

MASTER

Integral multi echelon planning vs integral single echelon planning to cope with uncertainties in the animal health supply chain

David, G.D.C.

Award date:
2013

[Link to publication](#)

Disclaimer

This document contains a student thesis (bachelor's or master's), as authored by a student at Eindhoven University of Technology. Student theses are made available in the TU/e repository upon obtaining the required degree. The grade received is not published on the document as presented in the repository. The required complexity or quality of research of student theses may vary by program, and the required minimum study period may vary in duration.

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain

Eindhoven, April 2013

**Integral Multi Echelon planning VS
Integral Single Echelon Planning to
cope with uncertainties in the Animal
Health Supply Chain**

By

G.D.C DAVID (Guillaume)

BSc Genie Industriel — INPG 2011

Student identity number 0786439

in partial fulfilment of the requirements for the degree of

Master of Science

in Operations Management and Logistics

Supervisors:

dr.ir. S.D.P. Flapper, TU/e, OPAC

dr. J.P. Gayon, INPG, ICL

-Integral Single Echelon planning VS Integral Multi Echelon planning to cope with uncertainties-

-Integral Single Echelon planning VS Integral Multi Echelon planning to cope with uncertainties-

TUE. School of Industrial Engineering.

Series Master Theses Operations Management and Logistics

Subject headings: Integral Planning, Single Echelon, Multi Echelon, Simulation,
Pharmaceutical supply chain, supply uncertainties



Animal Health

Integral Multi Echelon planning VS Integral Single Echelon Planning to cope with uncertainties in the Animal Health Supply Chain

Master thesis report

G.D.C DAVID (786439)

10/04/2013



Supervisors:

Ir. Dr. S.D.P. Flapper, TU/e OPAC

Dr. J.Waanders, MSD Animal Health

Dr. JP.Gayon, INP of Grenoble-Génie Industriel

Key words : Integral Planning, Single Echelon, Multi Echelon, Simulation, Pharmaceutical supply chain, supply uncertainties

Table of content

Glossary	7
Abstract	8
Preface.....	9
Management summary	10
Introduction.....	14
I. MSD animal Health’s description	16
II. Supply chain description	18
II.A Supply chains structure and activities	18
Pharmaceutical supply chain.....	18
Biological supply chain	19
II.B Supply chain coordination.....	21
II.C Supply chain uncertainties	22
Demand uncertainties	22
Supply uncertainties.....	22
III. Project context	25
III.A Project definition.....	25
III.B Multi Echelon concept versus Single Echelon concept	25
III.C Research questions.....	27
III.D Research approach.....	28
Conceptualization.....	28
Modeling.....	28
Model Solving.....	29
Implementation.....	29
III.E Project scope	29
IV. Conceptual model	31
IV.A Supply chain in scope	31
IV.B Single Echelon concept characterization.....	33
IV.C Multi Echelon concept characterization.....	34
IV.D Planning process and characteristics	35
IV.E Planning policy.....	37
IV.F Model characteristics	38
The customer demand	38
The supply uncertainties	38

-Integral Single Echelon planning VS Integral Multi Echelon planning to cope with uncertainties-

Service level.....	39
Objective function	40
Decisions variables	41
IV.G Model summary	42
V. Simulation models.....	43
V.A Simulation assumptions	43
V.B Multi Echelon Planning.....	44
V.C Single Echelon Planning.....	51
VI. Verification and Validation.....	57
VI.A Verification	57
VI.B Validation	57
VII. Results	59
VII.A Answer to the first research question: SE versus ME	59
VII.B Answer to the second research question: Scenario analysis	65
Conclusion/discussion	77
Recommendations	77
Limitations of my project	78
Further research.....	78
Table of Figures	80
Table of Tables.....	80
References.....	81
Definition of the tables' columns in the appendixes	83
APPENDIXES.....	85

Glossary

API	Active Pharmaceutical Ingredient
APICS	American Production and Inventory Control Society
APO	Advanced Planner Optimizer (module of SAP)
ARENA	Simulation software
BOM	Bill Of Material
BR	Batch Rejection
CODP	Customer Order Decoupling Point
DC	Distributor Center
EIO	Enterprise Inventory Optimization (module of SAP)
EOQ	Economic Order Quantity
ERP	Enterprise Resource Planning
FPP	Finish Product Packed
FPU	Finish Product Unpacked
Input Analyzer	Tool of AREANA to analyze data
ME	Multi Echelon
MPS	Merck Production System
MRP	Material Requirement Planning
MSDAH	MSD Animal Health
OptQuest	Tool of ARENA to optimize simulation parameters
OR	Operational Research
S&OP	Sales & Operations Planning
SAP	the Company which produces the ERP
SCM	Supply Chain Management
SCOP	Supply Chain Operation Planning
SE	Single Echelon
SKU	Stock Keeping Unit
SL	Service Level
VMI	Vendor Managed Inventory
X	Sub Product family considered in this study

Abstract

This master thesis compares the performances of two major planning concepts: the single echelon concept (currently used) and the multi echelon concept; taking into account uncertainties within MSD Animal Health. The research goals are to find out which planning concept is the best for MSDAH in order to get control of its supply chain, and what the impact of the supply uncertainties is.

To achieve those goals, a simulation study has been done on a particular pharmaceutical sub product family X. Two planning models are built and compared, one based on a single echelon concept and the second supported by a multi echelon concept. These two planning methods take as input data the same input parameters (demand, uncertainties, lead times), they have the same inventory management policy (R,s,Q), only the concept changes. The objective is to compute for the sub product family X's supply chain the optimal planning parameters of each echelon, in order to minimize the average supply chain cost while meeting a given service level. Then, a scenario analysis is conducted in order to study the impact of the supply uncertainties on the two planning performances.

It appears that the multi echelon concept is better for MSDAH and gives more control of the supply chain than the single echelon concept for coping with uncertainties. The single echelon concept is really sensitive to the supply uncertainties level. Therefore, there is an opportunity for MSDAH to switch from the current single echelon concept to a more advanced multi echelon concept.

Preface

This report is the result of my graduation project for the Master of Science degree in Operation Management and Logistics at the Eindhoven University of Technology and for the Engineering Diploma in Industrial Engineering at the Institut National Polytechnique de Grenoble (INP Grenoble-Génie Industriel).

The graduation project was carried out from September 2012 till March 2013 within the Supply Chain Management department of MSD Animal Health of Boxmeer. It has been a real pleasure to realize this project in such an interesting environment, and meet lots of interesting people. I have enjoyed working on this project which was really interesting and I have learnt a lot.

I would like to thank Jasper Waanders for giving me the opportunity to do my project within MSD Animal Health, for all the discussion we had, for his support and his advice along my project. I would like to thank Simme Douwe Flapper, my mentor from TU/e, for his guidance, his advice and his critical remarks during our meeting that always encouraged me to do better. I would like to thank Jean-Philippe Gayon, my mentor from Grenoble-INP, for his wise advice and continuous support throughout my project.

I would also like to thank the Operations Support's team members, for accepting me and creating a nice work environment, their advice and support.

Last but not least, I would like to thank my family and friends for showing their interest and support, and especially my parents who always supported me and believed in me.

Guillaume DAVID

Eindhoven, March 2013

Management summary

Introduction

This research project has been carried out within the company MSD Animal Health (MSDAH) of Boxmeer. MSD Animal Health is an international Pharmaceutical company which produces drugs and vaccines for animals. The Supply Chain Management department coordinates all the activities, people, capacities and materials along the complete supply chain. The pharmaceutical supply chain and the biological supply chain are one of the most complex supply chains to manage compared to the other industries. It has to deal with a lot of demand and supply uncertainties as well as a long lead time. The coordination of the complete network is not an easy job. The current planning is based on MRP which does not consider the supply chain uncertainties for computing its planning parameters. Thus, the SCM department wonders if a more advanced planning concept than the single echelon concept currently implemented with the MRP planning could bring more control and increase the performances of the supply chain.

The supply chain planning field is dedicated to this kind of research question. And from a literature review, two most important planning concepts are brought out, the single echelon (SE) planning concept and the multi echelon (ME) planning concept. Those statements lead to two research questions which are:

- 1) Which planning concept, the single echelon concept or the multi echelon concept, is the best adapted to plan the MSDAH's supply chain, taking into account the uncertainties?**
- 2) What is the impact of the supply uncertainties on the planning performances?**

In order to answer those questions a simulation study is chosen (software ARENA 13.9). The scope of the project is restricted to one pharmaceutical sub product family X, which is produced at the manufacturing site of Boxmeer and where the supply chain is subject to demand and supply uncertainties (lead time variation, batch rejection and output quantity fluctuation). The forecast of the demand for the FPPs (finish product packed) is a given for my project. The scheduling is out of scope (my planning should not be a scheduling planning) and the supply chain is considered with infinite capacity.

Methodology

In order to combine rigor and relevance in my research, the research model developed by Mitroff et al. (1974) has been followed along my project. This research model is composed of four steps: conceptualization, modeling, model solving and implementation.

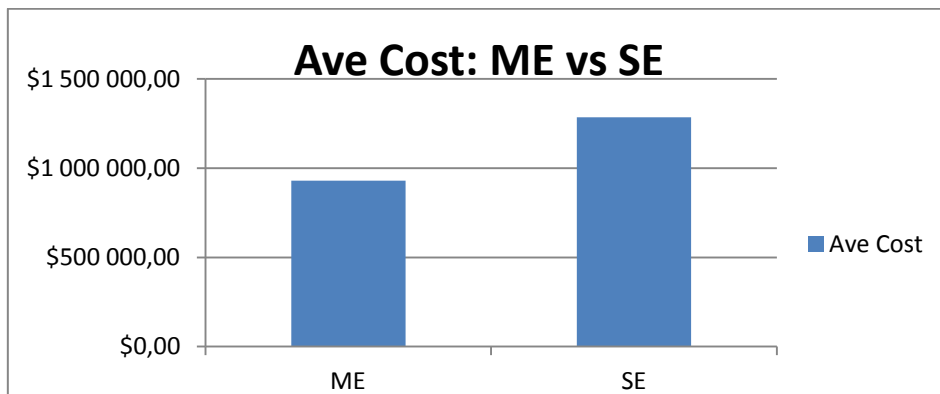
During the conceptualization the objective, constraints, input parameters and planning parameters are designed and quantified. In order to achieve that, interviews were done as well as data extract from SAP the ERP. The average cost formula and the service level formula are defined along this phase. The 98% service level requirement is selected and the uncertainties are quantified. The planning parameters of each echelon are the replenishment point s and the order quantity Q . The order quantity Q of an echelon is the quantity that needs to be produced if production is required for this echelon. The replenishment point s of an echelon is the threshold for the production decisions. If the physical inventory of an echelon goes below the s level, the production of Q is required. During the modeling phase, the simulation model is built and verified using ARENA 13.9 software. The

-Integral Single Echelon planning VS Integral Multi Echelon planning to cope with uncertainties-

objective is to optimize the planning parameters for a minimum average supply chain cost while meeting a given service level. To achieve that objective the OptQuest tool of ARENA is chosen. Thus, two planning models are built, one based on the single echelon concept and one based on the multi echelon concept. For both planning concepts, the planning performances have been compared. During the model solving phase, the OptQuest tool of arena is used. The optimization run takes 8 hours. This tool needs an optimization design (decision variable, objective, constraints) and used a Tabu search heuristic algorithm to optimize the planning parameters. Then, the SE planning results and ME planning results are analyzed. The implementation phase is done by a list of recommendations and implications because the best planning concept is not planned to be implemented during my project period.

Results

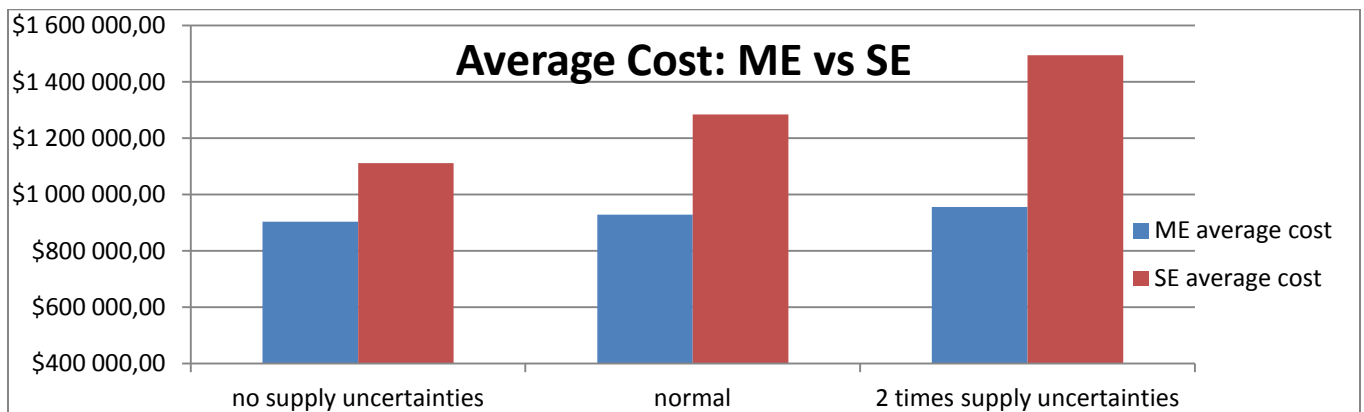
Answer to the first research question: the best planning concept for MSDAH is the ME concept because it has a lower average supply chain cost than the SE concept. The Average cost (SE)= 1 284 287 \$ per month while the Average cost (ME)= 928 899 \$ per month.



Answer to the second research question: a scenario analysis is carried out, and two scenarios are defined.

- Scenario 1: no supply uncertainties. In this scenario all supply uncertainties are deleted.
- Scenario 2: 2 times supply uncertainties: in this scenario all the supply uncertainties are doubled.

So, by adding the “normal” scenario, there are three scenarios for the analysis.



-Integral Single Echelon planning VS Integral Multi Echelon planning to cope with uncertainties-

The output of the scenario analysis is that the SE concept is very sensitive to supply uncertainties. With the ME concept, the supply chain is more controlled and the planning performances are less influenced by the supply uncertainties. The intern bullwhip effect is controlled by the ME concept.

Implications and recommendations

As MSDAH is subject to many uncertainties, the company can take advantages in the multi echelon planning concept. Switching from the current single echelon concept to a multi echelon concept is recommended. In order to do so, MSDAH must go on with the roll out of SAP in all manufacturing sites and all distributor centers to get a complete interconnected network. Once done, SAP Enterprise Inventory optimization (EIO) should be incorporated and designed to use the multi echelon functionality of this module (SAP APO does not support a multi echelon optimization). SAP EIO module can be incorporated in organizations using SAP R/3, and this is the case of MSDAH. Website links related to SAP EIO are given in Appendix 28.

The multi echelon simulation model can be used to optimize the planning parameters of the products. The input parameters need to be updated and the model implemented for all products in ARENA. The problem of seasonal products can be solved by dividing the time period in shorter periods when the demand is quite stationary and can apply the simulation on those time periods

Once the multi echelon concept has been implemented, the inventory levels will decrease and the supply chain will become more controlled. Then, the process problems will appear and become clearer. So, projects to improve the production and quality processes could be initiated to decrease the supply uncertainties, and decrease the lead times as much as possible.

This complete procedure is in line with the MPS logic of MSDAH.

Further research

For further research, it is recommended to improve the average supply chain cost function by introducing the ordering cost when an order is placed between echelons, and to study what differences can be noticed in the results. According to the role of my planning it is not required to introduce the ordering cost in this project. The planning in this project gives to the planner the quantity that needs to be produced during the lead time in order to cover the future demand. But in order to get a better operational validity, the ordering cost should be added in the objective function.

A further research could be to consider the capacity aspect of the supply chain (production capacity, transportation capacity and storage capacity). The planning in this project gives the quantities that need to be produced in order to satisfy the future demand but it does not take into account capacities. Are the capacities enough to produce the quantities required by the planning?

Another further research should be done on forecasting, because it appears that the forecast accuracy has an important impact on the supply chain performances (Teunissen, 2009), and this forecasting aspect has not been considered in this project at all.

Another further research should be to consider the biological supply chain. The supply uncertainties are higher in the biological supply chain than in the pharmaceutical supply chain. So the multi echelon concept could give to MSDAH a very good control of its biological supply chain.

-Integral Single Echelon planning VS Integral Multi Echelon planning to cope with uncertainties-

A last topic for further research could be to incorporate the suppliers or/and the customers on the supply chain scope. New echelons should be added. The information transparency brought by a multi echelon concept extended to the suppliers and customers could increase the performances of the supply chain and improve the relationship confidence between MSDAH and its suppliers and customers (De Kok et al, 2005).

Introduction

Context

Nowadays, in order to stay competitive in the market, a company cannot just develop new products and produce in mass. In fact, huge companies are constituted of a large number of departments and business processes which all link together. Furthermore, companies buy raw materials from different suppliers that are located over the world, and then companies produce and distribute their products to their worldwide customers. This leads to a complex network and a large number of persons and activities that have to be coordinated in order to get an efficient organization. This is how the paradigm of Supply Chain Management (SCM) was born.

Supply Chain Management is an important concept which is defined by APICS as the "design, planning, execution, control, and monitoring of supply chain activities with the objective of creating net value, building a competitive infrastructure, leveraging worldwide logistics, synchronizing supply with demand and measuring performance globally" (Lee, 1992) and (Lambert, 2000). The planning field has an important place within the Operational Research (OR) and within the SCM activities. Planning aims to coordinate all the strategies and activities of a company in long-term, mid-term and short-term horizon, and to balance inventory levels and resources utilization. In fact, along a supply chain hundreds of thousands of individual decisions have to be made and coordinated every minute. A planning supports decision-making by identifying alternatives and selecting a good one or even the best one. Thus a selected and implemented good planning concept is the key requirement for a company to save money and keep control of its supply chain. One of the main objectives is to minimize the supply chain cost while meeting a certain service level (Winter, 2005) and (Bisschop, 2007).

My project was carried out within the company MSD Animal Health (MSDAH) which is an international pharmaceutical company. According to (Shah, 2004), some sectors such as the pharmaceutical sector need sophisticated supply chain optimization techniques. The pharmaceutical supply chain and the biological supply chain are one of the most complex supply chains that we can encounter in the industry. In fact, it is subject to a lot of uncertainties and long lead times.

The current planning is based on an MRP logic supported by a single echelon concept in which the planning parameters are not computed taking into account uncertainties. The actual planning organization involves decentralized decisions that may lead to suboptimal performances of the supply chain management.

Thus, the company thinks that there is an opportunity to improve the supply chain performances and get a better control of the complete supply chain by using a new planning concept. This planning concept should plan the supply chain as a whole and should take into account the uncertainties. Indeed, planning the supply chain as a whole involves a centralized decision which could tend toward a global optimization of the supply chain in contrast with a sub optimization (Uquillas, 2010)

Project problem

Which planning and control concept can give to MSDAH a better control of its supply chain with a view to minimizing the supply chain cost while meeting a given service level?

Layout of this report

In chapter I, a description of MSDAH in a general way is given. Market, network and product portfolio complexity are presented.

In chapter II, a description of MSDAH from a supply chain perspective is given. Supply chain activities, characteristics and coordination are described.

In chapter III, the project context description is lead. A concept review and comparison is done. Research questions are put down, a research methodology is explained, the simulation approach is selected and the project scope is defined.

In chapter IV, the conceptual model for the simulation is defined and built.

In chapter V, the formal planning processes are presented through the software ARENA 13.9.

In chapter VI, the verification and validation of the model is achieved.

In chapter VII, the results of the two research questions are presented and a scenario analysis is achieved.

In a final part, a conclusion of my project is given and a discussion is lead.

-Integral Single Echelon planning VS Integral Multi Echelon planning to cope with uncertainties-

I. MSD animal Health's description

My project has been carried out within the company MSD Animal Health (MSDAH) in Boxmeer. This company offers veterinarians, farmers, pet owners and governments the widest range of veterinary pharmaceuticals, vaccines and health management solutions and services. MSD Animal Health is dedicated to preserving and improving the health, well-being and performance of animals. Moreover, this company is an international company with manufacturing sites, regional distributor centers, local distributor centers and customers allocated over the world and counts about 7000 employees worldwide.

The products sold are divided in two categories, pharmaceutical products which are mainly drugs and biological products which are vaccines.

The global market is divided in 5 species markets: Ruminants, companion animal, Swine, poultry and aqua/other. [Figure 1]

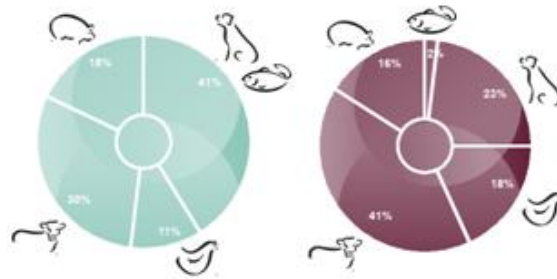


Figure 1: Global AH market by species and MSDAH's sales by species market (Source: 2010 Vetnosis and internal sales data)

MSD Animal Health's network

The MSD animal Health's network consists of 27 manufacturing sites and 50 distributor centers that deliver the end product to the worldwide external customer. [Figure 2]



Figure 2: MSDAH's Manufacturing Site network

-Integral Single Echelon planning VS Integral Multi Echelon planning to cope with uncertainties-

The 50 distributor centers located over the world (delivering into 140 countries) are divided into 5 different regions based on geographical location:

- Asia: Asia plus Australia and New Zealand
- Europe 1: North, West and Eastern Europe
- Europe2: Southern Europe and North Africa
- Latin America: South America
- North America: United States of America and Canada

The Figure 3 describes the global AH market by geographical region and the actual sales of MSDAH by geographical region. [Figure 3]

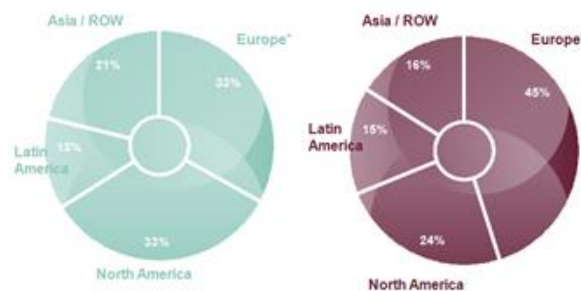


Figure 3: Global AH market by geographical region and MADAH's sales by geographical region (Source: 2010 Vetnosis and internal sales data)

Portfolio complexity

MSD Animal Health has an end product portfolio of about 6500 end products (pharmaceutical and biological products combined)

As a conclusion, the range of the market, the range of the MSDAH's network and the range of the product portfolio lead to a complex supply chain management exercise.

II. Supply chain description

Within this chapter, MSDAH is depicted from a supply chain perspective. It is essential to study, describe and understand the supply network of MSDAH as well as the activities and the actual supply chain coordination in order to orientate my research project and find an improvement way through a planning perspective. First, the supply chain structures and activities are presented. Secondly, the actual supply chain coordination is described. And finally, the uncertainties of the supply chain are defined and explained.

II.A Supply chains structure and activities

MSDAH manages two kinds of supply chains, the pharmaceutical supply chain and the biological supply. This paragraph is dedicated to the description of those two supply chains.

Pharmaceutical supply chain

The outputs of the pharmaceutical supply chain are pharmaceutical products (product without biological component) which are mainly drugs.

Pharmaceutical supply chain structure

In a general way, according to the typology description given by (Caillet, 2008), the pharmaceutical supply chain is structured as followed (from the upstream stage to the downstream stage): supplier, manufacturing site, stock point, packaging site, distributor center and external customer. The manufacturing site buys API (Active Pharmaceutical Ingredient), the quality is checked and API stocked at the stock point. Then it produces the medicine from API or a combination of APIs, and the quality is checked. Within the packaging site the final product is packed and shipped to the distributor center. Once at the distributor center, the product is transported to the end customer.

One can distinguish three key stockpoints, the stock of API at the manufacturing site, the stock of finish product unpacked (FPU) at the manufacturing site and the finish product packed (FPP) at the DC. Moreover, there are also stock points for additive materials and packaging materials but they are not considered in my project (out of scope).

The customer order decoupling point is located at the FPP stock point. This means that upstream to this point the supply chain is forecast driven and downstream to this point the supply chain is order driven. [Figure 4]

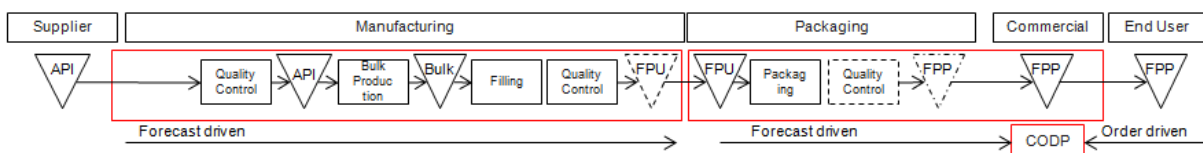


Figure 4: Pharmaceutical Supply Chain structure

Activities in the pharmaceutical supply chain

In this part more details are given regarding the pharmaceutical activities. Two kinds of activities along the supply chain are distinguished, the productions activities and the distribution activities.

-Integral Single Echelon planning VS Integral Multi Echelon planning to cope with uncertainties-

Production activities

APIs purchasing: APIs and basic material (water, Vaseline...) are purchased from external suppliers or sometimes supplied by another MSDAH’s manufacturing site. Once received, the API must be tested before released. The testing time is usually 3 weeks. The complete purchasing activity lead time can take a value from several weeks to one year. It depends on the product.

Bulk production: APIs and additive are inputs for the bulk production.

FPU production: A filling process is executed and results in several different presentations (FPU). Then a quality control is done. The production lead time plus the test lead time usually lasts from 3 to 6 weeks.

FPP production: A packaging process is executed in order to get the different FPPs which are country specifics. The planned lead time to get the product packed and ready to delivery is five weeks.

Distribution activities

Transportation to the DC: once the FPP produced it is transported to the DC. There are three types of distribution mode: by trucks, by planes or by ships, but ships are mainly used. The mode of selection depends on the shelf life, the value of the product and the location of the DC. A final test is done at the reception of the order at the DC.

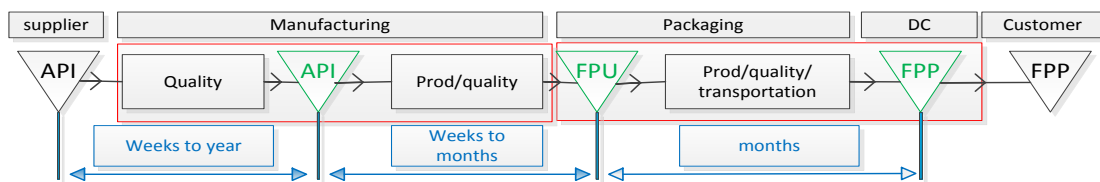


Figure 5: Lead Times description of the general pharmaceutical supply chain

Biological supply chain

The outputs of the biological supply chain are biological products (product that contains at least one biological component) which are vaccines.

Biological supply chain structure

In a general way the biological supply chain is identical to the pharmaceutical supply chain. But, instead of APIs purchasing step this is an antigen production step. The antigen are not purchased from external suppliers but are produced at the manufacturing sites. Considering this difference, the previous paragraph remains valid and true for the biological supply chain. [Figure 6]

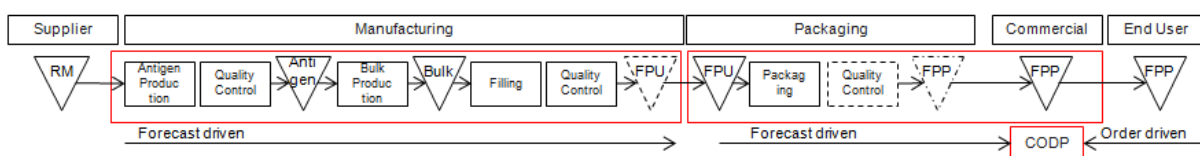


Figure 6: Biological Supply Chain structure

-Integral Single Echelon planning VS Integral Multi Echelon planning to cope with uncertainties-

Activities in the Biological supply chain

As mentioned previously the biological supply chain only differs from the pharmaceutical supply chain in one step which is the antigen production (antigen is the active component of the biological supply chain)

Production activities

Raw material purchasing: Raw materials are bought from external suppliers. The seeds are produced internally; they are outputs of the R&D department.

Antigen production: The antigen (API equivalent for the biological supply chain) is produced at the manufacturing site. Once produced, two tests are realized, a sterility test (takes 2 weeks) and a quality test (takes 6 weeks).

Bulk production: From the antigens and additive materials the bulk production is executed.

FPU production: A filling process is done which leads to different FPUs and tests are done. But, for particular products an additional freeze drying step is necessary.

FPP production: The FPP production is the same as the pharmaceutical supply chain.

Distribution activity

The distribution activity of the biological supply chain is the same as the pharmaceutical supply chain.

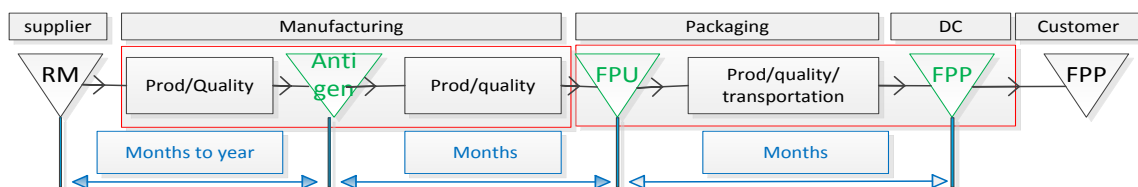


Figure 7: Lead time description of the general biological supply chain

To conclude this paragraph, it is noticeable that the supply network of MSDAH is made of two kinds of supply chain. The structure and the activities are roughly the same. But from a network perspective, the structure is quite complex. Indeed, the number of manufacturing sites and the number of end products (FPPs) lead to a complex network that is not easy to manage and control. The network is convergent from API/antigen to bulk and divergent afterward. It is also important to notice that the end to end lead time (E2E) from the supplier to the customer in the pharmaceutical industry is higher than in the other industries. This indicates the Cycle Time of the supply chain. It can take from several months to over a year [Figure 5 and 7]. To sum up, MSDAH is facing a complex international network with a huge portfolio of end product, and in an end to end perspective the lead time is relatively high. This leads to a complexity to plan and control this network. Now let's investigate the current supply chain coordination.

II.B Supply chain coordination

In order to coordinate its network, MSDAH has implemented an ERP which links all manufacturing sites and DCs together. The current logic of coordination and control of all activities is the MRP logic. The material requirement planning is the main tool of control of the supply chain. The MRP works with a planning horizon of 36 months. The demand planning and the stocks level at each controlled stock points of the network are input of the MRP system. The MRP run will generate production order propositions if the stock level goes below a replenishment point and purchase order propositions for the same reason. [Figure 8]

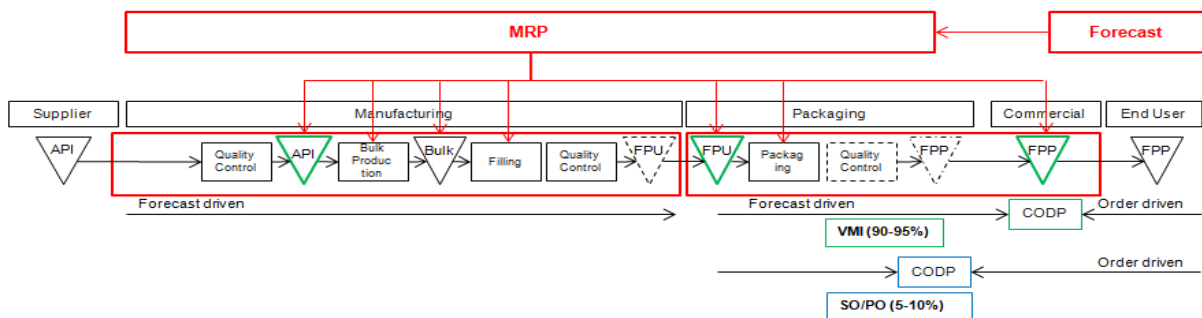


Figure 8: Current supply chain coordination

The actual inventory management policy implemented within the MRP system is the (R,s,Q) policy. Every R units of time the inventory position is checked and an MRP run is started. If the inventory position is below the order point s, an order quantity Q is ordered and after the lead time replenished. If the inventory position is above s, no production is started and the inventory position is reviewed the next period.

For the production process, fixed batch sizes are used during the bulk production and the FPU production. Nevertheless, for the FPP production, the batch sizes are computed with an adjusted Economic Order Quantity (EOQ) formula which takes into account the product shelf life (and many other aspects). This EOQ is the minimal production batch size for the packaging process and is also the minimum order quantity sent to the DC.

Also, MSDAH is using a VMI concept. This means that the responsibility of the FPP stock point at the DC is moved to the manufacturing site. In other words, the manufacturing site manages both the FPP stock points at the manufacturing site and at the DCs. This concept takes on board the expertise of the manufacturing site's manager in the distribution decisions and prevents against an abnormal (unexpected) DC orders quantity for whatever reasons.

Furthermore, in order to increase the coordination within the planning organization. The Sales & Operations Planning (S&OP) process is ongoing implementation. Within the S&OP process, a Global S&OP team and S&OP teams at each manufacturing site and DC are involved. The Sales & Operations Planning is a collaborative, interdependent decision making process. The local S&OP teams take decisions to resolve local or regional demand/supply mismatches due to market or production events, escalate issues to global S&OP team and agree to revisions of local consensus demand forecast. The global S&OP team takes decisions to resolve global demand/supply mismatches due to

-Integral Single Echelon planning VS Integral Multi Echelon planning to cope with uncertainties-

market or production events and communicates decisions back to local market and supply planning. This S&OP process creates an internal CODP which is located at the FPP stockpoint at the manufacturing site. However, this stockpoint is not a strategic stockpoint.

As expected, in order to plan and control the supply network MSDAH has implemented a planning concept (VMI) and a planning process (S&OP) to cope with its complex situation. But, one can notice that the current planning and control system is based on a simple MRP logic. Now let's analyze which uncertainties are present along the supply chains.

II.C Supply chain uncertainties

Both pharmaceutical and biological supply chains are subject to two kinds of uncertainties: demand uncertainties and supply uncertainties. [Table 1]

Demand uncertainties

The demand uncertainties are the result of unexpected customer behavior and unexpected outbreaks of diseases. Those two aspects are hardly manageable and only a good forecasting method can decrease the demand uncertainty. However, it has been decided that the Forecast of the demand is out of scope for my project. So, the demand uncertainty is investigated by taking the forecast of the demand as such.

Supply uncertainties

The supply uncertainties for MSDAH can be categorized within four groups:

- Output quantity fluctuations
- Quality uncertainty
- Lead time variability
- Yield fluctuations

Output quantity fluctuations

The output quantity fluctuation can be defined as followed: Quantity difference between the target output quantity and the actual output quantity of a batch being produced.

This output quantity fluctuation is a result of unexpected loss of material along the supply chain. For instance, it is not possible to use the complete bulk production because some production would be lost on the vessel. Or, during the labeling process some vials would be broken. These differences are determined for all different stock point (API/Antigen, Bulk, FPU, and FPP) for both pharmaceuticals and biologics. To calculate these quantity differences, the target quantity is compared to the actual quantity for each particular batch.

Quality uncertainties

If a complete batch has a quality problem or does not fulfill the quality requirements, the complete batch is rejected. This is called the batch rejection.

Lead time uncertainties

The lead time variability includes variability in both quality lead time and processing lead time. Moreover, some tests need to be repeated and this is not expected. So, lead time uncertainties also include test repetition.

Yield fluctuations

The yield is a particularity of the biological supply chain and represents the activity of the antigen produced.

The biological supply chain is subject to yield fluctuations, which is a problem for the supply chain management because if the antigen does not have the good yield, some products will not be able to be produced from this batch.

Table 1: supply chain uncertainties summary

Demand uncertainties	Supply uncertainties
-Outbreak of Diseases	-Lead time uncertainty
-Demand forecasting	-Output quantity fluctuation
-Seasonality	-Batch rejection
-Competitor out of stock	-Yield fluctuation

Summary:

According to the typology given by (Caillet, 2008) and the previous analyses, we notice that the pharmaceutical supply chain is subjected to:

- Long lead times
- Batch production and supply chain batch oriented
- Seasonal and static demand
- Bill of material: convergent in production step and divergent in packaging step. [Figure 9]
- Demand and supply uncertainties

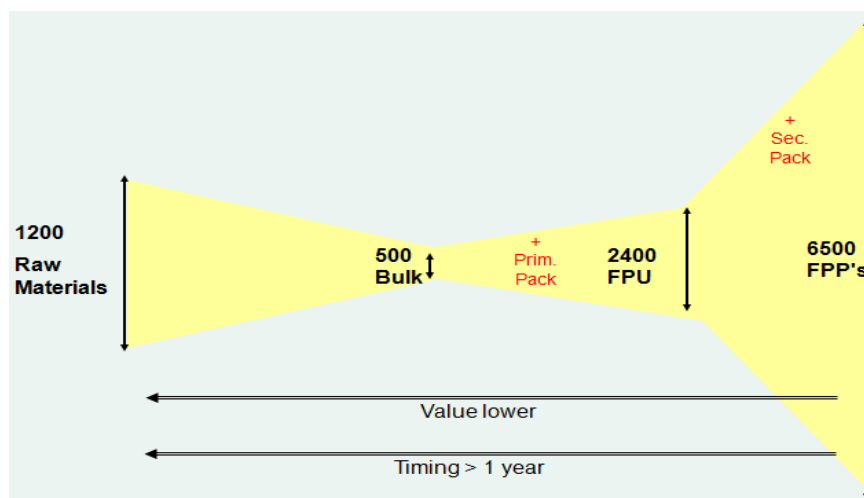


Figure 9: convergent and divergent characteristics of the supply chain

-Integral Single Echelon planning VS Integral Multi Echelon planning to cope with uncertainties-

To conclude this part, we can claim that the MSDAH's situation and network are complex and hardly manageable and controllable as a huge network. MSDAH has already understood this aspect and has introduced some advanced planning concepts and planning processes in order to plan and control the supply chain efficiently. Nevertheless, due to the importance of the uncertainties along the supply chain we can wonder whether this simple MRP logic is enough to plan and control the supply chain efficiently, what's more the MRP planning parameters have not been designed by taking into account the uncertainties. For instance, the safety stock levels are based on rules of thumb.

III. Project context

Within this chapter, a first project definition is given. This will lead to the study of two important planning concepts which are the single echelon planning concept and the multi echelon planning concept. Then, this study results in two research questions. Finally, the research scope of my project is depicted.

III.A Project definition

MSDAH wonders if the planning concept presently implemented (MRP) in order to plan its whole supply chain is the best. This leads to the following question: is there another planning concept that would be better adapted to the MSDAH environment and its supply network characteristics?

Which planning and control concept can give to MSDAH a better control of its supply chain with a view to minimizing the supply chain cost while meeting a given service level?

III.B Multi Echelon concept versus Single Echelon concept

From a supply chain perspective, a planning leads to coordinate flows of materials and resources along the supply chain while meeting the customer demand at minimum costs. This kind of planning problem is so called in literature a Supply Chain Operation Planning (SCOP) problem (De Kok and Fransoo, 2003). A planning and Control System is based around the following questions: What should be manufactured? How much should be manufactured? When should it be manufactured? It is composed of two things, **a planning concept** and **a policy**. The concept is a way of thinking and once defined; the policy is built and parameters are defined in order to support the planning concept. A planning is a decision support tool that gives a planning proposal with replenishment orders, production orders and distribution orders propositions as output (Silver et al, 1998).

It is really important for an organization to have a planning concept adapted to it as well as a decision support tool which provides a good and feasible plan. Indeed, bad decisions can lead to an important loss of money from the company. For instance:

- If a company purchases insufficient quantities of an item used in manufacturing (or the wrong item) it may be unable to meet contract obligations to supply products on time.
- If a company purchases excessive quantities of an item- the excess quantity ties up cash while it remains as stock and may never even be used at all.
- Beginning production of an order at the wrong time can cause customer deadlines to be missed.

This is why selecting a good planning and control concept is essential for MSDAH and is the aim of this report.

From a planning concept literature review, two general concepts brought out: the Single Echelon (SE) concept and the Multi Echelon (ME) concept (De Kok and Fransoo, 2003).

-Integral Single Echelon planning VS Integral Multi Echelon planning to cope with uncertainties-

With a Single Echelon concept, the network is optimized echelon by echelon without looking at the impact on the other echelons. And there is a lack of visibility from one echelon on another. Figure 10 shows the optimization process through a single echelon approach. [Figure 10]

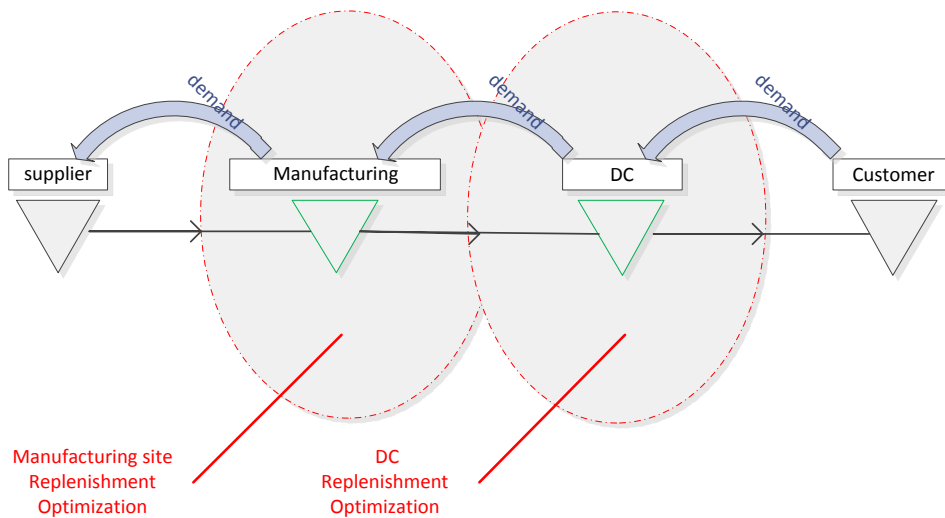


Figure 10: Multi echelon planning concept

With the Multi Echelon concept, inventory replenishment decisions are made at the enterprise level in a single optimization exercise rather than in a sequence of sub exercises for each echelon. The following Figure 11 shows the optimization process through a multi echelon approach. [Figure 11]

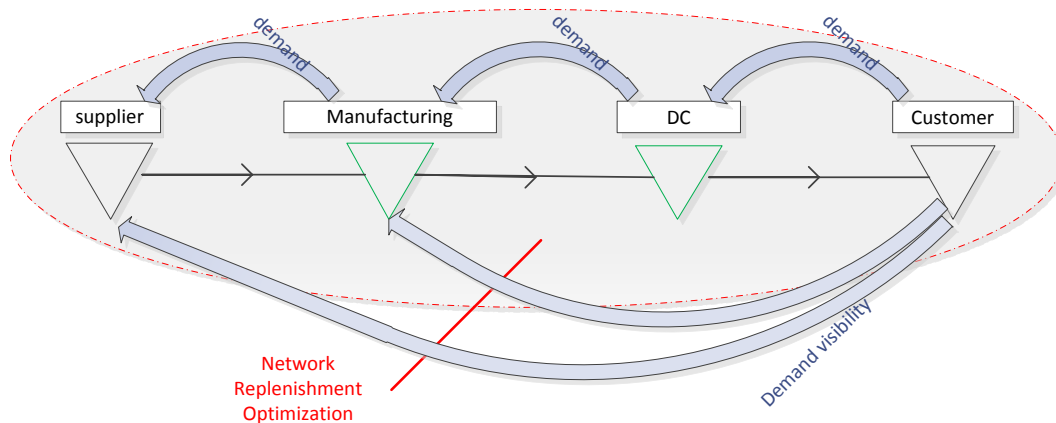


Figure 11: Single Echelon planning concept

A comparison between the two concepts characteristics is given on Table 2. This comparison is based on 5 criteria which are: Optimization Objective, Lead Times, Bullwhip Effect, Network visibility and Order synchronization. [Table 2]

Table 2: comparison between the Single Echelon concept and the Multi Echelon concept

Criteria	Single Echelon approach	Multi Echelon approach
Optimization Objective	Meet immediate customer's service requirements at minimum inventory (suboptimal for network)	Meet end customer service level at minimum inventory
Lead times	Uses immediate supplier lead times and lead time variability	Uses all lead times and lead times variation of upstream suppliers
Bullwhip Effect	Ignored	Effects measured and accounted for in overall replenishment strategy
Network Visibility	Immediate downstream customers demands and immediate upstream suppliers lead times	All echelon have complete visibility into other echelons; this visibility is exploited in the replenishment logic
Order synchronization	ignored	Full modeled to reduce unnecessary lags in network

It is important to mention that the MRP logic is part of the Single Echelon concept. And it seems, according to literature, that the Multi Echelon concept outperforms the single echelon concept. Thus, by just referring to the literature, I should say to MSDAH "you should move from your MRP planning to a multi echelon planning". But we need to quantify the difference between those two concepts. Furthermore, the current planning does not consider the supply chain uncertainties within the planning parameters computation. It is interesting to compare the Single Echelon planning concept performances and the Multi Echelon planning concept performances while the uncertainties are considered in the planning parameters computation.

III.C Research questions

The difference of performances of the two planning concepts (SE and ME) by taking into account the uncertainties for the computation of the planning parameters needs to be investigated. The first research question is the following:

Question 1: Which planning concept, the single echelon concept or the multi echelon concept, is the best adapted to plan the MSDAH's supply chain, to cope with the uncertainties?

Then, the impact of the supply uncertainties on both Single Echelon planning performances and Multi Echelon performances also needs to be investigated. The second research question is the following:

Question 2: What is the impact of the supply uncertainties on both planning performances?

III.D Research approach

In order to answer those two research questions, a simulation approach has been selected. In fact, due to the number of uncertainties, the model might be too complex for a formal mathematical analysis. Bertrand and Fransoo (2002), indicate that in case of high complexity, a simulation approach is often used. However, simulation may lead to lower scientific quality results than mathematical analysis, but the scientific relevance of the problem studied may be much higher (Teunissen, 2009)

Knowing that a simulation approach is chosen, the research approach followed to achieve the research objectives is presented. From the point of view of the philosophy of science it is really important to combine rigor and relevance within a research study, to ensure the usability and the understanding of the research in both academic field and practical field (Shrivastava, 1987). This aspect is even more important in the Operational Research field, and this is why I have decided to realize my research project in a company.

The research model elaborated by (Mitroff et al, 1974) is a good model to combine rigor and relevance within my project. The model has been used as a guideline along my project and is used as a guideline along this report. The Mitroff et al.'s research model consists of four phases, conceptualization, modeling, model solving and implementation. [Figure 12]

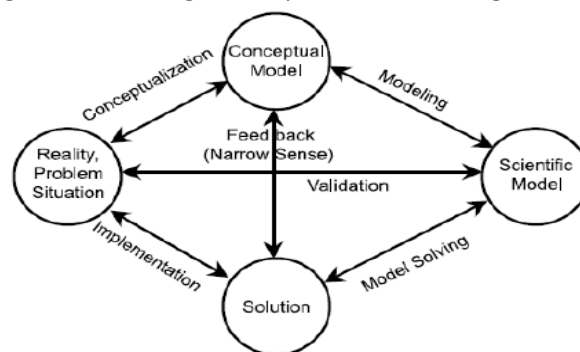


Figure 12: Research Model of Mitroff et al. (1974)

Conceptualization

The conceptualization is the first phase of the Mitroff et al.'s research model. Within this phase the conceptual model is defined. This means that the variables, parameters, inputs and outputs of the model are selected and defined. As a model is a simplification of the reality; it is decided what needs to take part of the model, what does not, and why. The conceptualization phase of my project is described in the chapter IV.

For my project, the planning parameters that need to be optimized must be defined as well as the parameters that represent the uncertainties. About the outputs, a service level definition and a cost function must be built.

Modeling

In the second phase, the quantitative model is built, that consists in defining and explaining the quantitative and causal relationships between variables defined during the conceptualization phase. The model must be presented in a formal form.

-Integral Single Echelon planning VS Integral Multi Echelon planning to cope with uncertainties-

For my project, a simulation approach is used to solve a planning problem. Thus, the planning process must be explained through a mathematical form. The Modeling phase is presented in chapter V.

Model Solving

In the third phase, the mathematical algorithms, methods or software required to solve the quantitative model are selected and used to solve the problem.

For my project, a simulation approach is chosen and the simulation software ARENA 13.9 has been selected to solve my problem. The mathematical model is translated in order to be adapted to this software. When a simulation approach is used, an optimization procedure must be designed in order to optimize the planning parameters in a right way. The OptQuest tool of ARENA has been used to achieve that.

To study the second research question, a sensitivity analysis combined to the OptQuest tool is achieved. This sensitive analysis is based on different scenarios consideration. The model solving phase is described in chapter VII.

Implementation

The final phase of the Mitroff et al.'s research model is the implementation. This phase consists in the integration process description of the solution and the results in an operational way (in real life situation).

For my project, the implementation phase is presented as recommendations and management implications and not as a process. In fact, the results of my project are not expected to be used in a short term but more in a mid term, and changes in the organization will occur within this time period.

III.E Project scope

In this paragraph, the scope of my project is depicted. [Figure 13]

- My research should be focus on the pharmaceutical supply chain because it is less complex than the biological supply chain.
- My study must consider a sub product family that is completely produced at the manufacturing of Boxmeer in order to facilitate the gathering of the required data.
- The planning should consider the complete network in an integral way (end to end from the API to the end customer) of the sub product family selected.
- The planning is based on a multi echelon environment and must manage the three important stockpoints which are the API level, the FPU level at the manufacturing site and the FPP level at the DC.
- Demand forecast is given by MSDAH.
- The contracts with the API's suppliers are out of scope. There are no constraints of maximum or minimum order quantity. There is no time restriction for ordering.
- The production batch sizes between API and FPU are registered, fixed and given by the company. These batch sizes cannot be changed.

-Integral Single Echelon planning VS Integral Multi Echelon planning to cope with uncertainties-

- However, the EOQ quantity between FPU and FPP is not a constraint for my project. The ordering quantities between FPU and FPP need to be defined.
- Scheduling is out of scope
- It is assumed infinite supply chain capacity

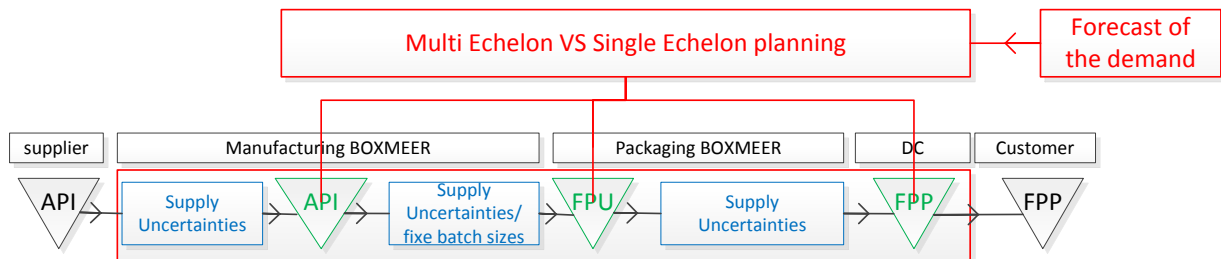


Figure 13: Scope of my project

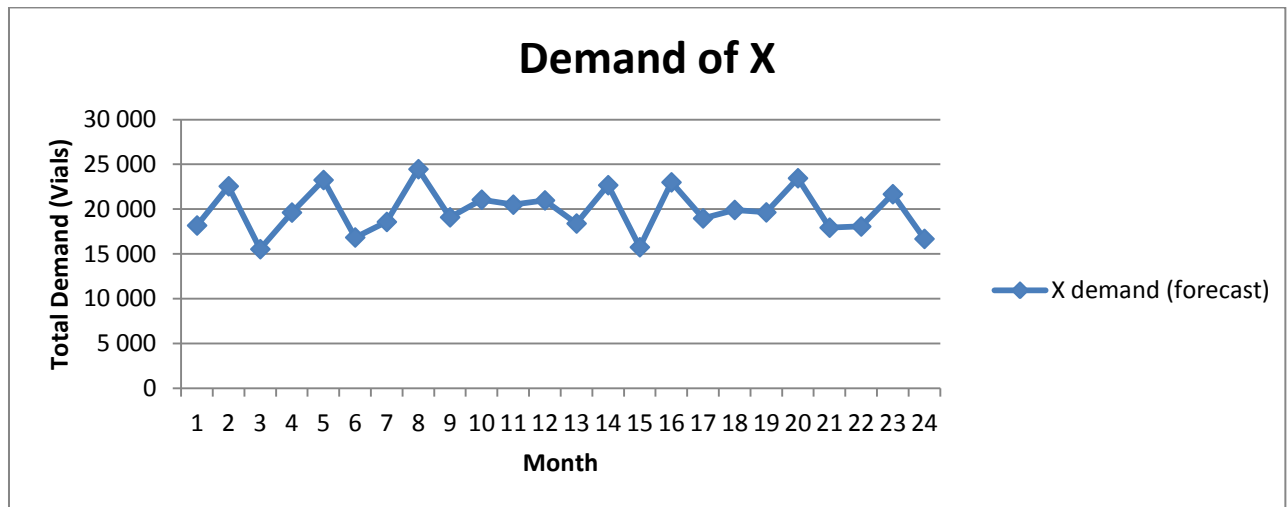
IV. Conceptual model

This chapter is dedicated to the conceptualization phase of the Mitroff's research model. First, the supply chain characteristics of the sub product family selected are presented. Secondly, the single echelon characterization is defined. Thirdly, the multi echelon characterization is given. Fourthly, the planning process and planning characteristics expected to be simulated are described. Fifthly, the planning policy supported by either the Multi Echelon concept or the Single Echelon concept is defined. And finally, the conceptual model is designed, starting by the customer demand consideration, then the supply uncertainties modeling, and the service level definition, the average supply chain cost function, finally the decision variables which are the planning parameters.

IV.A Supply chain in scope

In order to start my research study, a sub product family had to be selected. In agreement with MSDAH, a sub product family named X is selected. Why this sub product family? Because this sub product family X is produced at the manufacturing site of Boxmeer (from now "X" means sub product family X). X's network is not the easiest to study but not the hardest either. X's supply chain is subject to supply uncertainties, important for my project, and there is enough data available to do my research. Furthermore, X is representative of the business. X's demand is quite stationary. Indeed, by analyzing the total X's demand trend (sum of the FPPs demand forecasted by month) over the 24 months of forecast, we get the Graph 1.

Graph 1: Evolution of the total demand of X over the 24 months forecasted



The average total X's demand: sum of FPPs demand at the SKU (Stock Keeping Unit) level is 19.878 Vials by month, and the standard deviation over the 24 months of time horizon equals 2.522 Vials. So, the coefficient of variation of the total X's demand is:

$$CV(X) = \frac{Ave\ total\ demand\ (X)}{SD\ (X)} = 0.127$$

-Integral Single Echelon planning VS Integral Multi Echelon planning to cope with uncertainties-

X's network

First, at the most upstream part of the supply chain there are two APIs (API1 and API2). Those two APIs are blend to produce two different FPU, FPU1 which is a vial of 50ML, and FPU2 which is vial of 100ML. When the production starts for FPU1, it is produced in batches of 24200 vials of 50ML. When the production starts for FPU2, it is produced in batches of 3400 vials of 100ML. Those two quantities are the fixed batch sizes.

From FPU1, 31 FPPs can be produced (that corresponds to the same product but for different market/label). From FPU2, only one FPP is produced (only one market). The X's network is given in Appendix 1 and its characteristics in Appendix 2 to 5 (BOM, Fixed batch sizes and BOM numbers).

The lead time description of the X's supply chain is given on Figure 14. [Figure 14]

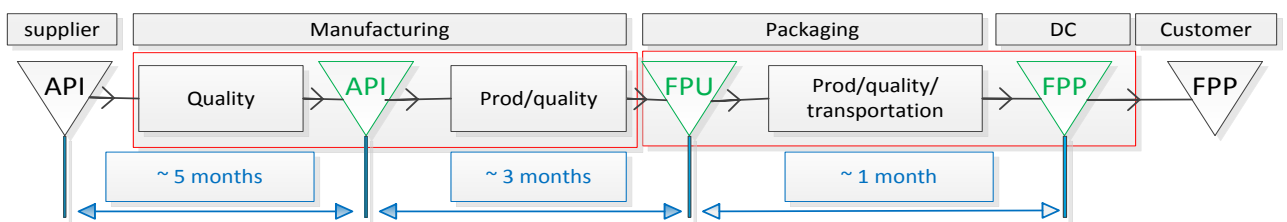


Figure 14: Lead time description of the X's supply chain

The supply uncertainties that occur along the X's supply chain are the lead time (production and quality), the output quantity fluctuation and the batch rejection. There is no yield consideration for pharmaceutical product, so no yield fluctuation for X. And there is no test repetition along the X's supply chain at all.

X is subject to three supply uncertainties:

- Lead time variation
- Output quantity fluctuation
- Batch rejection

Figure 15 shows the location of supply uncertainties through the X's supply chain. [Figure 15]

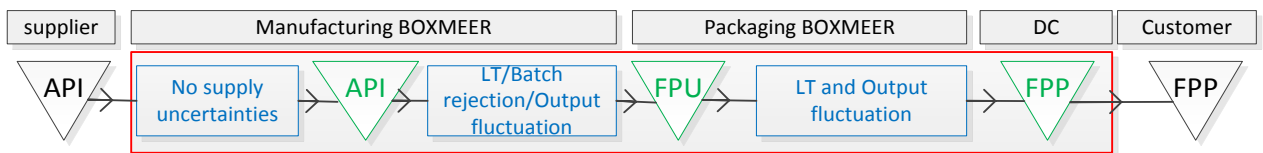


Figure 15: Location of the X's supply uncertainties within its supply chain

Research activities

First two supply chain planning simulation models for the sub product family X are built. One model will support a Single Echelon concept and the second model will support the Multi Echelon concept. The input parameters and variables will be exactly the same (they will use the same data); the output

-Integral Single Echelon planning VS Integral Multi Echelon planning to cope with uncertainties-

performance indicators will be defined exactly by the same formulas. Only the concept changes from one model to another. Then performances are compared.

Secondly, the second research question is investigated by doing a sensitive analysis based on scenarios in order to study the impact of the supply uncertainties on the two planning concepts.

IV.B Single Echelon concept characterization

The Single Echelon concept is depicted on two stock level (or inventory level) definitions (Silver et al, 1998). The Echelon stock ES and the Echelon Inventory position EIP . The definitions are the following:

- **Echelon Stock** of a stockpoint equals its physical stock minus its backorders. (1)
- **Echelon Inventory position** of a stockpoint equals its echelon stock plus all material in transit to that stockpoint. (2)

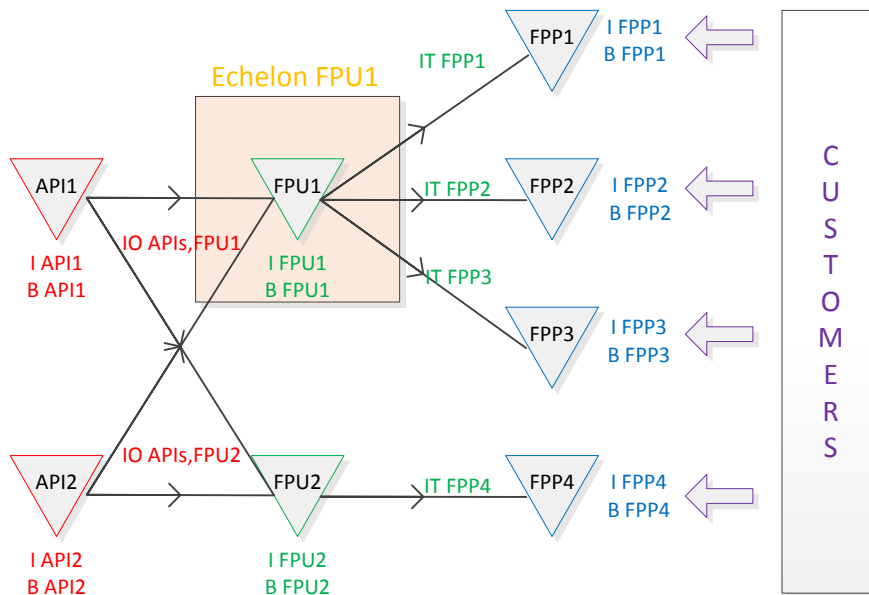


Figure 16: Single Echelon concept characterization

For instance [Figure 16],

$$\begin{cases} ES_{FPU1} = I_{FPU1} - B_{FPU1} \\ EIP_{FPU1} = ES_{FPU1} + IO_{API, FPU1} \end{cases}$$

Single Echelon Generalization

$\forall i$ an echelon

$$\begin{cases} ES_i = I_i - B_i \end{cases} \quad (1)$$

$$\begin{cases} EIP_i = ES_i + \sum_{j \in W(i)} IO_{j,i} \end{cases} \quad (2)$$

With, $W(i)$: direct predecessor of echelon i

IV.C Multi Echelon concept characterization

The Multi Echelon concept is also depicted by two stock level (or inventory level) definitions, the Echelon stock ES and the Echelon Inventory position EIP . They have the same names as in the Single Echelon concept but their definitions are quite different (Silver et al, 1998). The definitions are:

- **Echelon Stock** of a stockpoint equals the sum of its physical stock plus the amount in transit to or on hand at its downstream stockpoints minus backorders at its end-stockpoints. (3)
- **Echelon Inventory position** of a stockpoint equals its echelon stock plus all material in transit to that stockpoint. (4)

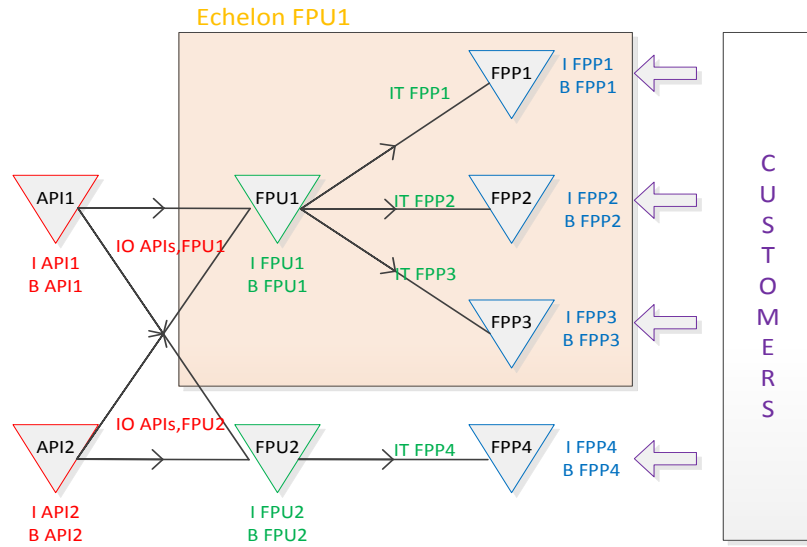


Figure 17: Multi echelon concept characterization

For instance [Figure 17],

$$\left\{ \begin{array}{l} ES_{FPU1} = I_{FPU1} + I_{FPP1} + I_{FPP2} + I_{FPP3} + IT_{FPP1} + IT_{FPP2} + IT_{FPP3} - (B_{FPP1} + B_{FPP2} + B_{FPP3}) \\ EIP_{FPU1} = ES_{FPU1} + IO_{API, FPU1} \\ \quad = I_{FPU1} + I_{FPP1} + I_{FPP2} + I_{FPP3} + IT_{FPP1} + IT_{FPP2} + IT_{FPP3} \\ \quad \quad - (B_{FPP1} + B_{FPP2} + B_{FPP3}) + IO_{API, FPU1} \end{array} \right.$$

Multi echelon generalization

$\forall i$ an echelon

$$\left\{ \begin{array}{l} ES_i = I_i + \sum_{j \in V(i)} (I_j + IT_j) - \sum_{k \in ends(i)} B_k \\ EIP_i = EI_i + \sum_{j \in W(i)} IO_{j,i} \end{array} \right. \quad (3)$$

$$\left\{ \begin{array}{l} ES_i = I_i + \sum_{j \in V(i)} (I_j + IT_j) - \sum_{k \in ends(i)} B_k \\ EIP_i = EI_i + \sum_{j \in W(i)} IO_{j,i} \end{array} \right. \quad (4)$$

With, $V(i)$: all successor of echelon i

$W(i)$: direct predecessor of echelon i

$ends(i)$: end stockpoint related to echelon i

IV.D Planning process and characteristics

For both SE and ME, the planning has a planning horizon T of three years. Due to a long cycle time for the complete supply chain it is not possible to get a planning with a planning horizon of one year. With two years of planning horizon, it gives only one complete cycle, which is not an acceptable limit. With three years of planning horizon, there is a problem because the forecast of the demand is given for 24 months. Nevertheless, as the demand for the sub product family X is quite stationary, it is possible to extend the demand forecast until the following year without taking a lot of risks. So, three years of planning horizon is good enough to get two complete cycles and not too much to keep a reliable extension of the forecast of the demand on the third year.

The planning is defined on a discrete planning review period basis. The discrete characteristic of the planning is selected because the current planning is discrete and it does not involve important changes within the management techniques in case of implementation. The planning is run and evaluated on each fixed period of time (review period). For the considered planning, the planning review period is one month.

The planning considered is a mid term planning (higher level than a short term planning). The activities are planned and coordinated on a mid term horizon instead of a short term horizon (more operational). The planning has for goal to give to the planners the quantities that need to be produced (when production is required) in order to cover the future demand. There is no scheduling consideration at all. The output of this planning is: we need to produce this quantity if production is required. But, planners can place orders strategically from an operational perspective, according to the capacity availabilities. For my project, there is infinite capacity. The real goal of my planning is to give to the planners the quantities that need to be produced and the amount of inventory that need to be kept in stock, but the scheduling and the operational production plan still need to be done. For instance in figure 18, my planning is depicted by the red line, when production is required Q_2 is produced. But from an operational perspective (green line), the planner would place for instance two orders of quantity Q_1 instead of one order of quantity Q_2 (maybe for capacity constraints) [Figure 18].

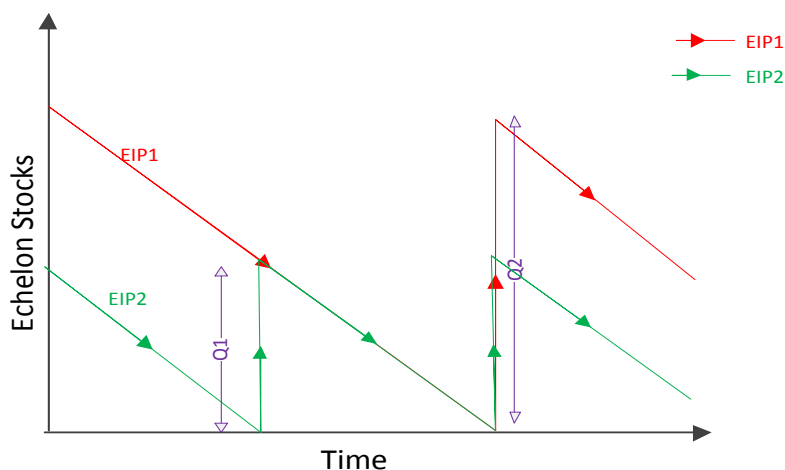


Figure 18: role of my planning

The planning considered in this project is a real mid term planning and it gets a higher level than an operational planning.

-Integral Single Echelon planning VS Integral Multi Echelon planning to cope with uncertainties-

Due to the long lead time and for a mid term planning, one month is an adequate review period to plan the future activities.

The planning process for both single planning and multi echelon planning is the following [Figure 19]:

- 1) Demand creation and demand fulfillment
- 2) Update inventory positions according to the demand fulfillment
- 3) Evaluation of the inventory positions
- 4) Production decisions
- 5) Update inventory positions according to the production decisions



Figure 19: Planning process for both SE planning and ME planning

IV.E Planning policy

It has been decided that the Single Echelon planning concept and the Multi Echelon planning concept for the sub product family X will be compared in an integral way. Thus, the planning concepts are known. Nevertheless, in order to take production decisions, the planning concept needs to be combined with an inventory management policy. Within this paragraph the inventory management policy is described.

According to the discrete aspect of the planning, the inventory policy must be discrete too. This means that the inventory will be evaluated at certain dates and not continuously over time. The actual inventory policy is a (R,s,Q) policy, which is a discrete policy. In order to stay in line with the actual inventory management and avoid a lot of changes in the organization from an implementation point of view, the same inventory policy is chosen for each planning concept and for each echelon of the sub product family X's supply chain.

According to (Silver et al, 1998), the (R,s,Q) policy works as follows: every R units of time (1 month) the inventory position is checked. If the inventory position goes below the replenishment point s, a quantity Q is ordered and afterwards the lead time replenished. If the inventory position is above s, no production is started and the inventory position is reviewed the next period. [Figure 20]

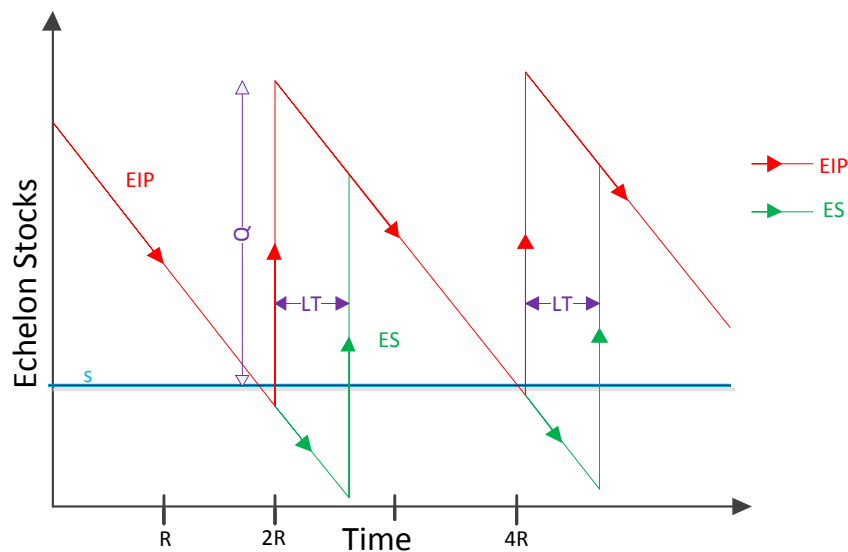


Figure 20: Planning policy for both SE planning and ME planning

For each planning (SE or ME) my goal is to optimize the planning parameters (s and Q) of each echelon in order to minimize the supply chain cost while meeting a given service level.

Note: the s level of the ME concept will obviously be higher than the s level of the SE concept for the FPU and API levels. The Multi Echelon characterization imposes that. The production decision of the ME planning is taken based on the complete downstream stock level of the supply chain.

$$s_{FPU}(SE) < s_{FPU}(ME) \text{ and } s_{API}(SE) < s_{API}(ME)$$

However, at the FPP level, the ME concept and the SE concept are similar because located at the most downstream part of the supply chain. Nothing can be forecasted about their s levels.

IV.F Model characteristics

In this paragraph the model's inputs, outputs and decision variables are presented. First, the customer demand consideration is treated. Secondly, the supply uncertainty modeling is depicted. Then, the model's outputs are presented through the service level definition and the objective function. Finally, the decision variables of the model are described.

The customer demand

For each FPP a stochastic customer demand is considered. This means that each month a random demand quantity is generated for each FPP. The random quantity is based on a probability distribution. In order to determine the distribution function of the demand for each FPP, the forecast of the monthly demand over the next 24 months is analyzed with the Input Analyzer tool of ARENA. The Input Analyzer tool takes the forecast data file as input and fits the data with a distribution function of your choice (exponential, gamma, poison, lognormal and so on). The problem now is to choose the good distribution function. In order to fit with the real life situation the random demand quantity must be discrete because MSDAH sells vials or box of vials. This constraint eliminates all continuous distribution functions. Furthermore, it seems that the best distribution should be the empirical one because this empirical distribution is based on the real data and not on a function that fits approximately the real data. Thus, by considering those two aspects, the discrete empirical distribution function for generating all random FPP's demands has been selected. The distribution functions for the FPP's demands are given in Appendix 6 and a reminder of the different probability distributions used in my project is given in Appendix 7.

The supply uncertainties

As mentioned before, the X's supply chain is subject to three kinds of supply uncertainties:

- Lead time variation
- Output quantity fluctuations
- Batch rejection

Let's analyze the study of those supply uncertainties in my simulation model

Lead time variation

For the lead time variation, it has been decided to generate a random lead time from a probability distribution. The same method as for the demand has been used. The history of the production times and quality times at each echelon have been extracted from SAP with the help of planners from the Manufacturing site. This Lead time history data file have been analyzed with the Input Analyzer tool of ARENA. The distribution function selected is the one which minimizes the Mean Standard Error (MSE) Appendix 8. A description of the different lead times given by echelon is presented in Appendix 9.

Output quantity fluctuation

This characteristic is incorporated in the simulation model via a deviation factor. This deviation factor is the percentage of the expected quantity which is lost during the process. In order to quantify this deviation factor, an output quantity history per SKU has been extracted from SAP (with the help of planners from the manufacturing site). Those output quantities have been compared to the expected

-Integral Single Echelon planning VS Integral Multi Echelon planning to cope with uncertainties-

output quantity to get a deviation factor, and the deviation factor used in the model is the average of those deviation factors.

For one production order step,

$$Devf (prod\ order) = 1 - \frac{Q\ produced}{Q\ expected}$$

Thus, the deviation factor for one SKU used in the simulation model is defined as followed:

$$Devf (SKU) = \frac{\sum_{prod\ order=1}^N Devf (prod\ order)}{N}$$

With, N the number of production order in the history.

Batch rejection

The batch rejection is introduced in the simulation model via a percentage of rejection. If a batch is rejected, the complete batch is lost. Batch rejection can only occur during the FPU production (in my project). A history of the batch production and batch rejection has been extracted and then the percentage of batch rejection is computed. From an ARENA model point of view, the batch rejection is model by a “decide” module which rejects a batch with a certain percentage (the batch rejection BR).

$$BR = \frac{Number\ of\ batch\ rejected}{Number\ total\ of\ batch\ produced}$$

Service level

The objective of this simulation is to optimize the planning parameters in order to minimize the supply chain cost while meeting a given service level. Thus, a service level definition needs to be given.

The FPP’s service level in period t is the proportion of the customer demand in t (in FPP) directly fulfilled from the stock at the DC.

$$SL_{FPP}(t) = \left(\frac{D_{FPP}(t) - MAX(B_{FPP}(t) - B_{FPP}(t-1); 0)}{D_{FPP}(t)} \right) * 100$$

Note: The MAX function is defined as followed:

$$\forall x, y \in R$$

$$\text{If } > y, MAX(x; y) = x$$

$$\text{If } < y, MAX(x; y) = y$$

The service level taken into account in the simulation is the average service level over the FPPs and over time. Three years correspond to a planning horizon $T=36$ months. The sub product family X's network is constituted by 32 FPPs. Thus, the average service level is defined like that:

$$SL = \frac{\sum_{t=1}^T \sum_{fpp=FPP1}^{FPP34} SL_{fpp}(t)}{32 * T}$$

So,

$$SL = \frac{\sum_{t=1}^T \sum_{fpp=FPP1}^{FPP34} \left(\frac{D_{fpp}(t) - \text{MAX}(B_{fpp}(t) - B_{fpp}(t-1); 0)}{D_{fpp}(t)} \right) * 100}{32 * T}$$

The required average service level is equal to 98%. The average service level constraint is:

$$SL = \frac{\sum_{t=1}^T \sum_{fpp=1}^{FPP} \left(\frac{D_{fpp}(t) - \text{MAX}(B_{fpp}(t) - B_{fpp}(t-1); 0)}{D_{fpp}(t)} \right) * 100}{32 * T} \geq 98\%$$

Objective function

As mentioned before the objective function of the optimization is the average supply chain cost. The objective is to minimize the average monthly supply chain cost. By considering only the average physical inventory cost of each echelon of the supply chain, the optimization will go in the right way. The s parameters will tend to decrease for obvious reasons, and the order quantity Q will tend to decrease too. Indeed, the value chain of the sub product family X increases from the API level to the FPP level, so if the order quantity is high, that means that the product will achieve an echelon stock point with a higher cost and remain high until being proceeded, that costs more money. The backordering cost is not considered because the optimization is Service level constrained.

Thus, the costs considered within the cost function are the Cost Prices (CP) of the product at each echelon (this is the value chain of the product). The different Cost Prices are given in Appendix 10.

$$\begin{aligned} & \text{Ave Cost} \\ & = \frac{\sum_{t=1}^T (\sum_{fpp=FPP1}^{FPP34} I_{fpp}(t) * CP_{fpp} + \sum_{fpu=FP1}^{FPU2} Inv_{fpu}(t) * CP_{fpu} + \sum_{api=API1}^{API2} Inv_{api}(t) * CP_{api})}{T} \end{aligned}$$

And the objective function is:

$$\min_{fpp, fpu, api} \left[\frac{\sum_{t=1}^T (\sum_{fpp=FPP1}^{FPP34} I_{fpp}(t) * CP_{fpp} + \sum_{fpu=FP1}^{FPU2} Inv_{fpu}(t) * CP_{fpu} + \sum_{api=API1}^{API2} Inv_{api}(t) * CP_{api})}{T} \right]$$

It is important to notice that according to the service level definition and the objective definition it would be useless to fulfill the backorders because the model does not punish for that. There is no backordering cost in the objective function. From a Mixed Integer Linear Programming perspective, those definitions will not lead to the fulfillment of the backorders because it will not be optimal. But this is not what the company wants. The backorders have to be fulfilled as soon as possible. The simulation approach used to solve the problem is able to overcome this problem. In fact, the

-Integral Single Echelon planning VS Integral Multi Echelon planning to cope with uncertainties-

implemented planning in ARENA will force the backorders fulfillment once an order received, and as the optimization tool will use the implemented planning as input, the backorders will be fulfilled during the optimization process.

From a Mixed Integer Linear programming perspective, the backorders would not be fulfilled. But by using the simulation approach, behaviors can be imposed and within the implemented planning in ARENA, backorders fulfillment is imposed.

As a conclusion, the input parameters are:

- The forecast of the demand for each FPP in order to get the demand distributions
- The lead time distribution functions for the different process between echelons
- The batch rejection percentage for the FPU production
- The deviation factors between each echelon
- The cost prices of X at each echelon
- The fixed batch quantities for the FPU production
- The given required average service level which is equal to 98%

Decisions variables

In the simulation model there are 36 echelons and for each echelon there are two planning parameters; s and Q for the FPP level and API level, and s and n for the FPU level (n represents the number of batch that needs to be produced). Thus, for each planning model, there are 72 planning parameters and by definition there are 72 decision variables. Appendix 11 presents the planning parameters by echelon.

A summary of the modeling phase is depicted in the Figure 21. [Figure 21]

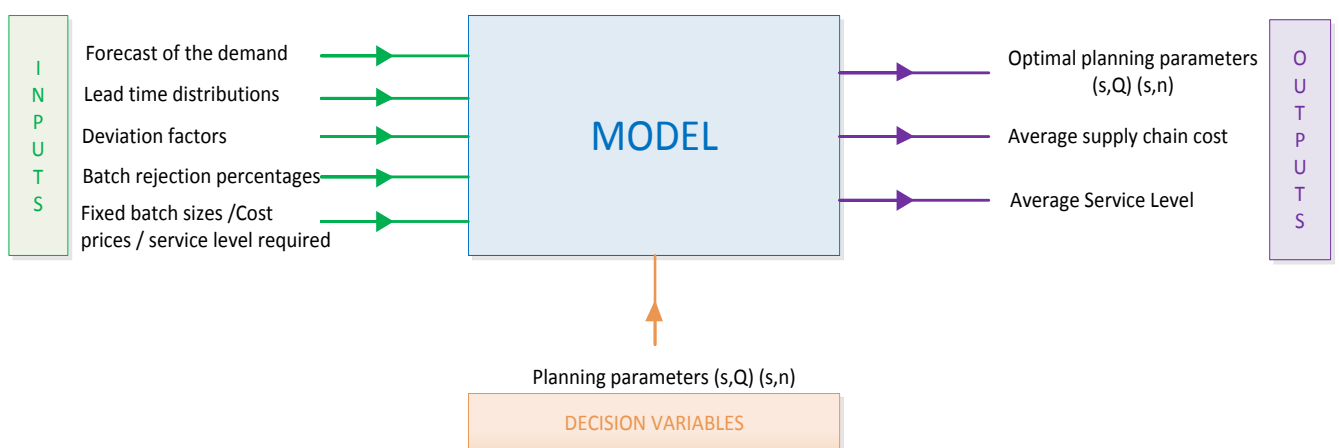


Figure 21: Model's inputs, outputs and decision variables overview

IV.G Model summary

Network characteristics

- 32 end products (FPPs)
- 36 echelons (32 FPPs, 2 FPU and 2 APIs)

Planning characteristics

- Planning horizon $T=36$ months
- Review period $t=1$ month
- Discretized time horizon: $[t, 2t, 3t, \dots, 35t, T]$
- s_i = First planning parameter of echelon i which is the replenishment point s
- Q_i = Second planning parameter of echelon i (for FPP level and API level) which is the ordering quantity when production is required at echelon i .
- n_{fpu} = Second planning parameter of echelon fpu (for FPU level) which is the number of batches required for production when production is required at echelon i .

Demand

- Stochastic demand in end echelon fpp (FPP level): D_{fpp} Value independent and identically distributed (i.i.d)

Supply uncertainties

- Stochastic replenishment lead time from echelon i to echelon j :
 LT EXPRESSION i to j (i.i.d)
- $devf_{ij}$ = the output quantity deviation factor from echelon i to echelon j
- BR_{ij} = batch rejection percentage from echelon i to echelon j

Stock definitions

- $EIP_i(t)$ = Echelon Inventory Position of echelon i in period t
- $ES_i(t)$ = Echelon Stock of echelon i in period t
- $I_i(t)$ = Physical Inventory of echelon i in period t
- $B_i(t)$ = Backorders of echelon i in period t

Cost

- CP_i = Cost price at the echelon i

Constraint

- SL= the average service level per month

Objective

- Ave Cost= the average supply chain cost per month

Compute the optimal planning parameters for each echelon in order to minimize the average supply chain cost while meeting a given service level (98%).

V. Simulation models

Within this chapter the simulation models and planning processes are depicted. First, the simulation assumption are listed and explained. Second, the multi echelon planning process is described through a formal approach. Then, the single echelon planning process is presented through a formal approach too. And finally, the verification/validation procedure is achieved (Kelton et al, 2003). A list of symbol used in the model is given in Appendix 12.

V.A Simulation assumptions

General assumptions

- [1] Network and paths are given. The location of the manufacturing sites and the DCs are not decision variables.
- [2] Production, quality, packaging and transportation processes are modeled by a black box and what is happening inside is not considered. They are modeled by a lead time.
- [3] There are no storage, production and transportation constraints. This is an infinite capacity problem.
- [4] Packaging material is not considered.
- [5] The FPP stockpoint at the packaging site is not considered at this level of planning.

Production assumptions

- [6] Batch sizes between API level and FPU level are registered, fixed and given by the company.
- [7] Only complete batches are produced between API level and FPU level.
- [8] Production lead times and quality lead times are stochastic. The transportation lead times are deterministic.
- **[9] It is not possible to place an order if the previous order has not been received. It seems normal because if the planning needs to place an order (for instance between FPU and FPP) before the previous one is received, that means that the planning parameters are not well defined.** This assumption is directly related to the goal of my planning and its mid term characteristic. For an operational planning this assumption is non sense. According to Figure 18 and from an operational perspective, planner can place order before receiving the previous one. But for my planning level this assumption makes sense.

Delivery assumptions

- [10] Partial delivery is allowed. If there is not enough in stock to fulfill the complete demand we fulfill the maximum we can.

Supply assumptions

- [11] Batch output quantity uncertainty. This is modeled by a factor.
- [12] Batch rejection uncertainty between API level and FPU level. Within the model this is a percentage of rejection of a batch; either the complete batch is accepted either the complete batch is rejected.
- [13] Stochastic lead times

Demand assumptions

- [14] Demand is stochastic
- [15] Demand is stationary
- [16] Customer demand occurs only at the end stockpoint. It is assumed that an external customer cannot order FPU or API.
- [17] Allocation rule in case of shortage is based on the average order quantity volume placed by the external customer. In case of shortage the customer with the highest average demand is fulfilled first.

Customer assumptions

- [18] Shortages are backordered

Supplier assumptions

- [19] Suppliers are reliable on lead time, quantity and quality. Everything is deterministic.

V.B Multi Echelon Planning

The multi echelon planning is a planning based on the Multi Echelon concept (equation (3) and (4)) supported by a (R, s, Q) policy for each echelon of the X's supply chain. The process described below follows the planning chronology.

1) Demand creation

At the beginning of each planning period (each month), the demand for each FPP is generated. This demand is random and the stochastic distribution of the demand is based on an empirical analysis of the demand forecast, assumption [14]. Thus, for each period and for each FPP, the FPP demand is generated (5):

$$D_{FPP}Value(t) := Demand\ FPP \quad (5)$$

From that FPP demand, a fictive demand in FPU (6) and APIs (7) is also generated to update the FPU and APIs echelons stocks

$$D_{FPP\ FPU}Value(t) := D_{FPP}Value(t) * BOM\ FPP\ FPU \quad (6)$$

$$D_{FPP\ API}Value(t) := D_{FPP\ FPU}Value(t) * BOM\ FPU\ API \quad (7)$$

2) Update inventory (demand)

Once all the FPP demands are generated, the demand in FPP is fulfilled and the inventory levels updated. First, the FPPs inventories (8) and (9):

$$ES_{FPP}(t) := ES_{FPP}(t) - D_{FPP}Value(t) \quad (8)$$

$$EIP_{FPP}(t) := EIP_{FPP}(t) - D_{FPP}Value(t) \quad (9)$$

Moreover, the physical inventory of FPP (10) and the backorders of FPP (11) are also updated

$$I_{FPP}(t) := \text{MAX}(ES_{FPP}(t), 0) \quad (10)$$

$$B_{FPP}(t) := \text{MAX}(-ES_{FPP}(t), 0) \quad (11)$$

The service level of each FPP in period t is then computed (12) after satisfying the demand in FPP:

$$SL_{FPP}(t) := \frac{D_{FPP}Value(t) - \text{MAX}(B_{FPP}(t) - B_{FPP}(t-1); 0)}{D_{FPP}Value(t)} * 100 \quad (12)$$

Secondly, the FPU inventories are updated (13) and (14). For each FPP related to the FPU considered:

$$ES_{FPU}(t) := ES_{FPP}(t) - D_{FPP FPU}Value(t) \quad (13)$$

$$EIP_{FPU}(t) := EIP_{FPP}(t) - D_{FPP FPU}Value(t) \quad (14)$$

Finally, the APIs inventories are updated (15) and (16). Since, the network is convergent between the API level and the FPU level, each FPP has an influence on the APIs level. For each FPP, we have:

$$ES_{API}(t) := ES_{API}(t) - D_{FPP API}Value(t) \quad (15)$$

$$EIP_{API}(t) := EIP_{API}(t) - D_{FPP API}Value(t) \quad (16)$$

3) FPP evaluation

In order to take production decisions on FPP, the model follows the echelon policy described in part IV.E. If the echelon inventory position of a FPP goes below the replenishment point s , we need to produce Q_{FPP} . Thus, for each period after updating the inventory levels:

For each FPP,

If $EIP_{FPP}(t) \leq \text{small } s \text{ FPP}$

$$\text{Do } QO_{FPP}(t) := Q_{FPP} \quad (17)$$

$$QO_{FPP FPU}(t) := Q_{FPP} * BOM_{FPP FPU} \quad (18)$$

$$D_{FPU}Value(t) := D_{FPU}Value(t) + QO_{FPP FPU}(t) \quad (19)$$

$$D_{FPU FPP}Value(t) := QO_{FPP FPU}(t) \quad (20)$$

$$\text{Else } D_{FPU}Value(t) := D_{FPU}Value(t) \quad (21)$$

$$D_{FPU FPP}Value(t) := 0 \quad (22)$$

End If

End for

If production of FPP is required, the quantity ordered (in FPP unit) is Q_{FPP} (17). This is translated in a quantity ordered in FPU unit (18). This increases the total demand in FPU (19), because this is

-Integral Single Echelon planning VS Integral Multi Echelon planning to cope with uncertainties-

realized for each FPP related to FPU. (20) is the variable related to the demand in FPU generated by the considered FPP in period t.

If no production of FPP is required in period t. the total demand in FPU does not increase with FPP (21) and the FPU demand generated from FPP is zero (22).

If we need to produce at least one FPP ($D_{FPU}Value(t) > 0$), only two things can happen. We have enough FPU In stock to produce the FPP demands. We do not have enough FPU in stock to produce the complete demand in FPP. We have assumed that partial delivery is allowed [10], thus the complete stock of FPU will be used in order to fulfill the maximum of the FPP demand.

In case there is not enough FPU in stock, we are facing an allocation problem. An allocation problem has to answer this question: which FPPs to produce first. In order to answer this question we need an allocation rule. The allocation rule is the following [17]: produce first the FPPs with the maximal average external demand (customer demand). This rule is based on order volume. Within ARENA, the FPPs related to FPU1 (50ml) have been ranked by descending average demand; this way, we will first fulfill the demand for the most important FPPs.

Return to the two cases:

If $Inv_{FPU}(t) \geq D_{FPU}Value(t)$

Do for each FPP that needs to be produced

$$QS_{FPU\ FPP}(t) := Q_{FPP} \quad (23)$$

$$QS_{FPU\ to\ FPP}(t) := D_{FPU\ FPP}Value(t) \quad (24)$$

$$Inv_{FPU}(t) := Inv_{FPU}(t) - D_{FPU\ FPP}Value(t) \quad (25)$$

$$EIP_{FPP}(t) := EIP_{FPP}(t) + QS_{FPU\ FPP}(t) * (1 - devf_{FPU\ FPP}) \quad (26)$$

Else for each FPP that needs to be produced

$$QS_{FPU\ to\ FPP}(t) := MIN(Inv_{FPU}(t), Q_{FPP} * BOM_{FPP\ FPU}) \quad (27)$$

$$QS_{FPU\ FPP}(t) := \frac{QS_{FPU\ to\ FPP}(t)}{BOM_{FPP\ FPU}} \quad (28)$$

$$Inv_{FPU}(t) := MAX(Inv_{FPU}(t) - Q_{FPP} * BOM_{FPP\ FPU}, 0) \quad (29)$$

$$EIP_{FPP}(t) := EIP_{FPP}(t) + QS_{FPU\ FPP}(t) * (1 - devf_{FPU\ FPP}) \quad (30)$$

End for

End If

-Integral Single Echelon planning VS Integral Multi Echelon planning to cope with uncertainties-

Note: The *MIN* function is defined as followed:

$$\forall x, y \in R$$

$$\text{If } > y, \text{MIN}(x, y) = y$$

$$\text{If } < y, \text{MAX}(x, y) = x$$

If the physical inventory at the FPU level is enough to produce the total demand in FPU, the quantity shipped (or produced) from FPU to FPP (in FPP unit) is Q_{FPP} (this is the order quantity of echelon FPP) (23), for each FPP that required production. The quantity shipped from FPU to FPP in FPU unit equals the demand in FPU generated by FPP (24). Then the physical inventory of FPU is updated (25). Finally, the echelon inventory position of FPP is updated (26) by taking into account the deviation factor of FPP.

If there is not enough FPU in stock to satisfy the total FPU demand, the allocation rule is applied and first the demand generated by the FPPs with highest average demand is fulfilled. According to the assumption [10], the quantity shipped from FPU to FPP (in FPU unit) is the maximum between the physical inventory level of FPU remaining and the demand in FPU unit generated by FPP (27). The quantity shipped in FPP unit is given by (28). Then, the physical inventory of FPU is updated (29). The echelon inventory position of FPP is also updated (30) taking into account the deviation factor of FPP. And the process is redone for the next FPP.

Once the order is received at the DC's (FPPs), the inventory levels need to be updated. First the echelon stock at the FPP level is updated (31) by taking into account the deviation factor.

$$ES_{FPP}(t) := ES_{FPP}(t) + QS_{FPU FPP}(t) * (1 - devf_{FPU FPP}) \quad (31)$$

Nevertheless, the model is supporting a multi echelon planning and the loss between the FPU echelon and the FPP echelon have to be take into account by each echelon even the API echelon. This is a characteristic of the multi echelon concept. Thus, the echelon inventories at the FPU level are updated (32) and (33) taking into account the loss of quantity between FPU and FPP.

$$EIP_{FPU}(t) := EIP_{FPU}(t) - QS_{FPU FPP}(t) * BOM_{FPP FPU} * devf_{FPU FPP} \quad (32)$$

$$ES_{FPU}(t) := ES_{FPU}(t) - QS_{FPU FPP}(t) * BOM_{FPP FPU} * devf_{FPU FPP} \quad (33)$$

Then, the echelon inventories at the API level are updated (34) and (35). For each API:

$$EIP_{API}(t) := EIP_{API}(t) - QS_{FPU FPP}(t) * BOM_{FPP FPU} * BOM_{FPU API} * devf_{FPU FPP} \quad (34)$$

$$ES_{API}(t) := ES_{API}(t) - QS_{FPU FPP}(t) * BOM_{FPP FPU} * BOM_{FPU API} * devf_{FPU FPP} \quad (35)$$

As mentioned in part IV.F, the backorder fulfillment is part of the planning process

For each FPP

$$I_{FPP}(t) := I_{FPP}(t) + QS_{FPU FPP}(t) * (1 - devf_{FPU FPP}) \quad (36)$$

If, $B_{FPP}(t) > 0$

Do If $B_{FPP}(t) \geq I_{FPP}(t)$

$$\text{Do } QS2_{FPP}(t) := I_{FPP}(t) \quad (37)$$

$$\text{Else } QS2_{FPP}(t) := B_{FPU}(t) \quad (38)$$

Else do nothing

End if

Once the order is received at the FPP echelon, the physical inventory of FPP increases by the shipped quantity (taking into account the deviation factor) (36).

If there are backorders at the FPP echelon, the minimum between the physical inventory of FPP and the backorders quantity is fulfilled (37) and (38).

Afterward, the physical inventory of FPP is updated (39) and the backorder level of FPP is updated too (40)

$$I_{FPP}(t) := \text{MAX}(ES_{FPP}(t), 0) \quad (39)$$

$$B_{FPP}(t) := \text{MAX}(-ES_{FPP}(t), 0) \quad (40)$$

4) FPU evaluation

Once the production decisions in FPPs taken, the FPU level is evaluated. The production decision process at the FPU level follows the same multi echelon policy as the FPP level. If the echelon inventory position of the FPU goes below the replenishment point s we produce $nFPU$ batches of quantity Q_{FPU} each (fixe quantity equals to 24200 vials for FPU1 and 3400 vials for FPU2, assumption [6]) in FPU. Nevertheless, between the API level and the FPU level the network is convergent, so for the FPU production decision we have to check the Physical inventory level of both API1 and API2.

If $EIP_{FPU}(t) \leq \text{small } s \text{ FPU}$

$$nFPUV := nFPU \quad (41)$$

Do for each API

$$D_{API \text{ FPU} Value}(t) := nFPUV * Q_{FPU} * BOM \text{ FPU API} \quad (42)$$

Else do nothing

If FPU production is required, a variable representing the number of FPU batches that needs to be produced is initiated at the value of the planning parameter $nFPU$ (41). And for each API, a demand in API is generated from the FPU requirement (42).

Only two things can happen. There is enough API1 and API2 in stock to produce the required order. There is not enough API1 and API2 in stock to produce. According to the assumption [7], only

-Integral Single Echelon planning VS Integral Multi Echelon planning to cope with uncertainties-

complete batch is produced between API and FPU. So, in the latest case, we will decrease the number of production batch until only complete batches can be produced.

If there is enough API1 and API2 in stock, the normal order quantity is placed by FPU (normal number of batches) (43). That generates a demand for each API in API unit, API1 (44) and API2 (45).

If $Inv_{API1}(t) \geq D_{API1 \ FPU}Value(t)$ AND $Inv_{API2}(t) \geq D_{API2 \ FPU}Value(t)$

$$\text{Do } QO_{FPU}(t) := nFPUV * Q_{FPU} \quad (43)$$

$$QO_{FPU \ API1}(t) := QO_{FPU}(t) * BOM_{FPU \ API1} \quad (44)$$

$$QO_{FPU \ API2}(t) := QO_{FPU}(t) * BOM_{FPU \ API2} \quad (45)$$

If there is not enough stock in API1 and API2, the number of required batches is decreased by one (46) and it is checked if this new order can be produced. If it can, we go to case 1. And if it cannot the number of batches is decreased by one. And, so on until a number of batches can be produced completely.

$$\text{Else } nFPUV := nFPUV - 1 \quad (46)$$

If $Inv_{API1}(t) \geq D_{API1 \ FPU}Value(t)$ AND $Inv_{API2}(t) \geq D_{API2 \ FPU}Value(t)$

Do the same actions as in the first "do"

Else do $nFPUV := nFPUV - 1$ and so on until we find a $nFPUV$ that works

End if

End if

Once the order quantities are defined, the quantities shipped are also defined. As the FPU's placed order can be produced, the quantity shipped in API1 to FPU is equals to the quantity ordered by FPU in API unit (47). And the quantity shipped from API1 in FPU unit is equal to the quantity ordered by FPU (49). We get the same for API2 (48) and (50).

$$QS_{API1 \ to \ FPU}(t) := QO_{FPU \ API1}(t) \quad (47)$$

$$QS_{API2 \ to \ FPU}(t) := QO_{FPU \ API2}(t) \quad (48)$$

$$QS_{API1 \ FPU}(t) := QO_{FPU}(t) \quad (49)$$

$$QS_{API2 \ FPU}(t) := QO_{FPU}(t) \quad (50)$$

Now it is time to update the inventory levels. First, the physical inventory of each API is updated (51) and (52). Then, the echelon inventory position of FPU is updated according to the deviation factor (53). But this is what is expected because batches can be rejected.

$$Inv_{API1}(t) := Inv_{API1}(t) - QS_{API1 \ to \ FPU}(t) \quad (51)$$

$$Inv_{API2}(t) := Inv_{API2}(t) - QS_{API2 \ to \ FPU}(t) \quad (52)$$

-Integral Single Echelon planning VS Integral Multi Echelon planning to cope with uncertainties-

$$EIP_{FPU}(t) := EIP_{FPU}(t) + QS_{API1\ to\ FPU}(t) * (1 - devf_{API\ FPU}) \text{ [Expected]} \quad (53)$$

As we check the physical inventory at the API level before placing an order, we ensure that complete batches are produced and above all, we ensure that there is no backorder at the API level (54) and (55).

$$B_{API1}(t) := 0 \quad (54)$$

$$B_{API2}(t) := 0 \quad (55)$$

Once processed, we know how many batches have been rejected and we have to update the inventory levels according to that. For instance, n batches have been rejected ($n \leq nFPUV$). At the FPU level, the echelon inventory position has to take into account this loss (56). Then, the echelon stock (57) and the physical inventory (58) are updated according to the batch rejection and the deviation factor.

$$EIP_{FPU}(t) := EIP_{FPU}(t) - n * Q_{FPU} * (1 - devf_{API\ FPU}) \quad (56)$$

$$ES_{FPU}(t) := ES_{FPU}(t) + (nFPUV - n) * Q_{FPU} * (1 - devf_{API\ FPU}) \quad (57)$$

$$Inv_{FPU}(t) := Inv_{FPU}(t) + (nFPUV - n) * Q_{FPU} * (1 - devf_{API\ FPU}) \quad (58)$$

According to the multi echelon concept characteristics the API level has to take into account those losses. The quantity output fluctuation and the batch rejection at the FPU level have an influence on the API echelon stocks. For each API, the echelon inventory position (59) and the echelon stock (60) are updated according to those losses.

(59)

$$EIP_{API}(t) := EIP_{API}(t) - n * Q_{FPU} * BOM_{FPU\ API} - (nFPUV - n) * Q_{FPU} * BOM_{FPU\ API} * devf_{API\ FPU}$$

(60)

$$ES_{API}(t) := ES_{API}(t) - n * Q_{FPU} * BOM_{FPU\ API} - (nFPUV - n) * Q_{FPU} * BOM_{FPU\ API} * devf_{API\ FPU}$$

We can notice that at the API level, the first part of the formula is dedicated to the batch rejection (we lose n batches) and the second part is dedicated to the quantity output fluctuation of the batches produced.

5) API evaluation

The production decision process at the API level follows the same multi echelon policy as the FPP level. If the echelon inventory position of the API goes below the replenishment point s we produce Q_{API} . At API echelon the process is quite easy because we have assumed the supplier is as reliable in time, quality and quantity (everything is deterministic) assumption [19].

If the purchasing of API is required, the quantity order to the supplier equals the planning parameters Q_{API} (order quantity in API) (61). Then, the echelon inventory position is updated (62).

-Integral Single Echelon planning VS Integral Multi Echelon planning to cope with uncertainties-

If $EIP_{API}(t) \leq \text{small } s \text{ API}$

$$\text{Do } QO_{API}(t) := Q_{API} \quad (61)$$

$$EIP_{API}(t) := EIP_{API}(t) + QO_{API}(t) \quad (62)$$

Else do nothing

Once the order is received, the echelon stock (63) and the physical inventory (64) are updated:

$$ES_{API}(t) := ES_{API}(t) + QO_{API}(t) \quad (63)$$

$$Inv_{API}(t) := Inv_{API}(t) + QO_{API}(t) \quad (64)$$

V.C Single Echelon Planning

The single echelon planning is a planning based on the single echelon concept (equations (1) and (2)) supported by a (R, s, Q) policy for each echelon of the X's supply chain. The process described below follows the planning chronology.

Warning: The SE planning process is exactly the same as the ME planning process. So explanations equation by equation will not be given for this SE planning.

1) Demand generation

The demand generation process for the single echelon planning is exactly the same as the one for the multi echelon planning. At the beginning of each planning period (each month), the demand for each FPP is generated. The demand is stochastic according to the assumption [14]. In the SE's case, no fictive demands are generated.

$$D_{FPP}Value(t) := Demand \ FPP \quad (65)$$

2) Update inventory (demand)

Once all the FPP demands are generated, the demand is fulfilled and the FPP echelon inventories are updated.

$$ES_{FPP}(t) := ES_{FPP}(t) - D_{FPP}Value(t) \quad (66)$$

$$EIP_{FPP}(t) := EIP_{FPP}(t) - D_{FPP}Value(t) \quad (67)$$

Moreover,

$$I_{FPP}(t) := MAX(ES_{FPP}(t), 0) \quad (68)$$

$$B_{FPP}(t) := MAX(-ES_{FPP}(t), 0) \quad (69)$$

Then, the service level of each FPP at period t is computed:

$$SL_{FPP}(t) := \frac{D_{FPP}Value(t) - MAX(B_{FPP}(t) - B_{FPP}(t-1); 0)}{D_{FPP}Value(t)} * 100 \quad (70)$$

The difference with the multi echelon planning is that we do not update the upstream echelon stocks according to the customer demand in FPP.

3) FPP evaluation

Once inventories updated and in order to take production decisions for FPP, the model follows the echelon policy described in part IV.E. If the echelon inventory position of a FPP goes below the replenishment point s , we need to produce Q_{FPP} . Thus, for each period:

For each FPP,

If $EIP_{FPP}(t) \leq \text{small } s \text{ FPP}$

$$\text{Do } QO_{FPP}(t) := Q_{FPP} \quad (71)$$

$$QO_{FPP \text{ FPU}}(t) := Q_{FPP} * BOM_{FPP \text{ FPU}} \quad (72)$$

$$D_{FPU \text{ Value}}(t) := D_{FPU \text{ Value}}(t) + QO_{FPP \text{ FPU}}(t) \quad (73)$$

$$D_{FPU \text{ FPP Value}}(t) := QO_{FPP \text{ FPU}}(t) \quad (74)$$

$$\text{Else } D_{FPU \text{ Value}}(t) := D_{FPU \text{ Value}}(t) \quad (75)$$

$$D_{FPU \text{ FPP Value}}(t) := 0 \quad (76)$$

End If

End for

If we need to produce at least one FPP ($D_{FPU \text{ Value}}(t) > 0$), only two things can happen. We have enough FPU in stock to produce the FPPs demand. We do not have enough FPU in stock to produce the complete demand in FPPs. We have assumed that partial delivery is allowed (assumption [10]), thus the complete stock of FPU will be used in order to fulfill the maximum of the FPP demand.

The allocation rule (assumption [17]) is the same as the multi echelon allocation rule, the FPPs related to FPU1 (50ml) have been ranked by descending average demand volume; this way we will first fulfill the demand for the most important FPPs.

And we still have the two cases (enough FPU in stock and not enough FPU in stock): The planning process is the same as for the ME planning. But the echelon inventories (ES and EIP) of FPU need to be updated because the quantity shipped is not considered in the single echelon characterization by opposition with the ME characterization. So, they are decreased by the demand in FPU.

$$EIP_{FPU}(t) := EIP_{FPU}(t) - D_{FPU \text{ Value}}(t) \quad (77)$$

$$ES_{FPU}(t) := ES_{FPU}(t) - D_{FPU \text{ Value}}(t) \quad (78)$$

If $Inv_{FPU}(t) \geq D_{FPU}Value(t)$

Do for each FPP that needs to be produced

$$QS_{FPU\ FPP}(t) := Q_{FPP} \quad (79)$$

$$QS_{FPU\ to\ FPP}(t) := D_{FPU\ FPP}Value(t) \quad (80)$$

$$Inv_{FPU}(t) := Inv_{FPU}(t) - D_{FPU\ FPP}Value(t) \quad (81)$$

$$EIP_{FPP}(t) := EIP_{FPP}(t) + QS_{FPU\ FPP}(t) * (1 - devf_{FPU\ FPP}) \quad (82)$$

End for

Else for each FPP that needs to be produced

$$QS_{FPU\ to\ FPP}(t) := MIN(Inv_{FPU}(t), Q_{FPP} * BOM_{FPP\ FPU}) \quad (83)$$

$$QS_{FPU\ FPP}(t) := \frac{QS_{FPU\ to\ FPP}(t)}{BOM_{FPP\ FPU}} \quad (84)$$

$$Inv_{FPU}(t) := MAX(Inv_{FPU}(t) - Q_{FPP} * BOM_{FPP\ FPU}, 0) \quad (85)$$

$$EIP_{FPP}(t) := EIP_{FPP}(t) + QS_{FPU\ FPP}(t) * (1 - devf_{FPU\ FPP}) \quad (86)$$

End for

End If

Once the order is received at the DC (FPP), we need to update the FPP echelon stock

$$ES_{FPP}(t) := ES_{FPP}(t) + QS_{FPU\ FPP}(t) * (1 - devf_{FPU\ FPP}) \quad (87)$$

Within the single echelon planning, the upstream echelons are not aware of the losses supported at the FPP level. Only the echelon considered can see that.

The backorder fulfillment is part of the planning process, so once the order received:

For each FPP,

$$I_{FPP}(t) := I_{FPP}(t) + QS_{FPU\ FPP}(t) * (1 - devf_{FPU\ FPP}) \quad (88)$$

If, $B_{FPP}(t) > 0$

Do If $B_{FPP}(t) \geq I_{FPP}(t)$

$$Do\ QS2_{FPP}(t) := I_{FPP}(t) \quad (89)$$

$$Else\ QS2_{FPP}(t) := B_{FPU}(t) \quad (90)$$

Else do nothing

End if

Moreover,

$$I_{FPP}(t) := \text{MAX}(ES_{FPP}(t), 0) \quad (91)$$

$$B_{FPP}(t) := \text{MAX}(-ES_{FPP}(t), 0) \quad (92)$$

4) FPU evaluation

The production decision process at the FPU level follows the same single echelon policy than the FPP level. If the echelon inventory position of the FPU goes below the replenishment point s we produce n_{FPU} batches of quantity Q_{FPU} (fixe quantity equals to 24200 vials for FPU1 and 3400 vials for FPU2 assumption [6]) in FPU. Nevertheless, between the API level and the FPU level, the network is convergent, so for the FPU production decision we have to check the Physical inventory level of both API1 and API2.

If $EIP_{FPU}(t) \leq \text{small } s \text{ FPU}$

Do for each API

$$n_{FPUV} := n_{FPU} \quad (93)$$

$$D_{API \text{ FPU} \text{ Value}}(t) := n_{FPUV} * Q_{FPU} * \text{BOM FPU API} \quad (94)$$

Else do nothing

In case of FPU production, only two things can happen. There is enough API1 and API2 in stock to produce the required order. There is not enough API1 and API2 in stock to produce the complete FPU demand. We have assumed that only a complete batch is produced between API and FPU (assumption [7]). So, in the latest case, we will decrease the number of production batch required until complete batches can be produced.

If $Inv_{API1}(t) \geq D_{API1 \text{ FPU} \text{ Value}}(t)$ AND $Inv_{API2}(t) \geq D_{API2 \text{ FPU} \text{ Value}}(t)$

Do $QO_{FPU}(t) := n_{FPUV} * Q_{FPU} \quad (95)$

$$QO_{FPU \text{ API1}}(t) := QO_{FPU}(t) * \text{BOM FPU API1} \quad (96)$$

$$QO_{FPU \text{ API2}}(t) := QO_{FPU}(t) * \text{BOM FPU API2} \quad (97)$$

Else $n_{FPUV} := n_{FPUV} - 1 \quad (98)$

If $Inv_{API1}(t) \geq D_{API1 \text{ FPU} \text{ Value}}(t)$ AND $Inv_{API2}(t) \geq D_{API2 \text{ FPU} \text{ Value}}(t)$

Do the same actions as in the first "do"

Else $n_{FPUV} := n_{FPUV} - 1$ and so on until we find a n_{FPUV} that works

End if

End if

The quantities shipped will be:

$$QS_{API1 \text{ to } FPU}(t) := QO_{FPU \text{ API1}}(t) \quad (99)$$

$$QS_{API2 \text{ to } FPU}(t) := QO_{FPU \text{ API2}}(t) \quad (100)$$

$$QS_{API1 \text{ FPU}}(t) := QO_{FPU}(t) \quad (101)$$

$$QS_{API2 \text{ FPU}}(t) := QO_{FPU}(t) \quad (102)$$

Now it is time to update the inventory levels:

$$Inv_{API1}(t) := Inv_{API1}(t) - QO_{FPU \text{ API1}}(t) \quad (103)$$

$$ES_{API1}(t) := ES_{API1}(t) - QO_{FPU \text{ API1}}(t) \quad (104)$$

$$EIP_{API1}(t) := EIP_{API1}(t) - QO_{FPU \text{ API1}}(t) \quad (105)$$

$$Inv_{API2}(t) := Inv_{API2}(t) - QO_{FPU \text{ API2}}(t) \quad (106)$$

$$ES_{API2}(t) := ES_{API2}(t) - QO_{FPU \text{ API2}}(t) \quad (107)$$

$$EIP_{API2}(t) := EIP_{API2}(t) - QO_{FPU \text{ API2}}(t) \quad (108)$$

$$EIP_{FPU}(t) := EIP_{FPU}(t) + QS_{API1 \text{ to } FPU}(t) * (1 - devf_{API \text{ FPU}}) \text{ [Expected]} \quad (109)$$

The echelon stocks of each API are decreased by the quantity shipped because the planning is supported by a single echelon concept. The quantities shipped are not intrinsic to the echelon.

Only the echelon inventory position of FPU is updated according to the deviation factor (because this loss is expected). But not according to the batch rejection because it is not known yet.

As we check the physical inventory at the API level before placing an order, we ensure that complete batches are produced and above all, we ensure that there is no backorder at the API level.

$$B_{API1}(t) := 0 \quad (110)$$

$$B_{API2}(t) := 0 \quad (111)$$

Once processed, we know how many batches have been rejected and we have to update the inventory levels according to that. If n batches have been rejected ($n \leq n_{FPUV}$), we get at the FPU level:

$$EIP_{FPU}(t) := EIP_{FPU}(t) - n * Q_{FPU} * (1 - devf_{API \text{ FPU}}) \quad (112)$$

$$ES_{FPU}(t) := ES_{FPU}(t) + (n_{FPUV} - n) * Q_{FPU} * (1 - devf_{API \text{ FPU}}) \quad (113)$$

$$Inv_{FPU}(t) := Inv_{FPU}(t) + (n_{FPUV} - n) * Q_{FPU} * (1 - devf_{API \text{ FPU}}) \quad (114)$$

The FPP level and the API level are not aware of these losses.

5) API evaluation

The production decision process at the API level follows the same single echelon policy as the one at the FPP level. If the echelon inventory position of the API goes below the replenishment point s we produce Q_{API} . At this echelon the process is quite easy because we have assumed the supplier is as reliable in time, quality and quantity (everything is deterministic) assumption [19].

If $EIP_{API}(t) \leq \text{small } s \text{ API}$

$$\text{Do } QO_{API}(t) := Q_{API} \quad (115)$$

$$EIP_{API}(t) := EIP_{API}(t) + QO_{API}(t) \quad (116)$$

Else do nothing

Once the order is received, we get:

$$ES_{API}(t) := ES_{API}(t) + QO_{API}(t) \quad (117)$$

$$Inv_{API}(t) := Inv_{API}(t) + QO_{API}(t) \quad (118)$$

VI. Verification and Validation

When using a simulation, the simulation model has to be verified and validated to ensure that it behaves as expected and gives the good output results according to the events that occur during the simulation run. This paragraph is dedicated to these verification and validation steps. This procedure has been executed for both ME planning and SE planning. First the verification of the model is presented, then the validation.

VI.A Verification

During the model building on ARENA, the model is verified part by part and intermediary outputs are created and checked to be correct. First the demand fulfillment from FPP to customer is modeled and checked. Next, the FPU level is added and checked. Finally, API level is modeled and checked too. For each level, the demand generated, the policy behavior, the backorders, the inventory levels, the quantity order and the quantity ship are checked. The real output (service level and cost) are checked according to the previous verification. If problems and incoherencies occur, the model is debugged and the verification process done again.

VI.B Validation

For the validation process, first the data validity is the responsibility of the users. For my part, the input data used for my simulation have been validated during the data gathering process in collaboration with MSDAH's planners.

The following step of the model validation process is to assess if the simulation model behaves as expected. In order to do that a scenario analysis is carried out. Three simulation model characteristics are studied; the demand, the inventory levels and the lead times. Those three criteria are analyzed in extreme conditions to observe how the model behaves.

Demand

Table 3: Simulation model behavior for two extreme Demand scenarios

Conditions	Behavior
FPP demand=0	Nothing is produced, no backorders
FPP demand=5000*average FPP demand	Production every month, backorders explode

In case of no demand, nothing happens, there is no production at all, the inventory levels remain constant and the backorders remains equal to zero.

In case of extreme demand, the production starts every month the backorders explode and an error message can be observe because it happens that internal orders are placed before the previous one has been received and this violates the assumption [9]. Thus, the R variable (Boolean variable) of the echelon which has to violate this assumption [9], takes the value of 1. The behaviors related to the Demand scenario analysis, are summarized in [Table 3].

Inventory levels

Table 4: Simulation model behavior for two extreme inventory level scenarios

Conditions	Behavior
Inventory=0	Production starts directly and demand is backordered, then after a while a normal planning behavior is observed
Inventory=5000*average FPP demand	Demand fulfilled directly every month, no production starts during the simulation run and inventory decreased each month

In case of no inventory, the first month all demand is backordered and production starts. After a while, once the quantities ordered are received, backorders are fulfilled and the system gets a stabilized behavior.

In case of extreme inventory, the demand is fulfilled every month (backorders equal zero) and there are no production requirements at all. The inventory levels decrease with the demand. The behaviors related to the inventory levels scenario analysis, are summarized in [Table 4].

Lead Times

Table 5: Simulation model behavior for two extreme Lead time scenarios

Conditions	Behavior
Lead time=0	The model behave normally, and the ES=EIP at each level and at each time of the simulation
Lead time=37 months>simulation run time	Production starts when required for the first time but is never received

In case no lead time, the model behaves normally but when production is required it is directly fulfilled form the previous echelon (if inventory level is enough).

In case of extreme lead time, at the beginning, the simulation behaves normally until the first production order is placed, because it will never be received. So, according to assumption [9] a message error can be observed because an order has to be placed before the previous one is received. Thus, the R variable (Boolean variable) of the echelon which has to violate the assumption [9], takes the value of 1. The two behaviors related to the Lead Times scenario analysis, are summarized in [Table 5].

As a conclusion, the results and statements of this scenario analysis are in line with the expectations and show that the simulation model behaves as it should. Therefore, those verification and validation steps enable us to conclude that the model implemented in ARENA is valid and can be used for answering my research questions.

VII. Results

Within this part, first are presented and analyzed the results for the SE planning and the ME planning subject to the real supply uncertainties in order to answer to the first research question. Then, in the second part a scenario analysis is achieved in order to answer the second research question which is the study of the impact of the supply uncertainties on the planning performances. For each simulation model, the planning parameters have been optimized by using the OptQuest tool of ARENA. A brief description of the OptQest tool is given in Appendix 13. The optimization run in OptQuest takes 8 hours by planning (8 hours for SE and 8 hours for ME). OptQuest tool is based on a Tabu Search metaheuristic algorithm which is described in Appendix 14.

VII.A Answer to the first research question: SE versus ME

The first research question is:

Which planning concept, the single echelon concept or the multi echelon concept, is the best adapted to plan the MSDAH's supply chain, taking into account the uncertainties?

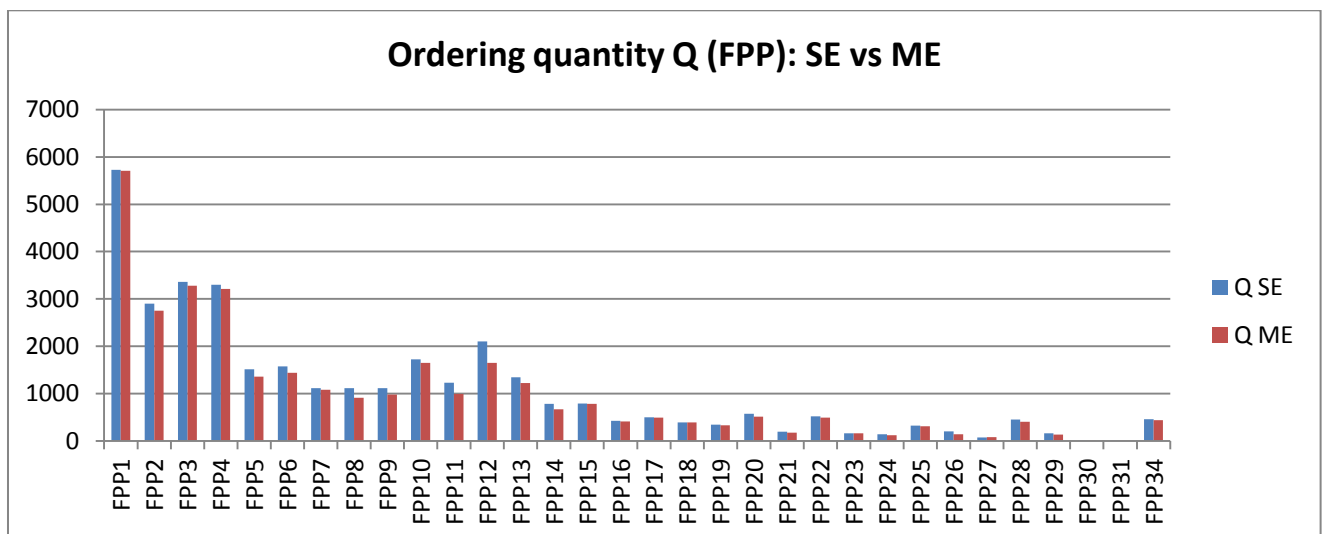
In this paragraph the answer to this question will be conducted by analyzing first the optimal orders quantity Q results, then the replenishment point s results and finally the average supply chain cost for both SE planning and ME planning and for each level of the X's supply chain. The supply uncertainties quantification is given in Appendix 15. In this part only the most important results and graphs are analyzed. The complete results of the SE planning are given in Appendix 18. The complete results of the ME planning are given in Appendix 19. And the comparison is done in Appendix 20.

Before starting the analyses, it is expected that the ME concept should lead to a lower average supply chain cost than the SE concept. The SE's ordering quantities should be higher than the ME's ordering quantities and the replenishment point s of the ME planning should be lower than the SE's s levels.

Order quantity Q analyses

FPP level (Graph 2)

Graph 2: Comparison between the optimal FPPs' Q quantities for SE and ME



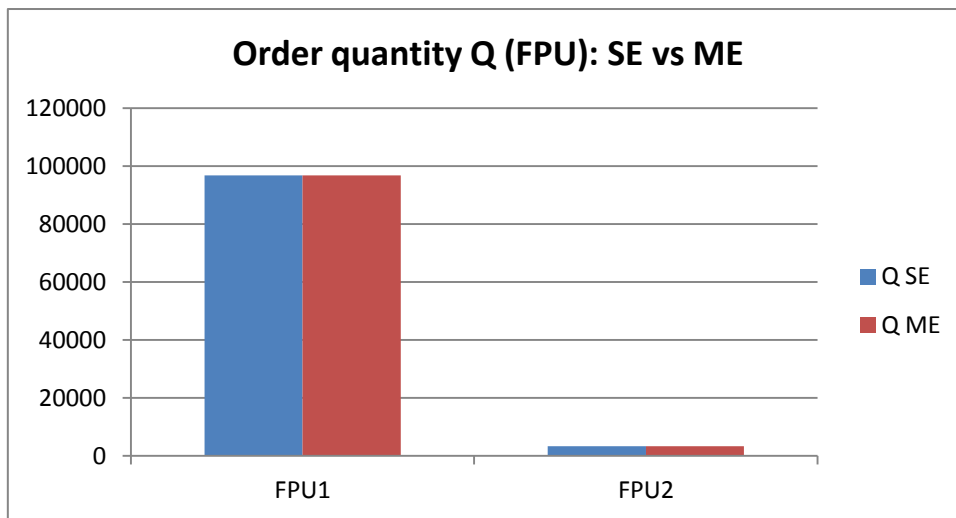
-Integral Single Echelon planning VS Integral Multi Echelon planning to cope with uncertainties-

At the FPP level, the order quantity Q results for SE and ME are quite similar. The sum of the order quantities for all FPP related to FPU1 (FPP1 to FPP31) is equals to 34100 Vials for SE and 29186 Vials for ME. This seems logical because for the FPP's echelons there is no big difference between the SE concept and the multi echelon concept. At this level of the supply chain, both plannings are based on a single echelon because we are at the most downstream part of the supply chain.

It is important to mention that the SE's Q quantities are a little bit higher than the ME's Q quantities. The sum of the order quantities for all FPP related to FPU1 (FPP1 to FPP31) is equal to 34100 Vials for SE and 31817 Vials for ME. And the QFPP34 (FPP related to FPU2) equals to 460 Vials for SE and equals to 440 for ME. Even if the echelon definition is the same at the FPP level for both planning, there is a difference in the results, but why? This can be explained. We are studying the supply chain in an integral way (end to end). For the SE planning the optimization is done echelon by echelon in a decentralized approach (so there is a lack of visibility on the other echelon) but for the ME planning the supply chain is optimized as a whole and from one echelon there is a complete visibility on the other echelon. This lack of visibility does lead to a higher order quantity Q for the SE echelon. SE planning requires higher order quantity in order to face to the uncertainties.

FPU level (Graph 3)

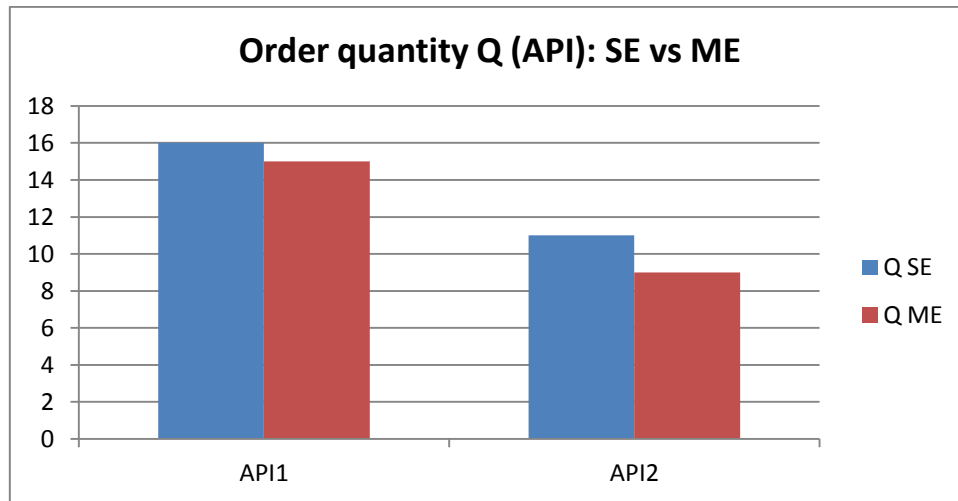
Graph 3: Comparison between the optimal FPU's Q quantities for SE and ME



At the FPU level, the results are exactly the same for both SE and ME. Both plannings require the same order quantity Q. Those results mean 4 batches for FPU1 ($98600=4*24200$) and 1 batch for FPU2. These results seem to be normal according to the FPPs order quantities which are quite the same for SE and ME, and the batch production characteristic of FPU.

API level (graph 4)

Graph 4: Comparison between the optimal APIs' Q quantities for SE and ME



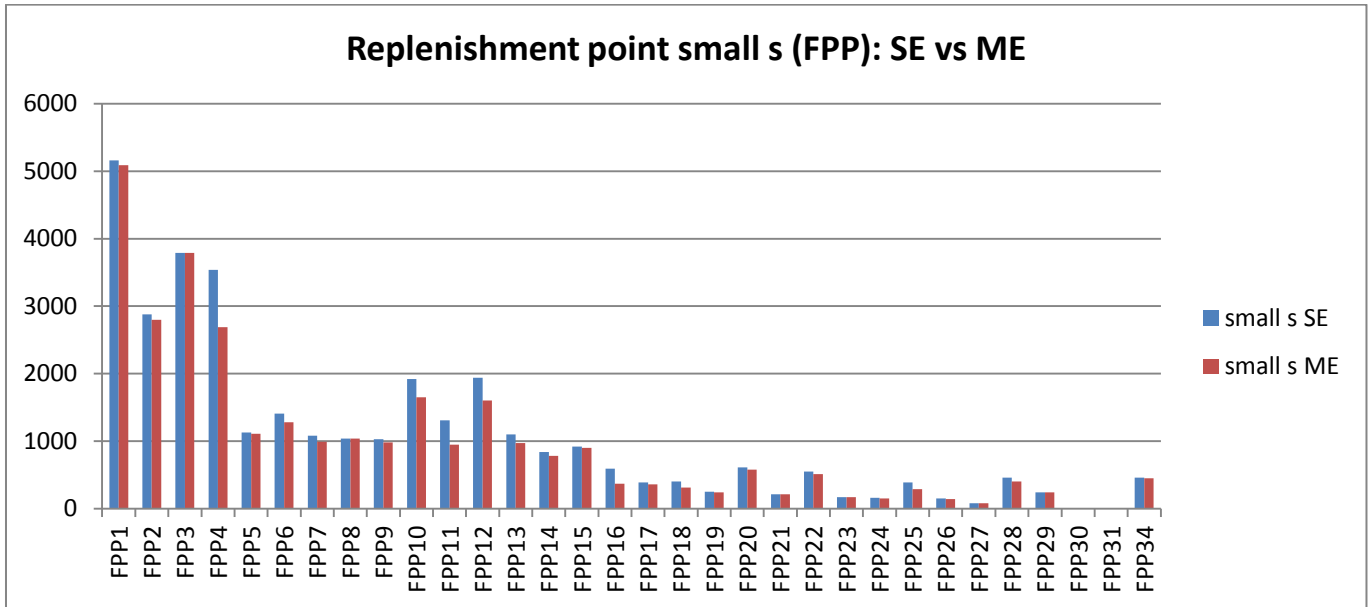
At the API level, the order quantities Q of the SE planning are higher than the ME planning. $Q_{API1} (SE) = 16$ Kg while $Q_{API1} (ME) = 15$ Kg and $Q_{API2} (SE) = 11$ Kg while $Q_{API2} (ME) = 9$ Kg. This can be explained by the same reason as the one given at the FPP level. This is the multi echelon characteristics and the complete visibility on the other echelon that gives this difference. But, this difference is bigger at the API level because we are at the more upstream part of the supply chain, and everything is known by the ME's API echelon. For instance if a FPU batch is rejected, it is taken into account in the API's stocks. So, in order to cope with this lack of visibility and the uncertainties, the SE planning requires higher order quantity Q than the ME planning.

This increase in the order quantities Q from the downstream part of the supply chain to the upstream part of the supply chain can be assimilated to an intern bullwhip effect. And it is clear that the ME planning gives more control to this bullwhip effect than the SE planning.

Replenishment point s analyses

FPP level (Graph 5)

Graph 5: Comparison between the optimal FPPs' s levels for SE and ME



At the FPP level, the same interpretation than the Q interpretation can be made. Indeed, the s levels are quite similar for both SE planning and ME planning. But, they are a little bit higher for the SE planning. The sum of the s levels for the FPPs related to FPU1 equals 33752 Vials for SE and equals 30680 Vials for ME. The s level for FPP34 is equal to 460 for SE and is equal to 450 for ME. The multi echelon characteristics lead to those results. The SE planning needs more safety stock to cope with the uncertainties.

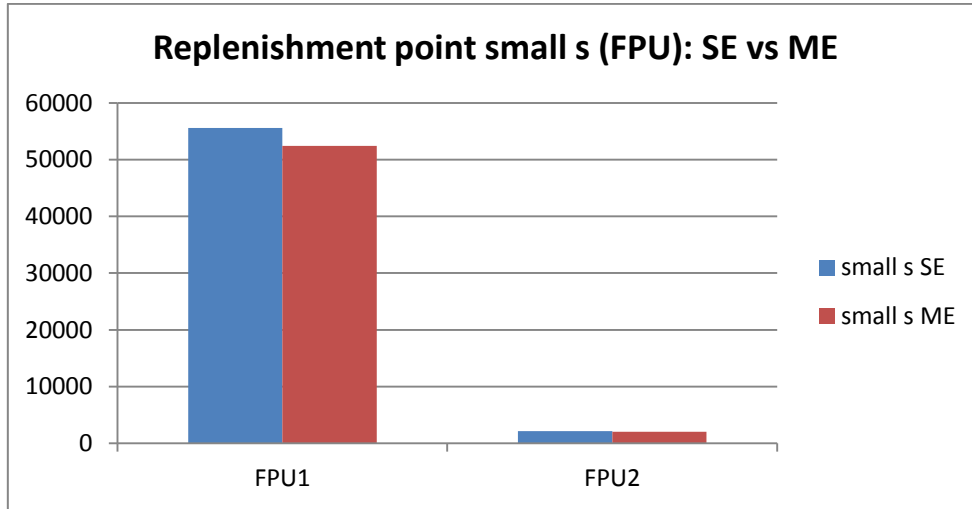
Before being able to compare the s levels of ME and s level of SE at the FPU and API levels, a transformation is required. As mentioned in part IV.E, the s level of ME is higher than the s level of SE and are not comparable because of the ME characterization. In order to compare those s levels at the FPU level, we do:

$$(119) \quad s_{FPU1}(ME)_{comparable} = s_{FPU1}(ME) - \sum_{fpp=FPP1}^{FPP31} s_{fpp}(ME) * BOM_{fpp} FPU1$$

$$(120) \quad s_{FPU2}(ME)_{comparable} = s_{FPU1}(ME) - s_{FPP34}(ME) * BOM_{FPP34} FPU2$$

FPU level (Graph 6)

Graph 6: Comparison between the optimal FPU's s levels for SE and ME



At the FPU level, the same tendency is observed; the SE planning requires a higher s level than the ME planning. From a comparable definition, $s_{FPU1}(SE) = 55600$ Vials while $s_{FPU1}(ME) = 52310$ vials, and $s_{FPU2}(SE) = 2150$ Vials while $s_{FPU2}(ME) = 2010$ Vials.

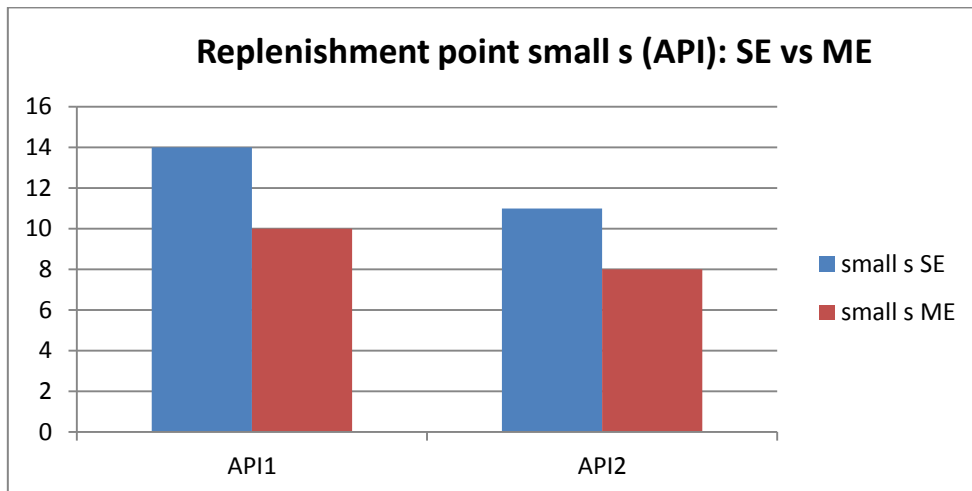
For the same reason as the FPU level, in order to be able to compare the s level of SE and the s level of ME at the API level, we do:

$$(121) \quad s_{API1}(ME)_{comparable} = s_{API1}(ME) - \sum_{fpu=FPU1}^{FPU2} s_{fpu}(ME) * BOM_{fpu} API1$$

$$(122) \quad s_{API2}(ME)_{comparable} = s_{API2}(ME) - \sum_{fpu=FPU1}^{FPU2} s_{fpu}(ME) * BOM_{fpu} API2$$

API level (Graph 7)

Graph 7: Comparison between the optimal APIs' s levels for SE and ME



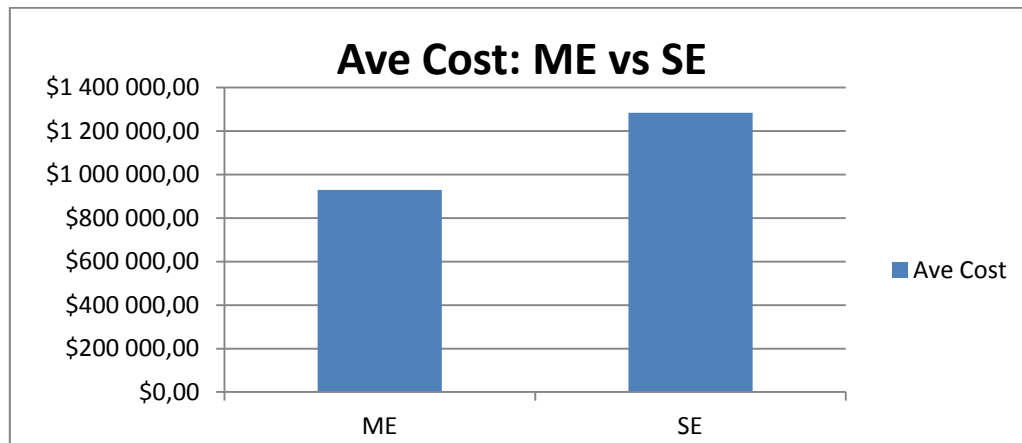
At the API level, this is the exact same tendency, but the difference between the SE's s levels and the ME's s levels is more pronounced. From a comparable definition, $s_{API1}(SE) = 14$ Kg while $s_{API1}(ME)$

-Integral Single Echelon planning VS Integral Multi Echelon planning to cope with uncertainties-

= 9.49 Kg, and $s_{API2(SE)} = 11$ Vials while $s_{API2(ME)} = 8.04$ Kg. Thus, the ME concept shows once time its benefits. The SE planning requires a higher s levels to cope with uncertainties.

Average supply chain cost analysis

Graph 8: Comparison between the average supply chain cost for SE and ME



This Graph 8 is clear; all the results presented so far support the cost analysis. Indeed, it is obvious that the ME planning leads to a lower average cost of the supply chain, so a lowest stock investment. The Average cost (SE)= 1 284 287 \$ per month while the Average cost (ME)= 928 899 \$ per month. The multi echelon concept has proved its benefits to cope with the X's supply chain uncertainties. The multi echelon concept is better than the current single echelon concept to plan and control the X's supply chain. The multi echelon concept characteristics give to an echelon a clear vision on the other echelon. Each echelon knows exactly the external demand and the supply uncertainties stay intrinsic to the echelon and are not external parameters like for the single echelon concept.

The multi echelon concept is the best for MSDAH in order to plan and control the sub product family x's supply chain face the uncertainties. But what is exactly the impact/influence of the supply uncertainties on the planning performances for both the SE planning and the ME planning?

VII.B Answer to the second research question: Scenario analysis

The second research question is:

What is the impact of the supply uncertainties on the planning performances?

In order to study the impact of the supply uncertainties on the planning performances, a scenario analysis is conducted. Two scenarios are considered:

Scenario 1 (no supply uncertainties): there is no supply uncertainty at all. All supply uncertainties are eliminated. In this scenario there are no lead time variations and all lead times become deterministic. There is no output quantity fluctuation and there is no batch rejection. The quantification of the supply uncertainties for the “no supply uncertainties” scenario is given in Appendix 16.

Scenario 2 (2 times supply uncertainties): it is considered twice the current supply uncertainties. This means that each supply uncertainty is doubled. The lead time uncertainty is double, for instance if the current lead time follows a Log-Normal distribution $LogN(\mu, \sigma)$, then the lead time in this scenario will follow a Log-Normal distribution $LogN(\mu, 2\sigma)$. The deviation factor is doubled as well as the batch rejection percentage. The quantification of the supply uncertainties for the “2 times supply uncertainties” scenario is given in Appendix 17.

By considering the case with the current supply uncertainties, we get three scenarios for the analysis. The current scenario is called “**scenario normal**”.

The optimization process takes 8 hours per planning concept and per scenario.

In this paragraph the answer to the second research question will be conducted by analyzing first the optimal orders quantity Q results, then the replenishment point s results and finally the average supply chain cost for both SE planning and ME planning and for each level of the X 's supply chain. In this part only the most important results and graphs are presented. Only the relevant graphs are presented in this paragraph.

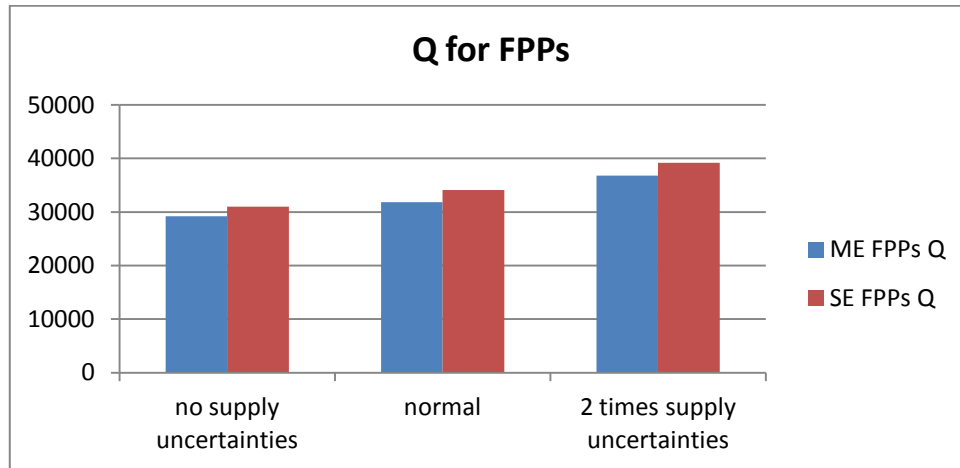
The complete SE results and ME results for the “no supply uncertainties” scenario are respectively given in Appendix 21 and Appendix 22. And, they are compared in Appendix 23. The complete SE results and ME results for the “2 times supply uncertainties” scenario is respectively given in Appendix 24 and Appendix 25. And, they are compared in Appendix 26. The percentage evolution results and analyses are presented in Appendix 27.

Before starting the analyses, it is expected that the ME concept should lead to better supply chain control than the SE concept. The gap of performances between the ME concept and the SE concept should increase with the increase of supply uncertainties level.

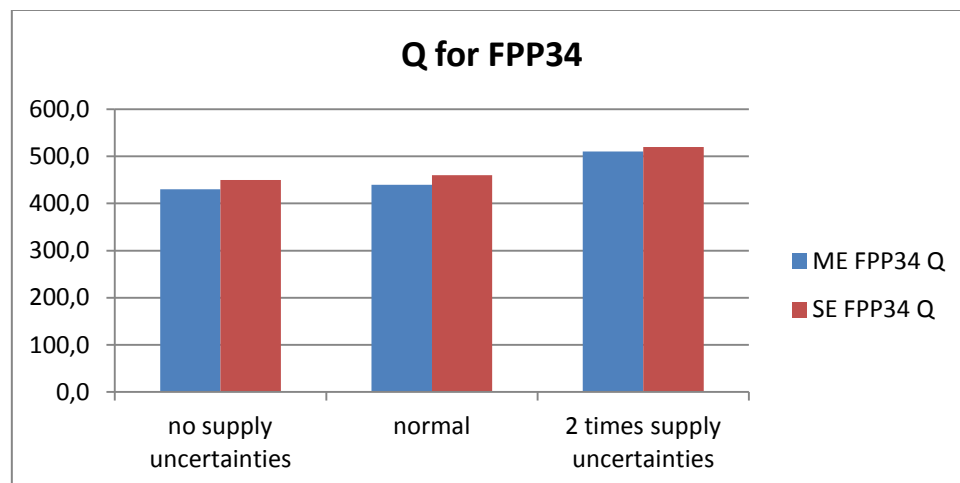
Order quantity Q analyses

FPP level (Graph 9 and Graph 10)

Graph 9: Comparison between the FPPs' Q quantities for SE and ME in 3 supply uncertainties scenarios



Graph 10: Comparison between the FPP34's Q quantities for SE and ME in 3 supply uncertainties scenarios



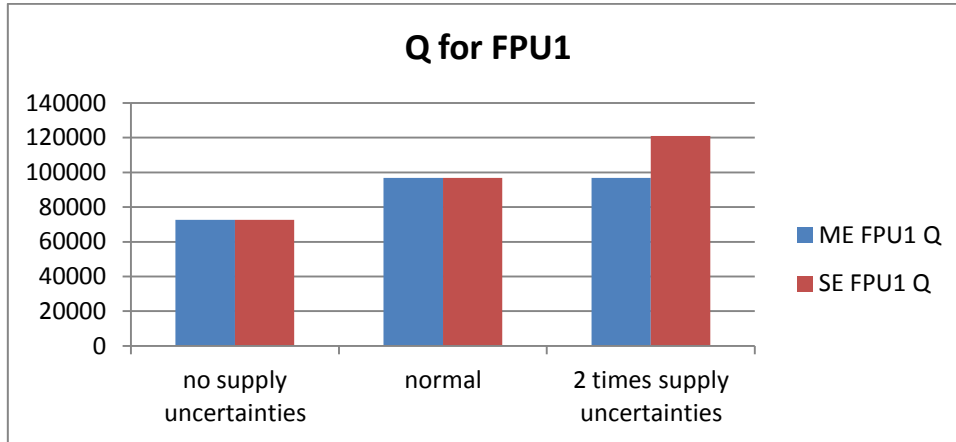
At the FPP level, two statements can be made. First, for both planning, the Q quantities increase with the level of the supply uncertainties. Secondly, for each scenario, the SE's Q quantities are higher than the ME's Q quantities.

The first statement was expected because if the supply uncertainties increase, we need to order more to cope with the uncertainties. The second statement was expected too, thanks to the benefits of the multi echelon concept. [Graph 9 and Graph 10]

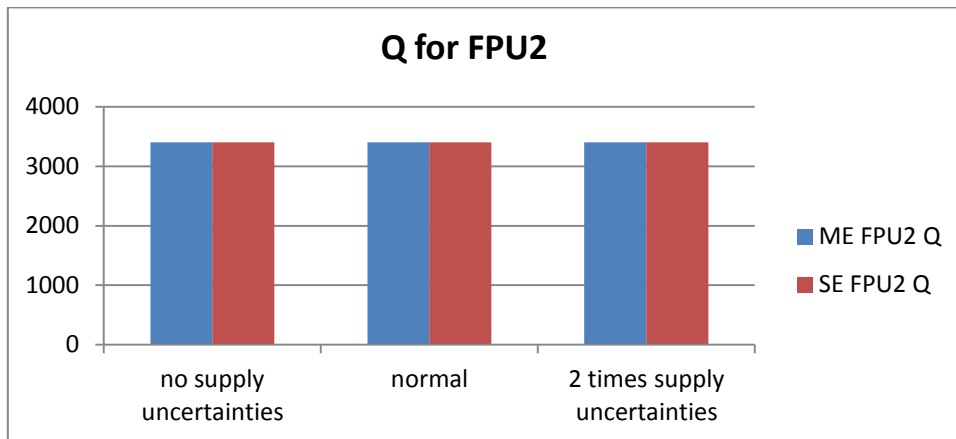
It is interesting to observe the difference in Q quantities for the scenario "no supply". Indeed, why is there a difference even if the supply uncertainties have been reduced to zero? This can be explained because the demand uncertainty is still present. And, this statement shows that the ME concept is better than the SE to cope with demand uncertainties. And it is easy to understand, because thanks to the multi echelon concept characteristics, the exact external demand is observable by all the echelon, even by the most upstream echelon of the supply chain. And this is not the case for the SE concept.

FPU level (Graph 11, Graph 12 and Graph 13)

Graph 11: Comparison between the FPU1's Q quantities for SE and ME in 3 supply uncertainties scenarios



Graph 12: Comparison between the FPU2's Q quantities for SE and ME in 3 supply uncertainties scenarios

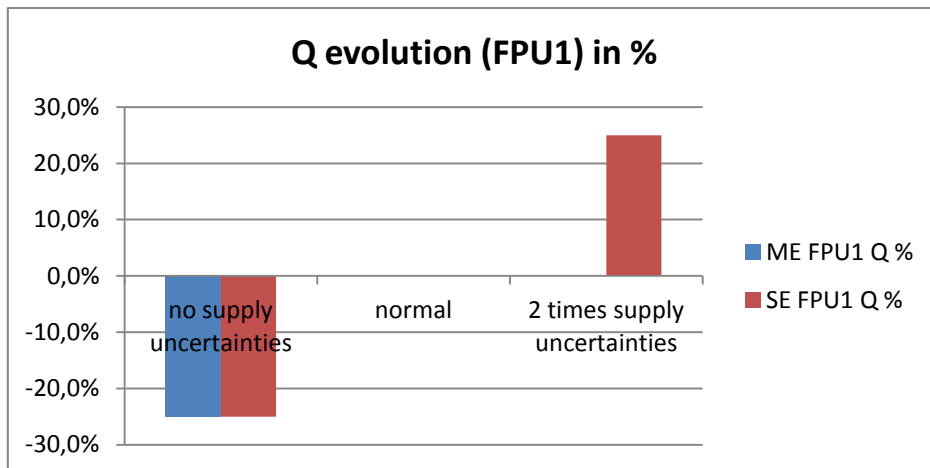


At the FPU level, the number of batch produces in FPU2 (which is one batch) is the same regardless the concept and the supply uncertainties level. This is explained because the production batch size of FPU2 is really high compared to its monthly demand. Thus, with one batch the supply chain can face the supply uncertainties. [Graph 12]

The most important at the FPU level is the analysis of FPU1. First, for the SE planning, the number of batches increases with the level of supply uncertainties. Scenario “no supply” requires 3 batches, scenario “normal” requires 4 batches and scenario “2 times supply” requires 5 batches (Graph 11). For the ME planning we get the same results as for the first two scenarios, but when the supply uncertainties are double, the number of batches required remains the same as for the “normal” scenario. This is observable in the Graph 13 where the percentage of decrease/increase of the FPU1's Q quantity is depicted by referring to the “normal” scenario.

-Integral Single Echelon planning VS Integral Multi Echelon planning to cope with uncertainties-

Graph 13: Comparison between the FPU1's Q evolution (%) for SE and ME in 3 supply uncertainties scenarios

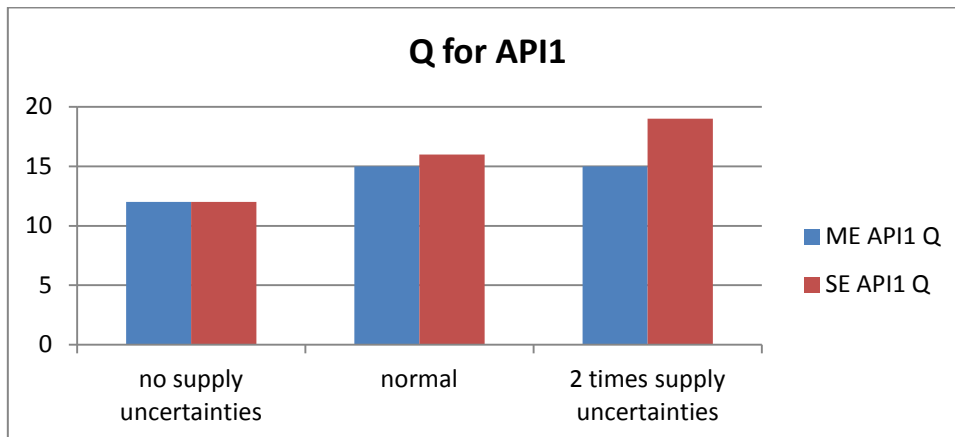


At the FPU1 echelon, for the “no supply uncertainties” scenario, the Q quantity decreases by -25% for both SE and ME. But, for the “2 times supply uncertainties” scenario, the Q quantity for ME increases by 0% while the Q quantity increases by 25% for SE. [Graph 13]

Thus, the multi echelon concept proves once more its benefits. Just by looking at the FPU1, we observe that the ME concept gives to MSDAH more control of the supply chain to face the increase of the supply uncertainties.

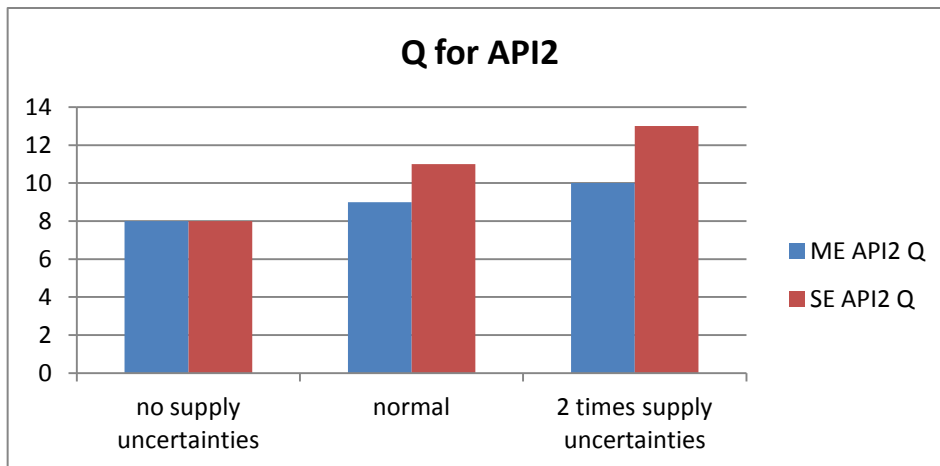
API level (Graph 14, Graph 15, Graph 16 and Graph 17)

Graph 14: Comparison between the API1's Q quantities for SE and ME in 3 supply uncertainties scenarios



-Integral Single Echelon planning VS Integral Multi Echelon planning to cope with uncertainties-

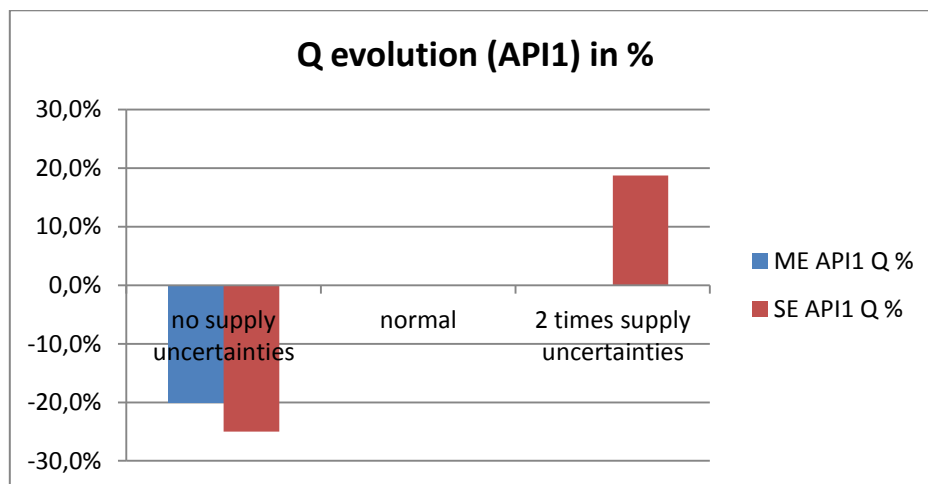
Graph 15: Comparison between the API2's Q quantities for SE and ME in 3 supply uncertainties scenarios



At the API level, first it is shown that regardless the planning concept, the Q quantities increase with the supply uncertainties level. This is logical. [Graph 14 and Graph 15]

By comparing SE and ME, for the scenario “no supply” the order quantities are the same, for the scenario “normal” the Q quantities are higher for SE than ME, and the difference is more visible with the scenario “2 times supply”. So, for the SE planning a kind of bullwhip effect over the supply uncertainties level is observable. This is observable in Graph 16. Those graphs are built in the same logic as Graph 13.

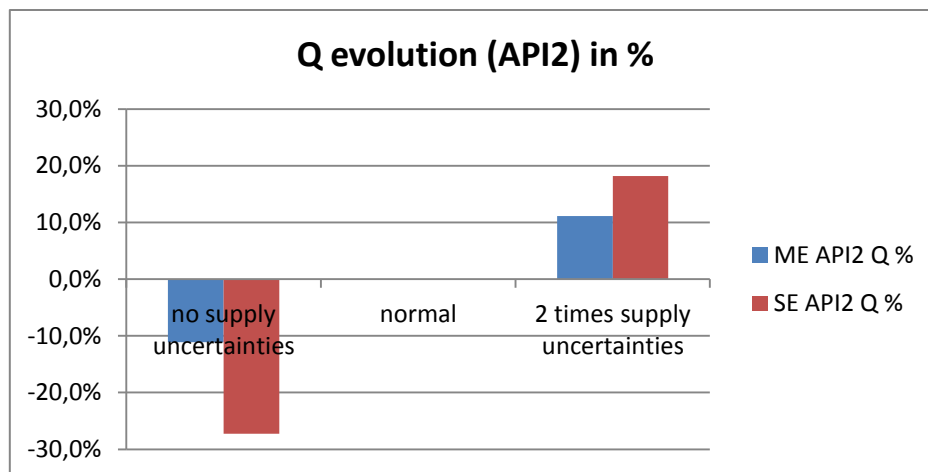
Graph 16: Comparison between the API1's Q evolution (%) for SE and ME in 3 supply uncertainties scenarios



At the API1 echelon, for the “no supply uncertainties” scenario the Q quantity decreases by -25% for SE while it decreases by -20% for ME. For the “2 times supply uncertainties” scenario the Q quantity increases by 18.8% for SE while it does not increase for ME. [Graph 16]

-Integral Single Echelon planning VS Integral Multi Echelon planning to cope with uncertainties-

Graph 17: Comparison between the API2's Q evolution (%) for SE and ME in 3 supply uncertainties scenarios



At the API2 echelon, for the “no supply uncertainties” scenario the Q quantity decreases by -27.3% for SE while it decreases by -11.1% for ME. For the “2 times supply uncertainties” scenario the Q quantity increases by 18.2% for SE while it increases by 11.1% for ME. [Graph 17]

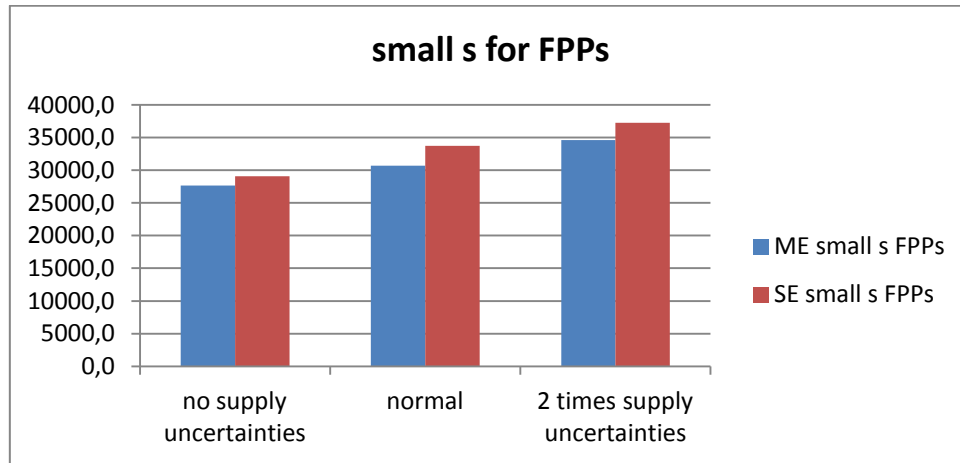
Those results can be explained by the FPU level results. Indeed, for the scenario “2 times supply”, the SE planning requires one more batch of FPU1 production than for the ME planning. So, this leads to the increase of the Q quantities difference at the API level between SE and ME.

As a conclusion, it has been proved by those Q quantities scenario analyses that the multi echelon concept gives more control of the supply chain and curbs the bullwhip effect amplified by the level of supply uncertainties. The SE concept is really sensitive to the supply uncertainties which lead to an amplification of the bullwhip effect.

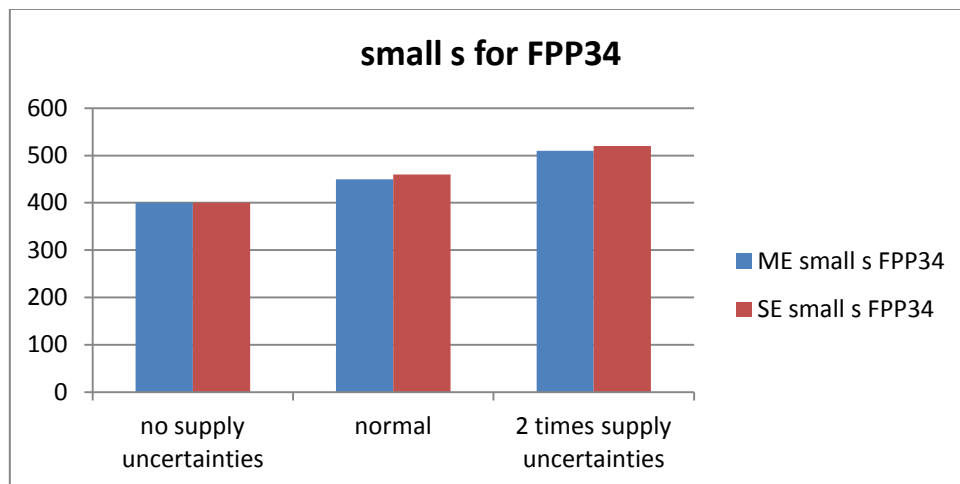
Replenishment point s analyses

FPP level (Graph 18 and Graph 19)

Graph 18: Comparison between the FPPs' s levels for SE and ME in 3 supply uncertainties scenarios



Graph 19: Comparison between the FPP34's s levels for SE and ME in 3 supply uncertainties scenarios



At the FPP level, the same analysis as the Q quantities analysis can be made. The s levels increase with the supply uncertainties level regardless the planning concept. And the s levels are higher for the SE planning than for the ME planning. Thus, in order to cope with supply uncertainties we need to keep more in stock if the supply uncertainties increase, and we need to keep less stock in the ME case thanks to the ME concept characteristics. [Graph 18 and Graph 19]

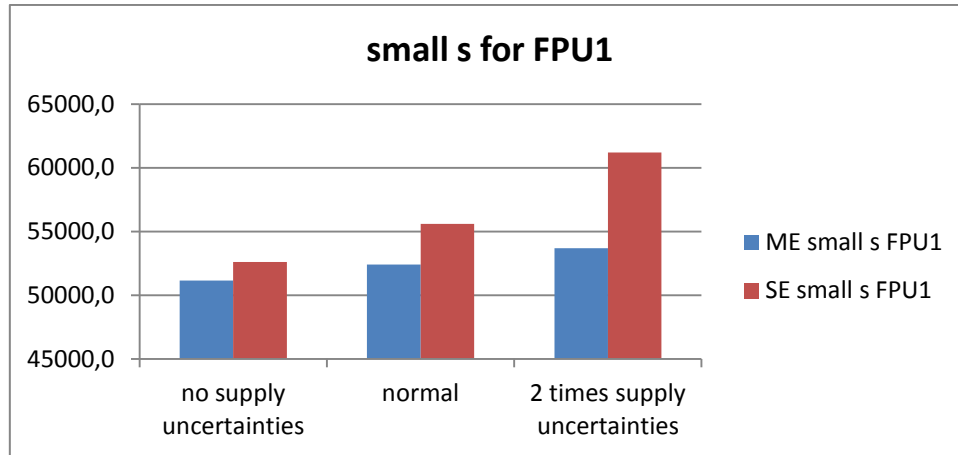
It is also observed that, by considering the "no supply" scenario, the ME concept is better to cope with demand uncertainty for the same reason as the Q quantity analysis.

-Integral Single Echelon planning VS Integral Multi Echelon planning to cope with uncertainties-

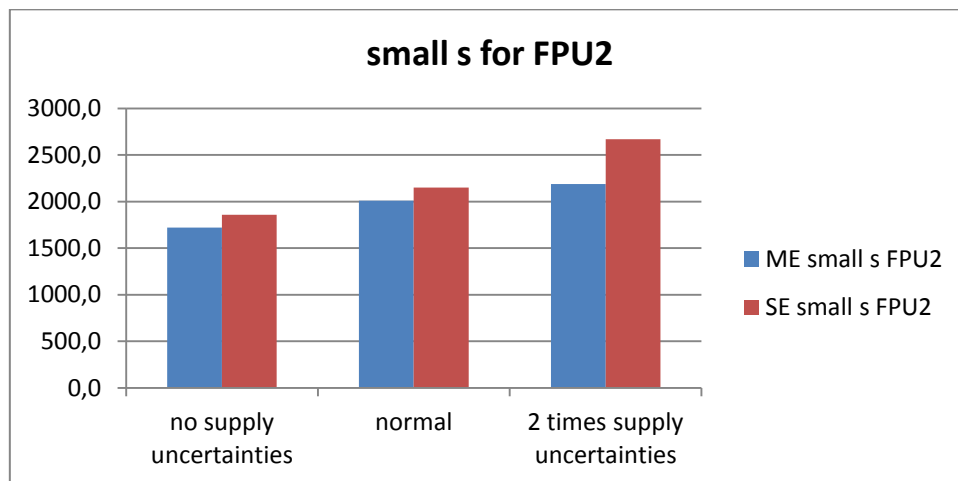
FPU Level (Graph 20, Graph 21, Graph 22 and Graph 23)

In order to compare the s levels of SE and ME at the FPU level, the equations (119) and (120) are used.

Graph 20: Comparison between the FPU1's s levels for SE and ME in 3 supply uncertainties scenarios



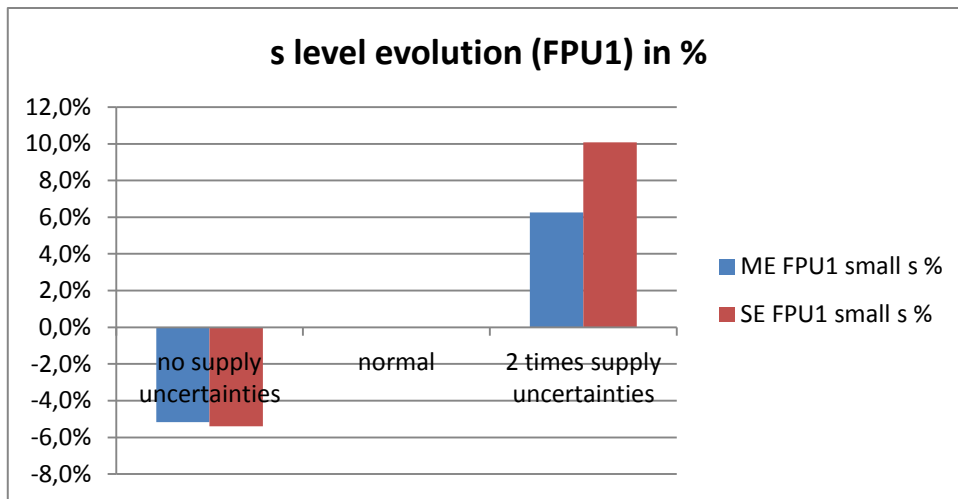
Graph 21: Comparison between the FPU2's s levels for SE and ME in 3 supply uncertainties scenarios



At the FPU level, the differences between SE and ME over the supply uncertainties level is more pronounced. Thus, we need to keep a high level of FPU stock to cope with supply uncertainties. [Graph 20 and Graph 21]

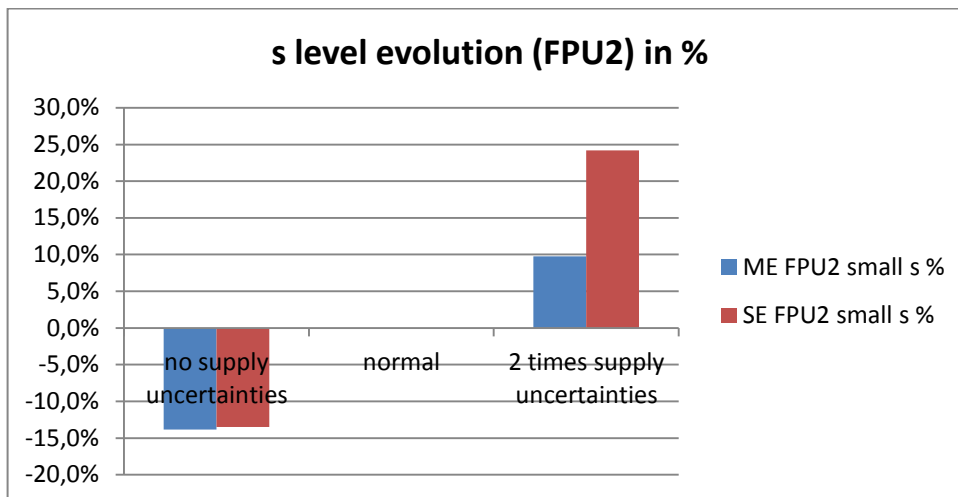
-Integral Single Echelon planning VS Integral Multi Echelon planning to cope with uncertainties-

Graph 22: Comparison between the FPU1's s levels evolution (%) for SE and ME in 3 supply uncertainties scenarios



At the FPU1 echelon, for the “no supply uncertainties” scenario the s level decreases by -5.4% for SE while it decreases by -5.2% for ME. And, for the “2 times supply uncertainties” scenario, the s level increases by 10.1% for SE while it increases by 6.3% for ME. [Graph 22]

Graph 23: Comparison between the FPU2's s levels evolution (%) for SE and ME in 3 supply uncertainties scenarios



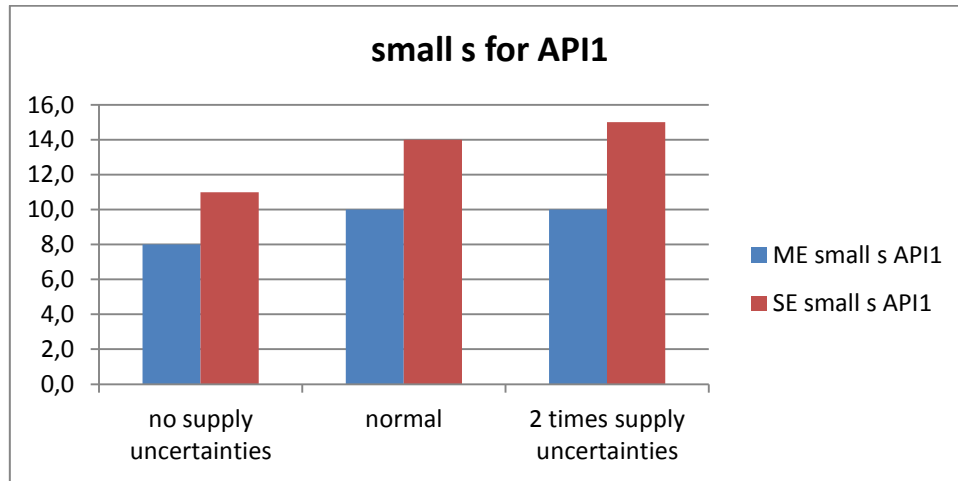
At the FPU2 echelon, for the “no supply uncertainties” scenario the s level decreases by -13.5% for SE while it decreases by -13.8% for ME. And, for the “2 times supply uncertainties” scenario the s level increases by 24.2% for SE while it increases by 9.8% for ME. [Graph 23]

-Integral Single Echelon planning VS Integral Multi Echelon planning to cope with uncertainties-

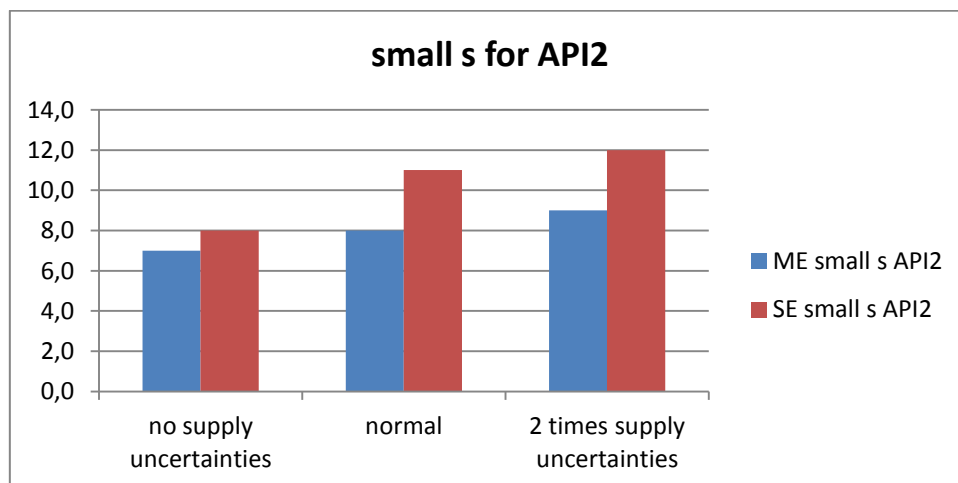
API level (Graph 24, Graph 25, Graph 26 and Graph 27)

In order to compare the s levels of SE and ME at the API level the equations (121) and (122) are used.

Graph 24: Comparison between the API1's s levels for SE and ME in 3 supply uncertainties scenarios



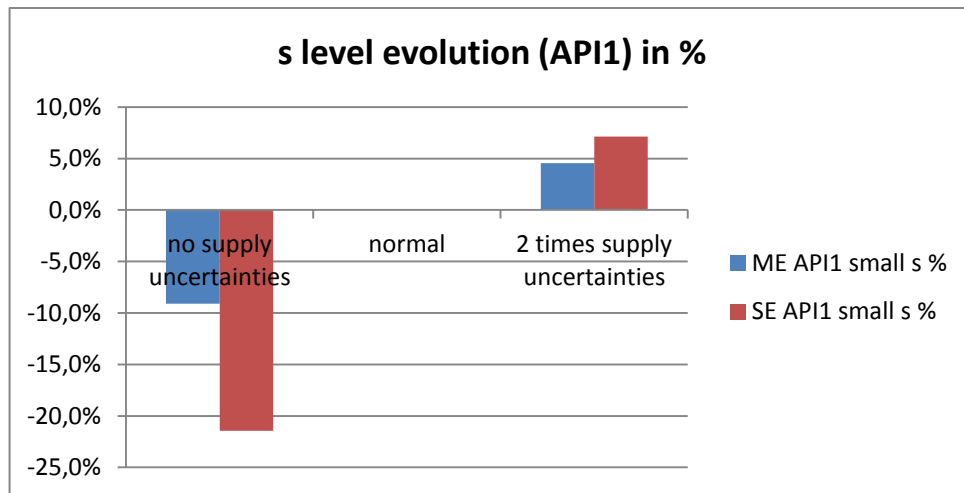
Graph 25: Comparison between the API2's s levels for SE and ME in 3 supply uncertainties scenarios



At the API level, the difference between SE and ME is again more pronounced than for the FPU level. This is triggered by the s levels at the FPU level. [Graph 24 and Graph 25]

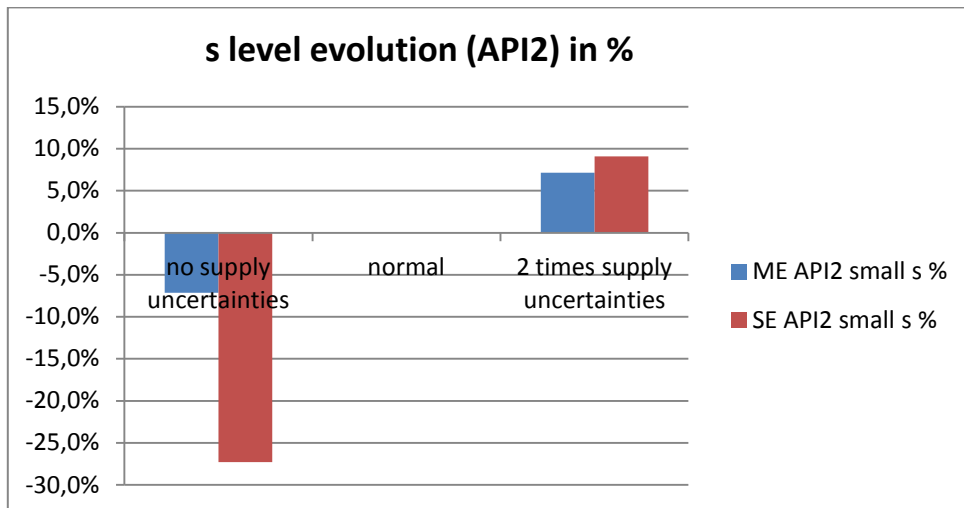
-Integral Single Echelon planning VS Integral Multi Echelon planning to cope with uncertainties-

Graph 26: Comparison between the API1's s levels evolution (%) for SE and ME in 3 supply uncertainties scenarios



At the API1 echelon, for the “no supply uncertainties” scenario the s level decreases by -21.4% for SE while it decreases by -9.1% for ME. And, for the “2 times supply uncertainties” scenario, the s level increases by 7.1% for SE while it increases by 4.5% for ME. [Graph 26]

Graph 27: Comparison between the API2's s levels evolution (%) for SE and ME in 3 supply uncertainties scenarios

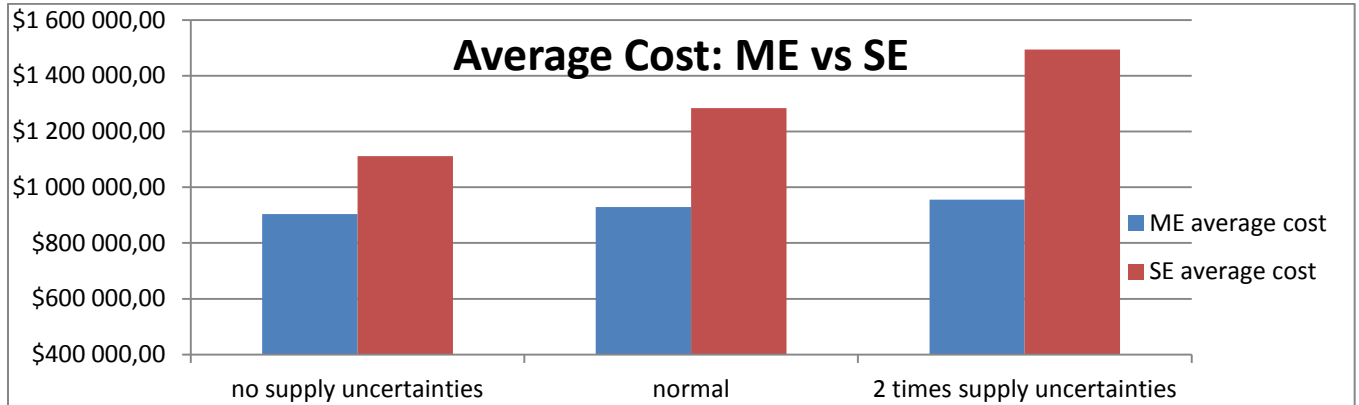


At the API2 echelon, for the “no supply uncertainties” scenario the s level decreases by -27.3% for SE while it decreases by -7.1% for ME. And, for the “2 times supply uncertainties” scenario, the s level increases by 9.1% for SE while it increases by 7.1% for ME. [Graph 27]

As a conclusion of the replenishment s level analyses, the SE concept is really sensitive to the supply uncertainties. When the supply uncertainties increase, the required stock level increases a lot in comparison with the ME concept. Thus, the ME concept gives more control to the supply chain face to supply uncertainties.

Average supply chain cost analyses

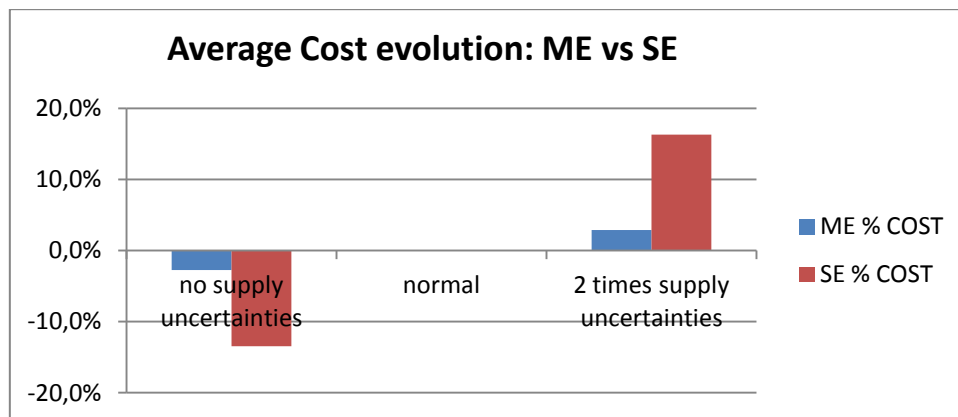
Graph 28: Comparison between the average supply chain cost for SE and ME in 3 supply uncertainties scenarios



For the “no supply uncertainties” scenario, cost(SE)= 1 111 377 \$ while cost(ME)= 903 450 \$. For the “normal” scenario, cost(SE)= 1 284 287 \$ per month while cost(ME)= 928 899 \$ per month. And, for the “2 times supply uncertainties”, cost(SE)= 1 493 913 \$ per month while cost(ME)= 955 639 \$ per month. [Graph 28]

Regardless the planning concept, the average cost increases with the supply uncertainties level. This is logical because we need to keep more in stock and order more. According to the previous analyses, this is normal. In each scenario the ME concept requires a lower average cost than the SE concept.

Graph 29: Comparison between the average supply chain cost evolution (%) for SE and ME in 3 supply uncertainties scenarios



The graph 29 depicts the Average monthly cost evolution (in %) for both plannings and for each scenario. The reference is the “normal” scenario. By looking at graph 29 we get in the case of “no supply uncertainties”, cost (SE)=-13.5% while cost (ME)=-2.7%. And, in the “2 times supply uncertainties” scenario we get, cost (SE)=+16.3 % while cost (ME)=+2.9 %. It is observed that the SE’s average cost is really sensitive to the supply uncertainties level. The ME concept gives more control of the supply chain face to supply uncertainties. [Graph 29]

Nevertheless, we can notice that the average cost of SE planning in the “no supply uncertainties” scenario is higher than the average cost of ME in the “2 times supply uncertainties” scenario. This can be explained by the results of (Teunissen, 2009), who shows that the demand uncertainties have a great impact on the pharmaceutical supply chain.

Conclusion/discussion

The two research questions were:

Which planning concept, the single echelon concept or the multi echelon concept, is the best adapted to plan the MSDAH's supply chain, taking into account the uncertainties?

What is the impact of the supply uncertainties on the planning performances?

By taking the example of one pharmaceutical sub product family (X), this project proves that the multi echelon concept is better to plan and control the X's supply chain in an integral way than the current single echelon concept. Indeed, the multi echelon concept is efficient to cope with supply uncertainties thanks to its concept characteristics. The supply uncertainties are intrinsic to the echelon. Every event is known and taken into account by each echelon for the production decisions. This conclusion can be extended to all pharmaceutical products that meet the model requirements. This project does not give a real answer to the first question because it has been studied only one product family and the biological supply chain has not been considered at all. But according to the results for the pharmaceutical sub product family X, the multi echelon concept seems better than the current single echelon concept to plan and control the pharmaceutical supply chain.

Furthermore, the answer at the second question is that the single echelon concept is really sensitive to the supply uncertainties level for X. By looking at the supply uncertainties level, this conclusion holds for all pharmaceutical products. Thus, for products with important supply uncertainties it is really essential to switch from a single echelon concept to a multi echelon concept.

The three SE planning's scenarios and the three ME planning's scenarios implemented in ARENA have been handled to MSDAH as well as the six optimization designs in OptQuest.

Recommendations

As MSDAH is subject to a many uncertainties, the company can take advantages in the multi echelon planning concept. Switching from the current single echelon concept to a multi echelon concept is recommended. In order to do so, MSDAH must go on with the roll out of SAP in all manufacturing sites and all distributor centers to get a complete interconnected network. Once done, SAP Enterprise Inventory optimization (EIO) should be incorporated and designed to use the multi echelon functionality of this module (SAP APO does not support a multi echelon optimization). SAP EIO module can be incorporated in organizations using SAP R/3, and this is the case of MSDAH. Website links related to SAP EIO are given in Appendix 28.

The multi echelon simulation model can be used to optimize the planning parameters of the products. The input parameters need to be updated and the model implemented for all products in ARENA. The problem of seasonal products can be solved by dividing the time period in shorter periods when the demand is quite stationary and can apply the simulation on those time periods

Once the multi echelon concept has been implemented, the inventory levels will decrease and the supply chain will become more controlled. Then, the process problems will appear and become clearer. So, projects to improve the production and quality processes could be initiated to decrease the supply uncertainties, and decrease the lead times as much as possible.

This complete procedure is in line with the MPS logic of MSDAH.

Limitations of my project

First of all, a simulation approach has been used. This means that the planning parameters are closed to optimal and cannot be claimed as optimal. Indeed, the design of the optimization has a role and the best solution given depends on the number of replication, number of simulation and the definition interval of the decisions variable.

Secondly, the model implemented in ARENA is specific for the sub product family X. It is not possible to use this model for other pharmaceutical products, because the network is not the same. Nevertheless, the conceptual model, by its variable definitions, input parameters definitions (uncertainties), cost function, service level definitions, is usable to study other products. And the general model skeleton created on ARENA can be followed.

Thirdly, for the average supply chain cost only the inventory cost is considered. As explained before, it is not useful to introduce a backordering cost because the problem is service level constraint and the simulation model imposes the backorders fulfillment. But, when an order is placed between echelons, an ordering cost could be introduced to get a better operational level.

Products with seasonal trend are not studied in this research project. But seasonal products with seasonal trend are present within the MSDAH's portfolio. For instance, some diseases occur in winter. Thus, this is a limitation to not study them. Nevertheless, the conceptual model could be used for seasonal product but only by applying the model on shorter period where the demand is quite stationary. Do that for one period, change the parameters according to the next period demand and do the same. This procedure is viable because the planning parameters optimization takes 8 hours.

Further research

For further research, it is recommended to improve the average supply chain cost function by introducing the ordering cost when an order is placed between echelons, and to study what differences can be noticed in the results. According to the role of my planning it is not required to introduce the ordering cost. The planning in this project gives to the planner the quantity that needs to be produced during the lead time in order to cover the future demand. But in order to get a better operational validity, the ordering cost should be added in the objective function. This has already been explained.

A further research could be to consider the capacity aspect of the supply chain (production capacity, transportation capacity and storage capacity). The planning in this project gives the quantities that need to be produced in order to satisfy the future demand but it does not take into account capacities. Are the capacities enough to produce the quantities required by the planning?

Another further research should be done on forecasting, because it appears that the forecast accuracy has an important impact on the supply chain performances (Teunissen, 2009), and this forecasting aspect has not been considered in this project at all.

Another further research should be to consider the biological supply chain. The supply uncertainties are higher in the biological supply chain than in the pharmaceutical supply chain. So the multi echelon concept could give to MSDAH a very good control of its supply chain.

-Integral Single Echelon planning VS Integral Multi Echelon planning to cope with uncertainties-

A last topic for further research could be to incorporate the suppliers or/and the customers on the supply chain scope. This means that new echelons should be added. The information transparency brought by a multi echelon concept extended to the suppliers and customers could increase the performances of the supply chain and improve the relationship confidence between MSDAH and its suppliers and customers (De Kok et al, 2005).

Table of Figures

Figure 1: Global AH market by species and MSDAH's sales by species market.....	16
Figure 2: MSDAH's Manufacturing Site network.....	16
Figure 3: Global AH market by geographical region and MADAH's sales by geographical region.....	17
Figure 4: Pharmaceutical Supply Chain structure	18
Figure 5: Lead Times description of the general pharmaceutical supply chain	19
Figure 6: Biological Supply Chain structure.....	19
Figure 7: Lead time description of the general biological supply chain	20
Figure 8: Current supply chain coordination.....	21
Figure 9: convergent and divergent characteristics of the supply chain	23
Figure 10: Multi echelon planning concept.....	26
Figure 11: Single Echelon planning concept.....	26
Figure 12: Research Model of Mitroff et al. (1974).....	28
Figure 13: Scope of my project.....	30
Figure 14: Lead time description of the X's supply chain	32
Figure 15: Location of the X's supply uncertainties within its supply chain.....	32
Figure 16: Single Echelon concept characterization.....	33
Figure 17: Multi echelon concept characterization	34
Figure 18: role of my planning	35
Figure 19: Planning process for both SE planning and ME planning.....	36
Figure 20: Planning policy for both SE planning and ME planning.....	37
Figure 21: Model's inputs, outputs and decision variables overview	41

Table of Tables

Table 1: supply chain uncertainties summary.....	23
Table 2: comparison between the Single Echelon concept and the Multi Echelon concept.....	27
Table 3: Simulation model behavior for two extreme Demand scenarios	57
Table 4: Simulation model behavior for two extreme inventory level scenarios	58
Table 5: Simulation model behavior for two extreme Lead time scenarios	58

References

- Bertrand J.W.M, Fransso J.C (2002). Modeling and Simulation: Operation Managements Research Methodologies Using Quantitative Modeling. *International Journal of Operations and Production Management*, 22(2), pp. 241-264.
- Bisschop J (2007). Supply Chain Performance Evaluation. *Master thesis, Eindhoven University of Technology, the Netherlands.*
- Boulaksil Y, Fransoo J.C, al (2006). A general approach to set safety stocks in multi-stage inventory systems under rolling horizon mathematical programming models. *OR Spectrum, Volume 31, Issue 1, pp. 121-140.*
- Caillet T (2008). SCM in a pharmaceutical Company. In: *Stadtler H, Kilger C (eds) Supply Chain Management and Advanced Planning, 4rd edn. pp. 415-430*
- Cui J, Engell S (2010). Medium-term planning of a multiproduct batch under evolving multi-period multi-uncertainty of a moving horizon strategy. *Computers and Chemical Engineering, Volume 34, Issue 5, pp. 598 – 619.*
- De Kok T.G, Doremalen F, Wachem E, Clerkx M, Peeters W (2005). Philips Electronics Synchronizes its supply chain to End the Bullwhip Effect. *Interfaces, Volume 35, Issue 1, pp. 37 – 48.*
- De Kok T.G, Fransoo J.C (2003). Planning supply chain operations: definition and comparison of planning concepts. In: *De Kok A.G, Graves SC (eds) Supply Chain Management: Design, Coordination, Operation (Handbooks in Operations Research and Management Science, Volume 11). North Holland, Amsterdam, pp. 1-146.*
- Fleischmann B, Meyr H, Wagner M (2008). Advanced Planning. In: *Stadtler H, Kilger C (eds) Supply Chain Management and Advanced Planning, 4rd edn. pp 81-106.*
- Glover F (1990). Tabu Search Fundamentals and Uses. *ORSA Journal on Computing, Volume 2, Issue 1, pp. 4 – 32.*
- Kelton W, Sadowski R, Sturrock D (2003). Simulation with Arena 3rd edn
- Kilger C, Reuter B, Stadtler H (2008). Collaborative Planning. In: *Stadtler H, Kilger C (eds) Supply Chain Management and Advanced Planning, 4rd edn. pp 263-284.*
- Kilger C (2008). The definition of a supply chain Project. In: *Stadtler H, Kilger C (eds) Supply Chain Management and Advanced Planning, 4rd edn. pp 287-307.*
- Lambert D.M, Cooper C.C (2000). Issues in Supply Chain Management. *Industrial Marketing Management, Volume 29, Issue 1, pp. 65 – 83.*
- Lee H.L, Billington C (1992). Managing Supply Chain Inventory: Pitfalls and Opportunities. *Sloan Management Review, Volume 33, Issue 3, p. 65.*
- Papageorgiou L, Rotstein G, Shah N (2001). Strategic Supply Chain Optimization for the Pharmaceutical Industries. *Industrial & Engineering Chemistry Research, Volume 40, Issue 1, pp. 275 – 286.*

-Integral Single Echelon planning VS Integral Multi Echelon planning to cope with uncertainties-

-Shah N (2004). Pharmaceutical supply chains: key issues and strategies for optimization. *Computers and Chemical Engineering, Volume 28, Issue 6, pp. 929 - 941*

-Shrivastava P (1987). Rigor and Practical Usefulness of Research in Strategic Management. *Strategic Management Journal, Volume 8, Issue 1, pp. 77 – 92.*

-Silver E.A, Pyke D.F, Peterson R (1998). Inventory Management and Production Planning and Scheduling 4rd edn.

-Spitter J.M, Hurkens C.A.J, Kok A.G, Lenstra J.K (2005). linear programming models with planned lead times for supply chain operations planning. *European Journal of Operational Research, Volume 163, Issue 3, pp. 706 – 720.*

-Sürie C, Wagner M (2008). Supply Chain Analysis. In: *Stadtler H, Kilger C (eds) Supply Chain Management and Advanced Planning, 4rd edn. pp 37-63.*

-Teunissen B (2009). A Multi Echelon Safety Stock Setting Procedure using Simulation: Coping with Supply and Demand Uncertainties in the Animal Health Industry. Master thesis, Eindhoven University of Technology, the Netherlands.

-Uquillas R (2010) An Integral Supply Chain Operations Planning System for a Global Pharmaceutical Company. Master thesis, Eindhoven University of Technology, the Netherlands.

-Winter J (2005) Safety stocks at Intervet international. Master thesis, Eindhoven University of Technology, the Netherlands.

Definition of the tables' columns in the appendixes

2 TIMES SUPPLY UN:	All characteristics related to the "2 times supply uncertainties" scenario (Lead times in days)
Ave Demand:	The average monthly demand according to the forecast for FPP considered
Batch size QFPU:	the expected number of vial of FPU produced in one batch. Batch sizes are fixed.
Component:	API 001148 or API 030767 or Bulk or FPU 50ml or FPU 100ml or FPP 50ml or FPP 100ml
Content:	the capacity of the vial sold (50ml or 100ml)
Country:	the abbreviation of the country destination of the FPP considered
Country Destination:	the country where the FPP considered is sold (market)
CP:	cost price in dollars
Demand Max:	The maximal monthly demand according to the forecast for FPP considered
Distribution function:	the distribution function of the demand for the FPP considered
ME 2 TIMES SUPPLY cost:	The average monthly supply chain cost for the ME planning under the "2 times supply uncertainties" scenario.
ME no supply cost:	The average monthly supply chain cost for the ME planning under the "no supply uncertainties" scenario.
ME normal cost:	The average monthly supply chain cost for the ME planning under the "normal" scenario.
MRP Transpo LT:	the lead time of the transportation activity for the process considered registered in SAP (in days)
Mean Production LT:	the average lead time of the production activity for the process considered (in days)
Mean Quality LT:	the average lead time of the quality activity for the process considered (in days)
NO SUPPLY UN:	All characteristics related to the "no supply uncertainties" scenario (Lead times in days)
NORMAL:	All characteristics related to the "normal" scenario (Lead times in days)
Packaging Unit:	the number of vial in the package sold
Param 1:	the first planning parameter of the echelon considered, the replenishment points.

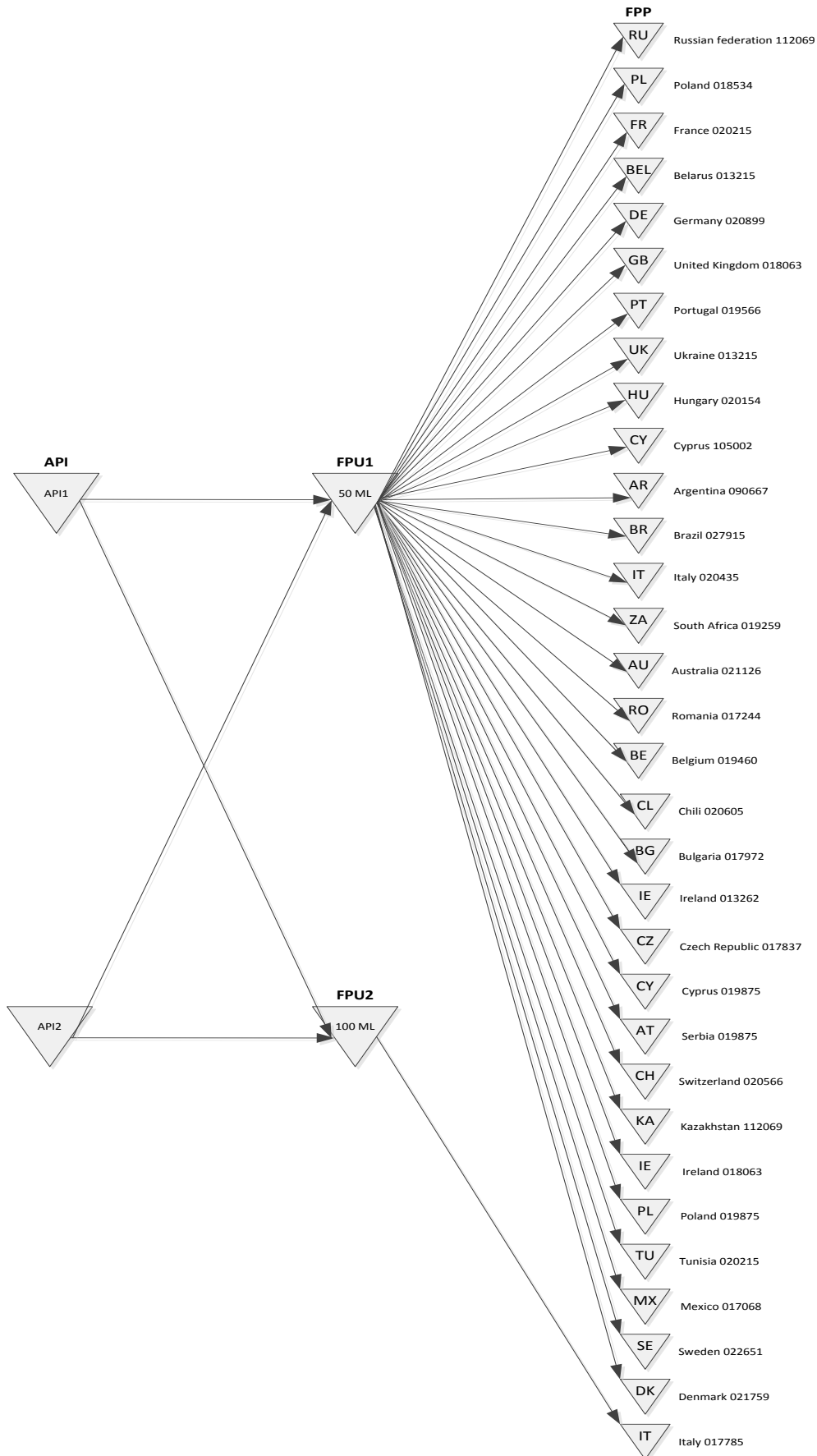
-Integral Single Echelon planning VS Integral Multi Echelon planning to cope with uncertainties-

Param 2:	the second planning parameter of the echelon considered, ordering quantity Q at the FPP and API level, and the number of batch n at the FPU level
Q ME:	The value of the optimal planning parameter Q for the ME planning
Q SE:	The value of the optimal planning parameter Q for the SE planning
Quantity:	fixe quantity of the component to produce
Small s ME:	The value of the optimal planning parameter s for the ME planning
Small s SE:	The value of the optimal planning parameter s for the SE planning
SE 2 TIMES SUPPLY cost:	The average monthly supply chain cost for the SE planning under the “2 times supply uncertainties” scenario.
SE no supply cost:	The average monthly supply chain cost for the SE planning under the “no supply uncertainties” scenario.
SE normal cost:	The average monthly supply chain cost for the SE planning under the “normal” scenario.
UIN:	Unique Identification Number of the FPP considered
Unit:	unit of measure of the quantity required

-Integral Single Echelon planning VS Integral Multi Echelon planning to cope with uncertainties-

APPENDIXES

Appendix 1: Supply network of sub product family X



Appendix 2: Supply network Characteristics of sub product family X

	Country	Country Destination	UIN	Packing Unit	Content	Demand Max	Ave Demand
FPP1	RU	RUSSIAN FEDERATION	112069	1 VL	50 ML	5500	5300
FPP2	PL	POLAND	018534	1 VL	50 ML	2500	2500
FPP3	FR	FRANCE	020215	1 VL	50 ML	3500	1533
FPP4	BEL	BELARUS	013215	1 VL	50 ML	3000	1250
FPP5	DE	GERMANY	020899	1 VL	50 ML	1100	1100
FPP6	GB	UNITED KINGDOM	018063	1 VL	50 ML	1290	938
FPP7	PT	PORTUGAL	019566	1 VL	50 ML	930	752
FPP8	UK	UKRAINE	013215	1 VL	50 ML	800	746
FPP9	HU	HUNGARY	020154	1 VL	50 ML	900	721
FPP10	CY	CYPRUS	105002	1 VL	50 ML	1723	688
FPP11	AR	ARGENTINA	090667	1 VL	50 ML	631	631
FPP12	BR	BRAZIL	27915	1 VL	50 ML	2000	458
FPP13	IT	ITALY	020435	1 VL	50 ML	950	427
FPP14	ZA	SOUTH AFRICA	019259	1 VL	50 ML	680	342
FPP15	AU	AUSTRALIA	021126	1 VL	50 ML	698	323
FPP16	RO	ROMANIA	017244	1 VL	50 ML	300	300
FPP17	BE	BELGIUM	019460	1 VL	50 ML	360	250
FPP18	CL	CHILI	020605	1 VL	50 ML	240	240
FPP19	BU	BULGARIA	017972	1 VL	50 ML	160	158
FPP20	IE	IRELAND	013262	1 VL	50 ML	570	149
FPP21	CZ	CZECH REPUBLIC	017837	1 VL	50 ML	120	120
FPP22	CY	CYPRUS	019875	1 VL	50 ML	494	120
FPP23	SER	SERBIA	019875	1 VL	50 ML	150	102
FPP24	CE	SWITZERLAND	020566	1 VL	50 ML	102	102
FPP25	KA	KAZAKHSTAN	112069	1 VL	50 ML	300	71
FPP26	IE	IRELAND	018063	1 VL	50 ML	100	62
FPP27	PL	POLAND	019875	1 VL	50 ML	60	60
FPP28	TU	TUNISIA	020215	1 VL	50 ML	386	46
FPP29	MX	MEXICO	017068	1 VL	50 ML	120	10
FPP30	SE	SWEDEN	022651	12 VL	50 ML	4	3
FPP31	DK	DENMARK	021759	12 VL	50 ML	2	2
FPP34	IT	ITALY	017785	1 VL	100 ML	450	375

	Batch size QFPU	UIN	Content
FPU1	24200 VL	004157	50 ML
FPU2	3400 VL	004156	100 ML

	UIN
API1	001148
API2	030767

Appendix 3: BOM of sub product family X

FPP 50ml					
component	quantity	unit	component	quantity	unit
API 001148	3,438	KG	Bulk	1250	KG
API 030767	1,638	KG			
Bulk	1250	KG	FPU 50ml	24200	VIALS
FPU 50ml	24200	VIALS	FPP 50ml	24200	VIALS

FPP 100 ML					
component	quantity	unit	component	quantity	unit
API 001148	0,976	KG	Bulk	355	KG
API 030767	0,465	KG			
Bulk	355	KG	FPU 100ml	3400	VIALS
FPU 100ml	3400	VIALS	FPP 100ml	3400	VIALS

Appendix 4: fixe batch sizes for FPU's production

	Quantity	Unit
API1	3,438	KG
API2	1,638	KG
BULK	1250	KG
FPU1 (50ML)	24200	VIALS

	Quantity	Unit
API1	0,976	KG
API2	0,465	KG
BULK	355	KG
FPU2 (100ML)	3400	VIALS

Appendix 5: BOM number

	Country	UIN	Packing Unit	Content	BOM FPP FPU1	BOM FPP FPU2
FPP1	RU	112069	1 VL	50 ML	1	
FPP2	PL	018534	1 VL	50 ML	1	
FPP3	FR	020215	1 VL	50 ML	1	
FPP4	BEL	013215	1 VL	50 ML	1	
FPP5	DE	020899	1 VL	50 ML	1	
FPP6	GB	018063	1 VL	50 ML	1	
FPP7	PT	019566	1 VL	50 ML	1	
FPP8	UK	013215	1 VL	50 ML	1	
FPP9	HU	020154	1 VL	50 ML	1	
FPP10	CY	105002	1 VL	50 ML	1	
FPP11	AR	090667	1 VL	50 ML	1	
FPP12	BR	27915	1 VL	50 ML	1	
FPP13	IT	020435	1 VL	50 ML	1	
FPP14	ZA	019259	1 VL	50 ML	1	
FPP15	AU	021126	1 VL	50 ML	1	
FPP16	RO	017244	1 VL	50 ML	1	
FPP17	BE	019460	1 VL	50 ML	1	
FPP18	CL	020605	1 VL	50 ML	1	
FPP19	BU	017972	1 VL	50 ML	1	
FPP20	IE	013262	1 VL	50 ML	1	
FPP21	CZ	017837	1 VL	50 ML	1	
FPP22	CY	019875	1 VL	50 ML	1	
FPP23	SER	019875	1 VL	50 ML	1	
FPP24	CE	020566	1 VL	50 ML	1	
FPP25	KA	112069	1 VL	50 ML	1	
FPP26	IE	018063	1 VL	50 ML	1	
FPP27	PL	019875	1 VL	50 ML	1	
FPP28	TU	020215	1 VL	50 ML	1	
FPP29	MX	017068	1 VL	50 ML	1	
FPP30	SE	022651	12 VL	50 ML	12	
FPP31	DK	021759	12 VL	50 ML	12	
FPP34	IT	017785	1 VL	100 ML		1

	Content	BOM FPU API1	BOM FPU API2
FPU1	50 ML	0,000142066	0,000067686
FPU2	100 ML	0,000287059	0,000136765

Appendix 6: FPPs demand (distribution function)

	Country	UIN	Demand Max	Ave Demand	Distribution function (discrete empirical)
FPP1	RU	112069	5500	5300	DISC(0.042,4300,0.333,5200,1,5500)
FPP2	PL	018534	2500	2500	DISC(1,2500)
FPP3	FR	020215	3500	1533	DISC(0.625,1020,0.750,2260,1,3500)
FPP4	BEL	013215	3000	1250	DISC(0.583,600,1,3000)
FPP5	DE	020899	1100	1100	DISC(1,1100)
FPP6	GB	018063	1290	938	DISC(0.083,650,0.25,810,0.417,970,0.833,1130,1,1290)
FPP7	PT	019566	930	752	DISC(0.125,186,1,930)
FPP8	UK	013215	800	746	DISC(0.125,640,0.417,720,1,800)
FPP9	HU	020154	900	721	DISC(0.042,580,0.667,740,0.917,820,1,900)
FPP10	CY	105002	1723	688	DISC(0.333,345,0.5,690,0.667,1034,0.833,1378,1,1723)
FPP11	AR	090667	631	631	DISC(1,631)
FPP12	BR	27915	2000	458	DISC(0.625,400,0.917,456,1,2000)
FPP13	IT	020435	950	427	DISC(0.417,350,0.583,500,0.958,650,1,950)
FPP14	ZA	019259	680	342	DISC(0.25,232,0.417,343,0.917,456,1,680)
FPP15	AU	021126	698	323	DISC(0.333,244,0.750,358,0.917,471,1,698)
FPP16	RO	017244	300	300	DISC(1,300)
FPP17	BE	019460	360	250	DISC(0.25,216,0.75,252,0.917,324,1,360)
FPP18	CL	020605	240	240	DISC(1,240)
FPP19	BU	017972	160	158	DISC(0.125,140,1,160)
FPP20	IE	013262	570	149	DISC(0.667,160,0.917,263,1,570)
FPP21	CZ	017837	120	120	DISC(1,120)
FPP22	CY	019875	494	120	DISC(0.667,99,0.750,296,0.917,395,1,494)
FPP23	SER	019875	150	102	DISC(0.25,80,0.333,90,0.667,100,0.833,110,0.917,120,1,150)
FPP24	CE	020566	102	102	DISC(1,102)
FPP25	KA	112069	300	71	DISC(0.667,60,0.958,240,1,300)
FPP26	IE	018063	100	62	DISC(0.083,17,0.167,22,0.25,34,0.33,39,0.417,44,0.5,50,0.75,80,1,100)
FPP27	PL	019875	60	60	DISC(1,60)
FPP28	TU	020215	386	46	DISC(0.833,77,0.917,232,1,386)
FPP29	MX	017068	120	10	DISC(0.917,24,1,120)
FPP30	SE	022651	4	3	DISC(0.042,2,0.5,3,1,5)
FPP31	DK	021759	2	2	DISC(1,2)
FPP34	IT	017785	450	375	DISC(0.25,330,0.333,360,0.375,390,0.875,420,1,450)

Appendix 7: Probability distributions

DISC ($P_1, a_1, P_2 + P_1, a_2, \dots, \dots, \sum_{k=1}^{i-1}(P_k) + P_i, a_i, \dots, \dots, \sum_{k=1}^{n-1}(P_k) + P_n, a_n$)

This is the name of the Discrete distribution in ARENA. The a_i 's are the different values that the output can take. P_i is the probability to get the value a_i . In order to understand the inputs of this distribution it is easier to take an example.

DISC (0.625,1020,0.750,2260,1,3500)

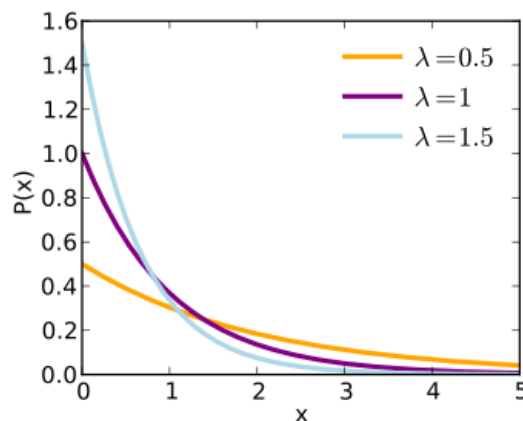
This means that the output can only take 3 possible values. That will be 1020 with a probability of 0.625, or 2260 with a probability of 0.125 (0.750-0.625=0.125), or 3500 with a probability of 0.250 (1-0.750=0.250). Within the expression, it is considered as the cumulative distribution.

EXPO(λ)

This is the name of the Exponential distribution in ARENA. The Exponential distribution is defined by one parameter λ (EXPO (λ)). The expected value of the exponential distribution is $\mu=1/\lambda$ (the mean).

Density function

$$f(x; \lambda) = \begin{cases} \lambda e^{-\lambda x}, & x \geq 0, \\ 0, & x < 0. \end{cases}$$

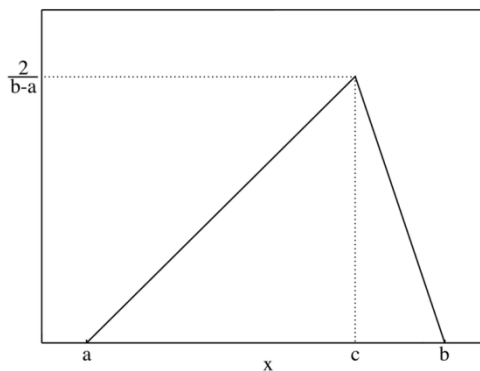


TRIA (a, b, c)

This is the name of the Triangular distribution in ARENA. The Triangular distribution is defined by 3 parameters a, b and c (TRIA (a, b, c)). a is the minimum value, b is the mean value and c is the maximum value that can be achieved.

Density function

$$f(x|a, b, c) = \begin{cases} 0 & \text{for } x < a, \\ \frac{2(x-a)}{(b-a)(c-a)} & \text{for } a \leq x \leq c, \\ \frac{2(b-x)}{(b-a)(b-c)} & \text{for } c < x \leq b, \\ 0 & \text{for } b < x, \end{cases}$$

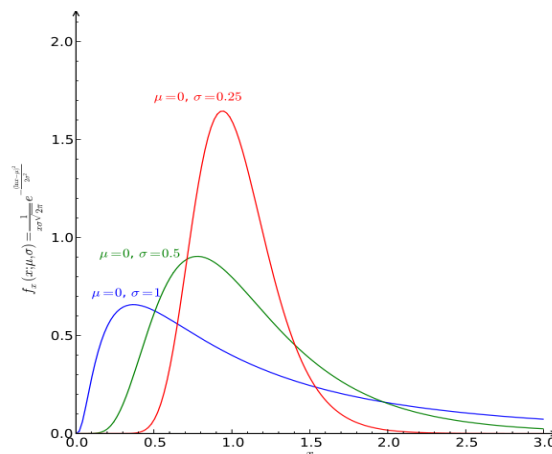


LOGN (μ, σ)

This is the name of the Log-Normal distribution in ARENA. The Log-Normal distribution is defined by 2 parameters, the mean μ (expected value) and σ the standard deviation. (LogN(μ, σ))

Density function

$$f_X(x; \mu, \sigma) = \frac{1}{x\sigma\sqrt{2\pi}} e^{-\frac{(\ln x - \mu)^2}{2\sigma^2}}, \quad x > 0$$



Appendix 8: Mean Square Error (MSE) definition

The MSE is a risk function and it measures the average of the square of the errors between the predicted values and the measured values. The square function is used in order to eliminate the possible compensation of errors with opposite signs.

If \hat{X} is a vector of n prediction, and X is the vector of the true values, then we get:

$$MSE = \frac{1}{n} \sum_{i=1}^n (\hat{X}_i - X_i)^2$$

Appendix 9: Lead time characteristics

	Country	UIN	Mean Quality LT	Mean Production LT	MRP Transportation LT
FPU1 to FPP1	RU	112069	0.56	10,1	7
FPU1 to FPP2	PL	018534	0.56	10,1	5
FPU1 to FPP3	FR	020215	0.56	10,1	2
FPU1 to FPP4	BEL	013215	0.56	10,1	5
FPU1 to FPP5	DE	020899	0.56	10,1	5
FPU1 to FPP6	GB	018063	0.56	10,1	2
FPU1 to FPP7	PT	019566	0.56	10,1	5
FPU1 to FPP8	UK	013215	0.56	10,1	7
FPU1 to FPP9	HU	020154	0.56	10,1	5
FPU1 to FPP10	CY	105002	0.56	10,1	6
FPU1 to FPP11	AR	090667	0.56	10,1	5
FPU1 to FPP12	BR	27915	0.56	10,1	5
FPU1 to FPP13	IT	020435	0.56	10,1	5
FPU1 to FPP14	ZA	019259	0.56	10,1	5
FPU1 to FPP15	AU	021126	0.56	10,1	5
FPU1 to FPP16	RO	017244	0.56	10,1	6
FPU1 to FPP17	BE	019460	0.56	10,1	6
FPU1 to FPP18	CL	020605	0.56	10,1	5
FPU1 to FPP19	BU	017972	0.56	10,1	5
FPU1 to FPP20	IE	013262	0.56	10,1	2
FPU1 to FPP21	CZ	017837	0.56	10,1	5
FPU1 to FPP22	CY	019875	0.56	10,1	6
FPU1 to FPP23	SER	019875	0.56	10,1	2
FPU1 to FPP24	CE	020566	0.56	10,1	5
FPU1 to FPP25	KA	112069	0.56	10,1	7
FPU1 to FPP26	IE	018063	0.56	10,1	2
FPU1 to FPP27	PL	019875	0.56	10,1	5
FPU1 to FPP28	TU	020215	0.56	10,1	5
FPU1 to FPP29	MX	017068	0.56	10,1	5
FPU1 to FPP30	SE	022651	0.56	10,1	2
FPU1 to FPP31	DK	021759	0.56	10,1	2
FPU2 to FPP34	IT	017785	0.56	10,1	5

	Mean Quality LT	Mean Production LT	MRP Transportation LT
API to Bulk	10,2	1,6	0
Bulk to FPU1	38,2	1,5	0
Bulk to FPU2	38,2	1,5	0

	MRP Quality LT	MRP Transportation LT
Supplier to API1	55	14
Supplier to API2	42	90

Appendix 10: Cost Prices of sub product family X

	Country	UIN	Packing Unit	Content	CP
FPP1	RU	112069	1 VL	50 ML	\$5,44
FPP2	PL	018534	1 VL	50 ML	\$5,44
FPP3	FR	020215	1 VL	50 ML	\$5,44
FPP4	BEL	013215	1 VL	50 ML	\$5,44
FPP5	DE	020899	1 VL	50 ML	\$5,44
FPP6	GB	018063	1 VL	50 ML	\$5,44
FPP7	PT	019566	1 VL	50 ML	\$5,44
FPP8	UK	013215	1 VL	50 ML	\$5,44
FPP9	HU	020154	1 VL	50 ML	\$5,44
FPP10	CY	105002	1 VL	50 ML	\$5,44
FPP11	AR	090667	1 VL	50 ML	\$5,44
FPP12	BR	27915	1 VL	50 ML	\$5,44
FPP13	IT	020435	1 VL	50 ML	\$5,44
FPP14	ZA	019259	1 VL	50 ML	\$5,44
FPP15	AU	021126	1 VL	50 ML	\$5,44
FPP16	RO	017244	1 VL	50 ML	\$5,44
FPP17	BE	019460	1 VL	50 ML	\$5,44
FPP18	CL	020605	1 VL	50 ML	\$5,44
FPP19	BU	017972	1 VL	50 ML	\$5,44
FPP20	IE	013262	1 VL	50 ML	\$5,44
FPP21	CZ	017837	1 VL	50 ML	\$5,44
FPP22	CY	019875	1 VL	50 ML	\$5,44
FPP23	SER	019875	1 VL	50 ML	\$5,44
FPP24	CE	020566	1 VL	50 ML	\$5,44
FPP25	KA	112069	1 VL	50 ML	\$5,44
FPP26	IE	018063	1 VL	50 ML	\$5,44
FPP27	PL	019875	1 VL	50 ML	\$5,44
FPP28	TU	020215	1 VL	50 ML	\$5,44
FPP29	MX	017068	1 VL	50 ML	\$5,44
FPP30	SE	022651	12 VL	50 ML	\$65,28
FPP31	DK	021759	12 VL	50 ML	\$65,28
FPP34	IT	017785	1 VL	100 ML	\$7,56

	Content	CP
FPU1	50 ML	\$5,11
FPU2	100 ML	\$6,98

	UIN	CP
API1	001148	\$10 770,00
API2	030767	\$26 002,00

Appendix 11: Planning parameters

	Param 1	Param 2
FPP1	s FPP1	Q FPP1
FPP2	s FPP2	Q FPP2
FPP3	s FPP3	Q FPP3
FPP4	s FPP4	Q FPP4
FPP5	s FPP5	Q FPP5
FPP6	s FPP6	Q FPP6
FPP7	s FPP7	Q FPP7
FPP8	s FPP8	Q FPP8
FPP9	s FPP9	Q FPP9
FPP10	s FPP10	Q FPP10
FPP11	s FPP11	Q FPP11
FPP12	s FPP12	Q FPP12
FPP13	s FPP13	Q FPP13
FPP14	s FPP14	Q FPP14
FPP15	s FPP15	Q FPP15
FPP16	s FPP16	Q FPP16
FPP17	s FPP17	Q FPP17
FPP18	s FPP18	Q FPP18
FPP19	s FPP19	Q FPP19
FPP20	s FPP20	Q FPP20
FPP21	s FPP21	Q FPP21
FPP22	s FPP22	Q FPP22
FPP23	s FPP23	Q FPP23
FPP24	s FPP24	Q FPP24
FPP25	s FPP25	Q FPP25
FPP26	s FPP26	Q FPP26
FPP27	s FPP27	Q FPP27
FPP28	s FPP28	Q FPP28
FPP29	s FPP29	Q FPP29
FPP30	s FPP30	Q FPP30
FPP31	s FPP31	Q FPP31
FPP34	s FPP34	Q FPP34

	Param 1	Param 2
FPU1	s FPU1	n FPU1
FPU2	s FPU2	n FPU2

	Param 1	Param 2
API1	s API1	Q API1
API2	s API2	Q API2

Appendix 12: List of symbols used in the simulation model

API	= Set of X's APIs
$B_{API1}(t)$	= Backorder level on API1 at the beginning of period t
$B_{API2}(t)$	= Backorder level on API2 at the beginning of period t
$B_{FPP}(t)$	= Backorder level on FPP at the beginning of period t
$BOM_{FPU\ API}$	= Bill of material number from FPU to API
$BOM_{FPU\ API1}$	= Bill of material number from FPU to API1
$BOM_{FPU\ API2}$	= Bill of material number from FPU to API2
$BOM_{FPP\ FPU}$	= Bill of material number from FPP to FPU
CP_{fpp}	= Cost Price of FPP
CP_{fpu}	= Cost Price of FPU
CP_{api}	= Cost Price of API
$D_{API1\ FPU}Value(t)$	=Demand in API1 generated by the requirement of FPU production in period t
$D_{API2\ FPU}Value(t)$	=Demand in API2 generated by the requirement of FPU production in period t
$D_{FPP}Value(t)$	=Demand for FPP (external demand) in period t
$D_{FPP\ FPU}Value(t)$	=Fictive demand for FPU in period t, generated by $D_{FPP}Value(t)$ (use to update FPU's echelon stocks)
$D_{FPP\ API}Value(t)$	= Fictive demand for API in period t, generated by $D_{FPP}Value(t)$ (use to update API's echelon stocks)
$D_{FPU}Value(t)$	= Total demand for FPU in period t, generated by the requirement of FPPs production at period t
$D_{FPU\ FPP}Value(t)$	= Demand for FPU in period t, generated by the considered FPP requirement of production
$Demand\ FPP$	= Name of the expression of the FPP demand (distribution function) in ARENA
$devf_{API\ FPU}$	= Deviation factor between API and FPU (output fluctuation uncertainty)
$devf_{FPU\ FPP}$	= Deviation factor between FPU and API (output fluctuation uncertainty)
$EIP_{API}(t)$	=Echelon inventory position of API at the beginning of period t
$EIP_{FPP}(t)$	= Echelon inventory position of FPP at the beginning of period t
$EIP_{FPU}(t)$	= Echelon inventory position of FPU at the beginning of period t

-Integral Single Echelon planning VS Integral Multi Echelon planning to cope with uncertainties-

$ES_{API}(t)$	= Echelon stock of API at the beginning of period t
$ES_{FPP}(t)$	= Echelon stock of FPP at the beginning of period t
$ES_{FPU}(t)$	= Echelon stock of FPU at the beginning of period t
FPP	= Set of X's FPPs
FPU	= Set of X's FPU
$Inv_{API}(t)$	= Physical inventory of API at the beginning of period t
$Inv_{API1}(t)$	= Physical inventory of API1 at the beginning of period t
$Inv_{API2}(t)$	= Physical inventory of API2 at the beginning of period t
$I_{FPP}(t)$	= Physical inventory of FPP at the beginning of period t
$Inv_{FPU}(t)$	= Physical inventory of FPU at the beginning of period t
n	=number of batch rejected during a production order of FPU
$nFPU$	=planning parameter of the FPU echelon. This is the number of batch that needs to be produced if the production of FPU is required.
$nFPUV$	=Number of FPU batches that are really produced when the FPU production is required
Q_{API}	= Order quantity in API (Planning parameter of the API echelon)
Q_{FPP}	= Order quantity in FPP (Planning parameter of the FPP echelon)
Q_{FPU}	= Order quantity in FPU (Planning parameter of the FPU echelon)
$QO_{API}(t)$	= Quantity ordered by API in period t
$QO_{FPP}(t)$	= Quantity ordered by FPP in period t
$QO_{FPU}(t)$	= Quantity ordered by FPU in period t
$QO_{FPP FPU}(t)$	= Quantity ordered by FPP in period t, translates in fpu quantity
$QO_{FPU API1}(t)$	= Quantity ordered by FPU in period t, translates in API1 quantity
$QO_{FPU API2}(t)$	= Quantity ordered by FPU in period t, translates in API2 quantity
$QS_{FPU FPP}(t)$	= Quantity shipped (produced) from FPU to FPP, in FPP quantity (expected quantity)
$QS_{API1 FPU}(t)$	= Quantity shipped (produced) from API1 to FPU, in FPU quantity (expected quantity)
$QS_{API2 FPU}(t)$	= Quantity shipped (produced) from API2 to FPU, in FPU quantity (expected quantity)
$QS_{API1 to FPU}(t)$	= Quantity shipped (produced) from API1 to FPU, in API1 quantity (expected quantity)
$QS_{API2 to FPU}(t)$	= Quantity shipped (produced) from API2 to FPU, in api2 quantity (expected quantity)

-Integral Single Echelon planning VS Integral Multi Echelon planning to cope with uncertainties-

$QS_{FPP}(t)$	= Quantity shipped in FPP to fulfill FPP backorders in period t
R_{FPP}	=The Boolean variable used as message error (take the value of 1) if an order is placed by the FPP echelon while the previous order has not been received yet
R_{FPU}	= The Boolean variable used as message error (take the value of 1) if an order is placed by the FPU echelon and the previous order has not been received yet
R_{API}	= The Boolean variable used as message error (take the value of 1) if an order is placed by the API echelon and the previous order has not been received yet
$SL_{FPP}(t)$	= Service level of FPP echelon in period t computed after satisfying the demand in FPP
$small\ s\ API$	= Replenishment point s of API (Planning parameter of the echelon API)
$small\ s\ FPP$	= Replenishment point s of FPP (Planning parameter of the echelon FPP)
$small\ s\ FPU$	= Replenishment point s of FPU (Planning parameter of the echelon FPU)
T	= planning horizon (number of month in the simulation)
t	=the period considered

Appendix 13: OptQuest tool

The OptQuest tool of ARENA is an optimizer action tool. OptQuest uses heuristic algorithm for the optimization process. The heuristic method is the well known Tabu Search method.

Before using the OptQuest tool, an optimization design must be done.

First, the simulation variables that need to be optimized have to be defined. They are called Control variables. A maximum of 100 controls can be used. For my part, the controls are the 72 planning parameters.

Secondly, the outputs need to be defined. They are called Responses. The Responses will be used in the constraints and the objective function. For my project, the Responses are the Average Service Level, the Average Cost function and the 36 R Boolean variables (one per echelon).

Thirdly, the optimization constraints are defined. For my part, the constraints are:

- Average Service Level at least to 98%
- The sum of the R different from Zero

Fourthly, the objective is defined. For my project this is to minimize the Average Cost.

Finally, the optimization characteristics are defined, like the number of simulations for the optimization (number of time that the control values change) and the number of replication of the same simulation (number of time the simulation is run with the same control values). For my project, 5000 simulations were done with 5 replications for each simulation. This is what is recommended by the OptQuest's manual when an optimization is run for a number of controls between 50 and 100.

Appendix 14: Tabu Search metaheuristic

Reference: Glover F (1990). Tabu Search Fundamentals and Uses. *ORSA Journal on Computing, Volume 2, Issue 1, pp. 4 – 32.*

Tabu Search (TS) is a metaheuristic local search algorithm. Tabu Search uses a local or neighborhood search procedure to iteratively move from one potential solution to an improved solution in the neighborhood of the potential solution.

Classic local search procedures often become stuck in areas where the solution is not optimal for the problem considered. The classic local search procedures may lead to suboptimal solution (local optimization) instead of the optimal solution (global optimization) by not exploring the good region. In order to avoid these pitfalls and explore regions of the search space that would be left unexplored by other local search procedures, Tabu Search carefully explores the neighborhood of each solution as the search progresses. The solutions admitted to the new neighborhood are determined through the use of memory structures. By using these memory structures, the search progresses by iteratively moving from the current solution to an improved solution.

These memory structures is known as the **tabu list**, a set of rules and banned solutions used to filter which solutions will be admitted to the neighborhood to be explored by the search. The memory structures used in Tabu Search can be divided into three categories:

- Short-term: The list of solutions recently considered. If a potential solution appears on this list, it cannot be revisited until it reaches an expiration point.
- Intermediate-term: A list of rules intended to bias the search towards promising areas of the search space.
- Long-term: Rules that promote diversity in the search process (i.e. regarding resets when the search becomes stuck in a plateau or a suboptimal dead-end).

The short-term memory only intensifies the search by temporarily locking in certain locally attractive attributes Intermediate and long-term structures primarily serve to intensify and diversify the search.

One major issue with Tabu Search is that is only effective in discrete spaces. For my project, the variables spaces are discrete. This is not an issue for the project.

Appendix 15: Supply uncertainties characteristics (“normal” scenario)

Lead times (in days)

	Country	UIN	NORMAL
FPU1 to FPP1	RU	112069	EXPO(1.79)+TRIA(9.2,10.1,10.9)+7
FPU1 to FPP2	PL	018534	EXPO(1.79)+TRIA(9.2,10.1,10.9)+5
FPU1 to FPP3	FR	020215	EXPO(1.79)+TRIA(9.2,10.1,10.9)+2
FPU1 to FPP4	BEL	013215	EXPO(1.79)+TRIA(9.2,10.1,10.9)+5
FPU1 to FPP5	DE	020899	EXPO(1.79)+TRIA(9.2,10.1,10.9)+5
FPU1 to FPP6	GB	018063	EXPO(1.79)+TRIA(9.2,10.1,10.9)+2
FPU1 to FPP7	PT	019566	EXPO(1.79)+TRIA(9.2,10.1,10.9)+5
FPU1 to FPP8	UK	013215	EXPO(1.79)+TRIA(9.2,10.1,10.9)+7
FPU1 to FPP9	HU	020154	EXPO(1.79)+TRIA(9.2,10.1,10.9)+5
FPU1 to FPP10	CY	105002	EXPO(1.79)+TRIA(9.2,10.1,10.9)+6
FPU1 to FPP11	AR	090667	EXPO(1.79)+TRIA(9.2,10.1,10.9)+5
FPU1 to FPP12	BR	27915	EXPO(1.79)+TRIA(9.2,10.1,10.9)+5
FPU1 to FPP13	IT	020435	EXPO(1.79)+TRIA(9.2,10.1,10.9)+5
FPU1 to FPP14	ZA	019259	EXPO(1.79)+TRIA(9.2,10.1,10.9)+5
FPU1 to FPP15	AU	021126	EXPO(1.79)+TRIA(9.2,10.1,10.9)+5
FPU1 to FPP16	RO	017244	EXPO(1.79)+TRIA(9.2,10.1,10.9)+6
FPU1 to FPP17	BE	019460	EXPO(1.79)+TRIA(9.2,10.1,10.9)+6
FPU1 to FPP18	CL	020605	EXPO(1.79)+TRIA(9.2,10.1,10.9)+5
FPU1 to FPP19	BU	017972	EXPO(1.79)+TRIA(9.2,10.1,10.9)+5
FPU1 to FPP20	IE	013262	EXPO(1.79)+TRIA(9.2,10.1,10.9)+2
FPU1 to FPP21	CZ	017837	EXPO(1.79)+TRIA(9.2,10.1,10.9)+5
FPU1 to FPP22	CY	019875	EXPO(1.79)+TRIA(9.2,10.1,10.9)+6
FPU1 to FPP23	SER	019875	EXPO(1.79)+TRIA(9.2,10.1,10.9)+2
FPU1 to FPP24	CE	020566	EXPO(1.79)+TRIA(9.2,10.1,10.9)+5
FPU1 to FPP25	KA	112069	EXPO(1.79)+TRIA(9.2,10.1,10.9)+7
FPU1 to FPP26	IE	018063	EXPO(1.79)+TRIA(9.2,10.1,10.9)+2
FPU1 to FPP27	PL	019875	EXPO(1.79)+TRIA(9.2,10.1,10.9)+5
FPU1 to FPP28	TU	020215	EXPO(1.79)+TRIA(9.2,10.1,10.9)+5
FPU1 to FPP29	MX	017068	EXPO(1.79)+TRIA(9.2,10.1,10.9)+5
FPU1 to FPP30	SE	022651	EXPO(1.79)+TRIA(9.2,10.1,10.9)+2
FPU1 to FPP31	DK	021759	EXPO(1.79)+TRIA(9.2,10.1,10.9)+2
FPU2 to FPP34	IT	017785	EXPO(1.79)+TRIA(9.2,10.1,10.9)+5

	NORMAL
API to Bulk	EXPO(0.098)+TRIA(1.1,1.6,1.9)
Bulk to FPU1	LOGN(38.2,8.2)+TRIA(1.2,1.5,1.95)
Bulk to FPU2	LOGN(38.2,8.2)+TRIA(1.2,1.5,1.95)

	NORMAL
Supplier to API1	69
Supplier to API2	132

-Integral Single Echelon planning VS Integral Multi Echelon planning to cope with uncertainties-

Output quantity deviation factor

	NORMAL
FPU to FPP	0,08%
API to FPU1	0,65%
API to FPU2	2,30%

Batch rejection percentage

	NORMAL
RB API to FPU1	2,00%
RB API to FPU2	1,50%
RB FPU to FPP	0,00%

Appendix 16: Supply uncertainties (“no supply uncertainties” scenario)

Led times (in days)

	Country	UIN	NO SUPPLY UN
FPU1 to FPP1	RU	112069	0.56+10,1+7
FPU1 to FPP2	PL	018534	0.56+10,1+5
FPU1 to FPP3	FR	020215	0.56+10,1+2
FPU1 to FPP4	BEL	013215	0.56+10,1+5
FPU1 to FPP5	DE	020899	0.56+10,1+5
FPU1 to FPP6	GB	018063	0.56+10,1+2
FPU1 to FPP7	PT	019566	0.56+10,1+5
FPU1 to FPP8	UK	013215	0.56+10,1+7
FPU1 to FPP9	HU	020154	0.56+10,1+5
FPU1 to FPP10	CY	105002	0.56+10,1+6
FPU1 to FPP11	AR	090667	0.56+10,1+5
FPU1 to FPP12	BR	27915	0.56+10,1+5
FPU1 to FPP13	IT	020435	0.56+10,1+5
FPU1 to FPP14	ZA	019259	0.56+10,1+5
FPU1 to FPP15	AU	021126	0.56+10,1+5
FPU1 to FPP16	RO	017244	0.56+10,1+6
FPU1 to FPP17	BE	019460	0.56+10,1+6
FPU1 to FPP18	CL	020605	0.56+10,1+5
FPU1 to FPP19	BU	017972	0.56+10,1+5
FPU1 to FPP20	IE	013262	0.56+10,1+2
FPU1 to FPP21	CZ	017837	0.56+10,1+5
FPU1 to FPP22	CY	019875	0.56+10,1+6
FPU1 to FPP23	SER	019875	0.56+10,1+2
FPU1 to FPP24	CE	020566	0.56+10,1+5
FPU1 to FPP25	KA	112069	0.56+10,1+7
FPU1 to FPP26	IE	018063	0.56+10,1+2
FPU1 to FPP27	PL	019875	0.56+10,1+5
FPU1 to FPP28	TU	020215	0.56+10,1+5
FPU1 to FPP29	MX	017068	0.56+10,1+5
FPU1 to FPP30	SE	022651	0.56+10,1+2
FPU1 to FPP31	DK	021759	0.56+10,1+2
FPU2 to FPP34	IT	017785	0.56+10,1+5

	NO SUPPLY UN
API to Bulk	11,8
Bulk to FPU1	39,7
Bulk to FPU2	39,7

	NO SUPPLY UN
Supplier to API1	69
Supplier to API2	132

-Integral Single Echelon planning VS Integral Multi Echelon planning to cope with uncertainties-

Output quantity deviation factor

	NO SUPPLY UN
FPU to FPP	0,00%
API to FPU1	0,00%
API to FPU2	0,00%

Batch rejection percentage

	NO SUPPLY UN
RB API to FPU1	0,00%
RB API to FPU2	0,00%
RB FPU to FPP	0,00%

Appendix 17: Supply uncertainties (“2 times supply uncertainties” scenario)

Led times (in days)

	Country	UIN	2 TIMES SUPPLY UN
FPU1 to FPP1	RU	112069	EXPO(1.79)+TRIA(8.3,10.1,11.7)+7
FPU1 to FPP2	PL	018534	EXPO(1.79)+TRIA(8.3,10.1,11.7)+5
FPU1 to FPP3	FR	020215	EXPO(1.79)+TRIA(8.3,10.1,11.7)+2
FPU1 to FPP4	BEL	013215	EXPO(1.79)+TRIA(8.3,10.1,11.7)+5
FPU1 to FPP5	DE	020899	EXPO(1.79)+TRIA(8.3,10.1,11.7)+5
FPU1 to FPP6	GB	018063	EXPO(1.79)+TRIA(8.3,10.1,11.7)+2
FPU1 to FPP7	PT	019566	EXPO(1.79)+TRIA(8.3,10.1,11.7)+5
FPU1 to FPP8	UK	013215	EXPO(1.79)+TRIA(8.3,10.1,11.7)+7
FPU1 to FPP9	HU	020154	EXPO(1.79)+TRIA(8.3,10.1,11.7)+5
FPU1 to FPP10	CY	105002	EXPO(1.79)+TRIA(8.3,10.1,11.7)+6
FPU1 to FPP11	AR	090667	EXPO(1.79)+TRIA(8.3,10.1,11.7)+5
FPU1 to FPP12	BR	27915	EXPO(1.79)+TRIA(8.3,10.1,11.7)+5
FPU1 to FPP13	IT	020435	EXPO(1.79)+TRIA(8.3,10.1,11.7)+5
FPU1 to FPP14	ZA	019259	EXPO(1.79)+TRIA(8.3,10.1,11.7)+5
FPU1 to FPP15	AU	021126	EXPO(1.79)+TRIA(8.3,10.1,11.7)+5
FPU1 to FPP16	RO	017244	EXPO(1.79)+TRIA(8.3,10.1,11.7)+6
FPU1 to FPP17	BE	019460	EXPO(1.79)+TRIA(8.3,10.1,11.7)+6
FPU1 to FPP18	CL	020605	EXPO(1.79)+TRIA(8.3,10.1,11.7)+5
FPU1 to FPP19	BU	017972	EXPO(1.79)+TRIA(8.3,10.1,11.7)+5
FPU1 to FPP20	IE	013262	EXPO(1.79)+TRIA(8.3,10.1,11.7)+2
FPU1 to FPP21	CZ	017837	EXPO(1.79)+TRIA(8.3,10.1,11.7)+5
FPU1 to FPP22	CY	019875	EXPO(1.79)+TRIA(8.3,10.1,11.7)+6
FPU1 to FPP23	SER	019875	EXPO(1.79)+TRIA(8.3,10.1,11.7)+2
FPU1 to FPP24	CE	020566	EXPO(1.79)+TRIA(8.3,10.1,11.7)+5
FPU1 to FPP25	KA	112069	EXPO(1.79)+TRIA(8.3,10.1,11.7)+7
FPU1 to FPP26	IE	018063	EXPO(1.79)+TRIA(8.3,10.1,11.7)+2
FPU1 to FPP27	PL	019875	EXPO(1.79)+TRIA(8.3,10.1,11.7)+5
FPU1 to FPP28	TU	020215	EXPO(1.79)+TRIA(8.3,10.1,11.7)+5
FPU1 to FPP29	MX	017068	EXPO(1.79)+TRIA(8.3,10.1,11.7)+5
FPU1 to FPP30	SE	022651	EXPO(1.79)+TRIA(8.3,10.1,11.7)+2
FPU1 to FPP31	DK	021759	EXPO(1.79)+TRIA(8.3,10.1,11.7)+2
FPU2 to FPP34	IT	017785	EXPO(1.79)+TRIA(8.3,10.1,11.7)+5

	2 TIMES SUPPLY UN
API to Bulk	EXPO(0.098)+TRIA(0.6,1.6,2.2)
Bulk to FPU1	LOGN(38.2,16.4)+TRIA(0.9,1.5,2.4)
Bulk to FPU2	LOGN(38.2,16.4)+TRIA(0.9,1.5,2.4)

	2 TIMES SUPPLY UN
Supplier to API1	69
Supplier to API2	132

-Integral Single Echelon planning VS Integral Multi Echelon planning to cope with uncertainties-

Output quantity deviation factor

	2 TIMES SUPPLY UN
FPU to FPP	0,16%
API to FPU1	1,30%
API to FPU2	4,60%

Batch rejection percentage

	2 TIMES SUPPLY UN
RB API to FPU1	4,00%
RB API to FPU2	3,00%
RB FPU to FPP	0,00%

Appendix 18: Results SE (“normal”

scenario)

SE NORMAL	Q SE	small s SE
FPP1	5730	5160
FPP2	2900	2880
FPP3	3360	3790
FPP4	3300	3540
FPP5	1510	1130
FPP6	1570	1410
FPP7	1110	1080
FPP8	1110	1040
FPP9	1110	1030
FPP10	1720	1920
FPP11	1230	1310
FPP12	2100	1940
FPP13	1340	1100
FPP14	780	840
FPP15	790	920
FPP16	420	590
FPP17	500	390
FPP18	390	400
FPP19	340	250
FPP20	570	610
FPP21	190	210
FPP22	520	550
FPP23	160	170
FPP24	140	160
FPP25	320	390
FPP26	200	150
FPP27	70	80
FPP28	450	460
FPP29	160	240
FPP30	6	8
FPP31	4	4
FPP34	460	460
Sum for FPU1	34100	
FPU1	96800	55600
FPU2	3400	2150
API1	16	14
API2	11	11

SE normal cost
\$1 284 287

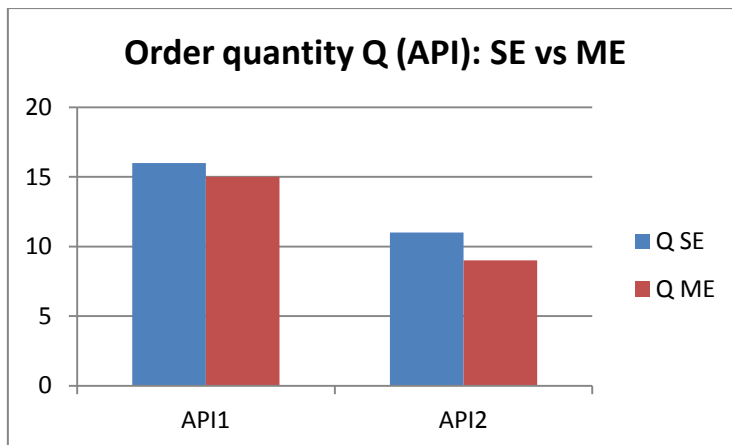
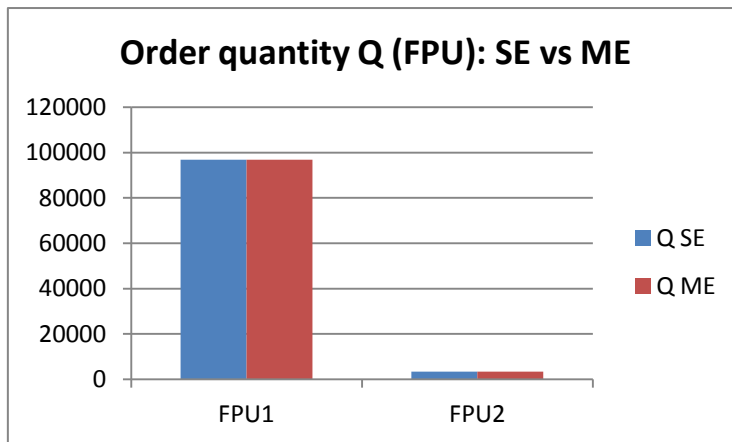
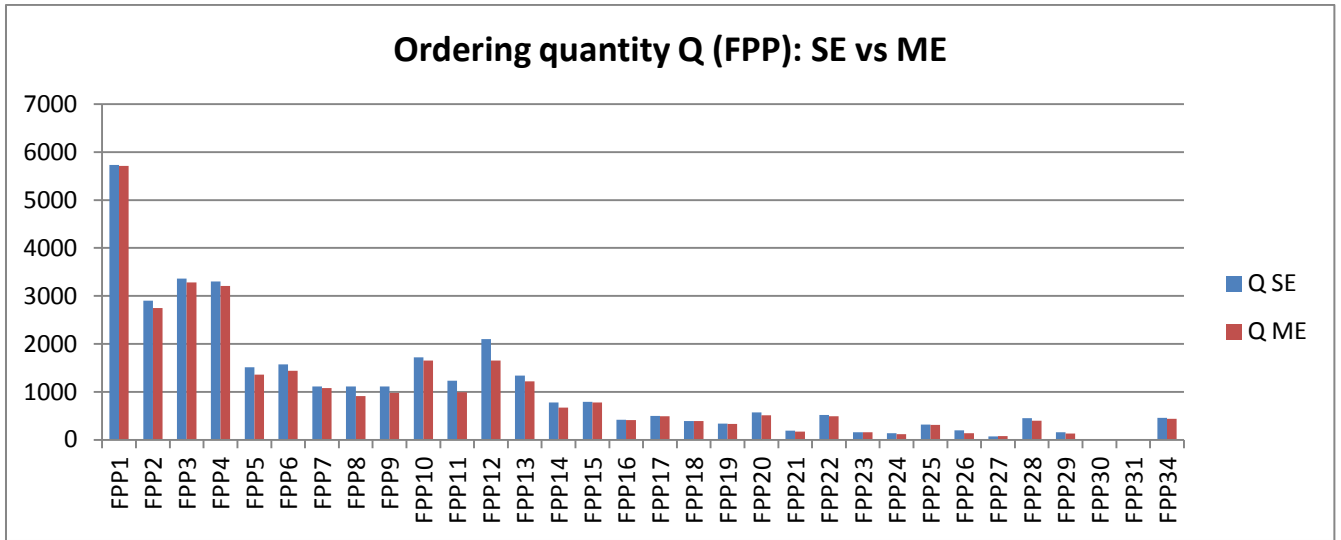
Appendix 19: Results ME (“normal” scenario)

ME NORMAL	Q ME	small s ME
FPP1	5710	5090
FPP2	2750	2800
FPP3	3280	3790
FPP4	3210	2690
FPP5	1360	1110
FPP6	1440	1280
FPP7	1080	990
FPP8	910	1040
FPP9	980	980
FPP10	1650	1650
FPP11	990	950
FPP12	1650	1600
FPP13	1220	970
FPP14	670	780
FPP15	780	900
FPP16	410	370
FPP17	490	360
FPP18	390	310
FPP19	330	240
FPP20	510	580
FPP21	170	210
FPP22	490	510
FPP23	160	170
FPP24	120	150
FPP25	310	290
FPP26	140	140
FPP27	80	80
FPP28	400	400
FPP29	130	240
FPP30	4	6
FPP31	3	4
FPP34	440	450
Sum for FPU1	31817	
FPU1	96800	83100
FPU2	3400	2460
API1	15	22
API2	9	14

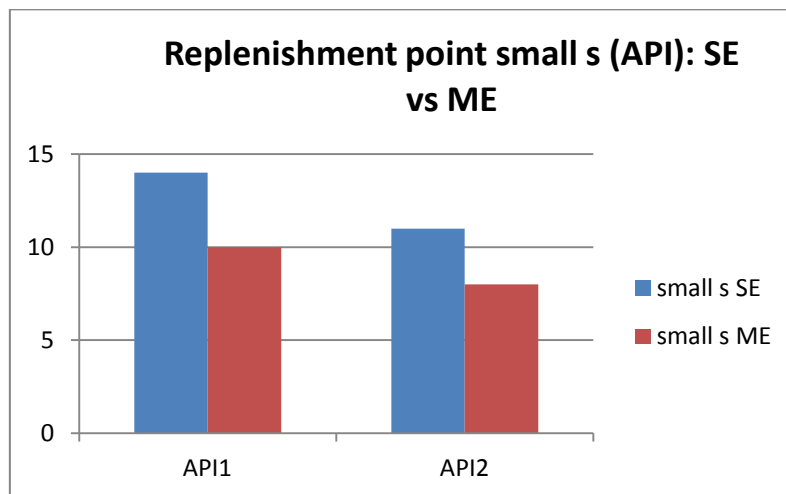
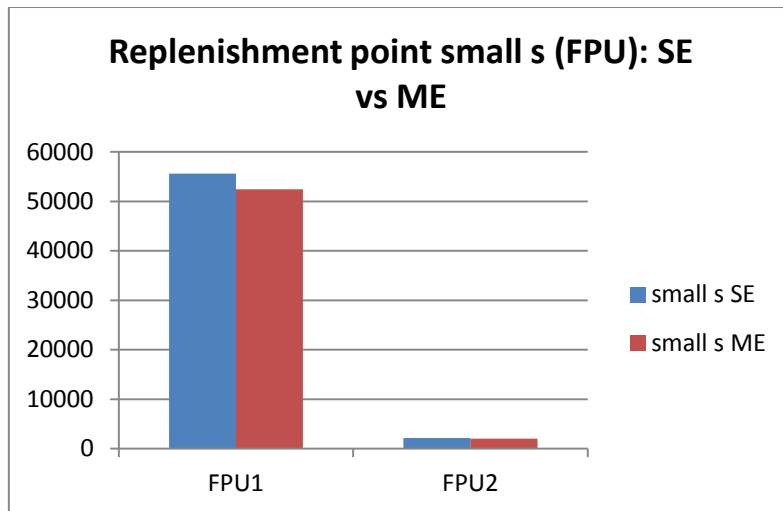
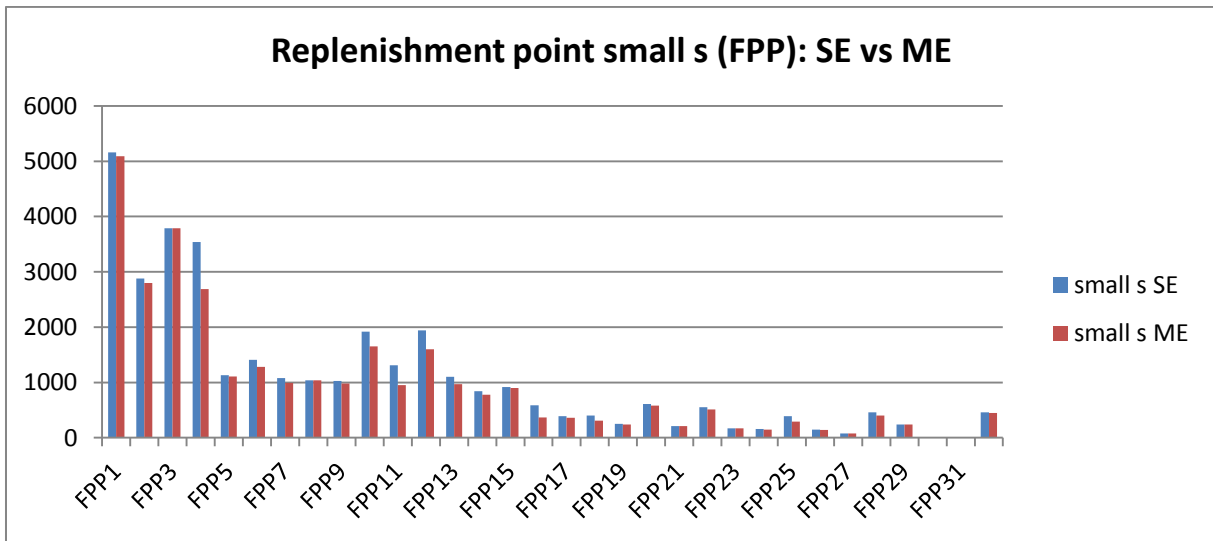
ME normal cost
\$928 899

Appendix 20: SE versus ME (“normal” scenario)

Q quantity analysis

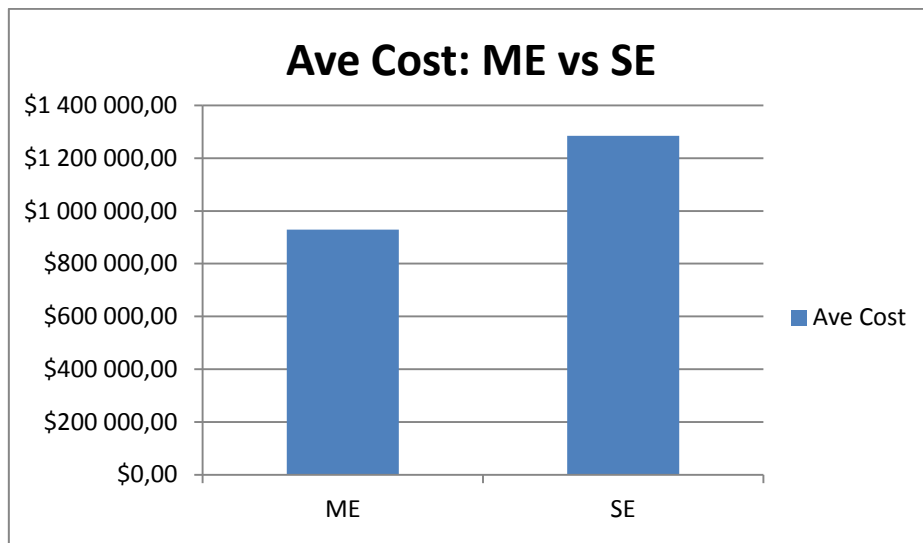


Replenishment point s analysis



-Integral Single Echelon planning VS Integral Multi Echelon planning to cope with uncertainties-

Average Cost Analysis



Appendix 21: Results SE (“no supply uncertainties” scenario)

SE no supply	Q SE	small s SE
FPP1	5460	4650
FPP2	2650	2700
FPP3	3270	3280
FPP4	2700	2630
FPP5	1440	1100
FPP6	1400	1300
FPP7	1050	980
FPP8	1110	960
FPP9	910	780
FPP10	1500	1770
FPP11	1190	640
FPP12	1650	1650
FPP13	1120	1050
FPP14	780	820
FPP15	770	810
FPP16	360	320
FPP17	500	360
FPP18	360	340
FPP19	180	230
FPP20	490	570
FPP21	150	210
FPP22	470	480
FPP23	160	160
FPP24	110	150
FPP25	320	290
FPP26	200	130
FPP27	70	70
FPP28	450	420
FPP29	140	210
FPP30	4	4
FPP31	2	2
FPP34	450	400
Sum for FPU1	30966	
FPU1	72600	52600
FPU2	3400	1860
API1	12	11
API2	8	8

SE no supply cost
\$1 111 377

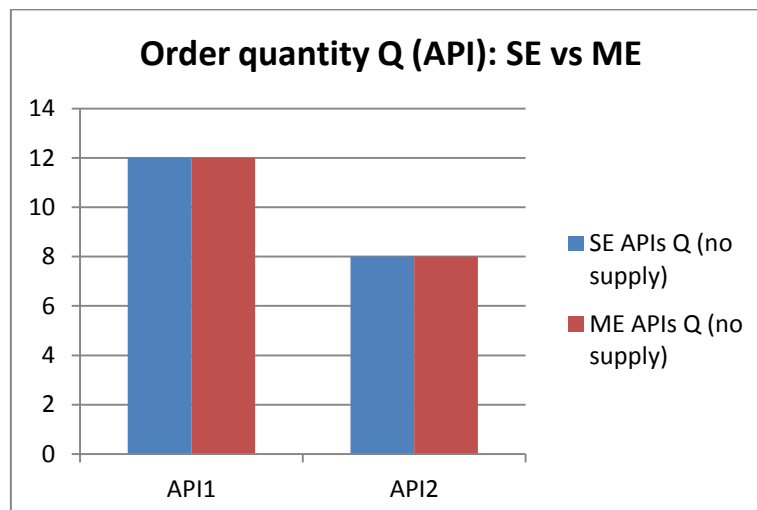
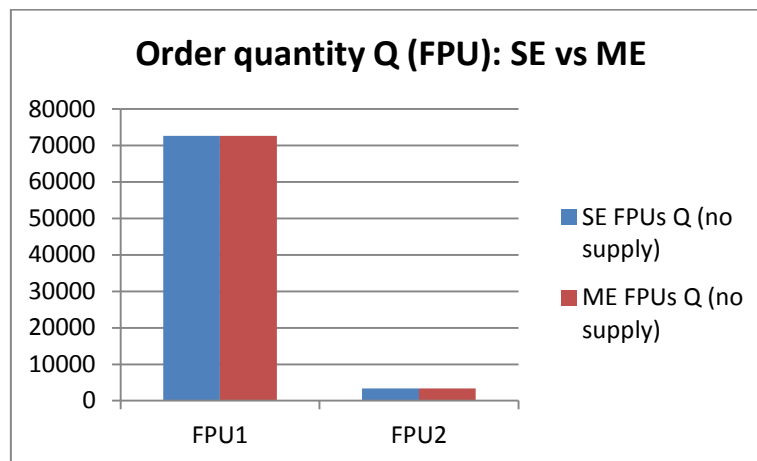
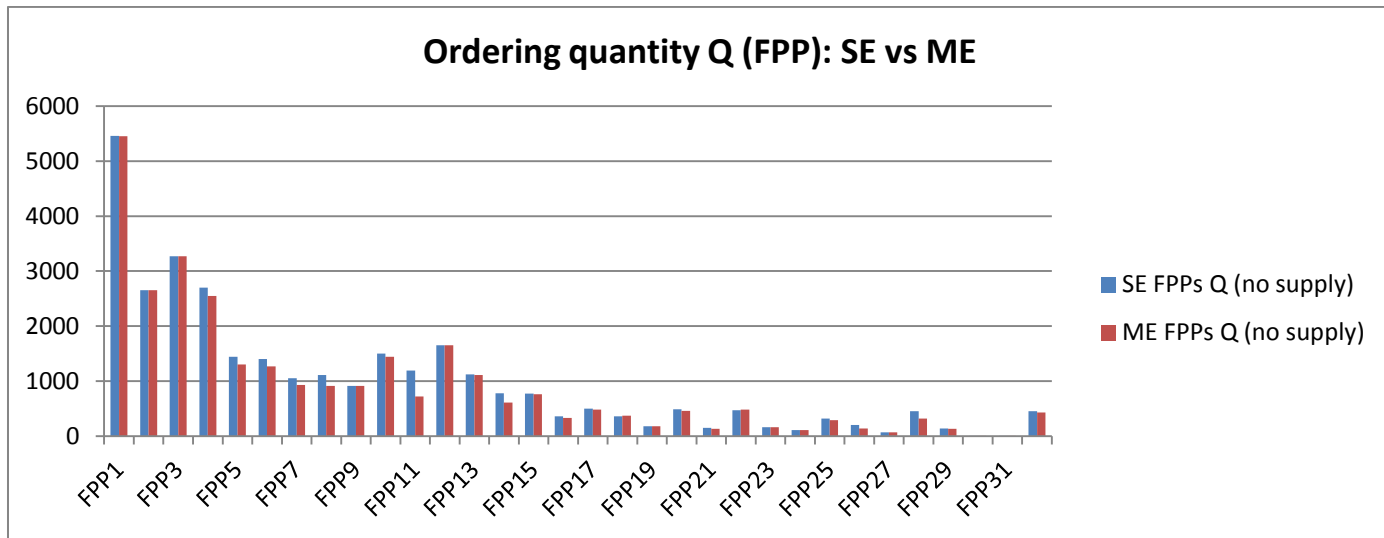
Appendix 22: Results ME (“no supply uncertainties” scenario)

ME no supply	Q ME	small s ME
FPP1	5450	4630
FPP2	2650	2670
FPP3	3270	3200
FPP4	2550	2470
FPP5	1300	1100
FPP6	1270	1200
FPP7	930	940
FPP8	910	960
FPP9	910	910
FPP10	1440	1640
FPP11	720	640
FPP12	1650	1420
FPP13	1110	760
FPP14	610	740
FPP15	760	810
FPP16	330	320
FPP17	480	360
FPP18	370	240
FPP19	180	160
FPP20	460	570
FPP21	130	170
FPP22	480	420
FPP23	160	160
FPP24	110	150
FPP25	290	260
FPP26	140	110
FPP27	70	70
FPP28	320	380
FPP29	130	190
FPP30	4	4
FPP31	2	2
FPP34	430	400
Sum for FPU1	29186	
FPU1	72600	78800
FPU2	3400	2120
API1	12	20
API2	8	13

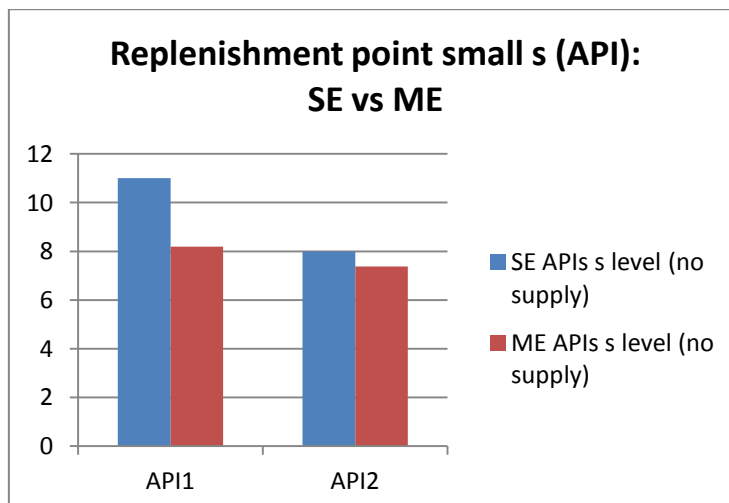
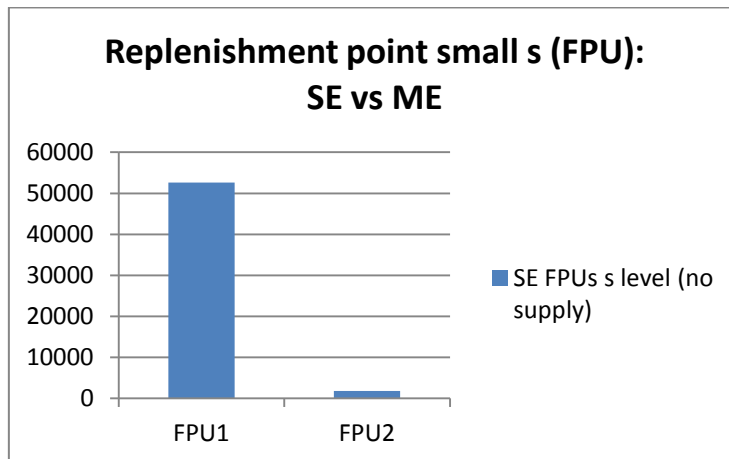
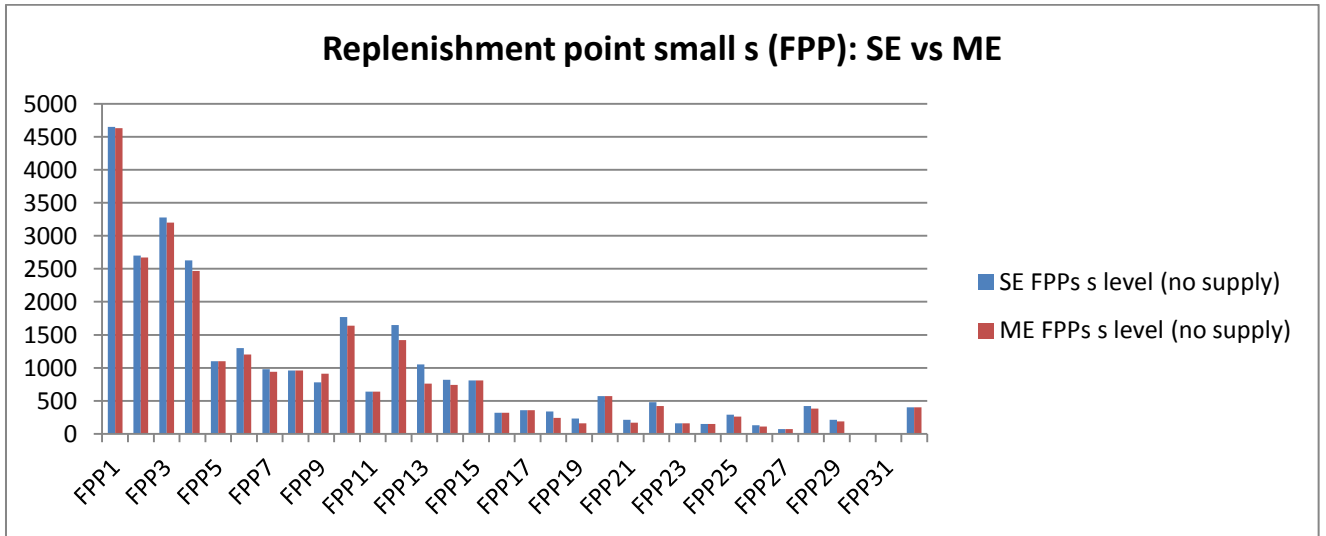
ME no supply cost
\$903 450

Appendix 23: SE versus ME (“no supply uncertainties” scenario)

Q quantity analysis

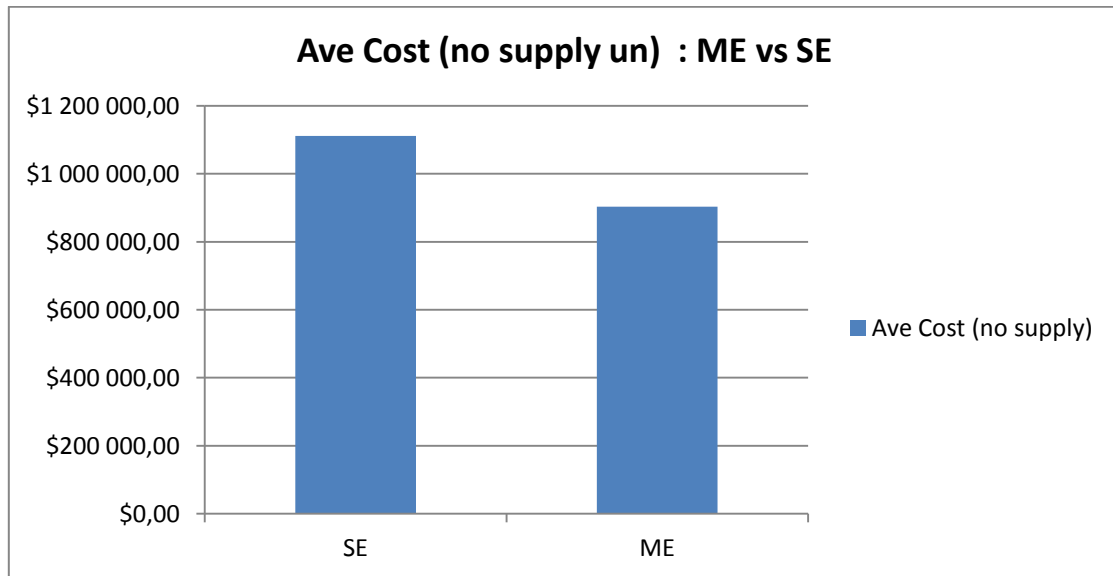


Replenishment point s analysis



-Integral Single Echelon planning VS Integral Multi Echelon planning to cope with uncertainties-

Average Cost Analysis



Appendix 24: Results SE (“2 times supply uncertainties” scenario)

SE 2 TIMES	Q SE	small s SE	SE 2 TIMES SUPPLY cost
FPP1	6560	5860	\$1 493 913,00
FPP2	3480	3610	
FPP3	4360	4150	
FPP4	3620	3620	
FPP5	1690	1270	
FPP6	1760	1640	
FPP7	1160	1250	
FPP8	1230	1210	
FPP9	1420	1130	
FPP10	1970	2020	
FPP11	1360	1360	
FPP12	2360	2040	
FPP13	1360	1180	
FPP14	820	850	
FPP15	960	920	
FPP16	480	590	
FPP17	520	440	
FPP18	470	460	
FPP19	360	290	
FPP20	670	650	
FPP21	230	260	
FPP22	560	570	
FPP23	170	200	
FPP24	160	180	
FPP25	460	430	
FPP26	200	210	
FPP27	90	90	
FPP28	490	480	
FPP29	210	290	
FPP30	8	8	
FPP31	5	5	
FPP34	520	520	
Sum for FPU1	39193		
FPU1	121000	61200	
FPU2	3400	2670	
API1	19	15	
API2	13	12	

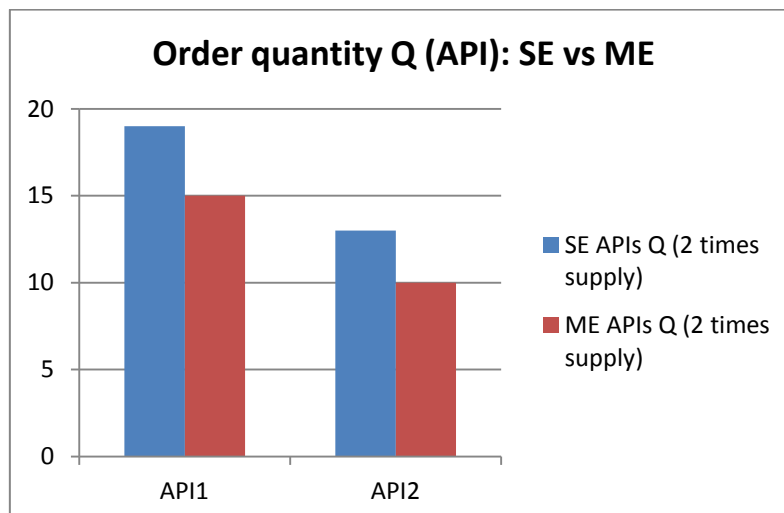
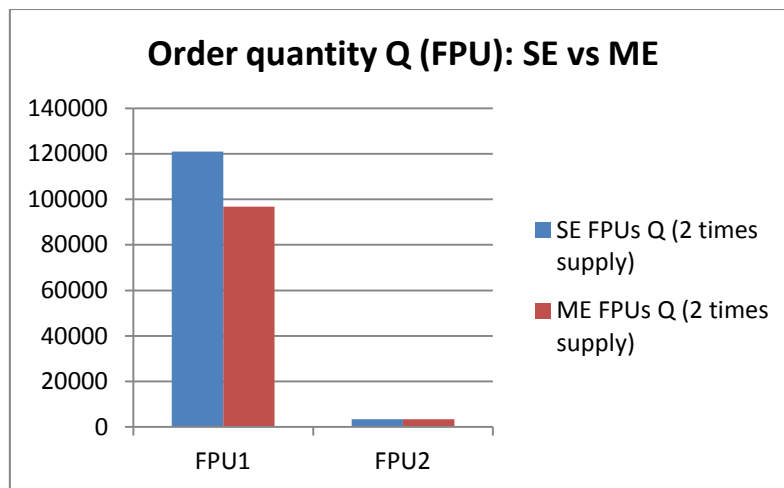
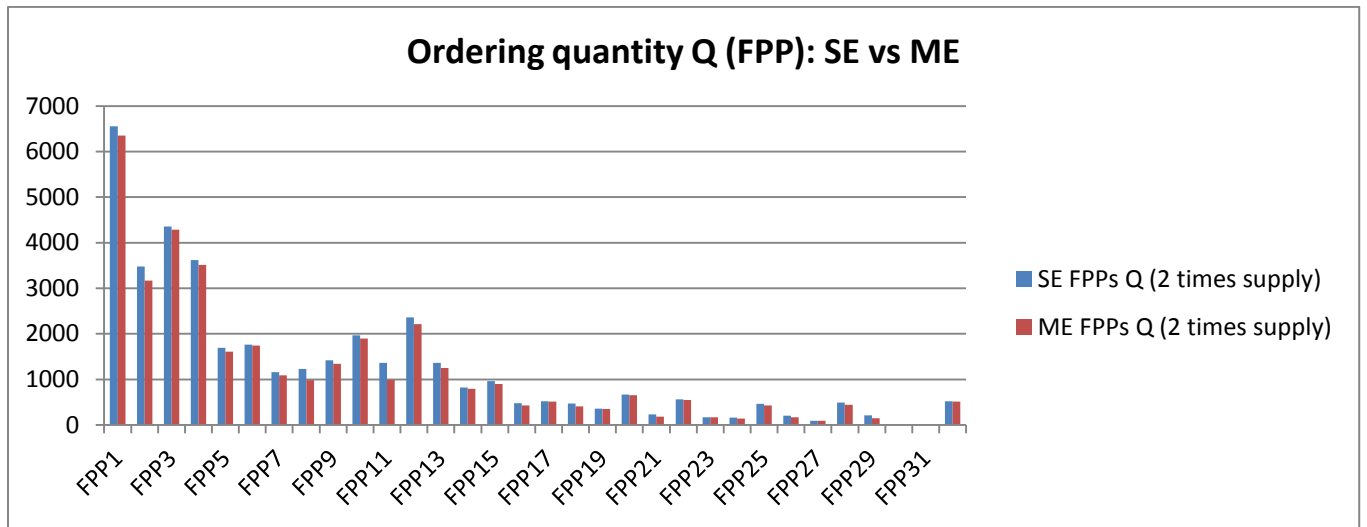
Appendix 25: Results ME (“2 times supply uncertainties” scenario)

ME 2 TIMES	Q ME	small s ME
FPP1	6350	5490
FPP2	3170	3470
FPP3	4290	3800
FPP4	3510	3170
FPP5	1610	1170
FPP6	1740	1580
FPP7	1090	1210
FPP8	980	1160
FPP9	1340	1090
FPP10	1900	1990
FPP11	990	950
FPP12	2210	2040
FPP13	1250	1040
FPP14	790	800
FPP15	900	910
FPP16	430	580
FPP17	510	410
FPP18	410	400
FPP19	350	260
FPP20	650	640
FPP21	180	230
FPP22	550	570
FPP23	170	180
FPP24	140	170
FPP25	430	390
FPP26	170	140
FPP27	90	90
FPP28	440	430
FPP29	150	250
FPP30	8	8
FPP31	4	4
FPP34	510	510
Sum for FPU1	36802	
FPU1	96800	88300
FPU2	3400	2700
API1	15	23
API2	10	15

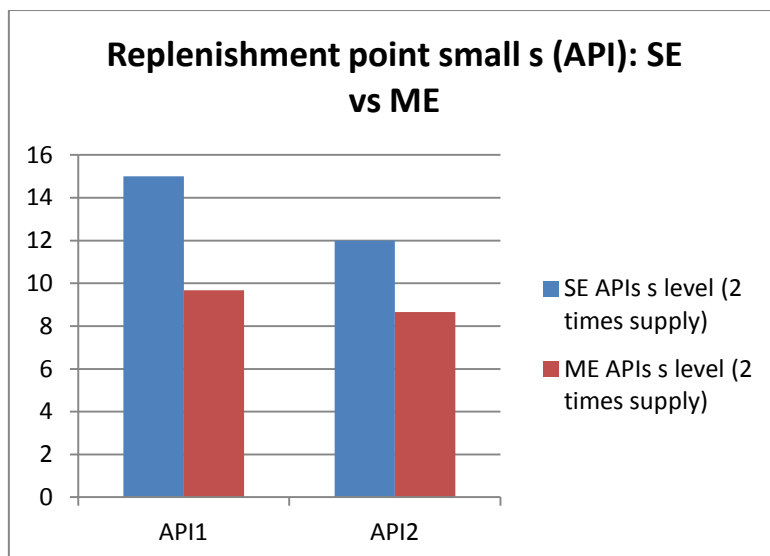
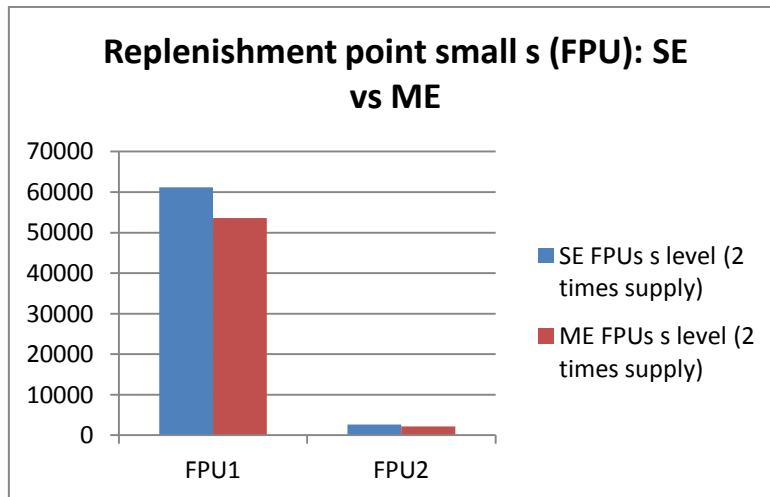
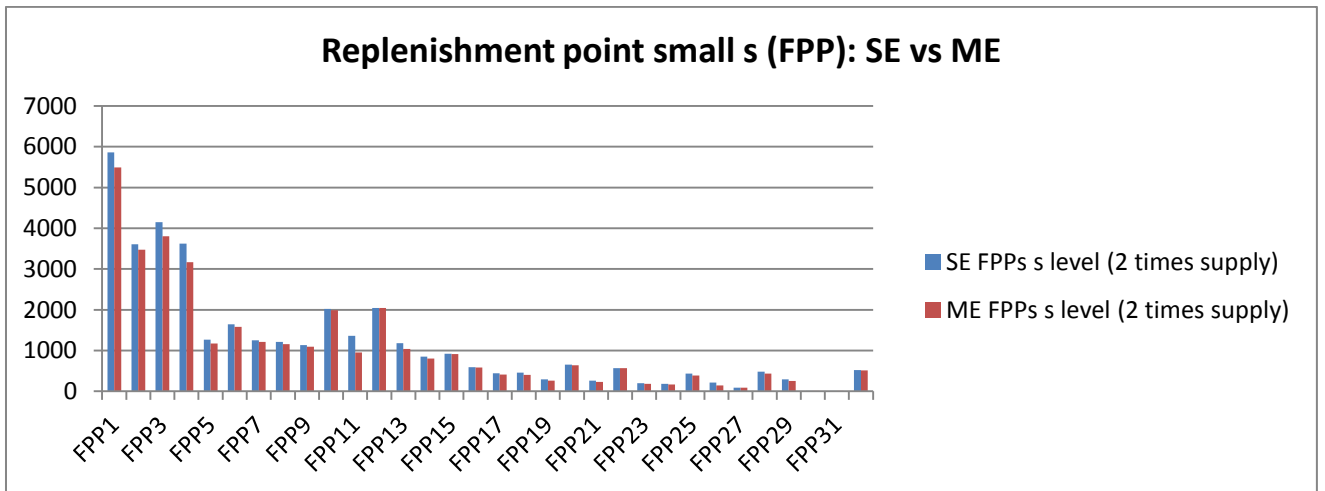
ME 2 TIMES SUPPLY cost
\$955 639,00

Appendix 26: SE versus ME (“2 times supply uncertainties” scenario)

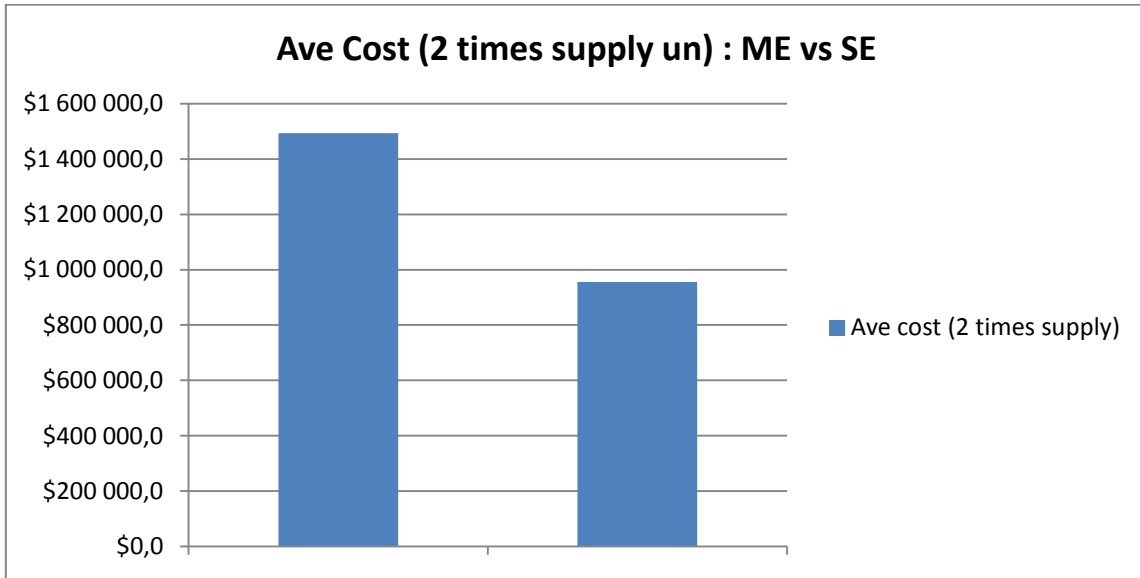
Q quantity analysis



Replenishment point s analysis



Average Cost Analysis



Appendix 27: Results scenario analysis

Q quantity analyses

	ME FPPs Q	ME FPP34 Q	ME FPU1 Q	ME FPU2 Q	ME API1 Q	ME API2 Q
no supply uncertainties	-8,3%	-2,3%	-25,0%	0,0%	-20,0%	-11,1%
normal	0,0%	0,0%	0,0%	0,0%	0,0%	0,0%
2 times supply uncertainties	15,7%	15,9%	0,0%	0,0%	0,0%	11,1%

	SE FPPs Q	SE FPP34 Q	SE FPU1 Q	SE FPU2 Q	SE API1 Q	SE API2 Q
no supply uncertainties	-9,2%	-2,2%	-25,0%	0,0%	-25,0%	-27,3%
normal	0,0%	0,0%	0,0%	0,0%	0,0%	0,0%
2 times supply uncertainties	14,9%	13,0%	25,0%	0,0%	18,8%	18,2%

Replenishment point s analyses

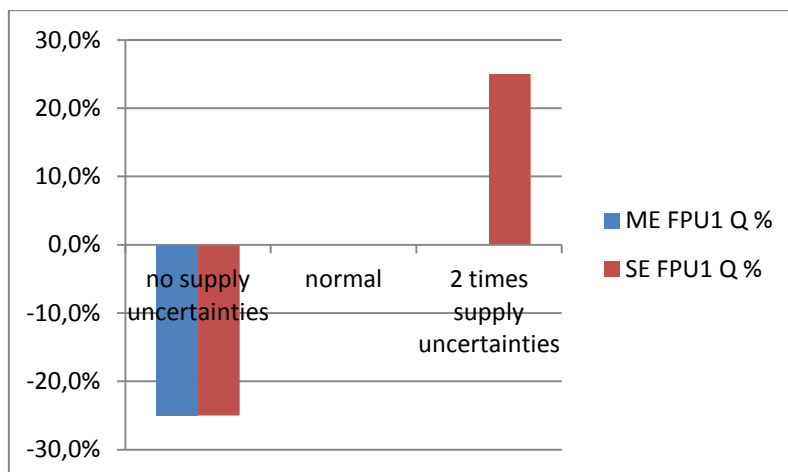
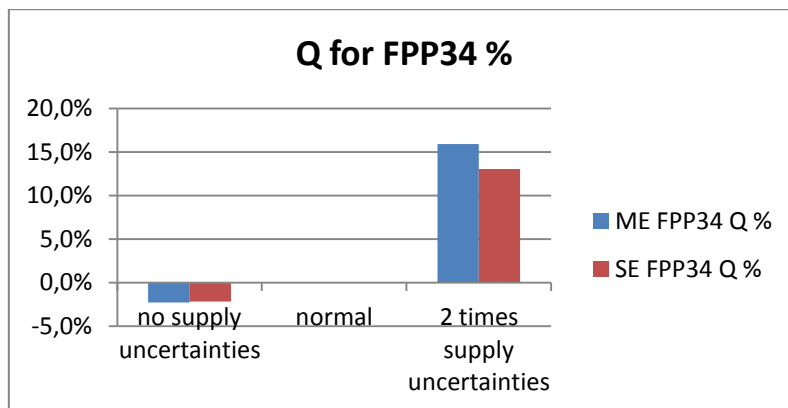
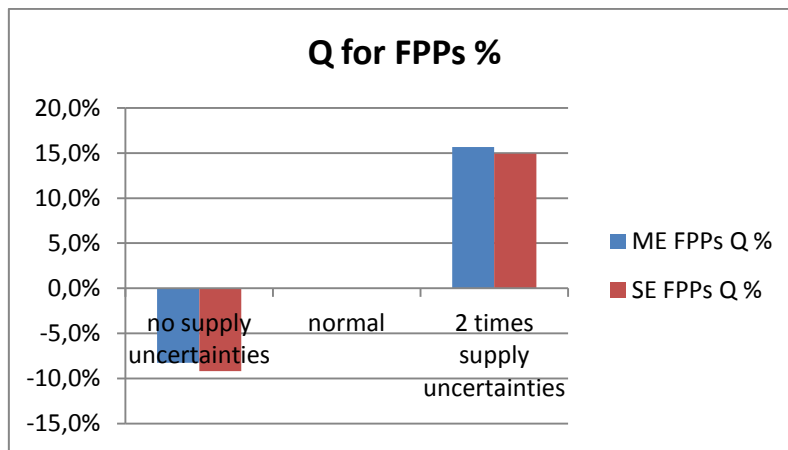
	ME FPPs s	ME FPP34 s	ME FPU1 s	ME FPU2 s	ME API1 small s	ME API2 s
no supply uncertainties	-9,9%	-11,1%	-5,2%	-13,8%	-9,1%	-7,1%
normal	0,0%	0,0%	0,0%	0,0%	0,0%	0,0%
2 times supply uncertainties	12,8%	13,3%	6,3%	9,8%	4,5%	7,1%

	SE FPPs s	SE FPP34 s	SE FPU1 s	SE FPU2 s	SE API1 s	SE API2 s
no supply uncertainties	-13,9%	-13,0%	-5,4%	-13,5%	-21,4%	-27,3%
normal	0,0%	0,0%	0,0%	0,0%	0,0%	0,0%
2 times supply uncertainties	10,4%	13,0%	10,1%	24,2%	7,1%	9,1%

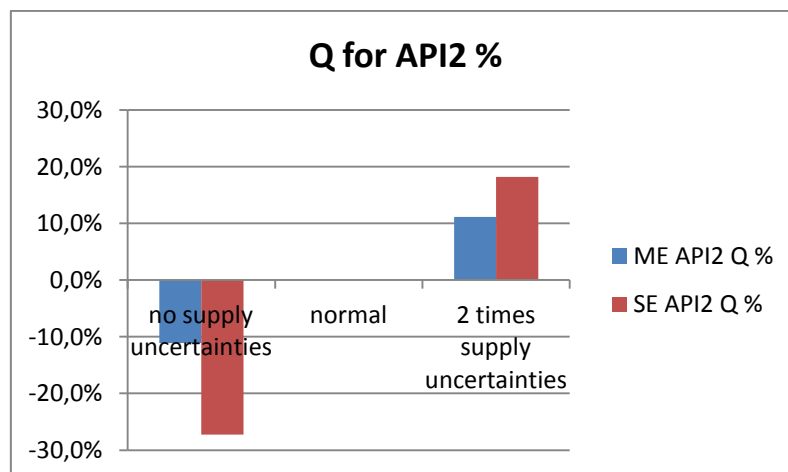
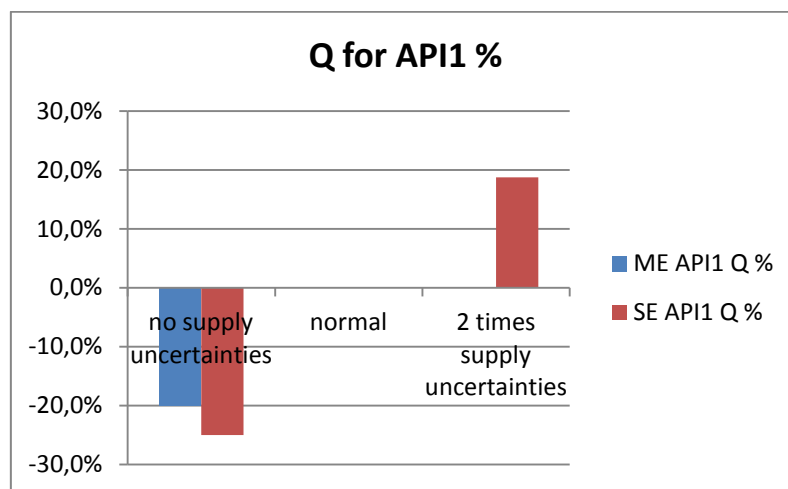
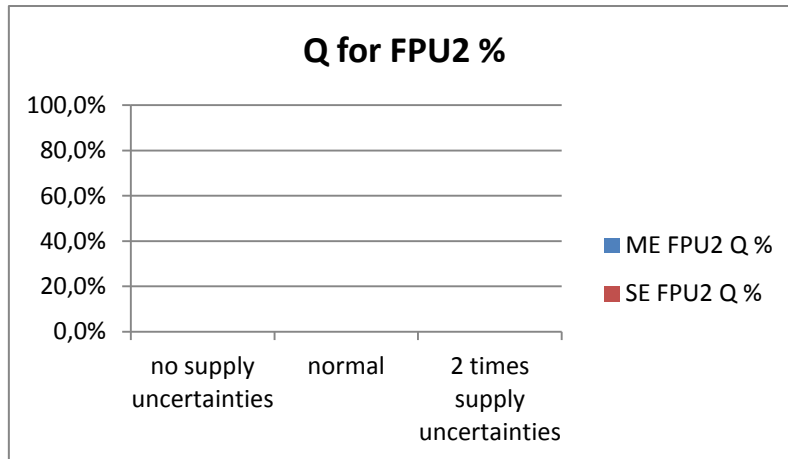
Average Cost Analysis

	ME cost	ME cost evolution	SE cost	SE cost evolution
no supply uncertainties	\$903 450,00	-2,7%	\$1 111 377,00	-13,5%
normal	\$928 899,00	0,0%	\$1 284 287,00	0,0%
2 times supply uncertainties	\$955 639,00	2,9%	\$1 493 913,00	16,3%

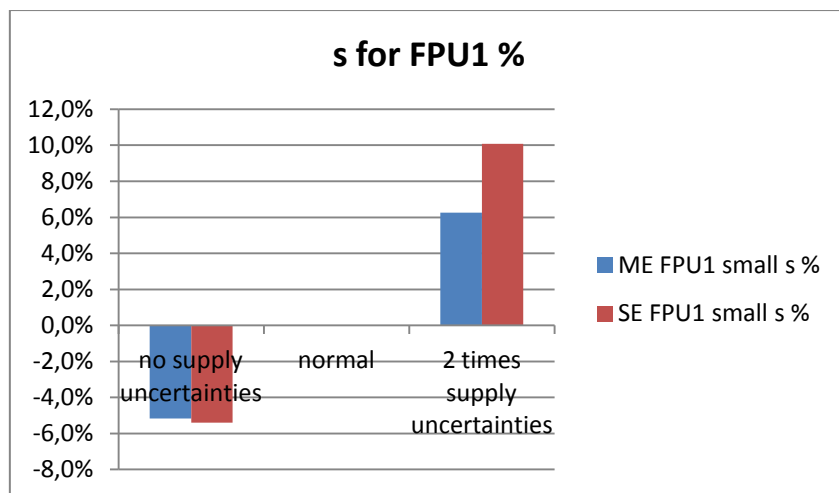
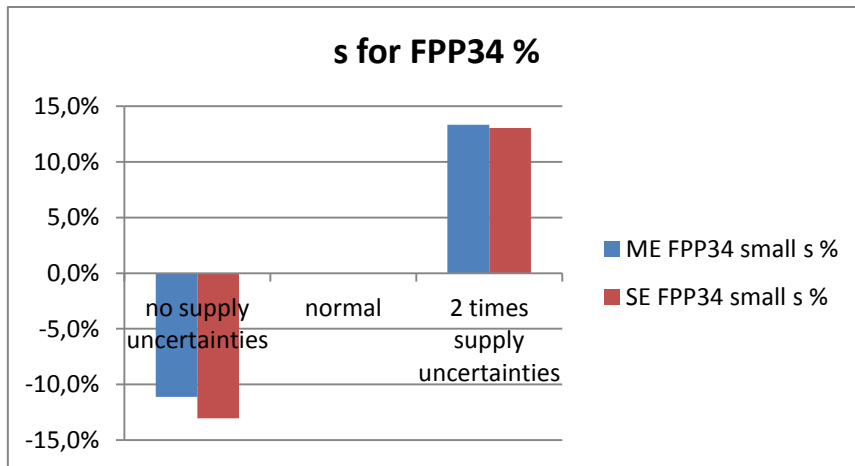
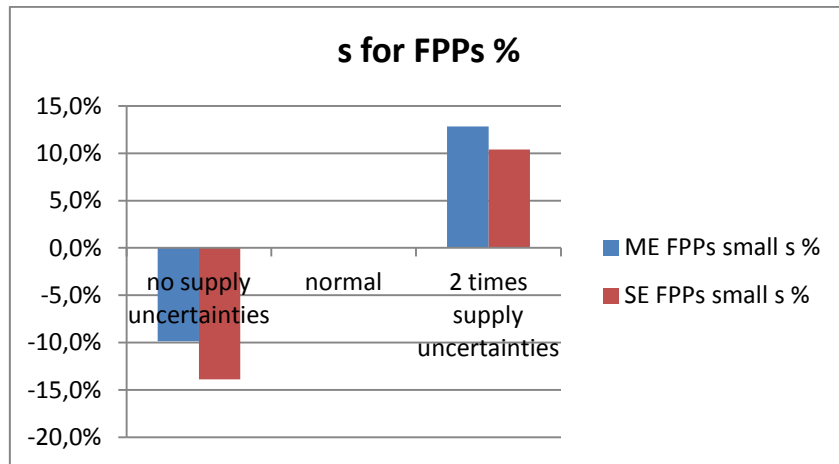
Q quantity analyses



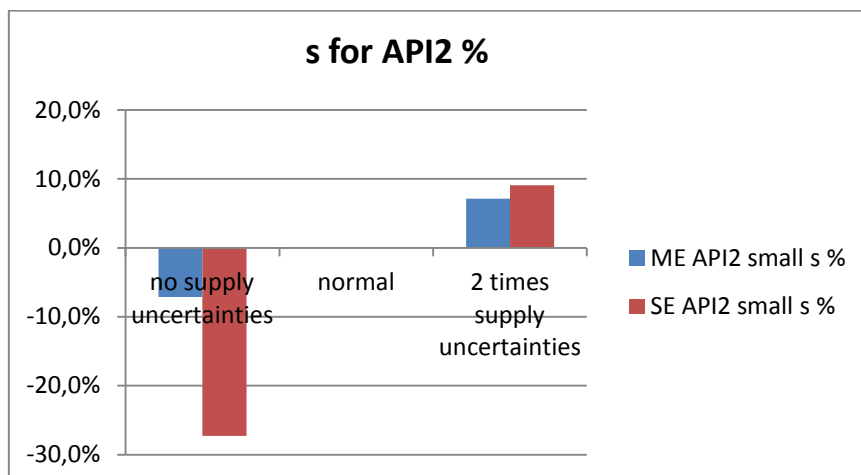
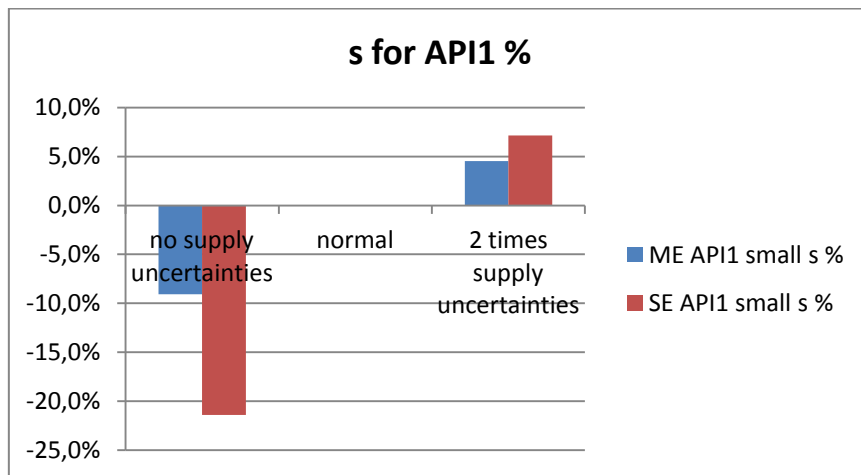
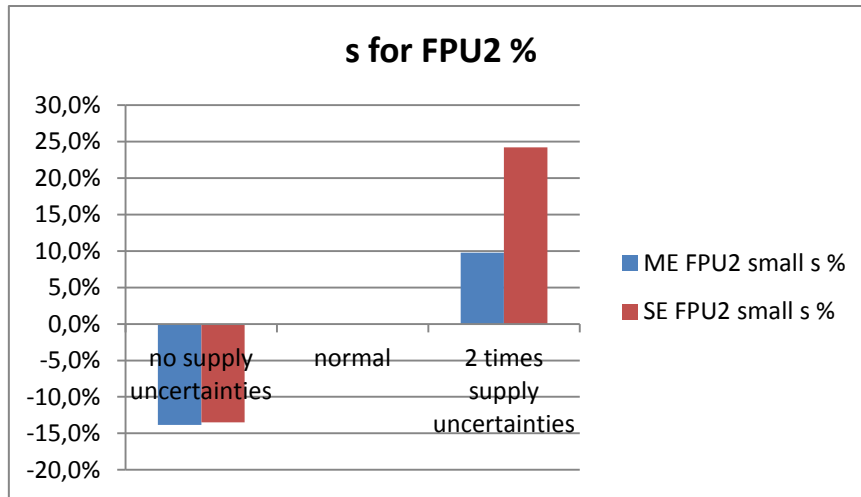
-Integral Single Echelon planning VS Integral Multi Echelon planning to cope with uncertainties-



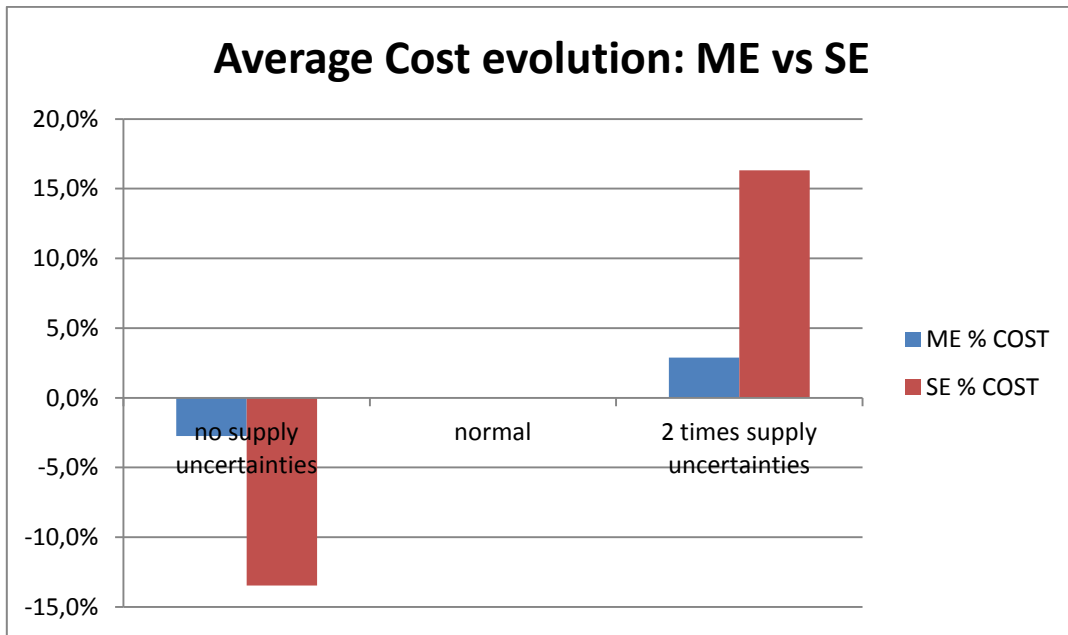
Replenishment points analyses



-Integral Single Echelon planning VS Integral Multi Echelon planning to cope with uncertainties-



Average Cost Analysis



-Integral Single Echelon planning VS Integral Multi Echelon planning to cope with uncertainties-

Appendix 28: SAP EIO

Definition

<http://startrinity.com/SupplyChainManagement/Resources/io11smartops.pdf>

Question about SAP EIO

<http://www.sdn.sap.com/irj/scn/go/portal/prtroot/docs/hub/uuid/4041c165-dd53-2b10-76bb-b447470b02d4>