marvelon have been too low. This is mainly caused by one exception. The results for Marvelon, Remeron 30, and Cerazette are given below in figure N.8 to N.10. Actual inventory levels for the period of October 2005 to April 2006 have been compared to the safety stock targets at that moment.

[49] Source: OP plans

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Figure N.8: Aggregated end inventory for Marvelon FP@LC level

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Figure N.9: Aggregated end inventory for Remeron FP@LC level

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Figure N.10: Aggregated end inventory for Cerazette FP@LC level

At the level of finished product at Local Company most times the inventory level fluctuates close to the safety stock. Of course, there are some exceptions, but no structural problem is found.

The safety stock targets at Local Companies are determined by an inventory coverage. The end inventory of month *t* should be able to cover the sales forecasts of some future months. For example, if the inventory coverage is 2 months, then the safety stock of month *t* should be able to cover the expected demand of month *t+1* and *t+2*. The way that the inventory coverage controls the inventories has some disadvantages. First, it increases the variation in replenishment orders if the sales forecast for the coming months is changed, because not only extra / less products are needed to fulfill the changed sales, but also because the safety stock increases / decreases. Second, for products that are not in a stable phase of their life cycle, the safety stock level always lags behind. This has the same reason as given above. Third, some Local Companies close down for a month during the summer, and therefore they have no sales in that month. Imagine a finished product with an inventory coverage of 1 month and a Local Company that closes down in August. Then the advised safety stock level for July would be zero.

N.4 The bullwhip effect

In section J.1 and section N.1 to N.3 we discussed several aspects of the supply chains of Organon. In this section we will focus on an aspect that cannot be placed under the heading 'Local Company' or 'POO' alone. In this section, the focus is on demand and supply variations in the supply chain; the bullwhip effect. To determine whether the variation upstream in the supply chain is larger than downstream, we analyzed the same four supply chains again: Marvelon, Remeron 30, Cerazette, and Orgametril. From the period of January 2005 to March 2006 we have looked at the monthly sales at Local Companies, the replenishment orders, the shipments from Oss to the Local Companies, the actual usage of bulk, and the production of bulk. In table N.7 the coefficients of variation are given. The underlying data can be found in appendix O. Table N.8 gives the sales variation coefficient for some specific finished products at Local Companies.

Coefficients of variation in the supply chain								
	Marvelon		Remeron 30		Cerazette		Orgametril	
	Full DP	All	Full DP	All	Full DP	All	Full DP	All
Aggregated sales@LC[50]								
Aggregated replenishment orders[51]								
Aggregated shipments PS to LC[52]								
Actual usage bulk[53]								
Bulk production[54]								

Table N.7: Coefficients of variation in the supply chain

In table N.7 a division is made between 'full DP' and 'All'. Full DP means that only the data of full DP Local Companies is used. 'All' means that information of all customers is used, including all Local Companies and replenishments of bulk tablets. It can be seen that the coefficient of variation of sales aggregated over all customers is larger than aggregated over only full DP Local Companies. This is because actual sales information is only known for full DP Local Companies. For light DP Local Companies, sales are assumed to be the same as the replenishment orders. It is easy to see that the coefficient of variation is much larger if you, for example, 'sell' a certain quantity in one month, and the following two months you 'sell' nothing.

[50] Source: ADB
[51] Source: Apollo
[52] Source: Apollo
[53] Source: Usage history report (USGHST_ddmmyy.xls)
[54] Source: Production contracts TPD

Coefficients of variation FP@LC				
	Marvelon	Remeron 30	Cerazette	Orgametril
Local Company 1				
Local Company 2				
Local Company 3				
Local Company 4				

Table N.8: Coefficients of variation of sales of finished products at Local Companies

Some interesting results can be found in table N.7. The table obviously shows an increase in variation upstream in the supply chain. First, variation is increased between aggregated sales at Local Companies and aggregated replenishment orders. Three reasons for this increase were already given in section N.2:

1. Not all finished products are ordered each month. Some are ordered only two or four times a year.
2. All orders are included in this analysis, while we could only include full DP Local Companies to determine sales variability. Variability is larger for replenishment orders of light DP Local Companies and for tender orders.
3. The size of a replenishment order is not always what it should be.

It is remarkable to see that the increase in variation for full DP Local Companies is that large, because most finished products that we have studied are high-category products, and therefore, they should be ordered each month. Furthermore, it is remarkable to see that coefficients of variation of aggregated replenishment orders for full DP Local Companies are larger than for all customers. We do not have a clear explanation for this result.

Second, variation is increased at the Packaging Department; for all supply chains the coefficient of variation of bulk usage is larger than of aggregated replenishment orders. This is caused by clustering stripping and sacheting orders, to use capacity more efficient by reducing changeover times. Especially smaller replenishment orders for finished products in the high-category are clustered. This means that two or three orders of the same finished product are stripped and sacheted at once.

Third, variation is increased by bulk production. Batches and campaign sizes at the production site are the main reason for this increase. For example, if demand is always exactly 0.5 batches, the production site will only produce once in two months. Unfortunately, it is unclear whether this reason explains all of the increase in variation.

N.5 Conclusion appendix N

In this appendix we have analyzed several logistical aspects related to Local Companies. We conclude that inventory levels have been controlled very well, and sales have been very stable. The sales forecast has been pretty stable, although this aspect could be improved. The variation in replenishment orders and the uncertainty in replenishment order forecasts have been too high in the studied period. Furthermore, we have seen that the increase in variability upstream in the supply chain has been large. We could give some explanations, but we could not explain the full increase in variability.

Appendix O: Actual demand and variations in the supply chain

Actual demand and variations in the supply chain: Marvelon								
in tablets	Sales@LC		Replenishment orders		Shipments		Usage	Production
	Full DP	All	Full DP	All	Full DP	All	Bulk	Bulk
Mar-06								
Feb-06								
Jan-06								
Dec-05								
Nov-05								
Oct-05								
Sep-05								
Aug-05								
Jul-05								
Jun-05								
May-05								
Apr-05								
Mar-05								
Feb-05								
Jan-05								
Average								
St.dev.								
Var. coef.								

Table O.1: Actual demand and variations in the supply chain of Marvelon

Actual demand and variations in the supply chain: Remeron 30								
in tablets	Sales@LC		Replenishment orders		Shipments		Usage	Production
	Full DP	All	Full DP	All	Full DP	All	Bulk	Bulk
Mar-06								
Feb-06								
Jan-06								
Dec-05								
Nov-05								
Oct-05								
Sep-05								
Aug-05								
Jul-05								
Jun-05								
May-05								
Apr-05								
Mar-05								
Feb-05								
Jan-05								
Average								
St.dev.								
Var. coef.								

Table O.2: Actual demand and variations in the supply chain of Remeron 30

Actual demand and variations in the supply chain: Cerazette								
in tablets	Sales@LC		Replenishment orders		Shipments		Usage	Production
	Full DP	All	Full DP	All	Full DP	All	Bulk	Bulk
Mar-06								
Feb-06								
Jan-06								
Dec-05								
Nov-05								
Oct-05								
Sep-05								
Aug-05								
Jul-05								
Jun-05								
May-05								
Apr-05								
Mar-05								
Feb-05								
Jan-05								
Average								
St.dev.								
Var. coef.								

Table O.3: Actual demand and variations in the supply chain of Cerazette

Actual demand and variations in the supply chain: Orgametril								
in tablets	Sales@LC		Replenishment orders		Shipments		Usage	Production
	Full DP	All	Full DP	All	Full DP	All	Bulk	Bulk
Mar-06								
Feb-06								
Jan-06								
Dec-05								
Nov-05								
Oct-05								
Sep-05								
Aug-05								
Jul-05								
Jun-05								
May-05								
Apr-05								
Mar-05								
Feb-05								
Jan-05								
Average								
St.dev.								
Var. coef.								

Table O.4: Actual demand and variations in the supply chain of Orgametril

It can be seen that sales at Local Companies are often smaller than replenishment orders, shipments, bulk usage, and bulk production. This is because there is only sales data available of the products that are produced and packed at POO in April 2006.

Appendix P: Evaluation of basic causes

In the second column of table P.1 the value 1 is given if the basic cause can be solved considering our position within Organon. The value 0 means that it can not be solved. For the basic causes that are within our abilities to solve, the third column gives a value between 1 and 5. A 1 means that taking away this basic cause will have a minor impact on the performance of Organon, while a 5 means that it will have a large impact.

Evaluation of basic causes		
Basic cause	**Solvable?**	**Impact on performance**
Uncertainty and variation in demand for bulk tablets		
Packaging planner reschedules packaging orders without communication	1	3
CR is very customer focused	0	
Customer has more power than production site	0	
Contractual agreement	0	
Forecasting is not main priority at LC's	0	
Market characteristics	0	
Difficult to forecast tender orders	0	
Efficiency improvement (batching and clustering)	1	3
Uncertainty and variation in supply of bulk tablets		
Storage life of bulk products	0	
Disapproval of bulk products	0	
Planning mistake made at production site	1	2
Problems at supplier	0	
Yield	0	
Machine breakdowns	0	
Uncertainty and variation in production lead time of bulk tablets		
Utilization rate operators > 90%	0	
Supply variations	*	
Demand variations	**	
Different routings per product	0	
Workload control	1	2
Planning method and capacity restrictions of operators in production		
Current safety stock is not based on uncertainties during total lead time	1	5
Capacity restrictions of operators in production	0	
High utilization rates of operators in production	0	
Demand and supply variations and uncertainties	* / **	
Lead time variations and uncertainties	***	
All backorders of Packaging projected in first week	1	3
Safety time at Packaging	1	3
No formal method to make a production plan	1	4
Record errors	0	
The plan is computed from scratch each time	1	2
Parameter changes	0	
Value changes	0	
No formal method to decide which production order to open first	1	4
Long and variable release process		
Capacity shortage of analysts and pharmacists	0	
Priority setting by PPO	1	2
* see supply uncertainty and variation		
** see demand uncertainty and variation		
*** see lead time uncertainty and variation		

Table P.1: Evaluation of basic causes

Appendix Q: Other alternative solutions

In this appendix, two alternative solutions we did not study in more detail are discussed. One of these is the cyclical plan, which is a slightly different approach to the capacity oriented strategy. The other one is a variant on the total control concept, namely using the AP system for short term planning. In this appendix, we will not only describe these two alternative solutions, but we will also discuss why we did not study them in more detail.

Q.1 Cyclical plan

According to Silver et al. (1998, pg. 452) there are two approaches to capacity oriented strategies; the run-out times plan, as discussed in chapter 4, and the cyclical plan. In a cyclical production plan, production orders are planned in a more or the less fixed order. One of the main goals is to keep the total cycle time stable, so it is known in advance when the next production run of a specific product will be. The most well known cyclical method is the Economic Lot Scheduling Problem (ELSP) (Elmaghraby, 1978), which was already mentioned above. The largest disadvantage of the ELSP is its deterministic approach. Several authors have studied the stochastic variant (SELSP) of the ELSP; in Sox et al. (1999) a review of the SELSP can be found.

A cyclic production schedule seems to be realizable considering the characteristics at Organon.

- Most bulk usage is stable. Silver et al. (1998) define 'stable' as a variation coefficient that is below 0.45. Of the four studied products, the three largest products (Marvelon, Cerazette, and Remeron 30) all satisfy this condition. Only for the small products, demand is not stable.
- There is a capacity bottleneck; utilization rates of operators are approximately xx% to xx%. Therefore, a capacity oriented approach, like the cyclical plan, may be needed.
- The lead times of the Production Department are under control. The average lead time is xx days, while the norm lead time is xx days, and the coefficient of variation is xx. On the other hand, the lead times of the release process are insufficient under control. On average the lead time is xx days, while the norm lead time is xx days, and the coefficient of variation is xx.

The largest advantage of a cyclic production schedule is a stable production plan. With a stable production plan, less effort is needed from the planners, and purchasing can be done more efficiently. Furthermore, the risk of making mistakes reduces in a stable environment, and the collaboration of the Production Department with QA and the Packaging Department can be improved, which could reduce the total lead time. It is hard to make a statement whether inventories will be controlled better.

A disadvantage of a cyclic production schedule is the risk of an inflexible system that can not adequately respond to important short term variations. Realizing that batch sizes are fixed, it is even more difficult to be flexible, because batch sizes can not be adjusted slightly if this is needed. A method in which batch sizes may be adjusted is given by Leachman and Gascon (1988). A second disadvantage of this new control structure is that it is hard, maybe even impossible, to implement it in the current control systems. This means that not only the control structure needs to be changed significantly, but also the information systems and the organization. It is questionable whether such a change is realizable. These two important restrictions are the reason that we did not study the feasibility of a cyclical plan in more detail.

Q.2 AP system for short term planning

The last alternative solution we would like to discuss is to extent the AP system to plan the short term too. The idea is to reduce the fixed period of the operational plan from xx to xx months. As can be seen in the lead time – decision structure in figure 2.6, with a fixed period of xx months the first order would already be opened within xx after the OP is solved. To prevent that MRP inventory projections are still used to plan production orders, an agreement should be made that the operational plan is implemented completely. This implies a fixed fence of about xx, with the disadvantage that larger safety stocks are needed to cope with the uncertainty during the fixed fence. Moreover, in this alternative solution there still is no instrument to allocate monthly production needs to a daily production schedule, and uncertainty in the capacity availability of operators at the short term is still not taken into account in this alternative solution. Therefore, we still need a planning method at the level of material coordination to determine which production order to open first.

Furthermore, reducing the fixed period of OP and blindly implementing the plan it has made, does not take the following disadvantages away:

- Monthly buckets are quite rough to make a plan for the short term. Especially rounding off lead times to zero or one month has implications on the quality of the plan.
- MTO products and tender orders are not modeled in OP, and their variable claim on capacity is not considered.
- There is no direct feedback on quality rejections or other important short term variations.
- The proposed plans can be unrealistic if operator capacity is taken into account.
- OP computes the optimal solution for the complete supply chain, while reality is that all actors in the supply chain try to increase their own performance in stead of the performance of the complete supply chain. The plan does not comply with the performance indicators of POO.

Of course, this option has its advantages too. The AP system considers the complete supply chain, and this multi-echelon view enables it to make a better production plan. Furthermore, the production plan will be more stable in the short run, because the plan that is made is implemented directly. Furthermore, it would be easy to implement this alternative, because only a small change in information systems, and no change in the organization is needed. However, these positive effects are not large enough to balance the negative effects. Therefore, this alternative solution has not been studied in more detail.

Appendix R: Product and demand characteristics

Product characteristics											
Product name	Product number	Demand model	Average demand size (*1000 tab)	St. dev. demand size (*1000 tab)	Probability of an arrival	Current safety stock (*1000 tab)	Batch size * yield (*1000 tab)	Campaign size	Probability of quality rejection	Capacity usage (h / 1000 tab)	Cost price (euro / 1000 tab)
CERAZETTE											
LIVIAL 2,5MG NS											
MARVELON Z.ME											
REMERON 30MG CTO NB											
DESO/EE-50/35 PS CT											
DESO/EE-100/30 PS CT											
EXLUTON											
MARVELON Z.ME CT											
MARVELON Z.ME ZO											
MERCILON											
MINISTAT											
ORADEXON 0,5MG											
ORADEXON 1,5MG											
ORGAMETRIL											
OVESTIN 1MG 6MM											
OVESTIN 1MG ZO											
OVESTIN 2MG											
OVESTIN 2MG ZO											
PLACEBO CT											
PLACEBO WIT ZO											
REMERON 15MG CTO NB											
THYRAX 0,025MG DT ZO											
THYRAX 0,1MG DT ZO											
TOLVON 10MG CT											
TOLVON 30MG CTO											
TOLVON 60MG CTO											
MTO											

Table R.1: Product characteristics of MTS products

Demand forecast characteristics									
Product name	Product number	Probability no change in demand	Probability small change in demand	Probability large change in demand	Model small change	Average size small change (*1000 tab)	St. dev. size small change	Autocor-relation in actual forecast	Autocor-relation in simulated forecast
CERAZETTE									
LIVIAL 2,5MG NS									
MARVELON Z.ME									
REMERON 30MG CTO NB									
DESO/EE-50/35 PS CT									
DESO/EE-100/30 PS CT									
EXLUTON									
MARVELON Z.ME CT									
MARVELON Z.ME ZO									
MERCILON									
MINISTAT									
ORADEXON 0,5MG									
ORADEXON 1,5MG									
ORGAMETRIL									
OVESTIN 1MG 6MM									
OVESTIN 1MG ZO									
OVESTIN 2MG									
OVESTIN 2MG ZO									
PLACEBO CT									
PLACEBO WIT ZO									
REMERON 15MG CTO NB									
THYRAX 0,025MG DT ZO									
THYRAX 0,1MG DT ZO									
TOLVON 10MG CT									
TOLVON 30MG CTO									
TOLVON 60MG CTO									
MTO									

Table R.2: Demand forecast characteristics of MTS products

Appendix S: Seasonal effects in demand

 # Deleted

Figure S.1: Average monthly demand for Marvelon and Cerazette over a period of 4 years

Appendix T: Architecture of the simulation models

In this appendix, the simulation models are described in more detail than in section 5.2. The focus is on the composition of the models, and the equations used to make the production decisions. Just like in section 5.2, we will first describe the input and performance sheet, then the product sheets, and last the capacity sheets of the three models.

T.1 Input and performance sheet

The input and performance sheet is (almost) similar for the three models. The only difference is that for the POS simulation model safety stock is part of this sheet, while for the COS simulation model, the critical level is part of this sheet. For the HCS simulation model, safety stock is given for slowmovers, and a critical level is given for the fastmovers. In figure T.1 and T.2, an example of the input and performance sheet of the HCS simulation model is given.

Input and performance sheet
hybrid control strategy

Input		CERAZETTE Product 1	...	OVESTIN 1MG ZO Product 16	...	TOLVON 60MG CTO Product 26
CL (h) and ss_j (*1000 tab)						
BS_j (*1000 tab)						
CS_j						
Pqr_j						
cu_j (h / 1000 tab)						
cp_j						
C (average)						
C (st. dev.)						
LTD (incl review period)						
Lead time						
Probability						
Cumulative						

Figure T.1 Input part of the input and performance sheet of the HCS simulation model

Performance	Total	CERAZETTE Product 1	...	OVESTIN 1MG ZO Product 16	...	TOLVON 60MG CTO Product 26
Total pos. inv. (*1000 tab)						
Av. pos. weekly inv. (*1000 tab)						
Av. weekly inv. investm.						
Total neg. inv. (*1000 tab)						
# stockouts (in weeks with order)						
Av. size stock-out (*1000 tab)						
# weeks with order						
% stock-out periods						
Total capacity						
Total usage MTS						
Total usage MTO						
Utilization rate						

Figure T.2 Performance part of the input and performance sheet of the HCS simulation model

Legend of figure T.2:

Total pos. inv.	:	Total positive inventory (per product summed over all weeks)
Av. pos. weekly inv.	:	Average positive weekly inventory
Av. weekly inv. investm.	:	Average weekly inventory investment
Total neg. inv.	:	Total negative inventory (per product summed over all weeks)
Av. size stock-out	:	Average size of a stock-out

T.2 Product sheets

The composition of the model

The product sheets have all been built in the same way. In the first 13 rows some variables are given a value, like demand size, batch size, safety stock etc. These values are converted from tablets to hours of operator work by a multiplication with cu_j. This is done because we do not calculate in tablets, but in hours of operator work. From row 20 to row 1019 each row represents a week, and all relevant data, like actual demand and end inventory, is given in the row. In table T.1 a modified version of a product sheet is given. This modified version is almost the same as the actual product sheet, but makes it easier to explain how the simulation model works.

Product sheet									
	Demand	**Demand forecast help 1** **Random number**			**Demand forecast help 2** **No restrictions**			**Demand forecast**	
Week	Actual demand	Demand forecast week t	...	Demand forecast week $t+\tau$	Demand forecast week t	...	Demand forecast week $t+\tau$	Demand forecast week t	...	Demand forecast week $t+\tau$
1										
2										
...	eq. T.1	eq. T.2		eq. T.3	eq. T.4		eq. T.5	eq. T.6		See T.6
1000										

Product sheet (continued)								
		Lead time production order						
Week	Production order	Rand()	L=7	Rejected?	...	L=12	Rejected?	Production order finished
1								
2								
...	eq. T.7	eq. T.8	eq. T.9	eq. T.10		See T.9	See T.10	eq. T.11
1000								

Product sheet (continued)						
	Inventory		**Run out time**			
Week	Inventory position	End Inventory	Expected inventory $t+L_{norm}-10$	...	Expected inventory $t+L_{norm}$	...	Expected inventory $t+L_{norm}+9$
1						
2						
...	eq. T.12	eq. T.13	eq. T.14		eq. T.15		eq. T.16
1000						

Table T.1: Architecture of the product sheets

The variables

Below, the variables are given that are used in the equations, which are given in MS Excel syntax. In most equations, we refer to a specific cell in the product sheet. In the list below, it can be found what information is found in these cells. All equations are taken from row 100, which therefore is our reference point.

$B$5	:	Pa_j
$C$8	:	$P\alpha$
$C$9	:	$P\varphi$
$C$13	:	σ_{SC_j}
$G$13	:	$\overline{SC}_j$
H$11 to M$11	:	*L* = xx to *L* = xx
$I$5	:	Pqr_j
$K$4	:	CS_j
$AA$5	:	$\overline{D}_j$
$AA$8	:	ss_j
$AA$9	:	PS_j
Column B	:	$D_{j,t}$: Computed in equation T.1
Column C to U	:	$\hat{D}_{j,t+\tau,t}$: Computed in equation T.6
Column V	:	$PO_{j,t}$: Computed in equation T.7
Column W	:	*rand()*: Computed in equation T.8
Column X,Z,AB,AD,AF,AH		Size of production order with *L = xx,xx,xx,xx,xx,xx*: Computed in equation T.9
Column Y,AA,AC,AE,AG,AI		Size of approved production order. Result of equation T.10 if *L = xx,xx,xx,xx,xx,xx*
Column AJ	:	Finished production order: Computed in equation T.11
Column AK	:	$Ipos_{j,t}$: Computed in equation T.12
Column AL	:	$I_{j,t}$: Computed in equation T.13
Column AP to BI	:	Help to compute run out time: Computed in equation T.14 to T.16
Column BK to CC	:	*rand()*: Computed in equation T.2 and T.3
Column CE to CW	:	$\hat{D}_{j,t+\tau,t}$ without restrictions: Computed in equation T.4 and T.5

The equations

Below, the equations are given in MS Excel syntax. We also refer to the equations in section 5.2 if a link exists.

Equation T.1: Actual demand in week *t*

B100=IF(RAND()>$B$5;0;MIN(6*$AA$5;ROUND(GAMMAINV(RAND();1;$AA$5);2)))

If there is an arrival, than there is demand that comes from an exponential distribution in this case.

Equation T.2 and T.3: Random number

BK100=RAND()

Because the same random number is needed more than one time in equation T.4 and T.5, we had to define equation T.2 and T.3.

Equation T.4: Demand forecast for week *t* at the start of week *t* without restrictions

*CE100=IF(BK100<$C$8;B100;ROUND(IF(AND(BK100>=$C$8;BK100<$C$9);IF(RAND()>$B$5;0;GAM MAINV(RAND();1;$AA$5));B100+GAMMAINV(RAND();$C$13;$G$13)*ROUNDUP(RAND()-0.5;0));2))*

Depending on the random number of equation T.2, the demand forecast changes not, small, or large. In the last case, a completely new demand forecast is computed in the same way is equation T.1 computes actual demand. In the case of a small change, a random number decides whether the small change is added or subtracted from the demand forecast of a week ago.

Please note that we compute the demand forecast the other way around. Starting with the actual demand, the demand forecast for week *t* in week *t* up to the demand forecast for week *t* in week *t-xx* is computed. We have made this modeling decision because otherwise the demand distribution of actual demand would get disturbed.

Equation T.5: Demand forecast for week *t* at the start of week *t-τ* without restrictions. (*τ = 1,2,..,xx)*

*CW100=IF(CC100<$C$8;CV101;ROUND(IF(AND(CC100>=$C$8;CC100<$C$9);IF(RAND()>$B$5;0;GAMMAINV(RAND();1;$AA$5));CV101+GAMMAINV(RAND();$C$13;$G$13)*ROUNDUP(RAND()-0.5;0));2))*

The difference between equation T.5 and T.4 is that in equation T.5 the demand forecast is based on the demand forecast of the week before, while in equation T.4 the demand forecast was based on the actual demand, because there is no demand forecast yet in the first forecast period.

Equation T.6: Demand forecast for week *t* at the start of week *t-τ* (*τ = 1,2,..,xx)*

*C100=MIN(MAX(0;CE100);6*$AA$5)*

The actual demand forecast is the demand forecast of equation T.4 and T.5 with the restriction that it is at least zero, and maximum xx times the average demand size.

Equation T.7: Actual production order in week *t*

V100='Capaciteit'!FV100

This equation refers to the capacity sheet, in which it is decided for which products a production order is opened. The capacity need for one production order is given here. In appendix T.3 it will be explained how the production decisions are made in the three planning strategies.

Equation T.8: Random number

W100=RAND()

Because the same random number is needed more than one time in equation T.9, we had to define equation T.8.

Equation T.9: The Production order opened in week *t* is assigned a lead time

X100=IF($W100<H$11;$V100;0)

Based on the random number of equation T.8, the production order is assigned a lead time, based on the lead time distribution.

Equation T.10: The production order opened in week *t* may be rejected by the Quality Department

Y100=IF($I$5=0;X100;(X100-X100/$K$4*CRITBINOM($K$4;$I$5;RAND())))

In our model, it is directly known whether one or more batches will be rejected. But for the production decision, this information comes available after the lead time.

Equation T.11: The production order is finished in week *t*

AJ100=AI88+AG89+AE90+AC91+AA92+Y93

After the assigned lead time, a production order is finished. It is given in the week that is finished.

Equation T.12: The inventory position in week *t*

AK100=AL99-SUM(C100:L100)+SUM(V91:V99)-X91-X92-Z91+AD90+AF90+AF89+AH90+AH89+AH88

The formula of the inventory position was already given in equation 5.6. In equation T.12 it is corrected if the lead time of a production order was not equal to the norm lead time.

Equation T.13: End inventory in week *t*

AL100=AL99-B100+AJ100

The end inventory of this week is the end inventory of last week minus actual demand in this week plus production orders that are finished in this week. This equation is related to equation 5.7.

Equation T.14, T.15 and T.16: Help to compute the run out time in week *t*

Eq. T.14: AP100=AQ100+C100
Eq. T.15: AZ100=AK100
Eq. T.16: BI100=BH100-U100

This set of equations start with the inventory position from equation T.12 and the demand forecast of week $t+\tau$ is added by it if $\tau < L_{norm}$ or subtracted from it if $\tau > L_{norm}$.

T.3 Capacity sheets

In this section it will be described how the capacity sheets have been built. Because these sheets differ for the three simulation models, we will describe them separately. In section T.3.1 the capacity sheet of the POS model is given, in T.3.2 the capacity sheet of the COS model, and in T.3.3 the capacity sheet of the HCS model.

T.3.1 Capacity sheet of the POS simulation model

The composition of the model

Just like in the product sheets, every row in the model represents a week, and on that row all information needed to decide for which products a production run should start can be found. We use hours of operator work in stead of tablets for the calculations.

Capacity sheet POS model										
	Production order need				**R.O. time**			**Rank help**		
Week	Product 1	...	Product 26	MTO Product 27	Product 1	...	Product 26	Product 1	...	Product 26
1										
2										
...	eq. T.17				eq. T.18			eq. T.19		
1000										

Capacity sheet POS model (continued)									
Rank			**Capacity begin wk *t***	$C_{0,t}$	C_t	**Capacity end wk *t***	**Cumulative production on**		
Product 1	...	Product 26	C_t-$Cneg_{t-1}$			$Cneg_t$	help	Rank 1	...
eq. T.20			eq. T.21	eq. T.22	eq. T.23	eq. T.24	eq. T.25	eq. T.26	

Capacity sheet POS model (continued)						
rank	**Cumulative capacity left**			**How many P.O.**	**Real production order**		
Rank 26	Rank 1	...	Rank 26	**possible?**	Product 1	...	Product 26
eq. T.27	eq. T.28			eq. T.29	eq. T.30		

Table T.2: Architecture of the capacity sheet of the POS simulation model

The variables

Below, the variables are given that are used in the equations, which are given in MS Excel syntax. In most equations, we refer to a specific cell in the capacity sheet. In the list below, it can be found what information is found in these cells. All equations are taken from row 100, which therefore is our reference point.

$A$1023	:	'1004'
$B$19 to $AA$19	:	'Product 1' to 'product 26'
$C$3	:	$\overline{C}$
$C$4	:	σ_C
DP$17 to EO$17	:	'1' to '26'
Column B to AB	:	$PN_{j,t}$*cu_j: Computed in equation T.17
Column AD to BC	:	$RO_{j,t}$: Computed in equation T.18
Column BF to CE	:	Rank help: Computed in equation T.19
Column CH to DG	:	Rank of the products: Computed in equation T.20
Column DJ	:	$C_t - Cneg_{t-1}$: Computed in equation T.21
Column DK	:	$C_{0,t}$: Computed in equation T.22
Column DL	:	C_t: Computed in equation T.23
Column DM	:	$Cneg_t$: Computed in equation T.24
Column DO	:	Help for cumulative production on rank: Computed in equation T.25
Column DP to EO	:	Cumulative production on rank: Computed in equation T.26 and T.27
Column ER to FQ	:	$C_{i,t}$: Computed in equation T.28
Column FT	:	How many production orders possible?: Computed in equation T.29
Column FV to GU	:	$PO_{j,t}$: Computed in equation T.30

The equations

Below, the equations are given in MS Excel syntax. We also refer to the equations in section 5.2 if a link exists.

Equation T.17: Need for a production order in week *t*

B100=IF('Product 1'!$AK100<'Product 1'!$AA$8;'Product 1'!$AA$9;0)

If the inventory position in week *t* falls below safety stock, then a production order with size batch size * campaign size is needed. In this sheet we refer to the product sheet. This equation is related to equation 5.9.

Equation T.18: Run out time in week *t*

AD100=IF(ISERROR(MATCH(0;'Product 1'!$AP100:$BI100;-1));0;MATCH(
0;'Product 1'!$AP100:$BI100;-1))

Based on the results of equation T.14 to T.16 it is computed what the run out time is. This equation is related to equation 5.8.

Equation T.19: Rank help in week *t*

*BF100=RANK(AD100;$AD100:$BD100;-1)+RAND()*0.1*

The products are ranked based on their run out time. If several products have the same run out time, a random factor will determine which product receives the highest rank.

Equation T.20: Rank of the products in week *t*

CH100=RANK(BF100;$BF100:$CF100;-1)

The actual rank of a product is determined by equation T.20, because the random factor of equation T.19 is also taken into account now. Equation T.19 and T.20 are related to equation 5.10.

Equation T.21 to T.24: Determination of available capacity in week *t*

Eq. T.21: DJ100=DM99+DL100
Eq. T.22: DK100=DJ100-AB100
Eq. T.23: DL100=NORMINV(RAND();$C$3;$C$4)
Eq. T.24: DM100=MIN(0;DK100-SUM(FV100:GV100))

With this set of equations the available starting capacity of each week is given. It is computed by subtracting the capacity need of MTO products and the negative capacity of last week from available capacity, which is a normally distributed variable. Equation T.21 and T.22 are related to equation 5.12. Equation T.24 is related to equation 5.11.

Equation T.25: Help for cumulative production on rank in week *t*

DO100=$A$1023-A100+1

This is just a small help function to be able to compute equation T.26.

Equation T.26: Cumulative production on rank in week *t* (rank 1)

DP100=HLOOKUP(HLOOKUP(DP$17;$CH100:$DH$1023;$DO100;FALSE);$B$19:$AB$1020;$A100+1;FALSE)

This equation looks for the production need of the product with rank 1 in week *t*. First, the lookup function looks for the product with rank 1 in week *t*, then it looks for the production need of that product in week *t*.

Equation T.27: Cumulative production on rank in week *t* (rank 26)

EO100=HLOOKUP(HLOOKUP(EO$17;$CH100:$DH$1023;$DO100;FALSE);$B$19:$AB$1020;$A100+1;FALSE)+EN100

This equation looks for the production need of the product with rank 26 in week *t*. The cumulative production need up to rank 25 in week *t* is added to it. This last aspect is the difference between equation T.26 and T.27.

Equation T.28: Cumulative capacity left on rank in week *t*

ER100=$DK100-DP100

In this equation, the cumulative production on rank in week *t* (computed in equation T.27) is subtracted from the available starting inventory from equation T.22.

Equation T.29: How many production orders are possible in week *t*?

FT100=IF(DK100<0;0;COUNTIF(ER100:FR100;">0")+1)

With this equation it is computed when equation T.28 becomes negative, to know how many production orders can be loaded in week *t*.

Equation T.30: Real production order in week *t*

FV100=IF($FT100-CH100>=0;B100;0)

If the rank of this product is smaller or equal to the number of products that can be loaded, a production order is generated for this product in week *t*. The value of equation T.7 comes from this equation. Equation T.26 to T.30 are related to equation 5.13 to equation 5.16, but a one-on-one relation can not be made.

T.3.2 Capacity sheet of the COS simulation model

The composition of the model

Just like in the product sheets, every row in the model represents a week, and on that row all information needed to decide for which products a production run should start can be found. We use hours of operator work in stead of tablets for the calculations.

Capacity sheet COS model									
	Inventory position			R.O. time			Rank help		
Week	Product 1	...	Product 26	Product 1	...	Product 26	Product 1	...	Product 26
1									
2									
...	eq. T.31			eq. T.32			eq. T.33		
1000									

Capacity sheet COS model (continued)							
Rank			Capacity begin wk *t*	$C_{0,t}$	C_t	Capacity end wk *t*	Sum inventory position	Total production need
Product 1	...	Product 26	C_t-$Cneg_{t-1}$			$Cneg_t$		
eq. T.34			eq. T.35	eq. T.36	eq. T.37	eq. T.38	eq. T.39	eq. T.40

Capacity sheet COS model (continued)									
Cumulative production on rank				Cumulative production need left			Cumulative capacity left		
help	Rank 1	...	Rank 26	Rank 1	...	Rank 26	Rank 1	...	Rank 26
eq. T.41	eq. T.42		eq. T.43	eq. T.44			eq. T.45		

Capacity sheet COS model (continued)					
How many P.O. need?	How many P.O. possible?	How many P.O.	Real production order		
			Product 1	...	Product 26
eq. T.46	eq. T.47	eq. T.48	eq. T.49		

Table T.2: Architecture of the capacity sheet of the COS simulation model

The variables

Below, the variables are given that are used in the equations, which are given in MS Excel syntax. In most equations, we refer to a specific cell in the capacity sheet. In the list below, it can be found what information is found in these cells. All equations are taken from row 100, which therefore is our reference point.

$A$1023 : '1004'
$B$19 to $AA$19 : 'Product 1' to 'product 26'
$C$3 : $\overline{C}$
$C$4 : σ_C
$E$3 : *CL*
$CH$12 to $DH$13 : PS_j
DS$17 to ER$17 : '1' to '26'
Column B to AA : $Ipos_{j,t}$: Computed in equation T.31
Column AD to BC : $RO_{j,t}$: Computed in equation T.32
Column BF to CE : Rank help: Computed in equation T.33
Column CH to DG : Rank of the products: Computed in equation T.34
Column DJ : $C_t - Cneg_{t-1}$: Computed in equation T.35
Column DK : $C_{0,t}$: Computed in equation T.36

Column DL	:	C_t: Computed in equation T.37
Column DM	:	$Cneg_t$: Computed in equation T.38
Column DO	:	$\sum_j Ipos_{j,t}$: Computed in equation T.39
Column DP	:	TPN_t: Computed in equation T.40
Column DR	:	Help for cumulative production on rank: Computed in equation T.41
Column DS to ER	:	Cumulative production on rank: Computed in equation T.42 and T.43
Column EU to FT	:	$TPN_{i,t}$: Computed in equation T.44
Column FW to GV	:	$C_{i,t}$: Computed in equation T.45
Column GY	:	How many production orders needed?: Computed in equation T.46
Column GZ	:	How many production orders possible?: Computed in equation T.47
Column HA	:	How many production orders to produce?: Computed in equation T.48
Column HC to IB	:	$PO_{j,t}$: Computed in equation T.49

The equations
Below, the equations are given in MS Excel syntax. We also refer to the equations in section 5.2 if a link exists.

Equation T.31: The inventory position in week *t*

B100='Product 1'!$AK100

From every product sheet the inventory position in week *t* is copied to this place.

Equation T.32: Run out time in week *t*

AD100=IF(ISERROR(MATCH(0;'Product 1'!$AP100:$BI100;-1));0;MATCH(0;'Product 1'!$AP100:$BI100;-1))

See equation T.18.

Equation T.33: Rank help in week *t*

*BF100=RANK(AD100;$AD100:$BD100;-1)-RAND()*0.1*

See equation T.19.

Equation T.34: Rank of the products in week *t*

CH100=RANK(BF100;$BF100:$CF100;-1)

See equation T.20.

Equation T.35 to T.38: Determination of available capacity in week *t*

Eq. T.35: DJ100=DM99+DL100
Eq. T.36: DK100=DJ100-'Product 27'!B100
Eq. T.37: DL100=NORMINV(RAND();$C$3;$C$4)
Eq. T.38: DM100=MIN(0;DK100-SUM(HC100:IC100))

With this set of equations the available starting capacity of each week is given. It is computed by subtracting the capacity need of MTO products and the negative capacity of last week from available capacity, which is a normally distributed variable.

Equation T.39: Sum of the inventory positions in week *t*

DO100=SUM(B100:AB100)

This is the sum of the inventory positions of all products in week *t* given by equation T.31. This equation is related to equation 5.17.

Equation T.40: Total production need in week *t*

DP100=MAX($E$3-DO100;0)

Just like in equation 5.18 it is computed how much we actually want to make in week *t* based on the total inventory position and the critical level.

Equation T.41: Help for cumulative production on rank in week *t*

DR100=$A$1023-A100+1

See equation T.25.

Equation T.42: Cumulative production on rank in week *t* (rank 1)

DS100=HLOOKUP(HLOOKUP(DS$17;$CH100:$DH$1023;$DR100;FALSE);$CH$12:$DH$13;2;FALSE)

See equation T.26.

Equation T.43: Cumulative production on rank in week *t* (rank 26)

ER100=HLOOKUP(HLOOKUP(ER$17;$CH100:$DH$1023;$DR100;FALSE);$CH$12:$DH$13;2;FALSE)
+EQ100

See equation T.27.

Equation T.44: Cumulative production need left on rank in week *t*

EU100=$DP100-DS100

In this equation, the cumulative production on rank (computed in equation T.27) is subtracted from the total production need from equation T.40.

Equation T.45: Cumulative capacity left on rank in week *t*

FW100=$DK100-DS100

See equation T.28.

Equation T.46: How many production orders are needed in week *t*?

GY100=IF(DP100=0;0;COUNTIF(EU100:FU100;">0")+1)

With this equation it is computed when equation T.44 becomes negative, to know how many production orders are needed in week *t*.

Equation T.47: How many production orders are possible in week *t*?

GZ100=IF(DK100<0;0;COUNTIF(FW100:GW100;">0")+1)

See equation T.29.

Equation T.48: How many production orders to produce in week *t*?

HA100=MIN(GZ100;GY100)

The minimum of equation T.47 and T.48 is the number of production orders that will be produced in week *t*.

Equation T.49: Real production order in week *t*

HC100=IF($HA100-CH100>=0;CH$13;0)

If the rank of this product is smaller or equal to the number of products that we decided to load in equation T.48, a production order is generated for this product in week *t*. The value of equation T.7 comes from this equation. Equation T.41 to T.49 are related to equation 5.13, 5.16, 5.19, 5.20 and 5.21, but a one-on-one relation can not be made.

T.3.3 Capacity sheet of the HCS simulation model

As said before, the HCS simulation model is a combination of the POS model and the COS model. Fastmovers are controlled by the COS, and slowmovers by the POS, and slowmovers have priority above fastmovers. The capacity sheet is therefore split in two parts: a slowmover part and a fastmover part. The 22 slowmovers are controlled by equation T.17 to T.30, and the fastmovers are controlled by equation T.31 to T.49. The only difference is that available capacity ($C_{0,t}$) for fastmovers in week *t* is not given by equation T.36, but it is the rest capacity of slowmovers in week *t*, given by equation t.28.

Appendix U: Warm up period and number of replications

In this appendix, we will show how the warm up period has been determined in section U.1, and we will give the Visual Basic macro to execute 25 simulation runs in a row in section U.2.

U.1 Warm up period

A steady state simulation implies that a simulation has reached a point in time where the state of the simulation is independent of the initial start-up conditions. The amount of time required to achieve steady-state conditions is referred to as the warm up period. Data collection begins after the warm up period is completed. We used the Welch graphical method to determine the warm up period in our simulation (Liman et al., 2004).

The warm up period is determined for all three simulation models under the same situation:

1. All parameters are set to the values currently used within Organon, including safety stock in the POS and the hybrid model.
2. The utilization rate of operators is set at ρ = xx%.
3. The starting inventory is computed by equation 5.4 for the POS and slowmovers in the HCS, and by equation 5.5 for the COS and fastmovers in the HCS. This ensures that inventories at the start of the simulation are already representative.
4. We made 10 replications for a period of 1000 weeks.

The observed variable to determine the warm up period is the amount of capacity stored in the inventories of the products. In figure U.1 a graphical representation can be found of the moving average over the average over the replications of the observed variable. (MA = 5 and MA = 20). Figure U.1 is the result of the COS model, but we have similar results for the POS model and the HCS model. It can be seen that the amount of capacity stored in the inventories stays approximately stable from the start, caused by the representative starting inventory. To be sure that we collect data from a steady state simulation, and for reasons of model building simplicity, we decide to set the warm up period at 100 periods. This means that we also use the warm up period of 100 periods when the simulation parameters are set at other levels. But because we used the most extreme case to determine the warm up period, it is valid to assume that a warm up period of 100 periods is enough to reach a steady state system in all other simulation runs.

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Figure U.1 Amount of capacity stored in inventories to determine warm up period

U.2 Visual Basic macro simulation models

```
Option Explicit

Sub Macro1()

' Macro1 Macro
' Macro recorded 21-9-2006 by N.V. Organon / Diosynth B.V.

Dim V As Long
Dim R As Long
Dim Num As Integer
Dim K As Long

Calculate

R = 2

For Num = 1 To 25
   Calculate
   R = R + 1
   For K = 2 To 146
      If Not IsError(Worksheets("Performance hulp").Cells(3, K)) Then
         V = Worksheets("Performance hulp").Cells(3, K)
      Else
         V = 0
      End If
      Worksheets("Uitkomsten").Cells(R, K) = V
   Next K

Next

Calculate

End Sub
```

Appendix V: Model error

A model is a simplified representation of the reality with the goal to obtain insights about the reality. But not every aspect of the reality can be integrated in the model, and therefore, applying the settings from the model in a real life setting can lead to different results. The difference in results from the model and from reality is called the model error, and the goal of this section is to gain more insight in the model error of our simulation study.

Simulation experiment with current settings

The current production and inventory strategy comes close to a product oriented strategy. Therefore, a first impression of the model error is obtained by running the POS simulation model with current safety stock settings. Because we are not sure about the exact utilization rate of operators, a simulation experiment is done with ρ = xx%, and one with ρ = xx%. The results are given in table V.1 and V.2. In these tables it is found what the simulated average service level was, what the simulated average utilization rate was, and what the simulated average inventory investment was. Furthermore, the lower and upper bound of the 95% confidence interval are given.

Current situation 1				
Goal:		**Utilization rate**	**xx%**	
	Strategy	*Service level*	*Utilization rate*	*Inventory investment*
Average	POS			
LB - UB				

Table V.1: Simulation results of current situation with ρ = *xx%*

Current situation 2				
Goal:		**Utilization rate**	**xx%**	
	Strategy	*Service level*	*Utilization rate*	*Inventory investment*
Average	POS			
LB - UB				

Table V.2: Simulation results of current situation with ρ = *xx%*

It is remarkable to see that the service level in the simulation experiments is much larger than the real service levels, which have been on average xx%. Probably, the most important reason for this difference comes from the fact that historical inventory levels have been too low. In figure J.4, we already showed historical inventory levels, and including leveling stock, the average inventory has been xx million tablets, while in the simulation experiment average inventory, excluding leveling stock, has been xx million tablets for ρ = xx%, and xx million tablets for ρ = xx%.

Although the analysis above already gives some insight in the model error, there are many more aspects that have an influence on the model error. First, reasons will be given how in reality higher availability levels can be obtained compared to the simulation study, and then it will be explained why lower availability levels can be obtained in reality.

Reasons why availability can be higher in reality

- Achieving the desired service level is not only done by safety stocks, but also by using slack capabilities. For example, lead times of the production or the release process can be reduced to some extent if this is needed, and therefore, products will be available before the end of the normal lead time. This is especially relevant if a product is disapproved by the Quality Department, because in that case, the lead time can be reduced with a few weeks.

- The planners of bulk tablets look forward in time, and therefore, to some extent, they can prevent capacity shortages in the future by rescheduling orders and building up some extra inventories or by requesting some extra operator capacity in the from of flexible workforce or overtime.

- Actual performance is based on bulk availability levels at the 'calculated RR'-date. This date is based on the actual replenishment order and the norm lead times of the packaging activities. The performance in the simulation model is based on the actual RR-date. This is the date at which bulk should be available based on the packaging order. The actual RR-date is on

average xx weeks before the actual bulk usage[55], while the calculated RR-date is on average xx weeks before the actual bulk usage[56]. Thus, in the simulation study, bulk should be available xx weeks earlier than in reality.

- The demand forecast for bulk tablets is assumed to be stable in the simulation study, but in reality we see that demand is over forecasted a little. On average, actual demand for bulk tablets is xx% lower than the demand forecast of xx weeks ago.

Reasons why availability can be lower in reality

The reasons that bulk availability can be lower in reality compared to the simulation study can be placed in three categories:

1. Neglected uncertainties in the simulation study
2. The method used to measure bulk availability
3. Current planning method versus product oriented strategy

1. *Neglected uncertainties in the simulation model*

- The lead time, including review time is never more than xx weeks in the simulation model. We made this modeling decision because we believe that any order can be released within xx weeks if it is really needed. But this positively influences the results of the simulation study.

- In reality there is a probability that the yield of a production order is disappointing, while in our simulation study it is assumed that the yield is deterministic. Furthermore, machine problems are not considered in the simulation model.

- In our simulation study, it is assumed that a production order can be released if there is any capacity left. This means that only 1 hour of capacity is enough to release an order. Although the excess capacity that is used in week t is corrected with the available capacity in week $t+1$, this assumption has a positive effect on the results of the simulation study.

- In our simulation study we have an overshoot. If we expect to go below safety stock in week $t+L_{norm}$, then a production order is released. Because this production order comes available in week $t+L_{norm}$, the lowest end inventory level is in week $t+L_{norm}-1$, and on average, this end inventory level is above safety stock.

- Bulk products can expire, or it can happen that a Local Company does not approve to receive an 'old' bulk product, with the consequence that some inventory just 'disappears'. This is not considered in the simulation study.

- API's or excipients can be unavailable when a production order needs to be opened, and therefore production must be started later. This is not considered in our model.

- In the simulation model it is not considered that setup times can be sequence dependent, while in reality, some sequences are preferred, because they lead to lower cleaning times.

- Only operator capacity is considered in the model. Although machines are not highly utilized, it is still possible that a production order cannot be opened yet because a machine is processing another order.

2. *The method used to measure bulk availability*

Actual bulk availability is measured in the following way:

- For each packaging order it is registered which bulk batch is used.
- Then it is checked whether this bulk batch was released at the calculated RR-date.
- The calculated RR-date is computed by subtracting the norm lead time of the packaging activities from the replenishment order date.

[55] This is computed by comparing expected demand for week $t+1$ with actual demand for all MTS bulk tablets for the period of June 2005 to May 2006.

[56] This is computed by comparing the date of opening a packaging order and the calculated RR date for all MTS bulk tablets for the period of August 2005 to July 2006.

This method to measure bulk availability negatively influences the performance. It is estimated by the responsible packaging planner that about xx% of the packaging orders do not use released bulk tablets, while there are released bulk tablets available. For example, if there are two small batches released, and one large batch is unreleased, the large batch is often preferred for a large packaging order. Another example is that a bulk batch is rejected for a certain Local Company. If that Local Company places a replenishment order, it can happen that an unreleased bulk batch needs to be used, while there is a released bulk batch available too.

In the simulation model, an out-of-stock is defined in another way. It is reported if the end inventory of a certain bulk product is negative and if there is demand for that bulk product in that week. The number of out-of-stocks is compared to the number of weeks with demand. Dividing these two by each other gives the bulk availability.

3. *Current planning method versus product oriented strategy*

   - The product oriented strategy is probably better than the current planning method, because the decision which production order should be released is made at the last possible moment. In reality, the production planner tries to keep the production plan of the coming xx months stable, and only makes considerable changes to the plan when he thinks it is really needed. Therefore, the production plan is mostly based on old information. Furthermore, in the simulation study, the production decision is only based on aspects like expected inventory levels and capacities, and cannot be negatively influenced by other less interesting factors.

   - The last two years, the focus was on high MRP-availability levels, in stead of high availability levels of released bulk tablets. Therefore, a lot of bulk products were packed unreleased. Often, bulk tablets were released after they were stripped.

Conclusion

Taken all the qualitative aspects described above into account it is very hard to make an estimation of the model error. But still, we need to make one. Considering the fact that our simulation experiment reached a much higher service rate with current safety stock settings than has been done in reality, we have decided that we need to model a service rate of xx% to obtain an xx% service rate in reality. However, because the low real service rates can be caused too by the current inventory levels that are quite low, we also decided to make some simulation experiments under an xx% service rate.

However, it should be realized that it does not have to be a problem if our estimation of the model error is not completely correct, because the goal of the simulation experiments is to compare the three planning strategies with each other, not with reality. Because the aspects given in this appendix have the same effect on the three simulation models, the model error does not influence the decision which strategy is best. For example, if we do not consider that API's can be unavailable, it does not matter whether the planning strategy is the POS, the COS, or the HCS.

Appendix W: Relation between utilization rate and lead times

Under stochastic demand, the lead time of an order is related to the utilization rate of the resource needed to produce the order. If a resource has a low utilization rate, than there is only a small probability that a new production order arrives and needs to wait until the resource becomes available again. However, under high utilization rates, the resource is probably not available if a new order arrives, and probably, there is even a queue of waiting orders in front of the new order. Therefore, the lead time under high utilization rates is much larger.

However, we assumed that the lead time distribution is the same in all simulation experiments (from a utilization rate of ρ = xx% to ρ = xx%). This can be assumed because a production order is only opened if there is enough capacity available, and the lead time only starts if a production order is opened. The waiting time of a production order, before it can be opened, is not part of the lead time. We have studied the waiting time before a production order can be opened under different simulation settings by performing extra simulation experiments. The results are given in table W.1. It can be seen that the waiting time is larger if the utilization rate is higher, which shows that there is a relation between lead times and utilization rates in our simulation experiments too. However, this waiting time is not part of our lead time, and therefore it can be assumed that the lead time distribution after the production order is opened, is the same in all simulation experiments.

Still, it can be argued that the production process will be done a little faster if ρ = xx% in stead of ρ = xx%. We agree on this point, but this is only a small difference, mainly caused by the way that detailed schedules are made, because the aim of detailed scheduling is to make sure that production orders are finished within the norm lead time, and because a production order will not be opened, if it is expected that it is not possible to finish it within the norm lead time.

A last point we would like to make is that the way to compute initial safety stocks for the POS model is not completely correct, because under infinite capacity, the lead time is just shorter than the lead time distribution we used. However, it must be noted that we compute *initial* safety stocks. We just need a starting point for the simulation experiments under higher utilization rates.

Average waiting time before a production order is opened					
	Service rate				
	Utilization rate				
Product name	Product ID	Average waiting time (in weeks)			
TOTAL					
CERAZETTE					
LIVIAL 2,5MG NS					
MARVELON Z.ME					
REMERON 30MG CTO NB					
DESO/EE-50/35 PS CT					
DESO/EE-100/30 PS CT					
EXLUTON					
MARVELON Z.ME CT					
MARVELON Z.ME ZO					
MERCILON					
MINISTAT					
ORADEXON 0,5MG					
ORADEXON 1,5MG					
ORGAMETRIL					
OVESTIN 1MG 6MM					
OVESTIN 1MG ZO					
OVESTIN 2MG					
OVESTIN 2MG ZO					
PLACEBO CT					
PLACEBO WIT ZO					
REMERON 15MG CTO NB					
THYRAX 0,025MG DT ZO					
THYRAX 0,1MG DT ZO					
TOLVON 10MG CT					
TOLVON 30MG CTO					
TOLVON 60MG CTO					

Table W.1: Average waiting time in weeks before a production order is opened

Appendix X: Detailed results of the simulation experiments

In this appendix, more detailed results of the simulation experiments are given. For each simulation experiment, the simulated service level, the simulated utilization rate, and the inventory investment can be found. Furthermore, the lower bound and the upper bound of the 95% confidence intervals are given. The lower and upper bound are computed by equation X.1 (Di Bucchianico, 2000).

$$C.I.(95\%) = \bar{x} \pm t_{\alpha/2,N-1} \cdot \frac{s}{\sqrt{N}} \qquad (X.1)$$

where;

$\bar{x}$	:	Average of the data set
$t_{\alpha/2,N-1}$	:	A value from the Student t-distribution, where *N-1* is the degrees of freedom and α = 0.05 (the level of significance)
s	:	Standard deviation of the data set
N	:	Number of simulation runs

To test whether one of the three strategies is significantly better than the others, we use equation X.2 and X.3 (Di Bucchianico, 2000). The inventory investment is the parameter used to compare the performance of the three strategies. However, equation X.2 and X.3 are also used to compare the simulated service level and the simulated utilization rate, because a fair comparison on inventory investment can only be made if there is no significant difference in simulated service level or simulated utilization rate.

$$|t_0| = \frac{|\bar{x}_1 - \bar{x}_2|}{\sqrt{\frac{s_1^2}{N_1} + \frac{s_2^2}{N_2}}} \geq t_{\alpha/2,v} \qquad (X.2)$$

$$v = \frac{\left(\frac{s_1^2}{N_1} + \frac{s_2^2}{N_2}\right)^2}{\frac{(s_1^2/n_1)^2}{n_1+1} + \frac{(s_2^2/n_2)^2}{n_2+1}} - 2 \qquad (X.3)$$

For each comparison between simulation experiments we made, no significant difference has been found between the simulated service level, and the simulated utilization rate, which is a good result.

Simulation experiments 1 to 3				
Goal:	**Service level**	**xx%**	**Utilization rate**	**xx%**
	Strategy	*Service level*	*Utilization rate*	*Inventory investment*
Average	POS			
LB - UB				
Average	COS			
LB - UB				
Average	Hybrid			
LB - UB				

Table X.1: Simulation experiment 1 to 3. Goal: Service level = xx%, ρ = xx%

The inventory investment for the POS is significantly lower than for the COS and the HCS in table X.1.

Simulation experiments 4 to 6				
Goal:	Service level	xx%	Utilization rate	xx%
	Strategy	*Service level*	*Utilization rate*	*Inventory investment*
Average **LB - UB**	POS			
Average **LB - UB**	COS			
Average **LB - UB**	Hybrid			

Table X.2: Simulation experiment 4 to 6. Goal: Service level = xx%, ρ = xx%

The inventory investments for the POS and the COS are significantly lower than for the HCS in table X.2.

Simulation experiments 7 to 9				
Goal:	Service level	xx%	Utilization rate	xx%
	Strategy	*Service level*	*Utilization rate*	*Inventory investment*
Average **LB - UB**	POS			
Average **LB - UB**	COS			
Average **LB - UB**	Hybrid			

Table X.3: Simulation experiment 7 to 9. Goal: Service level = xx%, ρ = xx%

The inventory investment for the POS is significantly lower than for the COS and the HCS in table X.3. The inventory investment for the HCS is significantly lower than for the COS in table X.3.

Simulation experiments 10 to 12				
Goal:	Service level	xx%	Utilization rate	xx%
	Strategy	*Service level*	*Utilization rate*	*Inventory investment*
Average **LB - UB**	POS			
Average **LB - UB**	COS			
Average **LB - UB**	Hybrid			

Table X.4: Simulation experiment 10 to 12. Goal: Service level = xx%, ρ = xx%

No significant differences in inventory investment can be found in table X.4.

Simulation experiments 13 to 15				
Goal:	Service level	xx%	Utilization rate	xx%
	Strategy	*Service level*	*Utilization rate*	*Inventory investment*
Average **LB - UB**	POS			
Average **LB - UB**	COS			
Average **LB - UB**	Hybrid			

Table X.5: Simulation experiment 13 to 15. Service level = xx%, ρ = xx%

The inventory investments for the POS and the COS are significantly lower than for the HCS in table X.5.

Simulation experiments 16 to 18 (N = 50)				
Goal:	**Service level**	**xx%**	**Utilization rate**	**xx%**
	Strategy	*Service level*	*Utilization rate*	*Inventory investment*
Average	POS			
LB - UB				
Average	COS			
LB - UB				
Average	Hybrid			
LB - UB				

Table X.6: Simulation experiment 16 to 18. Goal: Service level = xx%, ρ = xx%

The inventory investments for the POS and the COS are significantly lower than for the HCS in table X.6.

Distribution of stock over the products: POS compared to COS

(in 1000 tablets)	Product ID / Product name	Total	CERAZET TE	LIVIAL 2,5MG NS	MARVELO N Z.ME	REMERON 30MG CTO NB	DESO/EE-50/35 PS CT	DESO/EE-100/30 PS CT	EXLUTON	MARVELO N Z.ME CT	MARVELO N Z.ME ZO	MERCILO N	MINISTAT	ORADEXO N 0,5MG	ORADEXO N 1,5MG
Service rate	**POS - ss**														
Utiliz rate	POS - av inv														
	POS - %														
Critical level	COS - av inv														
COS (h cap)	COS - %														
	COS/POS		116%	117%	99%	114%	98%	92%	100%	104%	95%	88%	96%	76%	95%
Service rate	**POS - ss**														
Utiliz rate	POS - av inv														
	POS - %														
Critical level	COS - av inv														
COS (h cap)	COS - %														
	COS/POS		110%	117%	102%	117%	90%	95%	97%	100%	94%	72%	92%	76%	89%
Service rate	**POS - ss**														
Utiliz rate	POS - av inv														
	POS - %														
Critical level	COS - av inv														
COS (h cap)	COS - %														
	COS/POS		112%	123%	102%	118%	88%	90%	102%	100%	90%	73%	91%	69%	73%
Service rate	**POS - ss**														
Utiliz rate	POS - av inv														
	POS - %														
Critical level	COS - av inv														
COS (h cap)	COS - %														
	COS/POS		105%	120%	104%	119%	90%	89%	103%	103%	88%	70%	90%	69%	74%
Service rate	**POS - ss**														
Utiliz rate	POS - av inv														
	POS - %														
Critical level	COS - av inv														
COS (h cap)	COS - %														
	COS/POS		105%	118%	107%	111%	88%	88%	103%	99%	83%	67%	89%	68%	73%
Service rate	**POS - ss**														
Utiliz rate	POS - av inv														
	POS - %														
Critical level	COS - av inv														
COS (h cap)	COS - %														
	COS/POS		106%	118%	107%	115%	87%	92%	96%	96%	81%	65%	87%	70%	73%

Table X.7 continues at the next page

Distribution of stock over the products: POS compared to COS (continued)

(in 1000 tablets)	Product ID / Product name	ORGAMET RIL	OVESTIN 1MG 6MM	OVESTIN 1MG ZO	OVESTIN 2MG	OVESTIN 2MG ZO	PLACEBO CT	PLACEBO WIT ZO	REMERON 15MG CTO NB	THYRAX 0,025MG DT ZO	THYRAX 0,1MG DT ZO	TOLVON 10MG CT	TOLVON 30MG CTO	TOLVON 60MG CTO
Service rate	**POS - ss**													
Utiliz rate	POS - av inv													
	POS - %													
Critical level	COS - av inv													
COS (h cap)	COS - %													
	COS/POS	107%	100%	98%	98%	94%	93%	100%	76%	96%	92%	106%	109%	89%
Service rate	**POS - ss**													
Utiliz rate	POS - av inv													
	POS - %													
Critical level	COS - av inv													
COS (h cap)	COS - %													
	COS/POS	99%	103%	100%	98%	96%	94%	101%	78%	107%	101%	101%	109%	94%
Service rate	**POS - ss**													
Utiliz rate	POS - av inv													
	POS - %													
Critical level	COS - av inv													
COS (h cap)	COS - %													
	COS/POS	105%	98%	89%	111%	92%	95%	95%	72%	140%	130%	103%	118%	85%
Service rate	**POS - ss**													
Utiliz rate	POS - av inv													
	POS - %													
Critical level	COS - av inv													
COS (h cap)	COS - %													
	COS/POS	103%	102%	90%	108%	88%	91%	99%	73%	157%	127%	101%	121%	81%
Service rate	**POS - ss**													
Utiliz rate	POS - av inv													
	POS - %													
Critical level	COS - av inv													
COS (h cap)	COS - %													
	COS/POS	102%	97%	87%	106%	88%	93%	97%	76%	153%	146%	98%	114%	85%
Service rate	**POS - ss**													
Utiliz rate	POS - av inv													
	POS - %													
Critical level	COS - av inv													
COS (h cap)	COS - %													
	COS/POS	99%	95%	89%	99%	84%	91%	97%	81%	188%	171%	95%	107%	81%

Table X.7: Distribution of stock over the products

Legend of table X.7

POS ss	:	Safety stock of product *j* in the POS simulation experiment (in 1000 tablets)
POS av inv	:	Average weekly inventory of product *j* in the POS simulation experiment (in 1000 tablets)
POS %	:	Relative inventory of product *j* in the POS simulation experiment. Computed by equation X.4
COS av inv	:	Average weekly inventory of product *j* in the COS simulation experiment (in 1000 tablets)
COS %	:	Relative inventory of product *j* in the COS simulation experiment. Computed by equation X.4
COS/POS	:	Relative inventory of product *j* in the COS simulation experiment compared with relative inventory of product *j* in the COS simulation experiment. See equation X.5.

$$Irel_j = \frac{\bar{I}_j}{\sum_j \bar{I}_j} \qquad (X.4)$$

$$COS/POS = \frac{Irel_j(COS)}{Irel_j(POS)} \qquad (X.5)$$

Appendix Y: Outside inventory target rate and coefficient of variation in inter production times

Y.1 Product oriented strategy

Outside inventory target rate and coefficient of variation in inter production times (POS)									
		Service rate Utiliz rate		Service rate Utiliz rate		Service rate Utiliz rate		Service rate Utiliz rate	
Product name	Product ID	Outside inv target rate	Coef of var inter prod time	Outside inv target rate	Coef of var inter prod time	Outside inv target rate	Coef of var inter prod time	Outside inv target rate	Coef of var inter prod time
TOTAL									
CERAZETTE									
LIVIAL 2,5MG NS									
MARVELON Z.ME									
REMERON 30MG CTO NB									
DESO/EE-50/35 PS CT									
DESO/EE-100/30 PS CT									
EXLUTON									
MARVELON Z.ME CT									
MARVELON Z.ME ZO									
MERCILON									
MINISTAT									
ORADEXON 0,5MG									
ORADEXON 1,5MG									
ORGAMETRIL									
OVESTIN 1MG 6MM									
OVESTIN 1MG ZO									
OVESTIN 2MG									
OVESTIN 2MG ZO									
PLACEBO CT									
PLACEBO WIT ZO									
REMERON 15MG CTO NB									
THYRAX 0,025MG DT ZO									
THYRAX 0,1MG DT ZO									
TOLVON 10MG CT									
TOLVON 30MG CTO									
TOLVON 60MG CTO									

Table Y.1: Outside inventory target rate and coefficient of variation in inter production times (POS)

Y.2 Capacity oriented strategy

Coefficient of variation in inter production times (COS)					
		Service rate Utiliz rate	Service rate Utiliz rate	Service rate Utiliz rate	Service rate Utiliz rate
Product name	**Product ID**	coef of var inter prod time	coef of var inter prod time	coef of var inter prod time	coef of var inter prod time
TOTAL					
CERAZETTE					
LIVIAL 2,5MG NS					
MARVELON Z.ME					
REMERON 30MG CTO NB					
DESO/EE-50/35 PS CT					
DESO/EE-100/30 PS CT					
EXLUTON					
MARVELON Z.ME CT					
MARVELON Z.ME ZO					
MERCILON					
MINISTAT					
ORADEXON 0,5MG					
ORADEXON 1,5MG					
ORGAMETRIL					
OVESTIN 1MG 6MM					
OVESTIN 1MG ZO					
OVESTIN 2MG					
OVESTIN 2MG ZO					
PLACEBO CT					
PLACEBO WIT ZO					
REMERON 15MG CTO NB					
THYRAX 0,025MG DT ZO					
THYRAX 0,1MG DT ZO					
TOLVON 10MG CT					
TOLVON 30MG CTO					
TOLVON 60MG CTO					

Table Y.2: Coefficient of variation in inter production times (COS)

Appendix Z: New safety stock proposal

New safety stock											
		Service rate Utiliz rate		Service rate Utiliz rate		Service rate Utiliz rate		Service rate Utiliz rate					
Product name	**Product ID**	Investment in safety stock	Relative	Investment in safety stock	Relative	Investment in safety stock	Relative	Investment in safety stock	Relative	Average relative investment	Current investment	New safety stock investment	**New safety stock (*1000 tab)**
CERAZETTE													
LIVIAL 2,5MG NS													
MARVELON Z.ME													
REMERON 30MG CTO NB													
DESO/EE-50/35 PS CT													
DESO/EE-100/30 PS CT													
EXLUTON													
MARVELON Z.ME CT													
MARVELON Z.ME ZO													
MERCILON													
MINISTAT													
ORADEXON 0,5MG													
ORADEXON 1,5MG													
ORGAMETRIL													
OVESTIN 1MG 6MM													
OVESTIN 1MG ZO													
OVESTIN 2MG													
OVESTIN 2MG ZO													
PLACEBO CT													
PLACEBO WIT ZO													
REMERON 15MG CTO NB													
THYRAX 0,025MG DT ZO													
THYRAX 0,1MG DT ZO													
TOLVON 10MG CT													
TOLVON 30MG CTO													
TOLVON 60MG CTO													
Total investment													

Table Z.1: New safety stock proposal

Legend of table Z.1:

Investment in safety stock	:	This is the safety stock of product *j* of the simulation experiment multiplied by the cost price of product *j*. See equation Z.1
Relative	:	Relative investment in safety stock of product *j*. See equation Z.2
Average relative investment	:	This is the average over the four relative investments in safety stock of product *j*
Current investment	:	This is the current investment in safety stock of product *j*, computed by equation Z.1, where ss_j is the current safety stock.
New safety stock investment	:	This is the average relative investment of product *j* multiplied by the total current investment
New safety stock	:	This is the new safety stock investment of product *j* divided by its cost price.

Investment in safety stock of product j = $ss_{inv,j} = ss_j * cp_j$ *(Z.1)*

Relative investment in safety stock of product j = $ss_{rel.inv,j} = \frac{ss_{inv,j}}{\sum_j ss_{inv,j}}$ *(Z.2)*

The proposed safety stock for Product xy is much smaller than the current safety stock. The reason that the current safety stock is xx million tablets is because POO wants a safety cover to be able to deliver large tender orders from stock. Currently, there is a discussion at POO whether this large safety stock of xx million tablets is needed.

The proposed safety stock for Product yx is much larger than the current safety stock. Because most times demand is a full batch from the production site in Ireland, a smaller safety stock is possible.

Appendix AA: Initial safety stocks and standard deviation average weekly demand

Initial safety stocks and standard deviation average weekly demand				
Product name	**Product ID**	Initial safety stock (*1000 tab), service rate = xx%	Initial safety stock (*1000 tab), service rate = xx%	Standard deviation average weekly demand (*1000 tab)
CERAZETTE				
LIVIAL 2,5MG NS				
MARVELON Z.ME				
REMERON 30MG CTO NB				
DESO/EE-50/35 PS CT				
DESO/EE-100/30 PS CT				
EXLUTON				
MARVELON Z.ME CT				
MARVELON Z.ME ZO				
MERCILON				
MINISTAT				
ORADEXON 0,5MG				
ORADEXON 1,5MG				
ORGAMETRIL				
OVESTIN 1MG 6MM				
OVESTIN 1MG ZO				
OVESTIN 2MG				
OVESTIN 2MG ZO				
PLACEBO CT				
PLACEBO WIT ZO				
REMERON 15MG CTO NB				
THYRAX 0,025MG DT ZO				
THYRAX 0,1MG DT ZO				
TOLVON 10MG CT				
TOLVON 30MG CTO				
TOLVON 60MG CTO				

Table AA.1: Initial safety stocks and standard deviation average weekly demand

Appendix AB: Architecture of the operational tool

AB.1 Input sheet

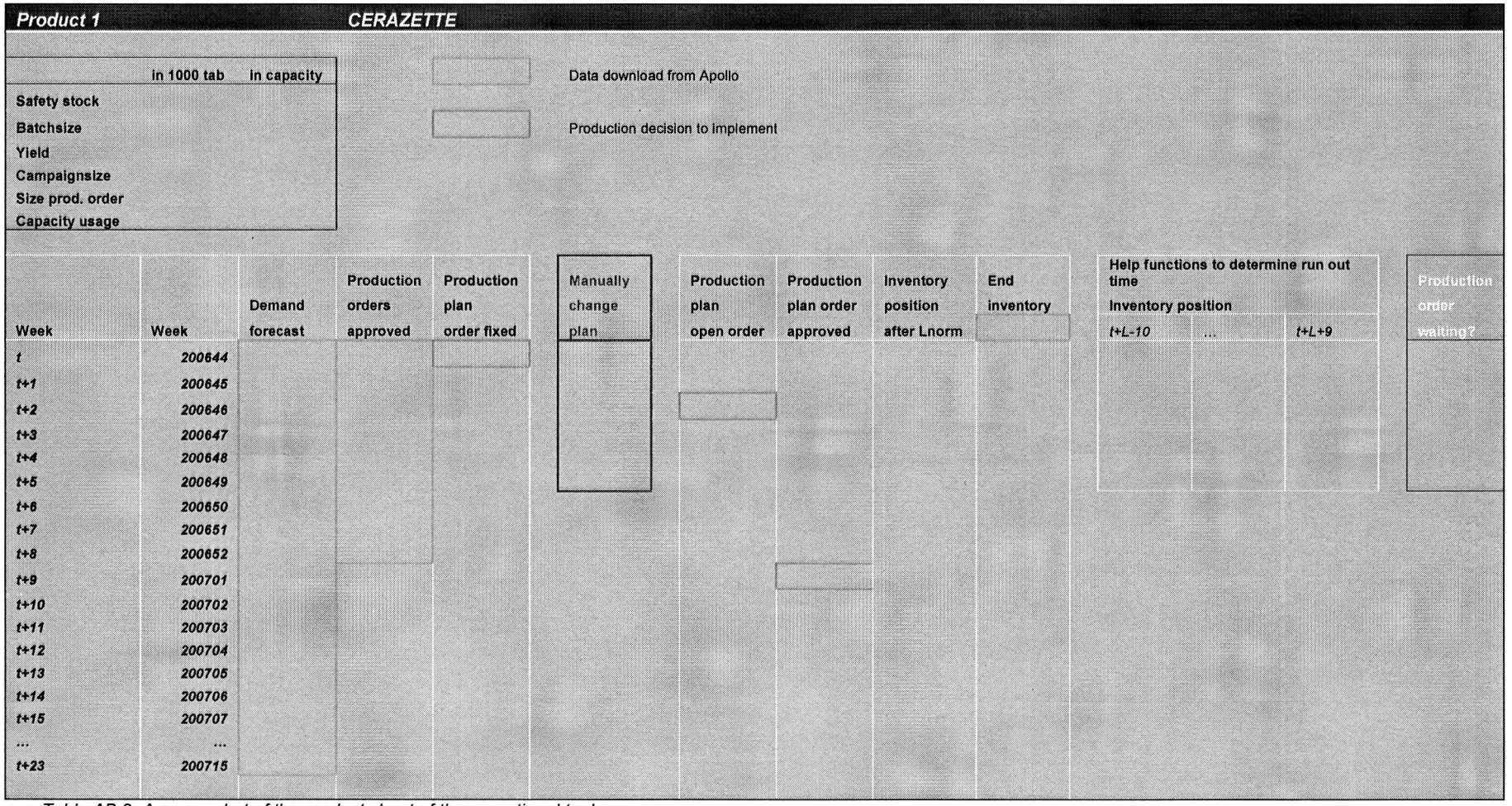
Operational tool Input sheet	product oriented strategy					
	MTS products -->					
Settings	CERAZETTE Product 1	LIVIAL 2,5MG NS Product 2	MARVELON Z.ME Product 3	REMERON 30MG CTO NB Product 4	DESO/EE-50/35 PS CT Product 5	... ...
Safety stock (in 1000 tab)						...
Batch size (in 1000 tab)						...
Yield (%)						
Campaign size						...
Capacity usage (h / 1000 tab)						...
Cost price (per 1000 tab)						...

Week	Available operator capacity (netto h)
t	
t+1	
t+2	
t+3	
...	
t+7	

The 'negative capacity' of last week is given here

Table AB.1: A screenshot of the input sheet of the operational tool

AB.2 Product sheet



Product 1	CERAZETTE

	in 1000 tab	in capacity
Safety stock		
Batchsize		
Yield		
Campaignsize		
Size prod. order		
Capacity usage		

Data download from Apollo

Production decision to implement

Week	Week	Demand forecast	Production orders approved	Production plan order fixed	Manually change plan	Production plan open order	Production plan order approved	Inventory position after Lnorm	End inventory	Help functions to determine run out time Inventory position t+L-10	...	t+L+9	Production order waiting?
t	200644												
t+1	200645												
t+2	200646												
t+3	200647												
t+4	200648												
t+5	200649												
t+6	200650												
t+7	200651												
t+8	200652												
t+9	200701												
t+10	200702												
t+11	200703												
t+12	200704												
t+13	200705												
t+14	200706												
t+15	200707												
...	...												
t+23	200715												

Table AB.2: A screenshot of the product sheet of the operational tool

The product sheet has been organized in the following way. Row 19 (week *t+5*) is taken as the reference row.

- In the upper left square surrounded by red lines, the data from the input sheet can be found.
  - *B4* : Safety stock of product *j*
  - *B5* : Batch size of product *j*
  - *B6* : Yield % of product *j*
  - *B7* : Campaign size of product *j*
  - *B8* : Production order size of product *j* = *B5*B6*B7*
  - *B9* : Capacity usage of product *j* (cu_j)
  - *C8* : Production order size of product *j* in hours of operator work = *B8*B9*

- In column B, the weeks for which the production plan is made are found. See equation AB.1. This data is imported into the 'production input sheet' from a report from Apollo.

  B19='Production input'!A11 *(AB.1)*

- In column C (Demand forecast) surrounded by orange lines, the demand forecast for the specific bulk product can be found. See equation AB.2. This data is imported into the 'demand input sheet' from a report from Apollo.

  C19=IF(ISERROR(HLOOKUP($B$1,'Demand input'!$1:$21,11,FALSE)/1000),0,HLOOKUP($B$1,'Demand input'!$1:$21,11,FALSE)/1000) *(AB.2)*

- In column D (Production orders approved), it can be found when it is expected that already opened production orders, or production orders in the fixed period are expected to be approved by the Quality Department. See equation AB.3. This data is imported into the 'production input sheet' from a report from Apollo.

  D19=IF(ISERROR(HLOOKUP($B$1,'Production input'!$1:$21,11,FALSE)/1000),0,HLOOKUP($B$1,'Production input'!$1:$21,11,FALSE)/1000) *(AB.3)*

- In column E (Production plan order fixed), the production plan can be found. The production order is found in the week when it needs to enter the fixed horizon. For MTS products, this data comes from the capacity sheet, because in the capacity sheet it is computed when which production order is opened. See equation AB.4. For MTO products, a production order is based on the inventory position of that product. Furthermore, for MTO products, it is checked whether the production plan has been changed manually in column G. See equation AB.5. For MTS products this check is done in the capacity sheet.

  E19=Capacity!GM19/$B$9 *(AB.4)*

  E19=IF(G14="";IF(K14<$B$4;$B$8;0);G14) *(AB.5)*

- In column G (manually change plan) it is given if the production plan has been changed manually in the production plan sheet. See equation AB.6.

  G19=IF('Production plan'!D34="";"";'Production plan'!D34) *(AB.6)*

- In column I (Production plan open order) the production plan is found in the week that the production order needs to be opened. This is just xx weeks later than the week in which the production order had been fixed.

- In column J (Production plan order approved) the production plan is found in the week that the production order is expected to be approved by the Quality Department. This is xx weeks later than the week in which the production order had been opened.

- In column K (Inventory position after Lnorm) the inventoy position is found. If the inventory position falls below the safety stock, a production need is created for MTS products, and a production order is created for MTO products. (For MTO products, the safety stock is zero.) The inventory position is computed by equation AB.7.

K19=L18+SUM(D19:D27)+SUM(J19:J27)-SUM(C19:C28) *(AB.7)*

- In column L (End inventory) the expected inventory at the end of the week bucket can be found. See equation AB.8.

L19=L18-C19+D19+J19 *(AB.8)*

- In column N to AG (Help functions to determine run out time) it is computed when the inventory position of MTS products is expected to fall below zero. For example, the expected inventory two weeks after the norm lead time is computed by equation AB.9.

Z19=Y19-C30 *(AB.9)*

- In column AI (Production order waiting?) it is given when a production order of a MTS product needs to be produced, but it has to wait, because there is not enough capacity available. See equation AB.10.

AI19=IF(AND(K19<$B$4;E19=0);"wait";"") *(AB.10)*

AB.3 Capacity sheet

To make it possible that the production plan proposed by the operational tool can be manually adjusted, and that a new plan is computed based on the manual adjustments, two equations of the POS simulation model had to be changed in the capacity sheet of the operational tool.

For MTS products, equation T.17 to compute the production need in week *t* has been changed in equation AB.11. Row 19 is the reference row.

D19=IF('Product 1'!$G19="";IF('Product 1'!$K19<'Product 1'!$B$4;'Product 1'!$C$8;0);
'Product 1'!$G19*'Product 1'!$B$9) *(AB.11)*

Equation AB.11 first checks if a manual change has been proposed in column G of the product sheet. If a manual change has been proposed, this manual change is the result of the equation, otherwise, the production need is computed based on the inventory position.

For MTO products, equation T.17 to compute the production need in week *t* has been changed in equation AB.12. Row 19 is the reference row.

AD19=IF('Product 27'!$G19="";'Product 27'!$E19'Product 27'!$B$9;'Product 27'!$G19*'Product 27'!$B$9)*
(AB.12)

Similar to equation AB.11, equation AB.12 first checks of the production plan has been changed manually. The difference between equation AB.11 and AB.12 is that for MTO products, the production orders are computed in the product sheets, instead of the capacity sheet. Therefore, the production order is already given for MTO products, and not the production need.

Equation T.19 to compute the rank help in week *t* has been changed in equation AB.13. Row 19 is the reference row.

BV19=IF('Product 1'!$G19="";RANK(AT19;$AT19:$BT19;-1)+RAND()*0.1;IF('Product 1'!$G19=0;
*100+RAND()*0.1;RAND()*0.1))* *(AB.13)*

If there is no manual change in the production plan, the rank help of equation AB.13 is similar to equation T.19. However, if the production order is manually set at zero, the product receives rank 100, and therefore, will never be produced. If a production order is manually created, the product receives rank 0, and therefore, it will have the highest priority.

AB.4 Production plan sheet

Production plan sheet

MTS products -->

Production order fixed Week	Production order open Week	Week	CERAZETTE Product 1	LIVIAL 2,5MG NS Product 2	MARVELON Z.ME Product 3	REMERON 30MG CTO NB Product 4	DESO/EE-50/35 PS CT Product 5	... ...
	t	200644						...
	t+1	200645						...
t	t+2	200646						...
t+1	t+3	200647						...
t+2	t+4	200648						...
t+3	t+5	200649						...
t+4	t+6	200650						...
t+5	t+7	200651						...

Production plan in the fixed period

Production decision to implement

MTS products -->

Manually change the production plan

Production order fixed Week	Production order open Week	Week	CERAZETTE Product 1	LIVIAL 2,5MG NS Product 2	MARVELON Z.ME Product 3	REMERON 30MG CTO NB Product 4	DESO/EE-50/35 PS CT Product 5	... ...
			Read this very carefully! Only enter a value in the cells below if you want to ...					
t	t+2	200646						
t+1	t+3	200647						
t+2	t+4	200648						
t+3	t+5	200649						
t+4	t+6	200650						
t+5	t+7	200651						

MTS products -->

Production order waiting?

Production order fixed Week	Production order open Week	Week	CERAZETTE Product 1	LIVIAL 2,5MG NS Product 2	MARVELON Z.ME Product 3	REMERON 30MG CTO NB Product 4	DESO/EE-50/35 PS CT Product 5	... ...
t	t+2	200646						...
t+1	t+3	200647						...
t+2	t+4	200648						...
t+3	t+5	200649						...
t+4	t+6	200650						...
t+5	t+7	200651						...

			MTS products -->					
Run out times								
Production order fixed Week	Production order open Week	Week	CERAZETTE Product 1	LIVIAL 2,5MG NS Product 2	MARVELON Z.ME Product 3	REMERON 30MG CTO NB Product 4	DESO/EE-50/35 PS CT Product 5	... ...
t	*t+2*	*200646*						...
t+1	*t+3*	*200647*						...
t+2	*t+4*	*200648*						...
t+3	*t+5*	*200649*						...
t+4	*t+6*	*200650*						...
t+5	*t+7*	*200651*						...

Table AB.3: A screenshot of the production plan sheet of the operational tool

AB.5 Inventory evaluation sheet

Inventory evaluation sheet									
Inventory projection in tablets Inventory projection in operator hours Inventory projection in monetary value									
Inventory projection in tablets						**MTS products -->**			
(* 1000 tab) **Week**	**Week**	Total positive negative	Total MTS positive negative	Total MTO positive negative		CERAZETTE **Product 1**	LIVIAL 2,5MG NS **Product 2**	MARVELON Z.ME **Product 3**	... ...
t-1	*current*								...
t	*200644*								...
t+1	*200645*								...
t+2	*200646*								...
...	...								...
t+14	*200706*								...

Table AB.4: A screenshot of the inventory evaluation sheet of the operational tool

In the inventory evaluation sheet, it is also given what the total positive inventory and what the total negative inventory (backorders) is for MTS products and for MTO products. The formulas used to compute positive respectively negative inventory are given by equation AB.14 and AB.15.

Equation AB.14

E17=SUMIF(I17:AH17;">0")

Equation AB.15

F17=SUMIF(I17:AH17;"<0")

In column I to AH, the inventories of the MTS products are given. In column AJ to AX, the inventories of the MTO products are given.

Appendix AC: Input levels MTO products[57]

Product characteristics MTO products							
Product name	Product ID	Safety stock (*1000 tab)	Batch size (*1000 tab)	Yield %	Campaign size	Capacity usage (h / 1000 tab)	Cost price (euro / 1000 tab)
CYCLESSA 100/25							
CYCLESSA 125/25							
CYCLESSA 150/25							
EE BLAUW ZO							
LIVIAL 1,25MG							
LO-LYNDIOL							
MIRCETTE 0/10							
MIRCETTE 150/20							
NANDORAL AUV ZO							
ORADEXON 2MG							
OVESTIN 1MG 9MM							
OVIDOL ZO Z.ME							
REMERON 45MG CTO NB							
THYRAX 0,150MG DT ZO							
TOLVON 20MG CT							

Table AC.1: Product characteristics of MTO products

[57] Sources: Apollo and normtijden TPD 2006

Appendix AD: Visual Basic macro operational tool

```
Sub Bijwerken_operationele_tool()

' Bijwerken_operationele_tool Macro
' Macro recorded 8-11-2006 by N.V. Organon / Diosynth B.V.

'Delete manually changed production plan of last week
Sheets("Production plan").Select
Range("D29:AS34").Select
Selection.ClearContents

'Insert Cneg(t-1)
Sheets("Capacity").Select
Range("EC14").Select
Selection.Copy
Sheets("Input").Select
Range("C20").Select
Selection.PasteSpecial Paste:=xlPasteValues, Operation:=xlNone, SkipBlanks _
    :=False, Transpose:=False

'Copy available operator capacity forecast of last week
Sheets("Input").Select
Range("C22:C26").Select
Selection.Copy
Range("C21:C25").Select
Selection.PasteSpecial Paste:=xlPasteValues, Operation:=xlNone, SkipBlanks _
    :=False, Transpose:=False

'Import production data
Sheets("Production input").Select
Cells.Select
Selection.ClearContents
Sheets("Pr inp help").Select
Cells.Select
Selection.ClearContents
Range("A1").Select

Dim interface_file1 As Variant

    interface_file1 = Application.GetOpenFilename("TXT Files (*.TXT), *.TXT", , "Open het nieuwe
    PL_4DM_PART_04.TXT bestand op fqdp:\Algemeen")

    If interface_file1 = False Then
        MsgBox " kies een file"
        Exit Sub
    End If

    With ActiveSheet.QueryTables.Add(Connection:= _
        "TEXT;" & interface_file1, Destination:=Range("A1"))
        .Name = "PL_4DM_PART_04"
        .FieldNames = True
        .RowNumbers = False
        .FillAdjacentFormulas = False
        .PreserveFormatting = True
        .RefreshOnFileOpen = False
        .RefreshStyle = xlInsertDeleteCells
        .SavePassword = False
        .SaveData = True
        .AdjustColumnWidth = True
        .RefreshPeriod = 0
```

```
        .TextFilePromptOnRefresh = False
        .TextFilePlatform = 437
        .TextFileStartRow = 1
        .TextFileParseType = xlDelimited
        .TextFileTextQualifier = xlTextQualifierDoubleQuote
        .TextFileConsecutiveDelimiter = False
        .TextFileTabDelimiter = True
        .TextFileSemicolonDelimiter = False
        .TextFileCommaDelimiter = False
        .TextFileSpaceDelimiter = False
        .TextFileOtherDelimiter = "#"
        .TextFileColumnDataTypes = Array(1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 2)
        .TextFileTrailingMinusNumbers = True
        .Refresh BackgroundQuery:=False
    End With

Range("A1").Select
Range(Selection, Selection.End(xlDown)).Select
Range(Selection, Selection.End(xlToRight)).Select
Selection.Sort Key1:=Range("A1"), Order1:=xlAscending, Header:=xlGuess, _
    OrderCustom:=1, MatchCase:=False, Orientation:=xlTopToBottom, _
    DataOption1:=xlSortTextAsNumbers
Selection.Copy
Sheets("Production input").Select
Range("A1").Select
Selection.PasteSpecial Paste:=xlPasteValues, Operation:=xlNone, SkipBlanks _
    :=False, Transpose:=True

'Import demand forecast data
Sheets("Demand input").Select
Cells.Select
Selection.ClearContents
Sheets("De inp help").Select
Cells.Select
Selection.ClearContents
Range("A1").Select

Dim interface_file2 As Variant

    interface_file2 = Application.GetOpenFilename("TXT Files (*.TXT), *.TXT", , "Open het nieuwe
    PL_4DM_PART_05.TXT bestand op fqdp:\Algemeen")

    If interface_file2 = False Then
        MsgBox " kies een file"
        Exit Sub
    End If

    With ActiveSheet.QueryTables.Add(Connection:= _
        "TEXT;" & interface_file2, Destination:=Range("A1"))
        .Name = "PL_4DM_PART_05"
        .FieldNames = True
        .RowNumbers = False
        .FillAdjacentFormulas = False
        .PreserveFormatting = True
        .RefreshOnFileOpen = False
        .RefreshStyle = xlInsertDeleteCells
        .SavePassword = False
        .SaveData = True
        .AdjustColumnWidth = True
        .RefreshPeriod = 0
        .TextFilePromptOnRefresh = False
```

```
        .TextFilePlatform = 437
        .TextFileStartRow = 1
        .TextFileParseType = xlDelimited
        .TextFileTextQualifier = xlTextQualifierDoubleQuote
        .TextFileConsecutiveDelimiter = False
        .TextFileTabDelimiter = True
        .TextFileSemicolonDelimiter = False
        .TextFileCommaDelimiter = False
        .TextFileSpaceDelimiter = False
        .TextFileOtherDelimiter = "#"
        .TextFileColumnDataTypes = Array(1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 2)
        .TextFileTrailingMinusNumbers = True
        .Refresh BackgroundQuery:=False
    End With

Range("A1").Select
Range(Selection, Selection.End(xlDown)).Select
Range(Selection, Selection.End(xlToRight)).Select
Selection.Sort Key1:=Range("A1"), Order1:=xlAscending, Header:=xlGuess, _
    OrderCustom:=1, MatchCase:=False, Orientation:=xlTopToBottom, _
    DataOption1:=xlSortTextAsNumbers
Selection.Copy
Sheets("Demand input").Select
Range("A1").Select
Selection.PasteSpecial Paste:=xlPasteValues, Operation:=xlNone, SkipBlanks _
    :=False, Transpose:=True

'End
Sheets("Input").Select
Sheets(Array("Input", "Production plan", "Inventory evaluation", "Capacity", _
    "Product 1", "Product 2", "Product 3", "Product 4", "Product 5", "Product 6", _
    "Product 7", "Product 8", "Product 9", "Product 10", "Product 11", "Product 12", _
    "Product 13", "Product 14", "Product 15", "Product 16", "Product 17", "Product 18", _
    "Product 19", "Product 20", "Product 21", "Product 22", "Product 23", "Product 24", _
    "Product 25", "Product 26", _
    "Product 27", "Product 28", "Product 29", "Product 30", "Product 31", "Product 32", _
    "Product 33", "Product 34", "Product 35", "Product 36", "Product 37", "Product 38", _
    "Product 39", "Product 40", "Product 41", "Production input", "Pr inp help", _
    "Demand input", "De inp help")).Select
Sheets("Input").Activate
Range("A1").Select
Sheets("Frontpage").Select
Range("A1").Select

Calculate

End Sub
```