MASTER

An integral supply chain operations planning system for a global pharmaceutical company

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An Integral Supply Chain Operations Planning System for a Global Pharmaceutical Company

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I. Abstract

In this study, the tangible benefits and operational validity of implementing an Integral Supply Chain Planning and Control System in a Global Pharmaceutical Company (GPC) are analyzed. Multi-echelon models for positioning stock of two relevant products of GPC are developed and the implications in the target stock setting process are analyzed. The study demonstrates that the integration through planning activities would imply lower capital investment. After the optimization, reductions were obtained for the total supply chain investment for both products. In addition, procedures for modeling different aspects of the supply network have been developed. A procedure to reduce the complexity of the BOM structure and standardize attributes in the network, using mono-equivalences along the chain, is presented. An aggregation study for modeling networks with the Synchronized Base Stock policy is extended. For supply networks with varying forecast error, a procedure for incorporating this evolving forecast is developed. The results suggest that it is possible to model non-stationary demand with stationary demand as long as relevant interactions and attributes are considered in the model. Finally, an assessment of the process requirements for increasing the operational validity of a multi-echelon tool, using Business Process Management techniques, is presented.

II. Preface

This thesis marks the culmination of the Master in Operations Management & Logistics at Eindhoven, University of Technology. The project was developed the second semester of the year 2009 at the Global Supply Chain Management (GSCM) Direction of a Global Pharmaceutical Company (GPC). This has been an enriching experience that has extensively contributed to my professional and personal development. I would like to express my gratitude to the people that have contributed to successfully initiate and complete the present project.

I would like to thank Jan Fransoo for mentoring me during the master program. His precise guidance and support during my studies and thesis project were an invaluable factor. Jan not only contributed extensively in all the aspects related to the present project but also represents a role model as a person. Similarly, I would like to thank the GSCM director, promoter of this project. His excellent supervision and leadership were essential to steer the project and overcome different barriers. I would like to thank the head of the support unit of GPC for initiating and supporting the project. Despite of his demanding agenda, he was able to support the project and challenge me with relevant ideas.

I also would like to thank my second supervisor Hajo Reijers and professor Ton De Kok for their valuable comments and ideas in their respective areas of research. Finally, I would like to thank the personnel of GPC for their effective guidance and collaboration during different stages of the project.

To conclude, I have an incommensurable debt of gratitude to my family and Luisa who have provided me their continuous support.

Roberto Uquillas

January 2010

Todas las teorías son legítimas y ninguna tiene importancia. Lo que importa es lo que se hace con ellas.
Jorge Luis Borges

¡Moltisimo Piu Avanti Ancora!
Si en vez de las estúpidas panteras
y los férreos, estúpidos leones,
encerrasen dos flacos mocetones
en la frágil cárcel de las fieras:
No habrían de yacer noches enteras
en el blando pajar de sus colchones,
sin esperanzas ya, sin reacciones,
lo mismo que dos plácidas horteras;
Cual Napoleones pensativos, graves,
no como el tigre sanguinario y maula,
escrutarían palmo a palmo su jaula,
buscando las rendijas, no las llaves...
Seas el que tú seas, ya lo sabes:
a escrutar las rendijas de tu jaula !
Almafuerte

III. Management Summary

In today's complex industrial environment where competing and changing at vertiginous velocities is required, operations around the world are being strongly pressured to rapidly increase their operational effectiveness. In order to fulfill this challenge, global integration is considered as one of the key strategies. This global integration involves the use of integral business models which present several advantages but also several difficulties related with their operational validity. In this sense, decoupled planning versus integral planning is a dilemma that several organizations are facing.

Decoupled Planning has been the general trend for coordinating the activities along the supply chain. In this kind of approach, self contained modules are controlled independently. This kind of models has a simpler mathematical tractability and faster execution of local decisions. On the other hand, they present lower levels of coordination, local optimality, and lower levels of systemic responsiveness capacity. In the case of integral planning, the interactions between elements are considered. Consequently, system optimality is obtained. This implies lower capital investment and more precise characterization of the system behavior. As a result of the higher degree of coordination inherent of these models, superior responsiveness capacity is achieved. The decisions are implemented in shorter time, and the system posses a faster reaction to changes. Nevertheless, this type of planning models present two main disadvantages: complex mathematical tractability, and lower level of feasible implementation.

In order to increase the tractability of integral models, several aspects can be considered in the modeling process. For instance, the mathematical complexity can be decreased by controlling integrally just the most representative variables. Nevertheless, this implies that mechanisms have to be generated to represent decoupled variables, adequately. This is the case when non-stationary demand has to be represented with models under assumptions of stationary demand. Similarly, optimization mechanisms of integrated variables can be generated assuming simpler numeric types. However, this entails the definition of conversion procedures for assuring accuracy in the results. This is the case when integer BOM numbers are assumed in optimization algorithms. Finally, the integration of real life supply chains involves the inclusion of several hundred of echelons. Consequently, less massive and more tractable problems can be obtained through aggregation procedures.

In order to increase the operational validity of integral models, it is necessary to adapt the involved business process. The implementation of an integral planning model implies a centralized control. As a result, it is necessary to define an owner of the model and his position in the organizational structure. Moreover, it is essential to align the responsibility and decision authority of the owner with his opportunity to control. Similarly, an integral control could involve the interaction of several hierarchies in the organization. Consequently, it is important to define the figures that are meaningful for the involved hierarchies and the interaction procedure for realizing a decision related to the model. Finally, there are several information requirements not only related to the generation of the integral model but also with the interface of the model and current systems. Accordingly, it is important to identify these necessities to create generation and interface mechanisms.

This project has been initiated by the Global Supply Chain Management (GSCM) board of a Global Pharmaceutical Company (GPC). This initiative has been made based on two facts: 1) An optimization of its supply networks is required to continue being competitive and 2) with the implementation of the new APS planning software the planning of the Pharmaceutical part (US and Europa for some products) and API manufacturing part is still decoupled. The vision of GPC GSCM is to increase the level of integration and reduce the inventories in the supply chains.

The objective of the project is to obtain insight regarding the benefits and feasibility of implementing an Integral Supply Chain Operations Planning and Control System in GPC in terms of operational validity and capital investment, e.g. from a level of integrated systems through reactive negotiations to a level of integration through planning activities. The research questions are:

1. Main question: Will the utilization of the integrated model for positioning stocks lead to a better optimization of the capital investment in the system than the current decoupled-system approach, in terms of the cost related for achieving a specific service level?

2. Which would be a possible structure and coordination mechanisms, in a specific process of the planning system, necessary to incorporate such centralized model?

With respect to the scope of the project, the supply chains used in the analysis are Omega and Aleph. The multi-echelon model does not consider products in the following phases: Introduction, discontinued products or obsolete products. The uncertainties covered are demand uncertainties. The stages integrated in the chain are API Production and Pharmaceutical Production (Distribution stage containing main affiliates has been extended for Omega).

For answering the first research question a multi-echelon model based on synchronized base stock policies is built. The software used is ChainScope [De Kok (2008)]. The main modeling considerations are: 1) Integration of one key variable, which in this case is stock positioning, 2) A mono-equivalence conversion procedure is used to decrease the complexity of BOM structure, 3) An aggregation approach is used to build the supply network, 4) A procedure to model non-stationary demand with a tool assuming stationary demand is defined. This procedure involves the analysis of forecast errors for different planning horizons. For answering the second research question, Business Process Management techniques are used.

Conclusions and recommendations obtained after using this methodology are:

It is concluded that the integral control of key variables reduces the inherent complexity of comprehensive models, and therefore, increases the operational validity of integral models. In this case, some variables, especially related to the scheduling process, were treated as given constants. Nevertheless, the consistency of the results, through different scenarios and through the comparison with the results of related projects in GPC, indicated that the integral control of key variables increases the level of coordination in the supply chain and maintain the degree of operational validity.

Using mono-equivalences along the chain reduces the complexity of the BOM structure and increases the mathematical tractability of models. Furthermore, it allows a standardized comparison of several attributes in the different stages. Consequently, it facilitates the visibility along the supply chain.

For supply networks with varying forecast error, a procedure for incorporating this evolving forecast is developed. The results indicate that it is possible to represent stationary demand with non-stationary demand models as long as the relevant attributes and interactions are taken into account. In this case, the non-stationary forecast error was controlled through sub-models and scenario analyses. Due to the construction of sub-models certain degree of synergies was lost. Nevertheless, the models represented reasonably well the reality.

Despite of the fact that in the current project all upstream echelons were modeled explicitly, a numerical analysis intended to extend the aggregation procedure developed by Bisschop (2007) when using the synchronized base stock policy was performed. The study indicates that it is not necessary to have equal parameters for the aggregation but relatively similar parameters could be aggregated. Second, items with extreme differences in certain parameters could be aggregated as long as the dominant parameters remain similar. Third, even if some dominant parameters are very different between aggregated items, they could be aggregated if they have opposed effects over the cumulative lead times.

In massive supply chains, it is valuable to define certain level of aggregation. Based on it, it is vital to generate indicators of various attributes in order to understand the supply chain behavior and optimization results.

Finally, the present project makes an initial effort to link Operations Management with Business Process Management (BPM) in order to increase the operational validity of decisions and establish a framework for the research analysis. In essence, any operation and its models are linked to decision processes. When we decide to modify our operations planning models, a reengineering of the related processes is required in order to make operational our decision. In the present project, the use of BPM techniques allows the identification of different interactions for releasing decisions that cannot be identified by typical theoretical models of Operations Management. Similarly, the framework of the BPM cycle which is typically applied to BPM related subjects demonstrates to be effective and applicable to other type of fields.

Conclusions and recommendations of first research question:

The analysis developed in the supply chains of Omega and Aleph demonstrates consistently that the integration through planning activities would imply lower capital investment. After the optimization, reductions were obtained for the total supply chain investment for both products. After the incorporation of supply uncertainties obtained in the pipeline visibility project, the study suggests that the supply chain investment for Omega and Aleph should be increased and maintained, respectively. Nevertheless, again, this can be considered as a relative advantage because additional uncertainties that are not considered in the current situation are taken into account.

Regarding the Omega supply chain, it is recommended to relocate the inventories downstream of the chain. Specifically, it is recommended to decrease the current targets for API Production (Raw materials and Intermediate I) and increase the inventory targets for Pharma (Bulk). The optimization indicates that 5% of relative advantage could be achieved by implementing this recommendation.

The studies in Aleph's chain primarily suggest a reallocation of inventories from Synthesis VII to Synthesis III and balanced levels of inventories between Synthesis III and API. This implies a reduction of inventories in Raw Materials, Synthesis VIII and particularly in Synthesis VII and V. This also implies an increment in API Micro, Granulate and largely in Synthesis III. The optimization indicates that 7% of relative advantage could be achieved by implementing this recommendation.

Furthermore, the results suggest the lower service levels than those required by end-echelons is required for intermediate echelons. For instance, in the case of Omega, a service level of 94% was required to the main API when the stocks were positioned in the optimal situation.

Finally, it is concluded that through a segmentation of target service levels relevant decrements in inventory investment could be achieved. Furthermore, the study suggests that customers with higher levels of demand volume have lower related variability. This implies that for achieving higher service levels in the most relevant customers (based on cost-volume) it is necessary to relatively invest less capital. Consequently, it is recommended to differentiate end customers using the variability of the products related to them as one of the reference variables and assign different service levels according to this segmentation.

Conclusions and recommendations of second research question:

First, it is essential to increase the coverage and precision of available information in terms of functional and structural attributes of the pipelines. It is also necessary to generate mechanisms to maintain the data. Several discrepancies in data were found.

An anticipational top-down approach is recommended to define the objectives. This approach implies that prior any decision released by a Top Level an evaluation of the Base Level behavior through an Anticipated Base Level Model (Multi-echelon model) should be performed. Conversely, the current target setting process involves a bottom up approach and occasionally a top down approach. The utilization of this anticipational top-down approach would entail the consideration of the synergies along the pipeline as well as the specific local implications of any decision. The result of this is a higher degree in the quality of decisions released.

It is necessary to increase the spectrum of pipeline indicators. At the present time, stocks levels are the only metric used for assessing the behavior of the pipeline. Nevertheless, inventory levels are the final consequence of other factors. Consequently, it is suggested to implement and follow up the next indicators per pipeline which are essential for having an accurate visibility: Service levels, variability, cost structure, lot sizes in terms of API Equivalent and along the pipeline.

Regarding the organizational structure, it is necessary to define a responsible entity of the model, and also assure that this entity has a comprehensive view of the network as well as an understanding of detailed figures. Consequently, it is suggested to assign the responsibility of the multi-echelon model to an Intermediate-Level responsible of controlling the entire pipeline.

Finally, it is recommended to define meaningful information in two aspects. First, it is suggested to generate meaningful figures for all the hierarchies involved in releasing a decision over the pipeline. Second, it is necessary to define an interface which couples the current planning parameters and multi-echelon model input and output parameters.

Conclusions and recommendations for future research:

It is suggested to identify research opportunities in which the mono-equivalence approach, developed in this project, could be used. In view of the fact that this approach allows a standardized comparison of different aspects as well as an easier mathematical tractability, it could be extended to other type of industries besides that pharmaceutical industry. In addition, for future research projects in which general structures are present and the software cannot treat non-integer numbers, a possible solution is to divide the network in partial subsystems composed by pure assembly or/and divergent systems. The drawback of this approach is that it will be unavoidable to lose certain degree of synergies.

Further research is suggested in aggregation procedures. These procedures increase the tractability of complex networks. Specifically, is recommended further study in the formalization of the new conditions required for aggregation related to the procedure of Bischop (2007) and the numerical example developed in the present project.

It is recommended to develop additional research projects in which the techniques of Operations Management and Business Process Management are combined.

IV. Table of Contents

1. Introduction

Let's consider the framework of the present industrial environment. What we see is a dynamic, heterogeneous and complex industrial playground where competing and changing at vertiginous velocities is required [Brown and Eisenhardt (1998)]. In view of these present characteristics, operations around the world are being strongly pressured to rapidly increase their operational effectiveness. As a result, the way of managing operations should be adapted to this complex situation. Brown and Eisenhardt (1998), based on complexity and evolutionary theories, have suggested that the right approach to compete on high-velocity, intensely competitive markets is to manage the change by reacting when necessary, anticipating wherever possible, and leading change when the circumstances are adequate. In fact, they suggest that the performance driver, in this model of strategy, is the ability to change. Consequently, the success of a specific industrial organization, industrial sector or area in general will be determined by its ability to continuously reinvent itself.

These trends and challenges are pushing the industry to be able to rapidly react to the changes and promptly improve its operational efficacy. In this line, Shah (2004) proposed key issues and strategies for a supply chain optimization in the pharmaceutical industry. According to this study, there is a general trend for companies to move towards a global supply chain reducing the excess capacity at local sites. The consequence of this trend is the formation of multiple complex coordination issues and much tighter capacity constraints. This implies the emergence of more integral models for planning and controlling supply chains. An adequate operations planning and control system should be able to make the global supply chain react appropriately to the requirements of the market. This entails that stock levels, capacities and other variables of all the elements involved in the planning process of the supply system should be effectively coordinated to allow this systemic rapid reaction. Furthermore, the planning system should be able to globally optimize its supply chains. This implies the consideration of all the resources along the global supply network. Consequently, in both requirements a holistic analysis of the system is a determinant factor for the Planning and Control System.

Conversely, the current planning models in the industry not always allow taking into consideration a systemic perspective of the supply chains due to the properties of the generally used planning structure. This structure is characterized by modularity of the elements composing the model, in which the decisions, with respect to different components in the supply chain, are analyzed independently from one another. The result of this decoupled planning approach is firstly, a local optimization of the used resources, and secondly, a reduced reaction capacity based on the complexity related with the synchronization of the elements.

In the case of integral planning, the interactions between elements are considered. Consequently, system optimality is obtained. This implies lower capital investment and more precise characterization of the system behavior. As a result of the higher degree of coordination, inherent of these models, superior responsiveness capacity is achieved. The decisions are implemented in shorter time and the system has a faster reaction to changes. Nevertheless, the superiority, design and implementation of such integrated system is also restricted and determined by two factors: complex mathematical tractability and lower level of feasible implementation.

In this report, the tangible benefits and operational validity of implementing an Integral Supply Chain Planning and Control System in a Global Pharmaceutical Company (GPC) are discussed. A multi-echelon model for relevant products of GPC is developed and the implications in the target stock setting process are analyzed. The present project has made seven relevant contributions.

First, insight to GPC is provided regarding the implications of an integral planning system in its operations. The study demonstrates that the integration through planning activities would imply lower capital investment. After the optimization, reductions were obtained for the total supply chain investment for significant products.

Second, based on a multi-echelon model and GPC context, relevant recommendations concerning the inventory positioning for the supply networks of the products Omega and Aleph are presented. This includes a detailed analysis of actual key functional and structural supply chain attributes to increase the conception of the operation and the quality of future decisions. This attribute analysis not only increases the understanding of supply chains in the pharmaceutical industry but also in similar supply networks.

Third, the understanding of comprehensive models for planning systems is increased in view of their possible advantages over the traditional decoupled approaches. In this case, it is demonstrated that the integral control of localized variables reduces the inherent complexity, and therefore, increases the operational validity of integral models.

Fourth, a procedure to reduce the complexity of the BOM structure, using mono-equivalences along the chain, is presented. This allows a standardized comparison of several attributes in the different stages, a clear visualization of the network structure, and the utilization of tools which do not process non-integer BOM numbers. This procedure is relevant for any supply network with one-item convergent-divergent structures.

Fifth, the aggregation study developed by Bisschop (2007) for modeling networks with the Synchronized Base Stock policy is extended. A numerical example of the impact of lot sizes, review periods and lead times in the aggregation feasibility for upstream echelons is provided.

Sixth, for supply networks with varying forecast error, a procedure for incorporating this evolving forecast is presented, using a stationary demand tool such as ChainScope [De Kok (2008)]. The results suggest that it is possible to model non-stationary demand with stationary demand as long as relevant interactions and attributes are considered in the model.

Finally, the present project makes an initial effort to link Operations Management with Business Process Management (BPM). The use of BPM techniques allows the identification of different interactions and requirements for the target stock setting process when the new technology (multi-echelon tool) is implemented.

The report has the following structure: In section one, the project context is presented. Section two describes the objective and research questions. In addition, the research approach and a synthesis of the literature review are included. Section three shows an analysis of functional and structural attributes of Aleph and Omega supply networks. Section four illustrates the main characteristics of the multi-echelon model. Primarily, it describes the procedures used to model the supply networks. Section five shows the specific characteristics of each product model as well as the optimization results. In section six, a qualitative analysis of the impact of the new technology is included, and a redesign of a specific process of the planning system is presented. Finally, section 7 provides the main conclusions of the project.

1.1 Global Pharmaceutical Company

This project has been initiated by the Global Supply Chain Management (GSCM) board of GPC. This initiative has been made based on two facts: 1) An optimization of its supply networks is required to continue being competitive and 2) with the implementation of the new APS planning software the planning of the Pharmaceutical part (US and Europa for some products) and API manufacturing part is still decoupled. The vision of GPC GSCM is to increase the level of integration and reduce the inventories in the supply chains.

1.1.1 Company's Profile and Organization

GPC is a global enterprise with core competences in the fields of health care, nutrition and high tech materials. GPC is organized in multiple subgroups and various service companies which operate independently. This project will involve two subgroups of the organization: Consultancy Group (CG) and GPC, being a support and business units, respectively.

1.1.2 GPC Global Supply Chain Management Strategy [GPC GSCM (2009)]

The objective of GPC is to achieve a net Inventory reduction target equivalent to 11,4% within the next two years. Essentially, there are three initiatives generated for a sustainable inventory optimization at GPC: 1) Enabler projects, the objective of which is to create transparency along the supply chain and build a fundamental basis for inventory optimization, 2) Inventory optimization projects which consider key inventory reduction levers. These key levers are: safety stock optimization, lead time reduction, forecast accuracy, and centralized determination of delivery volumes. 3) Mid and long term optimization approach which is more related with best practices and lesson learned between different units, the decrement of the portfolio complexity, and increment of levels of coordination.

A project related with the initiatives is the Global Inventory Management (GIM), the objective of which is to increate inventory visibility at different levels of aggregation. Even though some data can be obtained through coupling the systems, some planning parameters cannot be obtained. Parameters related to demand, forecast, and others for some marketing affiliates cannot be obtained. When mapping stock levels at SKU level several discrepancies were found.

One of the initiatives related with the present project is the Pipeline Risk Assessment, in which risk profiles are established for different stages along the pipelines. Based on this risk profile and the analysis of other uncertainties, safety stocks are determined with a high level of aggregation (stage). Similarly, there are initiatives to improve the forecast in sales affiliates which are related with the establishment of Sales and Operations Planning (S&OP) in marketing affiliates and the implementation of forecast accuracy targets at different levels of aggregation. The final result of this forecast accuracy improvement would be the inventory reduction.

In the same line, one of the main efforts is Inventory Target Setting. The objective of this initiative is to provide a procedure and/or tool with which the inventory targets could be identified. The approach indentified is a bottom up approach which takes into account supply chain setups, risk profile and service levels.

In terms of transparency, GPC GSCM is trying to generate standard key performance indicators for its supply networks. This involves the implementation of tools for obtaining data, and the processes related. Another key effort is the Pipeline Transparency project. The objective of this project is to assess the current situation of key products based on a comprehensive view of the supply networks. The basic idea of the project is that GPC GSCM is responsible for all the inventories in the globe from raw materials until the end customer. Consequently, GPC GSCM is responsible to generate initiatives to reduce inventories looking at the supply network as one pipeline. Based on this, several advantages could be obtained from the related synergy. For instance, the safety stocks along the pipeline could be redistributed in order to increment the effectiveness of the chain.

1.2 A comprehensive model

1.2.1 Supply Chain Planning Problem

The Supply Chain Operations Planning function is responsible for the coordination of activities along the supply chain, by making decisions on the quantities and timing of material and resource [De Kok & Fransoo (2005)]. The high complexity of the decision interactions within a supply chain as well as the necessity of an optimized plan, demand a decomposed decision model and the related control system. This is more evident in the case of a pharmaceutical supply chain due to the high necessity of coordination.

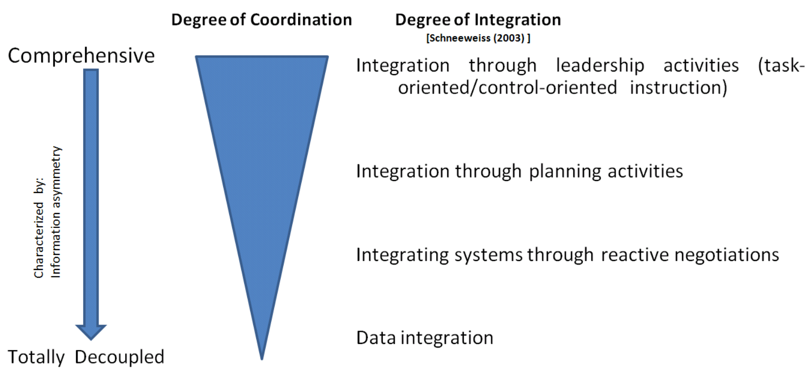

Figure 1-1 Relation between Coordination and Integration

There are different approaches for designing Supply Chain Planning and Control Systems based on the complexity of decision interactions: from completely decoupled to fully integrated. However, different levels of integration are related to different levels of coordination. In figure 1-1, the levels of integration of Schneeweiss (2003) have been linked to these different approaches for solving the supply chain planning problem and the degree of coordination.

1.2.2 Decoupled versus Integral Planning

Decoupled Planning has been the general trend [(Anthony (1965), Bertrand et al. (1990), Rohde et al. (2000) , Miller (0658) , Fleischmann et al. (2005)]. In this kind of approach, self contained modules are controlled independently. This kind of models has a simpler mathematical tractability and faster execution of local decisions. On the other hand, they present lower levels of coordination, local optimality, and lower levels of systemic responsiveness capacity. In the case of integral planning, the interactions between elements are considered. Consequently, system optimality is obtained. This implies lower capital investment and more precise characterization of the system behavior. As a result of the higher degree of coordination inherent of these models, superior responsiveness capacity is achieved. The decisions are implemented in shorter time, and the system posses a faster reaction to changes. Nevertheless, this type of planning models present two main disadvantages: complex mathematical tractability and lower level of feasible implementation. See figure 1-2.

In order to increase the tractability of integral models, several aspects can be considered in the modeling process. For instance, the mathematical complexity can be decreased by integrally controlling just the most representative variable, which - based on the company context - is the inventory positioning. See figure 1-3. Nevertheless, this implies that mechanisms have to be generated to represent decoupled variables, adequately. This is the case when non-stationary demand has to be represented with models under assumptions of stationary demand. Similarly, optimization mechanisms of integrated variables can be generated assuming simpler numeric types. However, this entails the definition of conversion procedures for assuring accuracy in the results. This occurs, for instance, when integer BOM numbers are assumed in optimization algorithms. Finally, the integration of real life supply chains involves the inclusion of several hundred of echelons. Consequently, less massive and more tractable problems can be obtained through aggregation procedures.

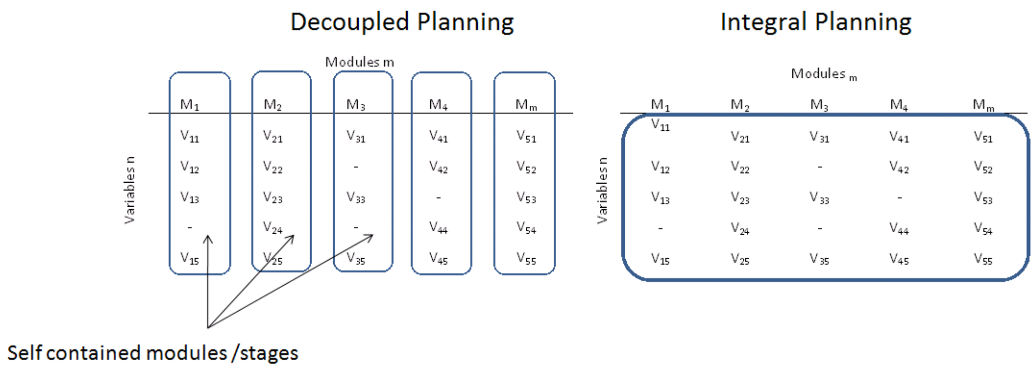

Figure 1-2 Decoupled and Integral Planning

To increase the operational validity of integral models, it is necessary to adapt the involved business process. The implementation of an integral planning model implies a centralized control. As a result, it is necessary to define an owner of the model and his position in the organizational structure. Moreover, it is essential to align the responsibility and decision authority of the owner with his opportunity to control. Similarly, an integral control could involve the interaction of several hierarchies in the organization. Consequently, it is important to define the figures that are meaningful for the involved hierarchies and the interaction procedure for realizing a decision related to the model. Finally, there are several information requirements not only related to the generation of the integral model, but also with the interface of the model and current systems. Accordingly, it is important to identify these requirements.

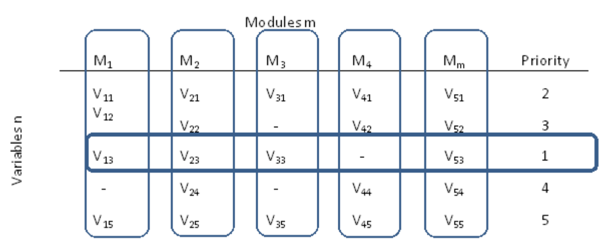

Figure 1-3 Integral Control of Localized Variables

2. Research Approach

2.1 Objective & Research Questions

The objective of the project is to obtain insight regarding the benefits and feasibility of implementing an Integral Supply Chain Operations Planning and Control System in GPC (GPC) in terms of operational validity and capital investment, e.g. from a level of integrated systems through reactive negotiations to a level of integration through planning activities

In order to define the research questions as well as the research approach, two main factors have been considered [Shrivastava (1987)]: rigor and practical usefulness.

The criteria used to assess the first factor were: 1) Conceptual adequacy, which has been completely developed in the previous document related with this master thesis and the initial section of this paper. 2) Methodological rigor & 3) Empirical evidence, which will be reflected in the research questions and the subsequent research approach.

With respect to the second factor, the main criteria used were: Goal relevance, meaningfulness, operational validity, and innovativeness. For identifying the aspects in GPC related with these criteria, several interviews were maintained in order to assess the relevance of the following proposed study:

We conduct a comparison study of a comprehensive approach versus the current decoupled approach to plan and control the operation of a specific Supply Chain. We expect that a holistic analysis of the system will lead to a global optimum solution. We also expect that this global optimum will be a better solution than the local optimums obtained when designing decoupled modules. In order to test this hypothesis a model to position stocks in a multistage inventory system that considers the decision of a higher central level would be used. The objective of the proposed study is to determine more insight into the following questions:

1. Main question: Will the utilization of the integrated model for positioning stocks lead to a better optimization of capital investment in the system than the current decoupled-system approach, in terms of the cost related for achieving a specific service level?
2. Which would be a possible structure and coordination mechanisms, in a specific process of the planning system, necessary to incorporate such centralized model?

2.2 Literature Review

In this section, literature review related with the previous research questions is discussed. In order to select the appropriate type of model it is essential to consider a model which first allows an effective comparison of the decoupled planning system with the integrated planning system and second, this model has to be operationally valid in order to identify the required decision structure for its implementation. Subsequently, the approach required to redesign the planning process considering the new model is discussed.

2.2.1 Multi-echelon models comparison

Basically, two different approaches exist for modeling the Supply Chain Operations Planning problem. One approach is based on stochastic models and other based on mathematical programming models. These two approaches were analyzed in the context of a pharmaceutical supply chain. The table 2-1 shows the main differences between different approaches.

Table 2-1 Main Differences between Different Approaches for Modeling the SCOP Problem

Factor	Stochastic demand models	Mathematical programming models
Demand	Stochastic variable	Forecast per period
Key decisions	Inventory positioning at the various stock points	Allocation of inventory at stock points
	Allocation of Inventory where product flow diverges	
	Safety stock determination	
Lead Times	Deterministic Input	Deterministic input or output variables
Capacity control	Workload control function	Aggregated constraints
	Demand management function	
Safety stock	Output	Input

De Kok and Fransoo (2003) developed a numerical comparison of both concepts. According to the results, they state that the stochastic control concept, the Synchronized Base Stock policy (SBS), outperformed the mathematical programming model. Other advantages present in the first case and mentioned in the same study are the short computational time as well as some insight into the decision hierarchies associated with the divergent systems and decision nodes. Nevertheless, the decision hierarchies of the factual organization not necessarily are aligned with the previous mentioned hierarchy. Another important positive point is that after some sensitivity analysis of demand variability the stochastic model showed stability in the results, e.g. the allocation of stocks was similar. On the other hand, an important consideration is that the results in this study have been obtained considering only stationary demand.

Similarly to the SBS policy, Graves and Willems (0658) developed a framework for modeling strategic safety stocks in a supply chain that is subjected to demand forecast uncertainty. The supply chain is modeled as a network composed of spanning trees, and each stage in the supply chain has a periodic-review base-stock policy. It is assumed that demand is bounded, and that there is guaranteed service time between every stage and its customers. The main limitations of the model include the consideration of deterministic lead-times, stationary demand, and the fact that the capacity constraints per stage are ignored. Based on this study, a commercial software application was developed, and its validity has been tested several times. For instance, the model was partially validated applying it to a product flow of Eastman Kodak. It was concluded that the implementation of the model helped Kodak to reduce its inventory, reposition its inventories in the supply chain, and increase the service performance. Nevertheless, information about its validation has not been found.

Recently, Schoenmeyr and Graves (2009) examined the placement of safety stocks in a supply chain with evolving forecast. They show that the inventory positioning in this kind of supply chain is equivalent to systems with stationary demand bounds and base-stock policies. They include a maximum cumulative forecast error in the optimization problem and make the safety stock to provide 100% of protection as long as the forecast errors are within the maximum cumulative forecast error for all lead times. They also assume that the cumulative forecast error is strictly increasing over the lead time. They tested the concept in a real supply chain. Apparently, the results showed that there was a significant opportunity of improvement from the consideration of evolving forecast. Nevertheless, a weak point was the lack of an actual comparison with the current situation of the supply chain under analysis.

Janssen (2004) developed a study in a pharmaceutical company, in which stochastic models, as discussed by De Kok and Fransoo (2003), were demonstrated to be not adequate for the supply chain analyzed. The stochastic models were modeled in the tool Supply Chain Optimizer and Evaluator (SCOE) [De Kok, Technische Universiteit Eindhoven].

Similarly, Boulaksil (2005) provides a number of arguments against the implementation of this stochastic model [De Kok and Fransoo (2003)]. He states that first, the pharmaceutical company under study operates in the batch process industry, and batch sizes play an important role in its operations. The stochastic model [SCOE, De Kok, Technische Universiteit Eindhoven] did not consider those batch sizes at that moment. Second, the stochastic model assumes stationary demand and stationary forecast errors while analysis of the supply chain showed that these forecast errors were non stationary. Third, it is stated that the network structure modeled by SCOE is rather static due to the difficulties related when changing the model. Finally, it is also mentioned that the tools present some difficulties when including yield effects and non-integer bill-of-material factors.

Additionally, in the same study, it is stated that the effect of the assumptions and limitations of the stochastic model [De Kok and Fransoo (2003)] are very significant for the case of the supply chain under analysis. In this case the Planning System of the chain was based on a mathematical programming model. It is also compared the performance of the stochastic model and a proposed model based on mathematical programming. Based on this comparison, it is concluded that the latter outperform the stochastic model. Finally, Boulaksil et al. (2007) conclude that their method based on simulation studies is suitable for companies that have implemented an APS, due to the characteristic of rolling horizon.

It is important to consider that some of the statements in which Boulaksil (2005) based his selection of the linear programming model are not fundamentally a motive for concluding that the linear program model could be more adequate than the stochastic model. For instance, it is mentioned that the tool SCOE is static due to some difficulties when changing the network structure. Nevertheless, the relative difficulty could be higher in a linear programming model because just adding one additional echelon would imply changing the linear program code in terms of objective function and different sets of variables and constraints related with the stage. Additionally, the computational time related with a linear programming model is higher. According to the model developed by Boulaksil (2005), the computational time for simulating one scenario would be from 10 to 12 hours, and after this it would be required some data processing for obtaining results. If one considers the fact that the safety stock model should be a tool allowing making decisions and interacting in real time, it presents a strong disadvantage in this point.

Evidently, the consideration of non-stationary forecast errors represents an advantage because the behavior of the supply network is represented more accurately. Nevertheless, even if a stochastic tool does not consider explicitly this variable, modeling techniques could be used to incorporate this factor in the analysis. In fact, it could be more time and cost effective to incorporate the forecast error in the stochastic model than generate a complete rolling simulation with a solver incorporated.

According to a study performed by De Kok (2009), the work of Boulaksil (2005) contains certain errors regarding the validation of SCOE. The main results of De Kok (2009) were: 1) the outcomes of SCOE were valid and, 2) SCOE outperformed the mathematical programming approach. Finally, De Kok (2008) developed an improved version of the tool SCOE. The new version, called CHAINSCOPE, included lot sizes. Nevertheless, the model does not include two relevant aspects: 1) treatment of non-stationary forecast, and 2) non-integer BOM numbers.

To conclude, the stochastic models such as those developed by Graves and Willems (0658) and De Kok appears to be a tool with high potential if its significant degree of operational validity is considered. Moreover, it could be aligned with the requirements of the pharmaceutical industry if some considerations such as non-integer BOM numbers treatment and non stationary forecast errors are incorporated to the model. On the other hand, even though a mathematical programming approach could lead to equal – or higher under certain considerations- performance, its operational validity has a lower degree in terms of cost efficacy, sustainability of the model, and responsiveness capacity. A closing decision factor is the fact that the APS of GPC is not completely implemented, consequently, the realization of such task is out of scope of the present project.

2.2.2 Process Redesign

Business Process Management theoretical background is used primarily to define a structured approach for analyzing supply networks, related processes and develop the required models. Second, the implementation of a new technology would imply the redesign of different related processes in order to adapt the tool to the planning system as well as some repercussions in the metrics related with the process. Consequently, an analysis of these implications and possible redesign has to be considered.

According to Van der Aalst et al. (2003), the business process management (BPM) life cycle is composed by the following steps: identification, discovery, diagnosis, planning, design, deployment, execution, and control. This is the main structure of the approach used to redesign the planning process.

In order to identify the innovation scope related to the implementation of the new technology, the following key activities are followed[Davenport, (1995)]: 1) enumerate major processes, 2) determine process boundaries, 3) asses strategic relevance of each process, 4) render high-level judgments of the health of each process, and 5) define manageable process innovation scope.

With respect to the discovery phase, the techniques and recommendations for modeling the As-Is process of Sharp and McDermott (0658) are followed: 1) Building the team, 2) Organizing and initiating the modeling session, 3) Getting started by building the handoff model, 4) Adding detail with a flow model, and 5) as necessary, developing a task model.

Sharp and McDermott (0658), provide some key steps to assess the As-Is situation prior the redesign of the defined process: 1) Confirm initial stakeholder assessment and process goals from framing. 2) Capture first impressions of process strengths and weaknesses. 3) Make the initial decision on what to do with the process, 4) Identify leverage points, and 5) asses by each enabler in turn.

The design phase has three different approaches [Reijers (2008), Technische Universiteit Eindhoven]: 1) evolutionary, 2) revolutionary, 3) reference models. The evolutionary design involves local updates in existing workflow, and gradual improvement of performance. The improvement is achieved through the implementation of best practices. A revolutionary design is a “green” approach in which the product or service of the process is the central concept. Accordingly, the product based workflow design (PBWD) is an approach in which a product data model is developed based on the product specifications, and a workflow process model is developed based on the product data model. In the case of the present project a reference model has been considered the best alternative based on the solid theoretical background developed by Schneeweiss (2003) in distributed decision making.

Brand and Van der Kolk (1995) identified four principal dimensions in the impact of a redesign process: Quality, Cost, Time, and Flexibility, belonging to the so called Devil’s quadrangle. According to the model developed by these authors, there is frequently a trade-off between the metrics of those dimensions when a redesign occurs. In this context, Reijers and Liman (2005), presented a framework of best practices in business process redesign in which the possible impact of different redesign heuristics is presented. In the final stage of the project, this framework is used as a reference to assess the possible impact of the inclusion of a new technology.

2.3 Scope

With respect to the model, it does not consider products in the following life cycle phases phases: Introduction, discontinued products or obsolete products. In addition, the uncertainties controlled come from the demand. Moreover, the stages considered in the integration are API Production and Pharmaceutical Production. Nevertheless, the distribution stage containing main affiliates has been extended for one product. Regarding the process redesign, the stages of execution and control are excluded.

2.4 Approach

The main research question is related to the tangible benefits of implementing an integral planning and control system. In order to answer this question, a model integrating the stages API production and Pharmaceutical production is built and the supply network is optimized. The results of the optimization compared with decoupled planning approaches are used to assess the potential benefits of the new planning approach. Based on the theoretical background exposed in section 1.2, the supply network is integrated through a key variable: stock positioning. Consequently, it is required to use a multi-echelon tool allowing an integral stock positioning along the supply network. In view of the results of the analysis of multi-echelon models exposed in section 2.2.1, the multi-echelon tool ChainScope [De Kok (2008)] is used to model the supply network.

The second question is related with the operational validity of such implementation. To answer this question, and in view of the time frame, one relevant related process is selected for analysis. The impact of the new technology (multi-echelon tool) on the selected process is assessed. Based on this assessment, the process is redesigned and recommendations related to the selected process are provided to make the implementation of the new technology feasible.

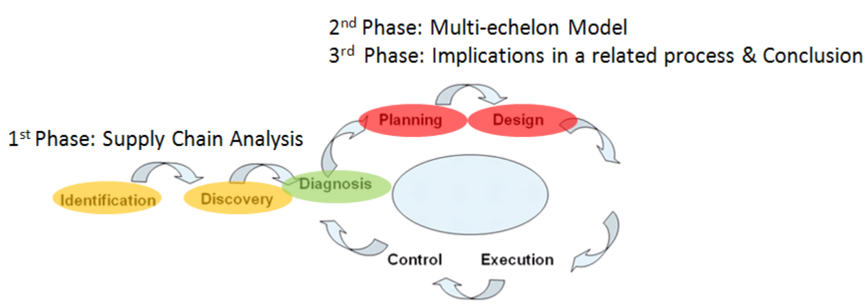

Figure 2-1 BPM Life Cycle [Technische Universiteit Eindhoven, (2008)]

The framework of business process management is used to define the research methodology. In this sense, the project consists in three phases. The first phase (Identification & Discovery) consists on supply chain analysis and understanding of the planning process. The outcome of this phase is the information grounding (Diagnosis) required for the next two phases: the determination of the supply chain stages to be considered in the model and the definition of the scope of the planning process to be redesigned. The second phase consists on developing multi-echelon models and different scenario analysis (Planning & Design). The first research question will be answered after this first stage. The third phase (Planning & Design) consists on redesigning a related process and building a workflow process model. The second research question will be the outcome of this phase.

2.4.1 First Phase: AS-IS Situation

The first stage of the project is an explorative phase. Initially, the attributes of the supply network and the characteristics of the planning system are analyzed. Base on this, the scope of the model and process redesign is completely defined and data required for the model is obtained. Several specific steps are involved in this stage. Initially, a team related to the project is built. This includes constructing a team matrix specifying support person per process involved and information required, and scheduling individual and group sessions. Secondly, the supply chains are analyzed in terms of structural and functional attributes. Individual sessions with personnel involved and automated mechanisms such as SAP are used. The structural attributes include: network structure, location of decoupling points, and capacity constraints per stage. The functional attributes include: products, lead times, production sequence, batch sizes, pattern of ordering, pattern of delivery, bill of materials, forecast data, and demand historical data. Subsequently, the planning procedure is analyzed. In addition, main operational functions and key initiatives of the company related to the planning process are identified. Finally, based on the previous points, the stages included in the integration are determined and the process to be redesigned is selected.

2.4.2 Second Phase: Integral Planning Model

This stage is related with all the steps involved in building, verifying, and validating the multi-echelon model. Initially, an analysis of the characteristics of the multi-echelon tool versus the supply network attributes obtained in the first phase is developed. Based on this, the main modeling considerations are defined. Three major misalignments are found. The multi-echelon tool considers stationary forecast error, integer BOM numbers and restricted number of echelons composing the supply network. Consequently modeling procedures have to be developed or incorporated in order to control these misalignments. Subsequently and taking into account the previous procedures, data tables required for built the models are developed. The supply network model is built layer by layer, and a verification and validation procedure is applied in each case. Finally, multiple comparative scenarios are generated.

2.4.1 Third Phase: Process Redesign & Conclusion

The third phase of the project treats the redesign process derived from a possible implementation of a multi-echelon tool in the planning system. Initially, the selected process, specified in the first phase, is characterized. For this characterization, interviews are carried out with people of involved areas and hierarchies of the company. In addition, a representation of the As-Is process is generated using Petri nets. Second, an assessment of the process is developed. Third, a reference model, taking into consideration the requirements of the new technology implementation, is incorporated in the analysis. Based on the previous points, the process is redesigned. The redesign includes a representation of the process using Petri Nets, a description of key aspects of the new process and a comparative analysis of the As-Is situation and the proposed process. Finally, the expected impact of the new technology on the selected process is analyzed. To conclude, final recommendations and conclusions of the project are generated.

3. Supply Chain Analysis

In this section, a characterization of the supply chains under analysis is developed. In addition, Appendix A shows a literature review of the supply networks in the pharmaceutical industry and analyze their key requirements.

3.1 Products

Various criteria are used for determining the supply networks to be analyzed. The first criterion is the full year 2008 sales. The selected products are ranked between the 20 best selling products of GPC. An additional factor is the company preference. GPC GSM recommended the analysis of one of the products selected and agreed in the analysis of the second. The third consideration is the availability of information. Finally, the possibility of directly interacting with the production people related to the products is the final factor.

3.2 Structural attributes

In this section, the most relevant structural attributes are discussed.

3.2.1 Network Structure

Basically, the network structure is composed by the following phases: procurement, primary manufacturing, secondary manufacturing, packaging, internal distribution, and local distribution. These basic phases can be observed in the figure 3-1:

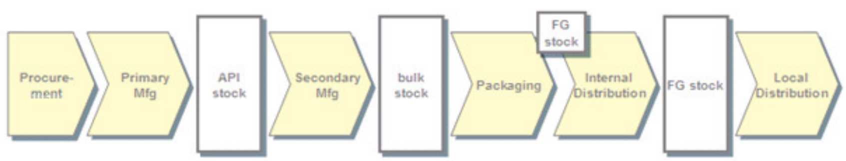

Figure 3-1 Basic Network Stages [GPC GSCM (2009)]

The result of the primary manufacturing is the active ingredient (API). The production of API is performed in the location GPC AG PH Location Epsilon. The output of the secondary manufacturing is bulk material (Unpacked material). This secondary manufacturing is performed in the location GPC AG PH Location Gamma. However, there are small volumes of API which are sold to marketing affiliates. The packaging process is developed in a significant portion of the total volume in the location GPC AG PH Location Gamma. Nevertheless, it can also be developed in plants of marketing affiliates in various other countries. The final products are distributed from the packaging plants to different marketing affiliates. For raw materials until the final local distribution the network could have several stages. The supply networks are massive and divergent having several Bulk products and some hundreds of final products.

3.2.2 Location of decoupling points

Decoupling points are located after the primary manufacturing, secondary manufacturing, and packaging process. In addition, within each process several decoupling points exist. In the case of packaging materials, inventory is hold just for primary materials.

With respect to Customer Order Decoupling Points (CODP), there are two production strategies: Make to Stock (MTS) used for consignment inventory with replenishment strategies, and Make to Order (MTO). For MTO, the CODP could be located after the second manufacturing. This is mostly likely in cases of small volume countries, countries with import approval, and other special cases such as affiliates with erratic demand. However, the CODP for MTO could also be located after the primary manufacturing. This is the case of special business opportunities such as government tender or global health care nonprofit organizations.

3.2.3 Other attributes

Other structural attributes can be seen in the table 3-1.

Table 3-1 Structural Attributes

Attributes	Detail	Omega	Aleph
Inventory Responsibility	Holder	Holding Company, Production Location	
	Owner	Holding Company, Production Location	
Network Structure	API Production	Pure Assembly System	
	Pharma	Pure Divergent System	
Degree of Globalization	Countries	118	51
	Holding Companies	59	58
Type of information exchanged	Data	Forecast and orders	

3.3 Functional attributes

In this section, the most relevant functional attributes are discussed. In addition, table 3-2 contains a detail of additional attributes.

3.3.1 SKUs Classes

In order to analyze the supply chain and the results of the multi-echelon model, the SKUs have been classified in different classes. For Omega, Class 1 is related with the type of products related to the SKUs (Type Y, Type X). Class 2 is defined based on the different production and distribution stages (Raw Material, Intermediate I, Intermediate II, Intermediate III, API, Bulk, Finished Product, Fp At LC). Class 3 is defined based on the forecast 2009 in terms of aggregated cost (A, B, C).

In the case of Aleph, Class 1 is based on the production type (Chemical, Pharma). Class 2 is based on the supply chain stages (Raw Material III, Raw Material II, Raw Material I, Synthese VIII, Synthese VII, Synthese VI, Synthese V, Synthese IV, Synthese III, Synthese II, Synthese I, API, API Micro, Granulate, Bulk, finished product at pack). Class 3 is defined based on the forecast 2009 in terms of aggregated cost (A, B, C).

3.3.2 Organization of the production process

There are two main steps: API production and Pharmaceutical production. In the case of Omega, API production consists on several steps that could be aggregated in three main intermediate stages. There are not decoupling points for intermediate 2 and 3. Nevertheless, there are significant amounts of work in progress (WIP). The final product of these intermediate stages is Moxifloxacin (Main AI). Similarly, the bulk production could be divided on 4 stages, producing different SKUs for different markets. In general, the entire production for all types of SKUs is performed in one run. In this case, WIP is less representative. Finally, after packaging, the Finished Products are stocked in the packaging sites, and or transported to the marketing affiliates.

For Aleph, API production has three parallel lines composed of several steps (five synthesis steps). The result of these parallel lines is the input for the production (3 synthesis steps) of Vardenafil (main API). In this case, the intermediate products along the API production hold inventory. After the production of the main API, it is transported to the Pharma production site and there are 2 subsequent additional steps before the bulk production. The first one is the production of API micro and the second one is the production of Granulate. Having the Granulate as input, the Bulk production is performed in one or two steps depending on the product. Finally, the products are packed and distributed.

3.3.3 Throughput times

In the case of Omega, due to a contractual agreement with the supplier, the procurement of Raw Materials is performed in the following way: Once a year (normally in June) an annual order quantity is placed at the supplier. The supplier needs 360 days for its own procurement, production and delivery processes. Consequently, after one year the total annual demand is delivered to Location Epsilon. In the case of Aleph, the raw materials can be supplied each 6 months. After this, there is a short period for quality check.

For the production stages, the throughput time is composed by production, quality and transportation times. Nevertheless, depending on the SKU, it is possible that the throughput time is composed just for one or two of these processes.

In the packaging stage, due to the fact that the lot size is dynamic and constantly optimized, the lead times in this process are also dynamic. As a result, average lead times based on average lot sizes have been considered for the production time. In addition, there are certain secondary components which are not stocked, and consequently, this time is also affecting the total lead time of the Formulation phase.

The throughput times in the local distribution are mainly determined by the transportation time. Nevertheless, there are several bulk products which are sent to other countries for local packaging and/or processing.

3.3.4 Lead Time Structure

The general lead time structure of the products produced in Location Gamma is presented in the figure 3-2. As it can be seen, the longer lead times are located in the primary procurement and manufacturing.

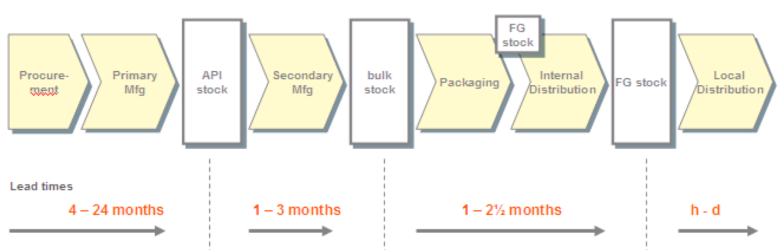

Figure 3-2 Lead Time Structure Location Gamma [GPC GSCM (2009)]

In order to determine the planning horizon per stage, the following definition is used: "The lead time is the throughput time between the moment of release of an order for the item and the moment at which the ordered item is available for usage in other items and/or delivery to customers." [De Kok (2009)]. For example, due to the fact that in all the stages the stations are not dedicated to Avalox, the processes times as previously described are increased by a component of the cycle time. In this sense, the average lead time, is defined as the aggregation of the throughput time t_i for item i, and half the execution cycle CT_i for item i. For instance, if an order is released from API requesting Raw Materials (RM), this order will be processed according to the supplier schedule. In this case, even if an order is released before the period 7 (See figure 3-3), the execution of the order will begin just in the period 7. This implies that in average, any order, released at any time from API to RM, will be executed in 540 [d]:

Similarly, an order released at any time for certain API 125 [d]. With respect to bulk and packaging, a similar approach is considered. Nevertheless, in packaging, taking into consideration that the order sizes are dynamic, average lost sizes will be used to estimate the average lead times.

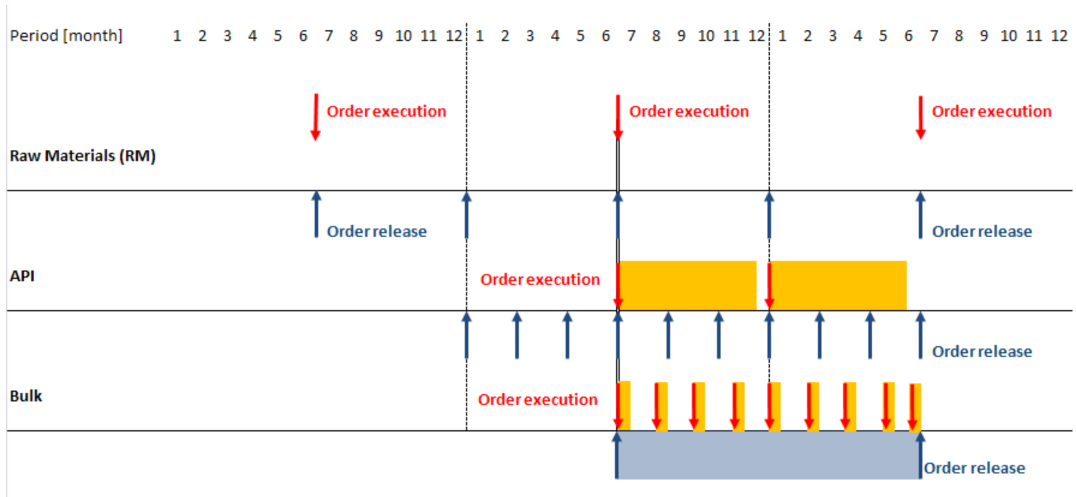

Figure 3-3 Lead Times & Cycle Times

The lead times computed with the previous approach represents an average response time and not the planning lead time. In fact this average lead time would be a too optimistic consideration because half of the time the lead time would be higher. A more precise consideration is:

$$Lp_i = t_i + CT_i \qquad (1)$$

The planning lead time used in practice is higher than the average lead time and slightly lower than the summation of the throughput time and the total cycle time (Equation 2). For instance, the general planning lead time used in the current planning procedure for the pharmaceutical part is 90 [d]. Then: Best case scenario < Average <Planning < Worst case scenario (38 [d] < 68 [d] < 90 [d] < 98 [d]). The planning lead time is located between the average and worse case, and closer to the last one.

This lead time becomes stable under the assumption that that the order frequency is synchronized with the production frequency. It is important to note that CHAINSCOPE models the lead time structure automatically when the throughput times and review periods are defined.

3.3.5 Omega Demand

Trend: Omega has an increasing demand with respect to the years 2006 and 2007. Nevertheless, the initial figures of the year 2009 have showed a decrement of 21% on the aggregated demand in terms of API Equivalent.

Composition: The figures are based on the forecast 2009. In the case of Class 1, it can be seen that most of the cost corresponds to the production of Type X. There are 184 SKUs with external demand and forecast 2009. Based on the total cost per SKU and forecast 2009, an ABC classification is developed in order to determine the relevance of each SKU (See figure 3-4). The most relevant final products (92) concentrate 97% of the demand. Similarly, an ABC classification of country related to SKU based on the same parameters is developed in order to determine the relevance of the local market in the network structure. In this case 80% of the sales is concentrated in 5 countries (US, CN, DE, IT, MX).

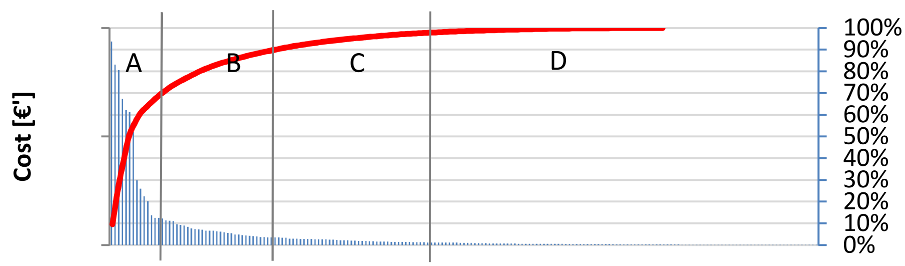

Figure 3-4 SKU ABC Classification

Seasonality: At an aggregated level, the extreme points in demand pattern can be identified in the figures showed in the Appendix. In the case of Type X and Type Y, the highest point of demand is produced in the first quarter of the year. In order to determine the relevance of the seasonality, the coefficient of variation of demand per quarter per year is estimated. For instance, in the year 2008 CV of 0,14 between demand quarters was obtained. Consequently, if the thresholds of moderate and high variability are set on 0,75 and 1,33 [Tan (2008)], it could be claimed that the seasonality is not high.

3.3.6 Aleph Demand

Trend: Aleph posses a stable demand with an increasing trend.

Composition: The same ABC classification is performed and 153 products represent 97% of the total final demand. Considering the Forecast 2009, by far, the US is the biggest consumer of the product, concentrating 55% of the global demand in terms of API Equivalence and 32% in terms of cost. The demand is concentrated in 9 countries (US, DE, VE, MX, BR, IT, RU, GR, FR). There is a small portion of bulk in the demand (16%), and the rest (84%) corresponds to finished products.

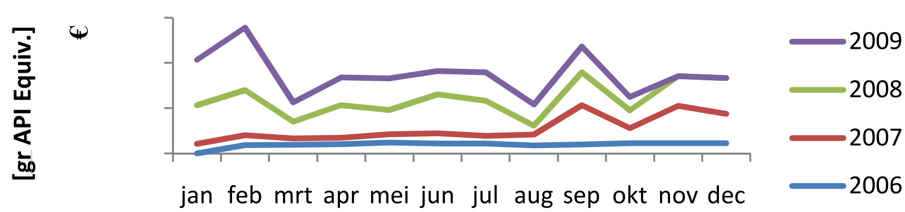

Figure 3-5 Aleph – Demand Seasonality

Seasonality: The demand of Aleph can be observed in figure 3-5. Similarly, it is obtained a CV of 0,12 between quarters for the year 2008. Consequently, the seasonality is low.

An example of this demand analysis is presented in the Appendix B.

3.3.7 Other attributes

The following table shows other functional attributes of the supply networks.

Table 3-2 Functional Attributes

Attributes	Detail	Omega	Aleph
Products Procured	Number	131	268
	Type	API, Bulk, Finished Products	Bulk, Finished Products
SKU Classes	Class1	Related with the type of products	Production type
	Class2	Based on the different production and distribution stages	
	Class3	ABC (Cost, Forecast 2009)	
Sourcing type	Raw Materials	Single	Main: 70%, Others: 30%
	Packaging Materials	Multiple	Multiple
Supplier lead time reliability	Raw Materials	Based on forecast, long lead times	
	Packaging Materials	Secondary Packaging materials (e.g. leaflet, carton, label): short and reliable, based on order. Primary Packaging materials (e.g. wraps, box, pallet, foil wrap): based on forecast, e.g. there is stock.	
Materials life cycle	Time	Long	
Organization of Production Process	API Production	Intermediates and API	
	Pharma	Formulation and packaging	API refinement, formulation and packaging
Repetition of Operations	API	Campaign	Campaign
	Bulk	Type X: Campaign, Type Y: Batch	Campaign
	Packaging	Dynamic optimized batch	
Resources allocation	Production Facilities	Not dedicated	
Availability of Future Demands	Forecast	Forecasted for all the stages	
Demand Curve	Trend	Decreasing	Stable
	Composition (Top Markets)	US, CN, DE, IT, MX	US, DE, VE, MX, BR, IT, RU, GR, FR
	Seasonality	Low	Low
Products life cycle	Shelf	At Bulk level at least 24 months	
Number of product	Types	Type X and Type Y	Type X
Degree of Customization	Products	Standard products (packaging country specific)	
BOM	Number types	Rational	
	Structure	API production convergent, Pharma divergent	
Distribution Structure	Steps	Multiple	Multiple

3.3.1 Inventory responsibility

Basically, GPC is working under two strategies: Make to Order (MTO), and Vendor Managed Inventory (VMI) [GPC (2009)].

IN VMI, two elements can be distinguished: The Supply Centers and the Affiliates. The Supply Centers have the planning and inventory responsibility. The affiliates have the responsibility of forecast generation and accuracy, and local product supply. Consequently, the Supply Centers will develop cost optimized delivery plans based on forecast, no orders. The interaction between Supply Centers and Affiliates is governed by supply agreements.

For MTO materials, the marketing affiliate has to release an additional order taking into consideration certain period. It is necessary to emphasize that even that this frozen period is directly related with the response lead time of the supply center; this frozen period is not exactly the lead time.

3.4 Metrics

The target service level used for all the final customers and affiliates is the fill rate. It is estimated to be 97% to affiliates and 99% to final customers. In the related projects, the metric used is P_2. Consequently, the same type of indicator is used in this project in order to have a commensurable comparison.

In parallel to this project, two related projects - Pipeline Visibility and Risk Assessment - are being developed. In the first case, the current target stocks are mapped and aggregated for the entire network. In the second case, aggregated safety stocks are determined. The uncertainties considered are demand and supply uncertainties. The safety stocks are determined using a one echelon approach. The supply uncertainties are obtained based on qualitative assessments of the risks of the most important echelons in the supply. The results of these projects are also used in comparative analysis in the following sections.

In the tables 3-3 and 3-4, the distribution of total inventory along the supply chain is described. In the case of Omega, most of the inventory (~60%) is concentrated upstream for the current situation and for the actual targets, being the most relevant stocks hold in Raw Materials and API. In the case of Aleph, in the current situation, the inventories are concentrated downstream. Nevertheless, the current targets try to increment the quantity of inventory in the initial stages of the chain, especially in Synthese III and API.

For Omega, 90% of inventory is concentrated in 21 Stock Holding Companies, 19 countries, and 49 SKUs. The countries that hold most of the inventory are 5. Aleph has a more centralized supply network in terms of location. Most of the inventory (90%) is concentrated in 5 countries, 13 Stock Holding Companies and 124 SKUs.

Figure 3-6 show the inventory composition. According to the current planning parameters of Omega, more than 70% of the inventory corresponds to Average Stock and can be considered as a Pipeline Stock. Within this Average Stock, the Cycle Stock is the most significant inventory. In the case of Aleph, more than 80% is Average Stock, and again the Cycle Stock represents a very significant 60% of the total inventory value. The safety stocks of Omega and Aleph represent 25% and 14%, respectively. Based on this figures, the relative opportunity of improvement is higher for Omega due to the fact that the Safety Stock is relatively higher in the network. For the validation process, it is important to note that the ratios Pipeline Stock versus Average Stock could be approximately located in a range from 0,2-0,5; depending on the Safety Stocks values.

The target coverage is the one determined in the Pipeline Visibility project. In the case of Omega, the current situation is close to norm. On the other hand, Aleph has inventory levels in terms of coverage out of the norm for Raw Materials 2 and 3, and Synthesis 5 and 7. Appendix C shows a detail of the target coverage per stage per product.

Table 3-3 Omega - Inventory Distribution

Stage	% Jun-09	% Target
Raw Material	29%	23%
Intermediate I	0%	9%
Intermediate II	0%	1%
Intermediate III	0%	1%
API	33%	22%
Bulk	14%	23%
Finished Product	7%	7%
Fp At LC	17%	13%
Total	100%	100%

Table 3-4 Aleph – Inventory Distribution

Stage	% Apr-09	% Target
Raw Material III	1%	0%
Raw Material II	0%	0%
Raw Material I	0%	0%
Synthese VIII	2%	0%
Synthese VII	11%	0%
Synthese VI	1%	0%
Synthese V	6%	6%
Synthese IV	1%	1%
Synthese III	0%	12%
Synthese II	8%	5%
Synthese I	3%	1%
API	3%	37%
API Micro	9%	4%
Granulate	1%	2%
Bulk	17%	11%
finished product at pack	13%	11%
finished product at loc	21%	10%
Total	100%	100%

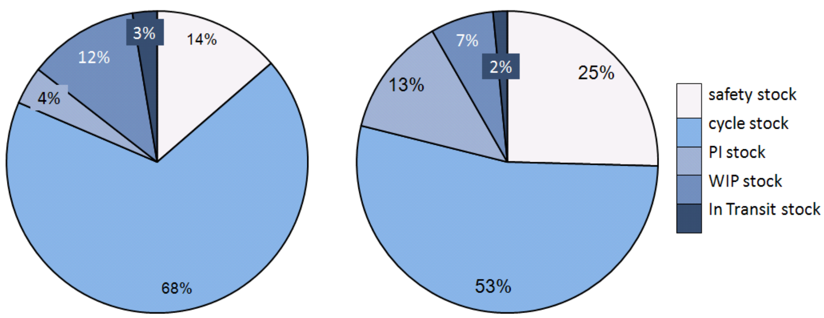

Figure 3-6 Aleph and Omega - Inventory Composition [GPC GSCM – Pipeline Visibility Project (2009)]

4. Multi-echelon Model

The present section describes the modeling procedures used when building the multi-echelon models. Section 4.1 discusses the characteristics of the synchronized base stock policies and their relation with the supply chains under analysis. Section 4.2 describes the main characteristics of the software ChainScope. Section 4.3 describes the procedure to model the BOM structure. Section 4.4 describes the procedure used to build the supply network structure and the related aggregation procedures. Section 4.5 and 4.6 treat demand and the approach for modeling the non-stationary forecast error. Finally, section 4.7 mention characteristics of the main remaining parameters.

4.1 Stochastic demand models

In this section the main concepts behind the optimization model are presented. Initially, the necessary and sufficient restrictions for Supply Chain Operations Planning are described. Afterwards, the main characteristics of the echelon concept are presented. Subsequently, fundamental characteristics of base stock policies for pure assembly systems and base stock policies for divergent systems are explained and related to the supply networks under analysis. Finally, synchronized base stock policies for general supply networks - Basis for ChainScope - are described.

4.1.1 Supply Chain Operations Planning Constraints

De Kok and Fransoo (2003) developed an assessment of various supply chain planning concepts for stochastic demand. This assessment is based on the fulfillment of a set of constraints required for Supply Chain Operations Planning. The constraints are derived from the material structure (BOM) and resource structure (BOP). We refer to De Kok and Fransoo (2003) for a detailed analysis of these constraints.

The following equations represent the necessary and sufficient material [De Kok and Fransoo (2003)]. The first equation guarantees that the increase of the backlog cannot exceed the exogenous demand. The second equation implies that all released quantities are non-negative, i.e. returns are not possible and released quantities together constitute a feasible plan. The third equation represents the inventory balance.

$$B_i(t+1) - B_i(t) \leq D_i(t), \forall i, t \geq 1 \quad (2)$$

$$r_i(t) \geq 0, \forall i, t = 1, \dots, T \quad (3)$$

$$I_i(t+1) - B_i(t+1) = I_i(t) - B_i(t) - G_i(t) - D_i(t) - r_i(t - L_i), \forall i, t = 1, \dots T \quad (4)$$

The next equations represent necessary and sufficient resource constraints. In the first equation, it is assumed that no orders are released before time 0.The second equation ensure that orders released at the start of period t are available for usage in period $t + L_i$. The third equation implies that the total capacity requirements for resource k associated with item orders released at the beginning of period t should not exceed the available capacity of resource k.

$$\sum_{s=1}^{t} r_i(s) \geq \sum_{s=1}^{t} q_i(s), \forall i, t = 1, \dots, T \quad (5)$$

$$\sum_{s=1}^{t} r_i(s) \leq \sum_{s=1}^{t+L_i-1} q_i(s), \forall i, t = 1, \dots, T \quad (6)$$

$$\sum_{i \in U_k} c_i q_i(t) \leq C_{kt}, \forall k, t = 1, \dots, T \quad (7)$$

$$q_i(t) \geq 0, \forall i, t = 1, \dots T \quad (8)$$

Where:

$p_i(t)$ Quantity of item $i$that becomes available at the start of period t from the transformation activity generating item i

$B_i(t)$ Backlog of item i at the start of period t, immediately before receipt of $p_i(t)$

$D_i(t)$ Independent demand for item i in period t

$r_i(t)$Quantity of item i released a the start of period t immediately after receipt of $p_i(t)$

$I_i(t)$ Physical inventory of item i at the start of period t, immediately before receipt of $p_i(t)$

$G_i(t)$ Dependent demand for item i in period t, i.e. demand in period t for item i, that is derived from demand for intermediate and end-items

L_i Throughput time between time of release of an order for item i and time at which t the ordered items are available for usage in other items and/or delivery to customers

$q_i(t)$ Amount of item i processed in period t, $t \geq 1$

C_{kt} Amount of capacity in units of time of resource k in period t, $k = 1, \dots, K, t \geq 1$, where K is the number of available resources.

U_k Set of items that can be processed on resource k

c_i Time required to process one unit of time i on its resource

4.1.2 Echelon Concept

Stochastic models can be differentiated by the variables used to derive the item orders: installation stock policies and echelon stock policies. This project is related with echelon stock policies. For general supply networks, the echelon inventory position and echelon stock are defined recursively as follows [De Kok and Fransoo (2003)]:

$$X_i(t) = J_i(t), \forall i \in E \tag{9}$$

$$Y_i(t) = X_i(t) + O_i(t), \forall i \in E \tag{10}$$

$$X_i(t) = J_i(t) + \sum_{j \in V_i} Y_j(t), \forall i \in I \tag{11}$$

$$Y_i(t) = X_i(t) + O_i(t), \forall i \in I \tag{12}$$

Where:

$X_i(t)$ Echelon inventory stock

$Y_i(t)$ Echelon inventory position

$O_i(t)$ Cumulative amount of orders outstanding at the start of period t

$J_i(t)$ Net inventory, i.e. physical inventory minus backorders, of item i at the start of period t, immediately before receipt of $p_i(t)$

a_{ij} number of items i required to produce one item j, $i = 1,2, \dots, N, j = 1,2, \dots, N$

E Set of end-items

I Set of intermediate items

In the echelon concept, the inventory position represents the coverage of future demand for sellable items. This interpretation is used for the development of order release policies in general supply networks [De Kok and Fransoo (2003)].

4.1.3 Base Stock Policies

A pure base stock policy operates as follows [De Kok and Fransoo (2003)], where S_i is the base stock level of item i:

$$r_i(t) = S_i - Y_i(t) \qquad (13)$$

According to the same authors, under pure base stock policies, it may be possible that the quantity release cannot be met due to lack of material.

Based on the initial analysis of the network structure of both supply chains, it is concluded that the networks are composed by 2 subsystems. The most upstream subsystem can be considered as a pure assembly system. The second subsystem can be considered as a divergent system.

In the case of pure assembly systems, there is one end-item and each item i has just one successor. A unique cumulative lead time can be defined per item i and the availability of successors can be taken into account. Rosling (1989) and Langenhof et al (1990) show that this policy is cost optimal. This type of policy is relevant for API production with just one API as final output.

After API Production, the networks could be considered as multi-echelon divergent systems. In this context, Diks et al. (1996), developed a review of the most important results in this type of system. In their paper, they characterize the divergent multi-echelon systems by the property that a stock point is supplied by exactly another stock point, and supplies one or more stock points, [Diks et al. (1996)]. Diks and De Kok (1998) derived the structure of average cost optimal policies for divergent systems based on the balance assumption. These policies satisfy generalized Newsboy equation. We refer to De Kok and Fransoo (2003) and Dicks and De Kok (1998) for a detailed study of the subject. De Kok and Fransoo (2003) conclude that for the combination of base-stock policies and linear allocation policies, it is possible to compute base-stock levels and allocation fractions. See Appendix D for a definition of balance assumption and a literature review of allocation rules in divergent systems.

The optimal policy derived for pure assembly systems cannot be applied to general assembly systems because there is not a method for allocation of a shortage to successors and the fact that there is not a unique lead time in case of multiple successors. In addition, in general assembly systems, it is not possible to find the clear decision structure present in a divergent system. In order to overcome this problem, De Kok and Visschers (1999) developed an approach based on an artificial hierarchy. Basically, the general network is converted in purely divergent muli-echelon divergent systems. Essentially, the hierarchy is based on cumulative lead times which are determined by the BOM and planned lead times. These authors proposed a class of policies that introduced uniquely defined stated variables analogous to those in pure assembly systems and allocations mechanisms derived from the analysis of divergent systems. This proposed mechanism is the so called Synchronized Base Stock Policy.

The artificial hierarchy derived from the structure of the general supply network is determined by the BOM and the planned lead times. Based on the cumulative lead times, a root node s is defined as follows [De Kok and Fransoo (2003)]:

$$s = arg(max_i\, L_i^c) \tag{14}$$

Where L_i^c is the cumulative lead time and $L_s^c \geq L_i^c, i \in I \cup E$

The cumulative lead times are defined as follows, where V_i is the set of successors of item i.

$$\mathrm{L_i^c} = \mathrm{L_i}, \mathrm{i} \in \mathrm{E} \tag{15}$$

$$\mathrm{L_i^c} = \mathrm{L_i} + \mathrm{max}_{\mathrm{j} \in \mathrm{V_i}}\, \mathrm{L_j}\, , \mathrm{i} \in \mathrm{I} \tag{16}$$

A hierarchical procedure based on the cumulative lead times is used to release orders, and a set of items $\hat{C}_i$ related to this hierarchy is defined. The first decision in the hierarchy is to order the item s at the start of the period t using a pure basic stock policy, as previously defined. When defining how much to order for subsequent items i, a coverage is created by a set of items for future demand related to end-items. This involves the creation of an artificial order up to level $S_{E(\hat{C}_i)\setminus E_i}$. Each order up to level is related to a decision node. This decision node is defined by set of items and end-items, and it is related to various nodes. Various end-items can be related to different decision node. The target coverage related to future demands of all end-items in $E(\hat{C}_i)$ is equal to $S_i + S_{E(\hat{C}_i)\setminus E_i}$.

Based on this, the order release of the synchronized base stock policy – as used in ChainScope - is defined in the following way. For detailed analysis of this policy and a comparison study with linear programming approached we refer to De Kok and Fransoo (2003):

$$r_i(t) = \max\left(0, S_i - q_i\left(S_i + S_{E(\hat{C}_i)\setminus E_i} - Z_{\hat{C}_i}(t)\right)^+ - Y_i(t)\right) \tag{17}$$

Basically, each item could have multiple base stock levels. In addition, the allocation fraction q_i per item i allows a differentiated target service level and is related to allocation analysis previously mentioned.

4.2 ChainScope

ChainScope is proprietary software. The logic of the software is based on the previously described synchronized base stock policies. It is important to mention that synchronized base stock policies are not cost-optimal. Nevertheless, efficient algorithms have been incorporated to ChainScope for determining close-to-optimal policies based on the relationship between generalized Newsboy equations and finite-horizon ruin probabilities. We refer to a work of De Kok (2003) for a higher detail of the optimization algorithm.

There are three main types of input: 1) echelon characterization, 2) network structure and 3) demand characterization.

The echelon characterization includes: a) SKU characterization which entails the codification and description of each echelon, b) expected lead times per echelon which can be interpreted as throughput times, c) added value of items which represent the incremental cost of the item after being processed in a specific echelon, d) review period, e) target stocks, f) lot sizes, g) items classification, h) releasing costs of items and i) yield.

With respect to the input parameters related to the network structure, they include the echelons of the supply network as well as the BOM numbers between successors and predecessors. It is important to note that ChainScope is not able to process non-integer BOM numbers.

Finally, the demand characterization includes a characterization of customers. In addition, stationary demand is represented by expected demand and expected standard deviation of demand. In the Appendix E, a schematic representation of the input parameters is showed.

In the remaining sections of this chapter, the input parameters are analyzed and the approach used is discussed. Sections 4.3 and 4.4 are related to network structure parameters, sections 4.5 and 4.6 are related to demand parameters, and section 4.7 is mainly related to the echelon characterization. The output parameters of ChainScope are described in Chapter 5: Results.

4.3 BOM

ChainScope cannot process non-integer BOM numbers. In some of the previous studies that have used the tool, this characteristic was not treated appropriately. For instance, BOM numbers were transformed into integer numbers without defining a BOM error or applying other modeling considerations to eliminate the BOM error. Apparently, this was one of the reasons why the results obtained in some of these studies were not satisfactory. Consequently, a special treatment is given to the analysis of the BOM numbers.

4.3.1 BOM Error

The following procedure has been defined in order to modify the input parameters of the model when non-integer numbers are not treated by an optimization tool.

The procedure consists on defining BOM integer numbers based on a maximum BOM error and transforming the units of the related parameters.

We define:

a_{ij} Actual BOM number (Quantity of j required to produce one unit of i)

f_{ij} Target rational number

ε_{ij} BOM error

ε_m Maximum error allowed

Where:

$$f_{ij} = \frac{r_{ij}}{sij} \tag{18}$$

$$sij = a^y \tag{19}$$

$$\varepsilon_{ij} = \frac{|a_{ij} - f_{ij}|}{a_{ij}} \tag{20}$$

$$\varepsilon_m = m \tag{21}$$

We need to find the r_{ij} (new BOM number) with which the minimum s_{ij} is obtained and allowing a maximum error of m.

$$\min s_{ij} \tag{22}$$

s.t.

$$\varepsilon_{ij} \leq \varepsilon_m \tag{23}$$

$$r_{ij,} y = int \tag{24}$$

If we want to define the new units in the decimal system, we have to use $a = 10$. Nevertheless, a lower *a* will trend to give lower values of s_{ij} , for the same BOM error. The disadvantage of this is that we lose the relative perspective that a decimal unit can provide.

In the case of Chainscope, we can define an additional constraint $a_{ij} \geq f_{ij}$. The model will provide always less material of *i* to the successor *j*. The difference could be compensated setting up the yield input with a similar value than the maximum error.

It is also necessary to generate a factor k_j associated with the new BOM number r_{ij} and required to convert the units $[u_j]$ into $[u_j']$. If we have that $i, j, k, \ldots\ldots z$ are successive items in the same chain. The factor k is:

$$k_j = s_{ij} \tag{25}$$

$$k_k = k_j s_{jk}$$

$$k_z = k_j k_k \ldots\ldots\ldots\ldots s_{yz}$$

This approach presents two main disadvantages. The first one is that in long chains with very small non-integer BOM numbers, the factor *k* for downstream echelons could have extreme values (k_z). In the case of Omega, these *k* numbers reached up to 1E+19. This type of numbers is not always tractable (The case of ChainScope). The second disadvantage is that if the BOM error is not small enough, the final error in final echelons could be very significant due to the multiplicative effect. For example in the case of Omega a 1% of error was set for all the echelons. In the worst case, after 11 tiers, an error of 10% was present in the final echelon. Moreover, there is an inverse relation between k and ε_m. Consequently, is not possible to improve ε_m without making *k* more extreme. See Appendix F for numeric example.

On the other hand, this approach could provide good results if BOM numbers are not small. For instance, this method could be used in the intermediate steps within API Production, Bulk or Packaging. To overcome the disadvantages mentioned in the previous approach, other procedure has been developed. It is described in section 4.3.2.

4.3.2 Mono-Equivalence[1]

To overcome the disadvantages mentioned in the previous approach, other procedure has been developed. The procedure consists on convert all the BOM numbers in 1. Thus, the units of all SKUs are transformed in such a way that relationships between predecessor and successor have always a 1:1 proportion. In order to do this, it is necessary to define one reference echelon on which all the upstream echelons are converging and from which all the downstream echelons are diverging. For instance, the echelons enclosed in figure 4-1 fulfill with the previous conditions.

[1] Based on suggestions provided by De Kok (2009) and a procedure of Van Halm (2009)

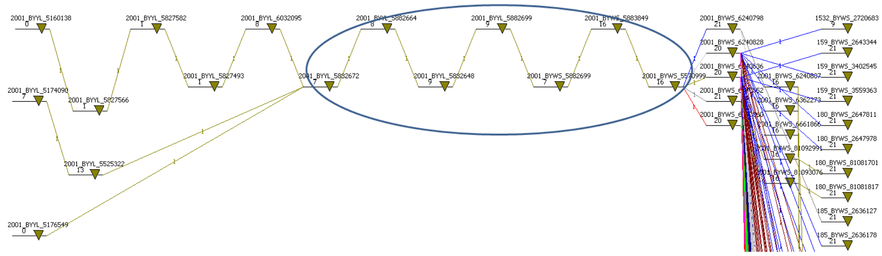

Figure 4-1 Mono-Equivalence Conditions of Convergence and Divergence

We define a chain S as the successive set of items n_i $(i = 1,2,3,4,5, \dots, m)$, where $n_j (0 < j < m)$ is the reference item on which n_i $(i = 1,2, \dots, j-1)$ are converging (upstream items) and n_i $(i = j+1, \dots, m)$ are diverging (downstream items). We also define a_{ij} as the actual BOM number.

The objective is to define a factor e_i related to the conversion of the BOM number a_{ij} to 1 so that the related modeling parameters can be transformed.

$For\ i = 1, 2, \dots, j-1$:

$$e_{j-1} = \frac{1}{a_{j-1j}} \tag{26}$$

$$e_{j-2} = \frac{e_{j-1}}{a_{j-2j-1}}$$

$$e_{j-3} = \frac{e_{j-2}}{a_{j-3j-2}}$$

$$e_1 = \frac{e_2}{a_{12}}$$

$For\ i = j+1, \dots, m$:

$$e_{j+1} = a_{jj+1} \tag{27}$$

$$e_{j+2} = e_{j+1} a_{j+1j+2}$$

$$e_{j+3} = e_{j+2} a_{j+2j+3}$$

$$e_m = e_{m-1} a_{jm-1m}$$

$For\ i = j$:

$$e_j = 1 \tag{28}$$

4.3.3 Parameters Conversion

The conversion of BOM numbers implies a modification in the units of measure of the input and output parameters. This modification depends on the parameter type. In this case we identify two types: volume related parameters and cost related parameters.

In the present project, the following volume related parameters have been considered (ChainScope notation is stated in parenthesis): target stocks (CPT), maximum stocks (MaxStock), lot sizes

(LotSize), expected demand (ED), standard deviation of demand (SD). In the case of cost related parameters, the parameters considered are: Added value of the item (AddValue).

We define a volume parameter v_i related to an item n_i and BOM conversion factor e_i. The modified factor v_i' would be:

$$v_i' = e_i v_i U \quad (29)$$

Where U is a units related constant that allow us to make an additional conversion in terms on conventional units to reduce or increase the size of the volume parameters units. In this case, this additional constant was considered in view of the fact that the program was unable to process the model when the expected demands were small numbers. In addition, a relatively better perspective of the figures was obtained with this conversion.

For instance, If we have defined a parameter v_i', the new unit of v_i' could be $[Kg_j]$, where n_j is the reference item on which n_i $(i = 1,2, \dots, j-1)$ converge and n_i $(i = j+1, \dots, m)$ diverge. If we want to transform $[Kg_j]$ to $[g_j]$ we have to set U as 1000.

We also define the cost parameters c_i as the total value of an item after being transformed in item i, and g_i as the added value in item i, which is the value that is added to the item during the transformation process in item i. Where $c_i \geq g_i$.

Similarly, c_i and g_i are related to an item i and BOM conversion factor e_i. The modified factor c_i' would be:

$$c_i' = \frac{c_i}{e_i U} \quad (30)$$

If a set of items i converge in the item j, then:

$$g_j' = c_j' - \sum_i c_i' \quad (31)$$

$$g_j' = \frac{c_j}{e_j U} - \sum_i \frac{c_i}{e_i U} \quad (32)$$

4.4 Network Structure

4.4.1 SKU characterization

Each item in the model network represents an SKU. The basic SKU characterization is the material number. Nevertheless, there are other considerations which make necessary to increase the complexity of this characterization.

After a transformation process has been completed, the material number is changed. Nevertheless, an SKU will have the same material number after the transportation to a different location. This implies that the same material number could be present in several locations. On the other hand, especially in the case of affiliates, there is not always a productive location. This implies that the material is directly linked to a stock holding company.

Another factor is that stock holding companies own inventory in several productive locations even if the company is not owner of the facility. Moreover, it is not always possible to map the required information using the stock holding company as key. In some occasions, it is necessary to use the production facility and vice versa. Particularly, this happens in the case of Omega.

In view of the previous considerations, each SKU is defined as a combination of stock holding company, location and material number codes. This is also aligned with the second research question. The recommended target inventories have to be disaggregated in different levels in order to make the recommendation operationally valid.

The general structure for Aleph with the SKU characterization is presented in figure 4-2. The general structure for Omega and complete structure of both supply chains is presented in the Appendix G.

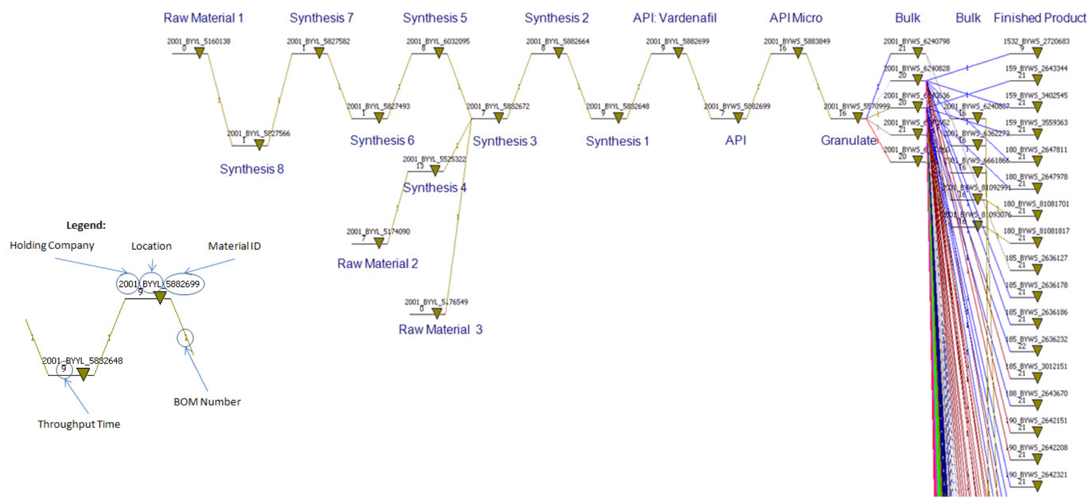

Figure 4-2 Aleph - Supply Network

4.4.2 Aggregation Level

Taking into account that the main research question is related to the benefits of integrated API Production and the Pharmaceutical part, all the SKUs involved in these macro processes have been mapped. Subsequently, a reference item fulfilling the conditions for a Mono-Equivalence conversion has been defined in order to develop possible aggregation analysis upstream and downstream of this reference item. In the supply networks of Omega and Aleph multiple items fulfill these conditions. Nevertheless, it has been chosen the main API as a reference item j due to the fact that it is intended to have in the future metrics related to this API equivalence.

Upstream aggregation

In the case of upstream items, for Omega and Aleph all the relevant SKUs have been modeled explicitly. Nevertheless, an additional procedure and a numeric example using the concept of Mono-Equivalence have been developed for cases in which aggregation in pure assembly systems is required. This procedure is an extension of a previous procedure developed by Bisschop (2007), relating it with the Mono-Equivalence procedure previously presented.

In a pure assembly (sub)system – the case of Omega, Aleph and multiple supply networks in GPC-, each item n_i has one and only one successor and all of them converge in one item n_j.

The Synchronized Base Stock Policy - on which ChainScope is based - has a divergent decision structure. In this decision structure, items with longer cumulative lead times are seen as input of items with shorter cumulative lead times. Moreover, the coefficient of variation in each echelon (CV), of items with similar BOM structures and similar lead times, is the same, [Bischop (2007)]. Consequently, it is feasible to aggregate different items without losing the specific characteristics of the system when the aggregated items have similar BOM structures and similar lead times. Based on this, Bischop (2007) developed an aggregated procedure in which three conditions were necessary for pure assembly subsystem aggregation: equal lead times, equal review periods, and equal BOM levels.

We define a chain S as the set of items n_i ($i = 1,2,3,4,5,\dots,m$), where $n_j(0 < j < m)$ is the reference item on which n_i ($i = 1,2,\dots,j-1$) are converging (upstream items) and n_i ($i = j+1,\dots,m$) are diverging (downstream items). We also define a_{ij} as the actual BOM number, volume related output v_i, cost parameters c_i, and the added value g_i related to an item n_i, Mono-Equivalence BOM conversion factor e_i, review period R_i and BOM level b_i.

$For\ i = 1,2,\dots,j-1$, according to Bischop (2007) procedure:

An item n_d is defined as the aggregating item of various n_i which could be aggregated if:

$$n_i \equiv n_d \qquad (33)$$

$$L_i = L_d \qquad (34)$$

$$R_i = R_d \qquad (35)$$

$$b_i = b_d \qquad (36)$$

Based on the fact that the Mono-Equivalence conversion is performed, every $a_{ij} = 1$, including a_{dj}.

In this case, the input parameters related with cost of the item n_d aggregating various items n_i would be:

$$c_i' = \frac{c_i}{e_i U} \qquad (37)$$

$$g_i' = c_i' \qquad (38)$$

$$g_d' = \sum_{i \equiv d} g_i' \qquad (39)$$

As output, a unique stock quantities for n_d would be obtained, and this volume should be converted to the stocks of the aggregated n_i.

$$v_i' = \frac{v_d'}{U e_i} \qquad (40)$$

Downstream aggregation

Due to the fact the current license of ChainScope allows 250 nodes, it is necessary to aggregate various end-items. We define E as the set of end-items:

$$E = \{n_i | a_{ij} = 0, i = 1,2,\dots,m, j = 1,2,\dots,m\} \qquad (41)$$

In addition, we obtain the set of end-items to be modeled explicitly M and N the set of nodes to be aggregated, were $M \cup N = E$ based on:

$$\frac{\sum_{i \in M} c_i \hat{x}_i}{\sum_{i \in E} c_i \hat{x}_i} = \gamma \qquad (42)$$

$$c_{i \in M} \hat{x}_{i \in M} > c_{i \in N} \hat{x}_{i \in N} \qquad (43)$$

Where c_i is the cost of item i, $\hat{x}_i$ the forecast of item i, and γ is the level of explicitness based on the aggregated cost. Basically, an assessment of the relevance of each final echelon is performed taking as a base the demand volume in terms of cost. In this case, the final echelons representing 97% of the total demand volume are represented explicitly in the model. For Aleph 158 final products are included and for Omega 97. The remaining 3% has been aggregated to the demand of predecessors. The items are aggregated trying to fulfill the previously exposed conditions. Nevertheless, due to the lower importance of aggregated items, it is not expected any major impact.

The affected parameters are expected demand (ED) and standard deviation of demand (SD)

$For\ i = 1, 2, \ldots, j-1$:

The aggregated demand of the aggregating item n_d would be:

$$v'_d = \sum_{i \in N} e_i v_i U \qquad (44)$$

For the definition of the standard deviation of demand, an actual correction of the demand variability has been performed. In the next section this is described in detail.

Other factors

It is necessary to mention some aspects not mentioned in the procedure of Bischop (2007) could be treated in future research.

First, when the aggregation occurs, unique parameters have to be assigned to the dummy item n_d. This implies that certain parameters that are not common for the aggregated items n_i have to be defined. For instance in the upstream items, maximum stocks and target stocks are highly unlikely to be equal among n_i. In the case of target stocks, the evaluation run could be performed using the lowest v'_d because the successor of n_d , finally, will be able to "assemble" after having all aggregated components n_i.

If $v = CPT$, then:

$$v'_d = \min\{e_i v_i U, \ldots, e_m v_m U\} \qquad (45)$$

In the case of maximum stocks applicable for evaluation and optimization runs, the same approach could be used. If there is an item n_i with certain capacity restriction, this would imply that the stocks would be assigned to the successors or more downstream. If that occurs, it is not necessary to maintain stocks in the items n_i without capacity restrictions.

Another important factor to be considered is that lot sizes were incorporated to ChainScope. Consequently, lot sizes should be incorporated in the aggregation procedure. An additional restriction that should be taken into account would be:

$$k'_i = k'_d \qquad (46)$$

Where k'_i and k'_d are the converted lot sizes through Mono-Equivalence for the aggregated and aggregating items, respectively.

In the present case it is possible to model explicitly all upstream echelons, and in the downstream aggregation, it was feasible to aggregate items with similar parameters. Nevertheless, in more complex networks such as complex assembly systems, the procedure of Bischop (2007) represents a very strict analysis of the requirements for the aggregation. In fact, the essential aggregation requirement could be seen in this way: after the Mono-Equivalence conversion, any item n_i could be aggregated as long as the final stocks output is equal for all n_i, when the items n_i are modeled explicitly. If we go back to the procedure of Bischop (2007) and add the restriction of lot sizes, this essential condition will be fulfilled. Basically, we could aggregate items that are redundant. Nevertheless, depending on the specific parameters, in other scenarios, where the conditions established by Bischop (2007) are not fulfilled, items n_i. Namely, there are cases in which items n_i with different lead times, review periods and lot sizes can be aggregated.

In order to analyze this, an additional numerical example was developed. The analysis consisted on identify under which conditions the Raw Materials of Omega could be aggregated. The results of it suggest that that it is not necessary to have equal parameters for the aggregation but relatively similar parameters could be aggregated. Second, items with extreme differences in certain parameters could be aggregated as long as dominant parameters remain similar. Third, even if some dominant parameters are very different between aggregated items, they could be aggregated if they have opposed effects over the cumulative lead times. See Appendix H for details about this example.

4.5 Demand

The values of demand correspond to the forecast per SKU provided by GPC. Similarly, these values have been transformed according to the mono-equivalence procedure. In the figure 4-3, the aggregated demand for the main API is presented. See Appendix B for aggregated demand of Omega.

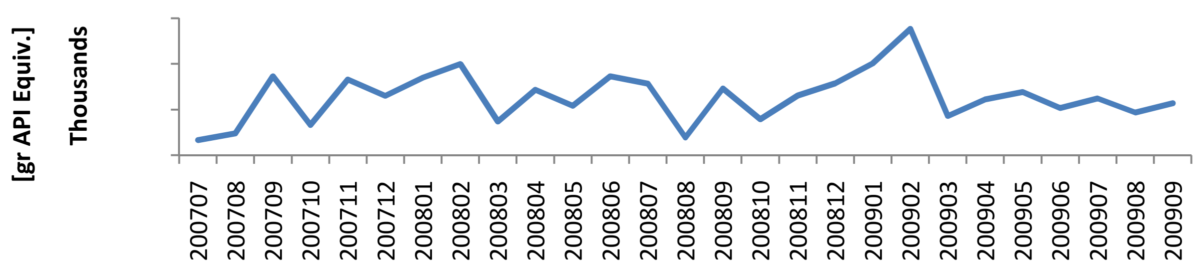

Figure 4-3 Aggregated Demand API Equivalence

4.6 Variability Analysis

The Synchronized Base Stock policy assumes stationary demand with a random distribution. The input parameters representing this stationary demand are the expected demand and the expected standard deviation of the demand. This implies that non stationary variability is not considered in ChainScope itself. Nevertheless, this non-stationary variability could have a significant impact in specific echelons of the chain. Consequently, it is necessary to conduct a special treatment and analysis of demand variability. In this section, first, it is presented a procedure for determining the variability affecting a final item n_i as a function of planning horizon. Second, the effect of commonalities in the variability is discussed. Finally, a procedure to model non-stationary forecast errors is presented.

4.6.1 Forecast Error

The objective of the present procedure is to measure the predictability of future demands as a function of the planning horizon. Based on this, the expected standard deviation, used as input parameter in the SBS policy of ChainScope, is determined for final items. An analogous procedure than the one used by Boulaksil (2005) and Silver et al. (1998) is used.

We define a chain S as the set of items n_i, mono-Equivalence BOM conversion factor e_i, and units transformation constant U.

$$x_i'(t) = e_i x_i(t) U \tag{47}$$

Where $x_i(t)$ is the demand in item n_i in period t and $x_i'(t)$ is the demand in the item n_i in period t in terms of j equivalence.

We determine the forecast error as a function of the various planning horizons h. In order to measure this forecast error, the following equation is used to define the mean square error (MSE), based on Silver et al. (1998).

$$MSE_i'(h) = \frac{1}{n}\sum_{p=-n}^{p=-1}[x_i'(t+p) - \hat{x}_i'(t+p-h, t+p)]^2 \tag{48}$$

Where n is the number of periods involved in the analysis, and $\hat{x}_i'(t-h, t)$ is the forecast made in period $t-h$ for the demand in period t.

Similarly, the standard deviation, and coefficient of variation of forecast error as a function of the planning horizon h are defined in the following way:

$$\sigma_i'(h) = \sqrt{true\ MSE_i'(h)} \tag{49}$$

$$C_{v_i}(h) = \frac{\sigma_i'(h)}{\mu_i'} \tag{50}$$

Where μ_i' is the demand mean of item n_i.

$$\mu_i' = \sum_{p=-n}^{p=-1} x_i'(t+p) \tag{51}$$

It is also necessary to define the same parameters when an aggregation of demand has occurred. In this case the new demand of aggregating item n_d is defined as well as the forecast error measure. Standard deviation, coefficient of variation and mean are determined in a similar way.

$$x_d'(t) = \sum_i x_i'(t) \tag{52}$$

$$MSE_d'(h) = \frac{1}{n}\sum_{p=-n}^{p=-1}[x_d'(t+p) - \hat{x}_d'(t+p-h, t+p)]^2 \tag{53}$$

Finally, for n_i and n_d the expected standard deviation is obtained using the forecasted mean and the coefficient of variation of forecast error as a function of the planning horizon.

In the figure 4-4, the actual standard deviation of forecast error for a final product of Omega is presented. As expected, the predictability of demand decreases with longer planning horizons. It can be seen that the variability in the planning horizons of finished products and bulk is relatively low. On the other hand this variability becomes significantly higher for raw materials.

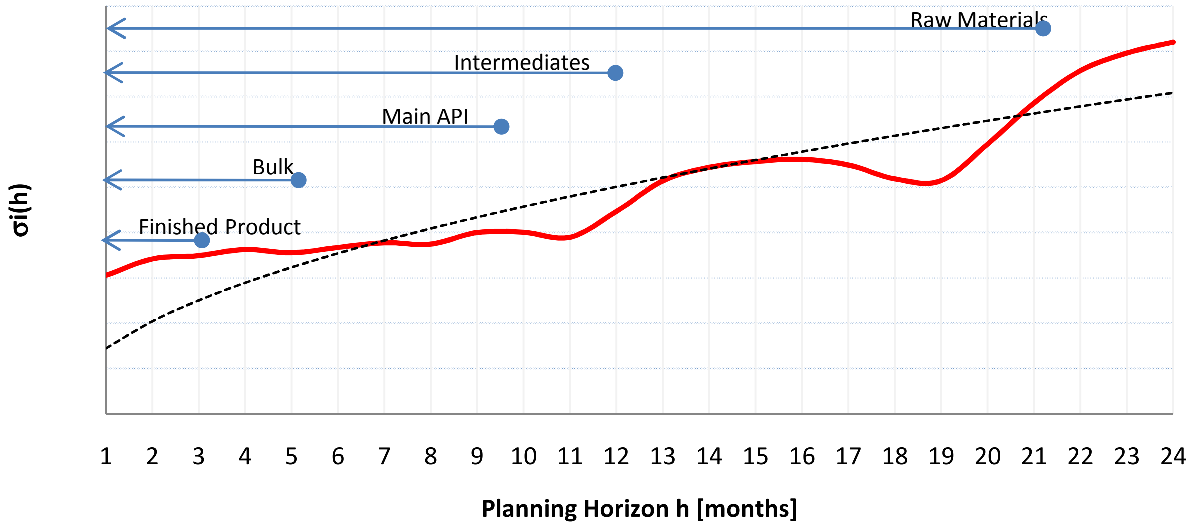

Figure 4-4 Final Product Omega - Standard Deviation of Forecast Error as A Function of the Planning Horizon H

4.6.2 Commonalities

The previous procedure is useful for adjusting the parameters of variability of final echelons. Nevertheless, setting the parameters of variability in last echelons does not assure that the variability is propagated in the model according to the reality. In fact, intermediate and downstream items are affected by two factors: 1) the decrement of forecast accuracy with an increasing planning horizon which leads to a higher variability, discussed in the previous section and 2) the presence of commonalities in their children demand which leads to a lower variability.

In order to measure the impact of commonalities, experiments were performed for Omega and Aleph using the propagated coefficient of variation in ChainScope. After the optimization, the coefficient of variation obtained for different tiers demonstrates that the commonalities play a key role and have a very significant impact in the variability. In the tables 4-1 and 4-2, the average coefficient of variation for different tiers is showed. Tier 1 represents the final items of the chain and tier 15 represents raw materials.

Table 4-1 Aleph – Propagated Coefficient of Variation

Tier	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
CV	0,575	0,477	0,179	0,188	0,188	0,186	0,186	0,186	0,186	0,186	0,186	0,186	0,186	0,186	0,186

Table 4-2 Omega – Propagated Coefficient of Variation

Tier	1	2	3	4	5	6	7	8	9	10	11
CV	0,863	0,804	0,660	0,537	0,268	0,230	0,204	0,204	0,204	0,204	0,204

In the case of Aleph the 15 tiers include API Production and Pharma. The final items have a coefficient of variation significantly higher than the main API (Tier 6). The last 10 tiers represent API production. Based on the fact the API Production can be considered a pure assembly system, it is logical that the all the final tiers have the same coefficient of variation.

Similarly in Omega, the items included in API production (Tiers 7-11) present the same coefficient of variation, being this stage a pure assembly system. The figures of Omega show notably the influence of commonalities in the decrement of variability. Especially in API production, the coefficient of variation is decreased substantially. The coefficient of variation reaching raw materials is more than 4 times lower than the one faced by the final products. This can be observed in figure 4-5.

This decrement in the variability is produced by the fact that commonalities have a pooling effect. The higher the level of commonalities, the higher the pooling effect. This is the reason why after bulk production the effect is substantially lower. This phenomenon is also related with the aggregation of items and has to be taken into account.

Finally, it is important to emphasize that ChainScope does not consider non-stationary demand. Consequently, the effect presented in this commonalities analysis just represents partially the reality.

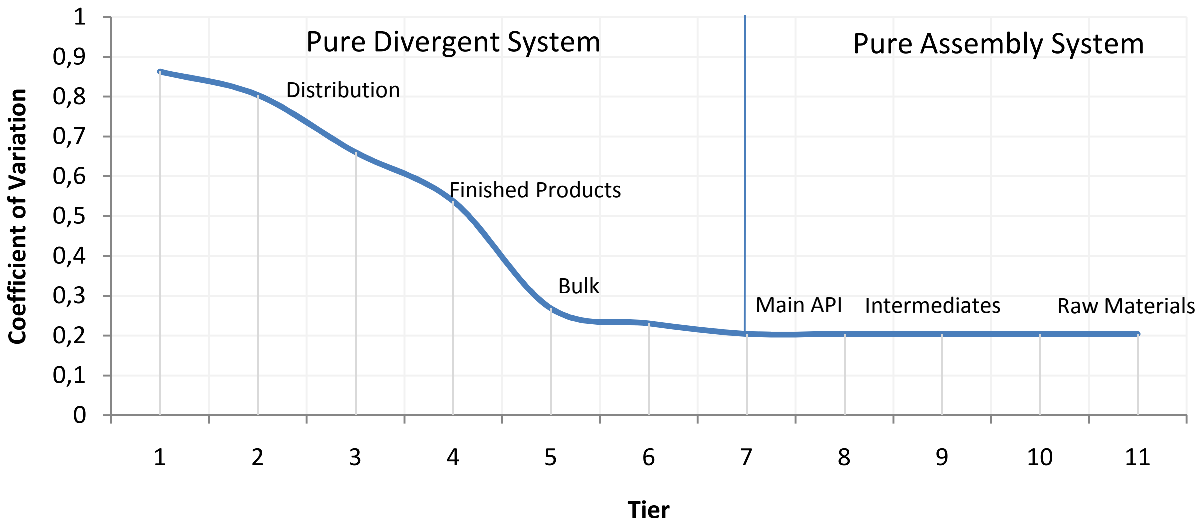

Figure 4-5 Omega – Commonalities Effect

4.6.3 Variability Modeling Procedure

There are two phenomena related to the variability that have to be considered in the multiechelon-model. One of them – commonalities – is already incorporated in ChainScope. Consequently, it is necessary to incorporate the non-stationary forecast errors. The present section describes a procedure for this incorporation. The following procedure is based on a previous study of Fransoo (200X) in which it was concluded that coupling echelons through service levels leaded to a near optimal integration.

We consider $C_{v_i}(h)$ the actual coefficient of variation and C_{vp_i} the propagated coefficient of variation in the model, for an item n_i. When the actual coefficient of variation $C_{v_i}(h)$ and the propagated coefficient of variation C_{vp_i} are not equal, it is necessary to modify C_{vp_i} in such a way that it represents the reality. Due to the specific characteristics of ChainScope, this is just possible by dividing the system in partial subsystems. Nevertheless, this division could cause the lost of synergies along the chain. Namely, we are decoupling the system again when determining non-integrally the stocks in the network. Consequently, it is necessary to establish another coordinating variable in order to couple the modules. In this case, this coupling variable is the service level.

We define a network Z as a set of items n_i. Initially, an optimization of the entire network Z is performed having as a result an optimazed network Z'. The propagated coefficient of variation C_{vp_i} and the service level P_i in the item n_i for downstream echelons are obtained. A maximum error in the coefficient of variation is defined:

$$\varepsilon_{C_{v_i}} = \frac{C_{vp_i} - C_{v_i}(h)}{C_{v_i}(h)} \tag{54}$$

Items n_i are identified based on the relevance of its hierarchical level in the distribution structure, the error in the coefficient of variation, and the level of required detail. The relevance within the distribution structure is based on the level code of the echelons, and relative relevance of the related stocks levels. The item n_i defines the frontier of a new subsystem Z_1. The items n_i are the end echelons in the new subsystem Z_1.

$$Z' = Z_1' \cup Z_2' \tag{55}$$

Subsequently, the service level P_i and $C_{v_i}(h)$ are incorporated as input parameters in the optimization of the new subsystem Z_1. A new optimization is performed in Z_1 and an optimized subsystem $Z_1''$is obtained. The final optimized network is defined as:

$$Z'' = Z_1'' \cup Z_2' \tag{56}$$

The same approach can be used recursively. After obtaining the optimized network Z_1'', it is possible that we want to increase the precision of the variability of the items inside n_i. Consequently, we can use the same approach and divide Z_1'':

$$Z_1'' = Z_{11}'' \cup Z_{12}'' \tag{57}$$

Adjust the coefficient of variation in Z_{11}'' and obtain a new optimized Z_{11}'''. The final optimized network would be:

$$Z''' = Z_1''' \cup Z_2' = (Z_{11}''' \cup Z_{12}'') \cup Z_2' \tag{58}$$

$$Z'''' = Z_1'''' \cup Z_2' = \left((Z_{111}'''' + Z_{112}''') \cup Z_{12}''\right) \cup Z_2'$$

Even though the subsystems are coupled through service levels, certain degree of synergies is definitely lost. The initial optimization step does not consider variability levels with enough precision in upstream items. Moreover, after defining Z_1' and Z_2', the stock levels of Z_2' are fixed and the new optimization Z_1'' will not have an impact on them. Consequently, it is necessary to define a balance between the division in subsystems and the accuracy of the variability.

One possible approach to control the variability and at the same time do not disaggregate the system dramatically, is the utilization of sensitivity analysis. In each subsystem, some items still have an error $\varepsilon_{C_{v_i}} > 0$. For instance, in the case of subsystem Z_1 it is possible that upstream echelons – raw materials – could have a higher error in the coefficient of variation. Consequently, it is necessary to analyze the impact of increasing $C_{v_i}(h)$ up to $\max\{C_{v_i}(h), C_{v_{i-1}}(h), \dots, C_{v_{i-m}}(h)\}$.

4.6.4 Numerical Examples

We consider the supply Network of Omega. A first optimization is performed. After the analysis of the propagated coefficient of variation and actual coefficient of variation, we find that big deviations are affecting API production. In addition, the items in API production have the highest hierarchical level in the network (See LLCode in table 4.3). Finally, the inventories are the most significant of the network. Consequently, it is necessary to make a readjustment in the variability parameters.

Table 4-3 Variability Modeling Procedure – Numerical Example

Item no.	C_{vp_i}	$C_{v_i}(h)$	LLCode	Class2	%
0973_LOC1_181653737	0,19	0,79	10	Raw Material	76%
0973_LOC1_181739216	0,19	0,79	10	Raw Material	76%
0973_LOC1_186312152	0,19	0,63	9	Intermediate I	71%
0973_LOC1_185163935	0,19	0,63	8	Intermediate II	71%
0973_LOC1_186669220	0,19	0,63	5	Intermediate III	71%
0973_LOC1_186669204	0,19	0,63	6	API	71%

We define API production as the subsystem Z_1. This is a pure assembly subsystem. Consequently, the coefficients of variation propagated in ChainScope are equal. Nevertheless, due to the fact that raw materials, intermediates and the main API have different planning terms, the actual coefficients of variation $\mathrm{C_{v_i}(h)}$ cannot be equal. Secondly, the value of $\mathrm{C_{v_i}(h)}$ is significantly higher. This can be seen in figure 4-6.

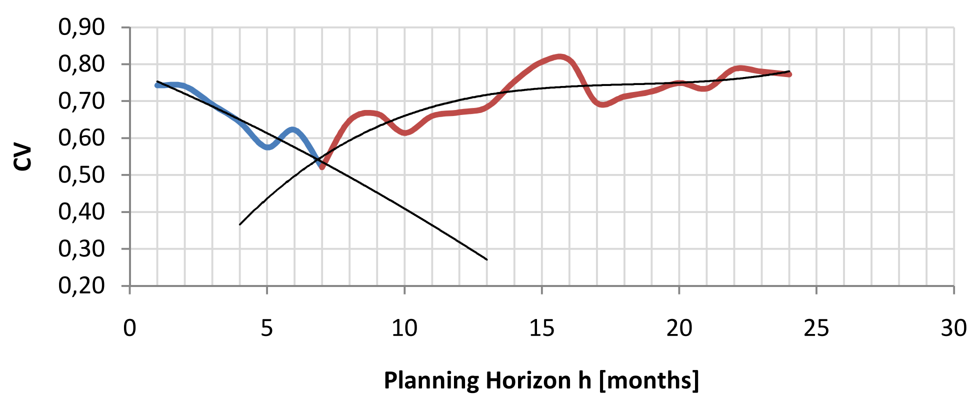

Figure 4-6 Omega – Coefficient of Variation API Production

The shape of this curve can be explained by the combined effects of commonalities and forecast error. The lowest point of the curve has approximately the same planning horizon when the highest commonality effect occurs.

Based on this, a second optimization is performed just for API production. In this new optimization, the fill rate required for the main API is set in 0,934 which is the value obtained in the first optimization. In addition, the value of the standard deviation is increased according to the actual coefficient of variation $\mathrm{C_{v_i}(h)}$ for the main API. See figure 4-7.

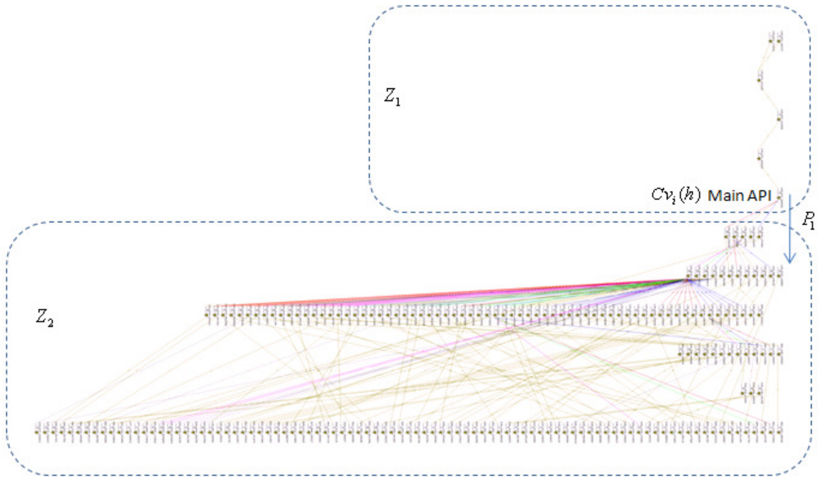

Figure 4-7 Non-stationary forecast error incorporation

After the second optimization and corrections through sensitivity analysis, the required average inventory cost for API production was increased in 106%. In table 4-4 the variation in the stock allocation can be observed. The items with higher variation are raw materials.

Table 4-4 Omega – Variation in stock positioning after variability correction

Class 2	Corrected Stock [Kg API Equivalence]	1st Optimization Stock [Kg API Equivalence]	Variation
Raw Material	16771	3657	359%
Raw Material	16771	3657	359%
Intermediate II	0	0	0%
Intermediate I	274	336	-18%
Intermediate III	0	0	0%
API	22227	8381	165%

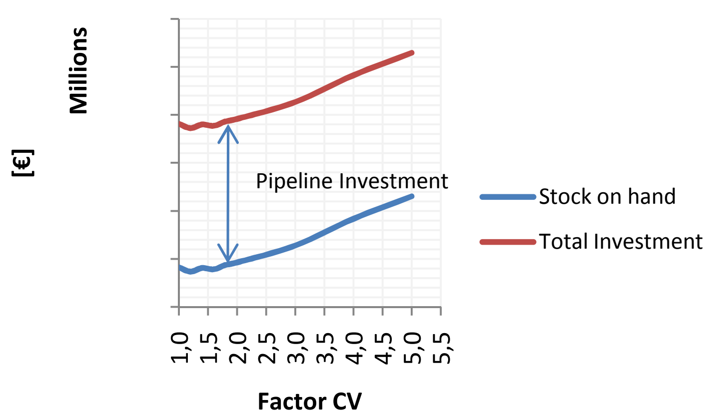

Figure 4-8 Omega – Coefficient of Variation Sensitivity Analysis

Finally, a sensitivity analysis of the coefficient of variation in the initial total network Z is performed in order to assure that the assumptions with respect to C_{vp_i} in Z_2 are correct. As it can be observed in figure 4-8, up to more than one hundred fifty percent of increment in the variability in the last echelons of the initial system does not have a significant impact in the overall supply chain investment. Consequently, we can consider that our assumptions were correct.

The same approach is used for Aleph. A subsystem is defined. This susbsystem is represented by API production. Similarly, the API production can be considered as a pure assembly system. In this case, the actual coefficient of variation of Aleph has more pronounced differences depending on the planning horizon. For instance, the variability faced in raw materials is more than two times the variability faced in the main API production. See figures 4-9 and 4-10.

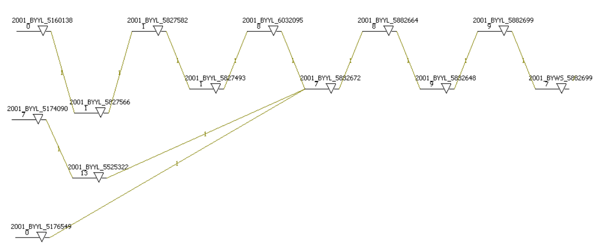

Figure 4-9 Aleph – API Production: Pure Assemble System

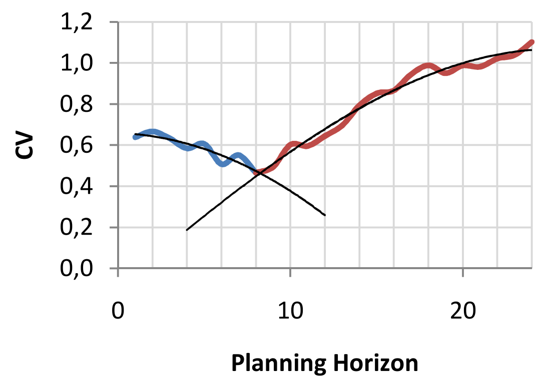

Figure 4-10 Aleph – Coefficient of variation API Production

Subsequently, a second optimization step is performed incrementing the coefficient of variation and setting as a target service level the one previously obtained. Finally, a sensitivity analysis in the API production is developed incrementing the coefficient of variation of the main API up to 1,2 (Coefficient of variation faced by raw materials) and the final stocks are defined.

4.7 Echelons Characterization

The lot sizes were defined in the following way:

$$k_i = max\{k_{c_i}, k_{b_i}\} \qquad (59)$$

Where k_{c_i} is the campaign size of item i and k_{b_i} is the batch size of item i

The lead times were defined as:

$$L_i = L_{P_i} + L_{Q_i} + L_{T_i} \qquad (60)$$

Where L_{i_P}, L_{i_Q}, L_{i_T} are the lead times for Production, Quality and Transport.

$$L_{i_P}, L_{i_Q}, L_{i_T} \geq 0$$

With respect to the yield, it was not considered due to the fact that BOM numbers already included it. Finally, it is considered that a year has 260 working periods.

5. Supply Chain Optimization

The optimization for both supply chains is performed in several steps. Initially, a model containing all the production stages is optimized. Subsequently, a variability analysis based on section 4.6.3 and 4.6.4 is performed in order to correct the coefficient of variation of API production and Bulk. Based on this analysis, sub-models containing SKUs up to main API and main Bulk materials are built. Inventories are corrected according to the optimization of these sub-models. Finally, taking into account the limitations from data availability or data precision, sensitivity scenarios are performed for certain key parameters to guarantee the accuracy of the conclusions. The parameters used in both models can be found in the data base related with this project. A graphical representation of the sub-models is presented in the Appendix I.

For Omega, the integration is extended up to main affiliates. In addition, an analysis integrating just API production and Pharma is performed in order to increase the robustness of the results taking into consideration that data for affiliates was not always available or precise. For Aleph the integration included API production and Pharma. All upstream and intermediate echelons are modeled explicitly. Downstream, the final echelons representing 97% of sales in terms of cost are modeled explicitly. The remaining 3% modeled according to the aggregation procedure of section 4.4.2.

Figure 5-1 shows the corrected coefficient of variations for Omega after applying the variability modeling procedure. Being considered the API production as a pure assembly system, the coefficients of variation are equal in the model for all the stages from raw materials up to main API. In the case of Bulk, a separate increment is performed.

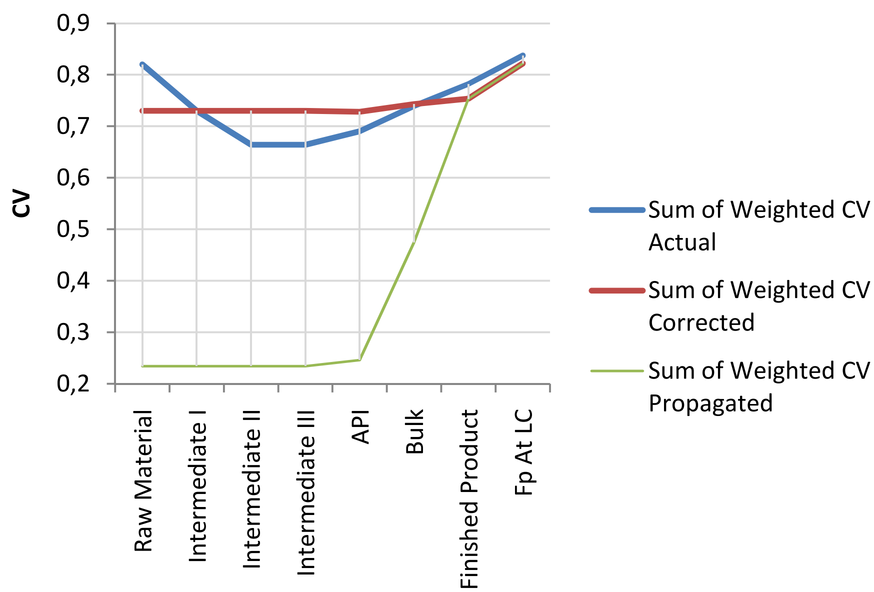

Figure 5-1 Omega – Actual CV vs. Corrected CV

For Omega, after the initial increment of variability, it is necessary to increase the level of inventories in API production and Bulk. Even though the CV represents the reality, this representation is not one hundred per cent accurate. Consequently, sensitivity scenarios increasing the CV from 0,63 (Main API) up to 0,79 (Raw Materials) are performed. The results of these sensitivity scenarios demonstrate that there is not significant impact in the inventory levels based on the difference of variability between main API and raw materials. This is produced by the fact that API production has big lot sizes and review periods. Consequently, cycle and pipeline stocks act like big inventory buffers.

The difference in the degree of variability between different stages is higher in Aleph. This is originated by longer lead times composing the chain. Similarly, variability levels are corrected and sensitivity scenarios performed. See figure 5-2.

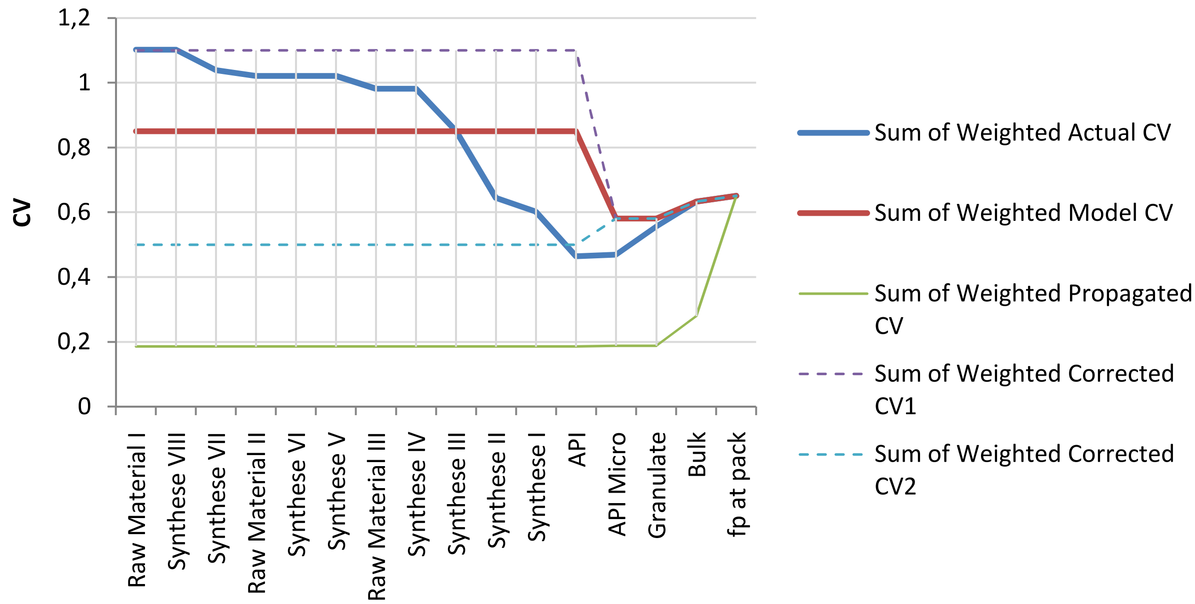

Figure 5-2 Aleph – Actual CV vs. Corrected CV

Correspondingly, sensitivity analyses of lead times are developed intended to control a possible underestimation of this parameter or variations of related parameters such as review periods and lot sizes. After the analysis, the results are consistent in terms of stocks positioning.

Finally, the stability of the algorithm was assessed checking for various scenarios of lead times, variability, demand levels, and service levels the consistency of results.

5.1 Omega Results

5.1.1 Main Results

Figure 5-3 shows the macro results of the optimization when API production and Pharma are integrated. Total stocks per month and average stocks are obtained from a tool developed by CG. According to these results, 15% of inventory reduction with respect to the average inventory situation could be achieved with the integration of these stages. In the right side of the figure, the development of inventories the last 8 months can be seen. Similarly, the current inventory target is presented.

It is important to mention that the present project does not consider supply uncertainties. Nevertheless, in parallel to this project, GPC is assessing additional supply uncertainties through a risk mitigation project. In this project, the risks involved in each production stage were identified and additional stocks levels were established for each stage. Using the results of the multi-echelon model for covering demand uncertainties and the results of the risk mitigation project to cover supply uncertainties, the results indicate that a 3 % of reduction in inventories could be achieved.

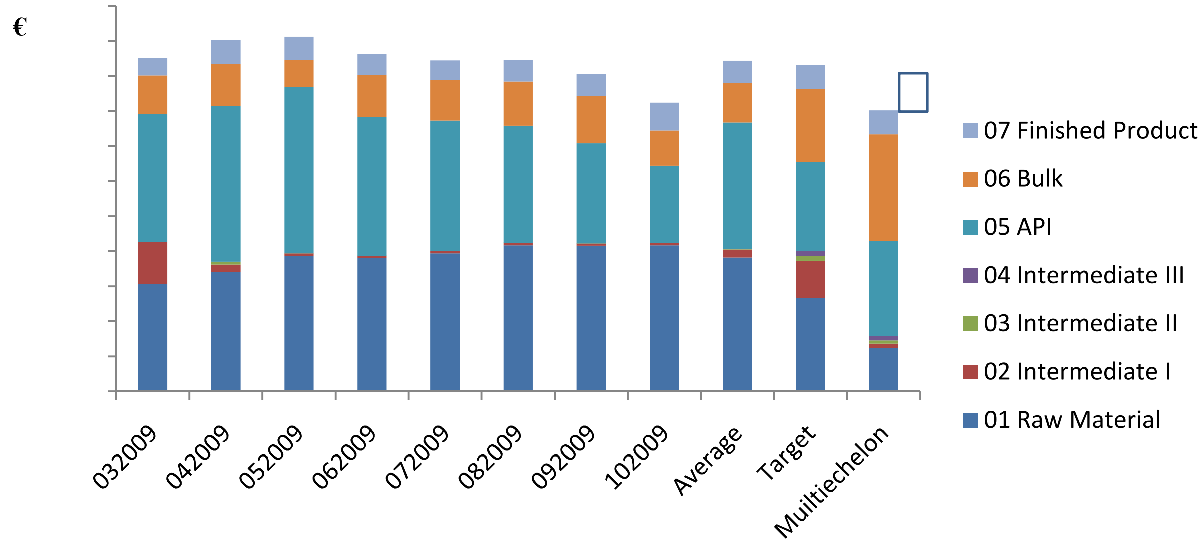

Figure 5-3 Omega – Results Macro: Chemical + Pharma (Source: CG)

Similarly, after integrating the distribution network, initial results show that 5% of inventory reduction could be achieved with respect to the average stocks. When the results of supply uncertainties are added up, no reduction is achieved and an increment of 7% is necessary to mitigate the risks considered for strategic inventories. This outcome is aligned with the results of the pipeline visibility and risk mitigation analysis of GPC. These results indicate that in order to control the specified risk it would be necessary to increase the inventory levels. Nevertheless, in this case, there is still an advantage because more uncertainty would be covered with less relative investment.

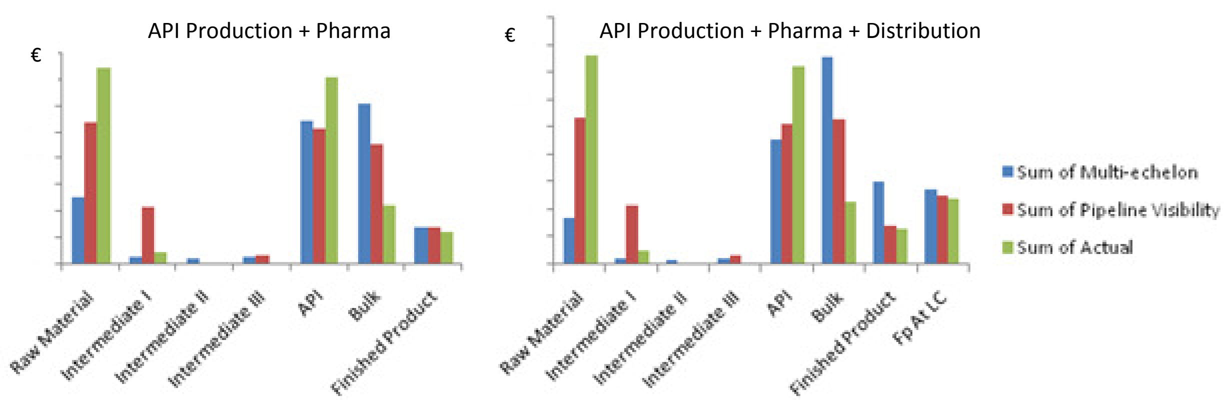

Figure 5-4 Omega – Results Composition [€] (Source: Pipeline Visibility)

Going to a lower level of disaggregation, figure 5-4 shows a comparison of inventory levels for the current average inventories, the norm established in the pipeline visibility project and the results of the multi-echelon model. In the figure, the outcome of the integration of API and Pharma is presented. If we compare the actual average inventories with the multi-echelon model outcome, the results suggest that relocating inventories from raw materials to Bulk could imply a lower capital investment.

The same analysis is performed for the integration of API production, Pharma and Distribution. The results are consistent and suggest again that through reducing raw materials inventory and incrementing bulk inventory, lower costs could be achieved. For both cases, the main characteristic is that inventories are pushed downstream. This is more noticeable in the second model, when it is even suggested to increase the inventory of Bulk in affiliates. In the second model, an increment of inventories in finished products is also suggested. Nevertheless, the accuracy of this could be limited due to the availability and precision of data of affiliates.

Finally, at SKU level, table 5-1 shows the recommendations over some of the most representative SKUs. Besides the recommended decrement of SKUs stocks in main API and raw materials, it is remarkable to note that Type X play a dominant role in the increment of Bulk inventories. The SKU 0973_LOC2_1746522327 and its predecessor drive the performance of the Type X chain and Omega chain in general. A considerable increment in the inventory of this SKU is recommended. It is also recommended an increment in the bulk material primarily related to the market in North America. With respect to the Type Y network, it is important a recommended increment in the stocks of Type Y API 0973_LOC1_186033768 and material 0973_LOC2_1746245676.

A detailed output containing all the SKUs is presented in the data base related to this project. The output describes per SKU the following data: ready rate (P1), fill rate (P2), standard deviation, coefficient of variation, stock time, stock investment, dead stock, remnant stock, effective stock, pipeline stock, safety stock, hierarchical level code, and expected number of items backordered. In addition, recommended planning parameters per SKU such as expected order size and period for releasing the orders are presented. A representation of the output of ChainScope is presented in the Appendix E.

Table 5-1 Omega – Results Most Relevant SKUs

Item no.	Class 2	Target Recommended Action	%
0973_LOC1_181653737	Raw Material	Decrement	-66%
0973_LOC1_181739216	Raw Material	Decrement	-69%
0973_LOC1_186669204	API	Decrement	-30%
0973_LOC2_1746522327	Bulk	Increment	83%

When comparing the actual targets (Pipeline Visibility) with the outcome of this project, it is clear that in both cases, the inventories are pushed downstream. This is more evident in the case of the multi-echelon approach. This allocation of stocks in Omega is driven primarily by a trade off of cost structure, variability, big lot sizes and review periods. In the figures 5-5 and 5-6, the cost structure for Omega is presented.

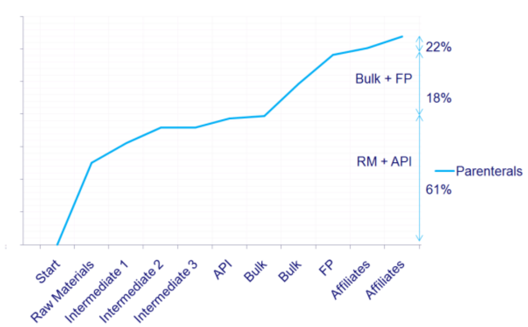

Figure 5-5 Omega – Cost Structure Type Y

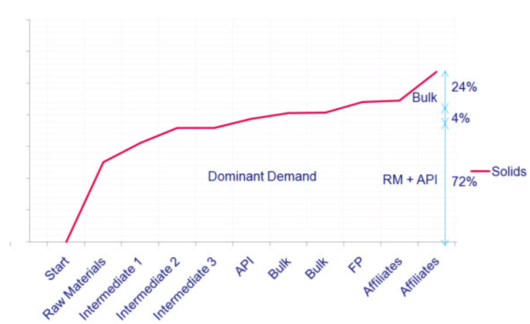

Figure 5-6 Omega – Cost Structure Type X

As previously mentioned, Type X have a dominant role in the chain. The cost structure of Type X is characterized by a no significant difference between the cost of Bulk and API. In addition, for Type Y and Type X, the raw materials represent a big percentage of the cumulative added value. Due to this concave cost structure there is not relevant advantage in allocating inventory in upstream echelons. In fact, most of the cumulative value has been already reached after the main API. In addition to this, upstream echelons present big lot sizes and review periods which already produce big cycle and pipeline stocks which are "natural" buffers of the chain. This can be observed in figure 5-7.

Finally, the variability in Bulk is lower than in raw materials. Nevertheless, the effect of it is relatively small if we consider that the difference is less than one decimal. Consequently, the inventories are pushed downstream. Figure 5-8 shows a clear comparison of the current situation, current targets, and the results obtained through the multi-echelon model. The current targets are already directing the inventories more downstream. This is suggested in a higher degree in the case of the model.

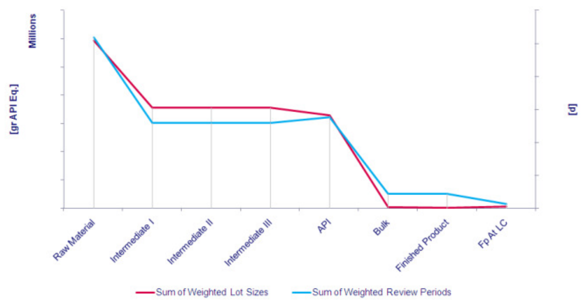

Figure 5-7 Omega – Lot Sizes and Review Periods

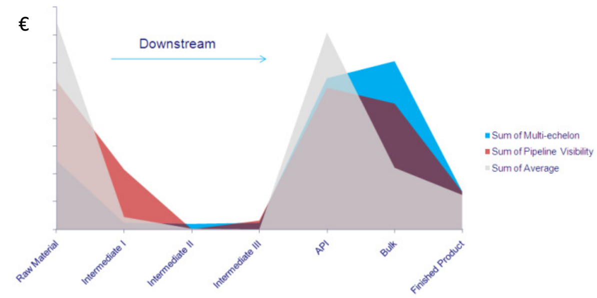

Figure 5-8 Omega – Allocation direction

5.2 Aleph Results

Figure 5-9 shows the macro results of Aleph. The outcome suggests that 7% of inventory reduction with respect to the current situation could be achieved integrated API production and Pharma. If the supply risks of the risk mitigation analysis were considered, no reduction would be achieved but additional uncertainties could be covered with less investment.

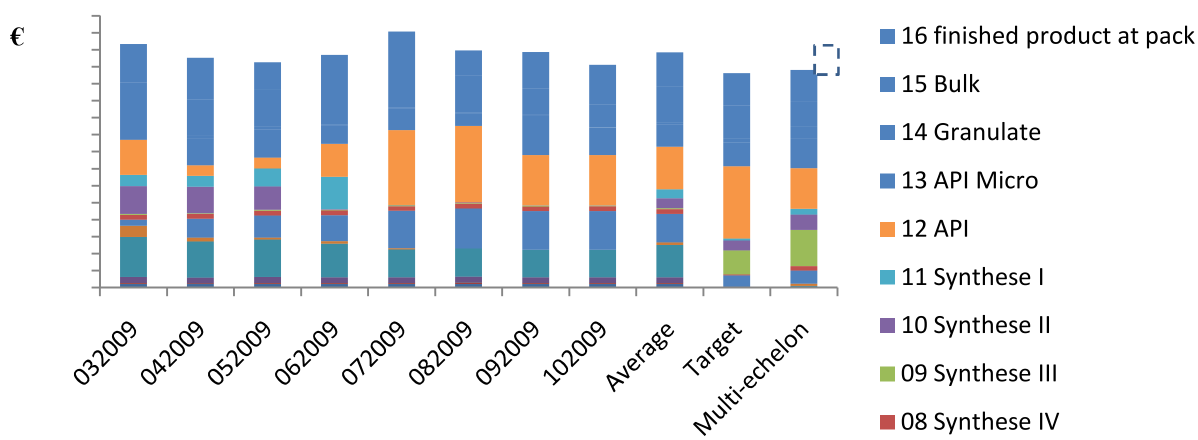

Figure 5-9 Aleph - Results Macro (Source: CG)

In a higher level of detail, the outcome primarily suggests a reallocation of inventories from Synthesis VII to Synthesis III and balanced levels of inventories between Synthesis III and API. In a lower level, the multi-echelon model indicates that higher level of stocks should be allocated to Synthesis II, Granulate and API Micro. See figure 5-10.

Comparing the actual targets (Pipeline Visibility) with the outcome of the Multi-echelon approach, it is interesting to note two major differences. The first difference when using the multi-stage approach is a higher allocation of stocks in Sinthesis III. Secondly, it is suggested to maintain the levels of API and in minor quantities to increase API Micro and Granulate while the current targets propose an extreme increment in main API.

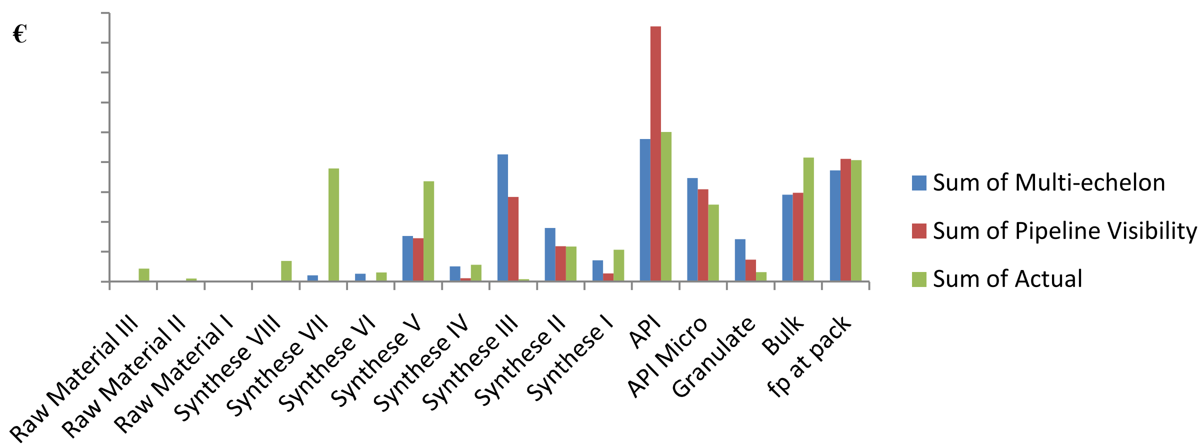

Figure 5-10 Aleph – Results Composition (Source CG)

At SKU level, the outcome of the multi-echelon model was highly similar with the current targets. In fact there was a consistency of approximately 5% of difference in inventory level. Nevertheless, major differences were found for API production and in the initial echelons of Pharama, as previously exposed. Table 5-2 shows relevant SKUs with the most important recommendations with respect to current targets.

Table 5-2 Aleph - Results Most Relevant SKUs

Item no.	Class2	Target Recommended Action	%
0658_LOC1_185882664	Synthese II	Increase	51%
0658_LOC1_185882672	Synthese III	Increase	50%
0658_LOC2_1745882699	API	Decrease	-44%
0658_LOC2_1742720691	Bulk	Decrease	-10%
0658_LOC2_1745570999	Granulate	Increase	92%
0658_LOC2_1745883849	API Micro	Increase	12%

This allocation is driven by a trade off of three factors: cost structure, variability and lot sizes. The cost structure plays a dominant role in this supply network. Aleph presents a clearly convex cost structure. This makes strongly advantageous to locate inventory in the upstream echelons. Figure 5-11 shows the big difference in cost between Raw Materials, Synthesis III and API. Coming back to the comparison between the current targets and the multi-echelon approach, it is gainful to locate inventories in Synthesis III rather than in API. This characteristic differs with the cost structure of Omega. A superposed figure of the cost structure of Omega and Aleph shows this difference.

On the other hand, another dominant factor that plays a role in pushing the inventories downstream is the big lot sizes in API production. After making a comparison of lot sizes and review periods for all the stages, it can be seen that the review periods for API and Synthesis III are equal. Synthesis V-VII have the biggest lot sizes of the network which already give to this stages a natural buffer. With respect to the variability, it increases importantly from Synthesis III up to Raw Materials. For instance, the variability is higher in Synthesis III than in API and Bulk. This can be observed in figures 5-12 and 5-13.

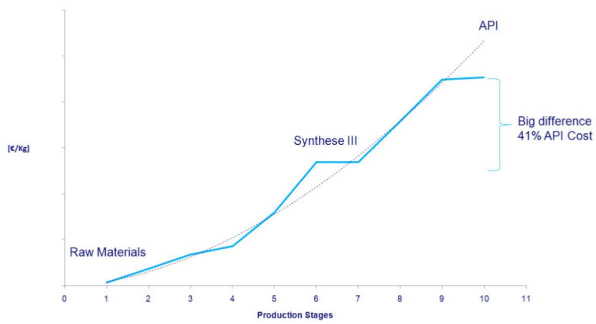

Figure 5-11 Aleph – Cost Structure

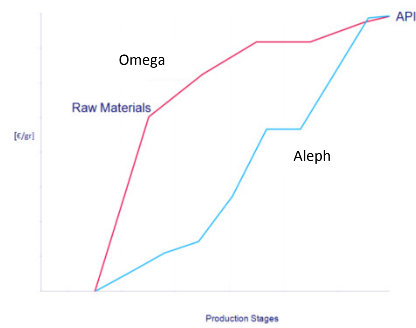

Figure 5-13 Cost Structure Comparison

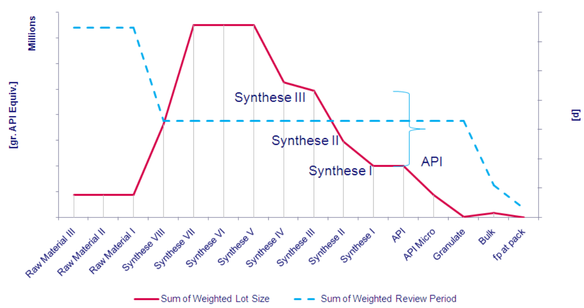

Figure 5-12 Aleph – Lot Sizes and Review Periods

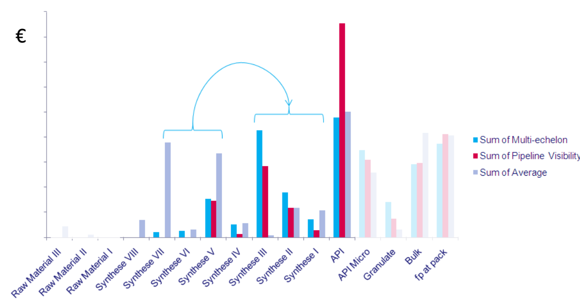

Figure 5-14 Aleph – Main recommendations

As a consequence of this trade-off, first, it is less beneficial to position relevant quantities of inventory in Synthesis VII and V considering the higher variability and considerably bigger lot sizes in these stages. This implies that inventories have to be moved downstream. Second, due to the cost structure of Aleph, the model suggests that it would be more beneficial to increase the targets of Synthesis I, II, and III. Moreover, the cost structure explains a balanced allocation between Synthesis III and API. See figure 5-14.

5.3 Other analysis

Taking into consideration a possible service level segmentation, an analysis of the variability for different types of SKUs is performed. In the case of Omega the results are showed in table 5-3. As expected, items with higher volumes showed lower variability. This is explained by the fact that orders of items with higher volumes, in general, are more consistent. Each type of item is assigned a different service level and an optimization is performed.

Table 5-3 Service Level Segmentation

Class 3	CV	Assigned service level
A	0,8	99%
B	0,9	95%
C	1,2	93%

After the optimization, a global service level of 97,2% is obtained and a substantial decrement in the inventory levels is reached. This demonstrates the possible advantages of a service level segmentation. Related to this service level segmentation, it is considered necessary to define the service level of different stages considering a target service level of 99%.. Based on the optimization analysis it is concluded that a service level of 93,5 % is required in the case of Omega.

Finally, a sensitivity analysis of demand is performed in order to determine the impact on the stocks allocation if the demand decreased. Eighty percent represent eighty percent of the current forecasted demand. It is assumed that the variability remains constant. The results suggest that it would be more beneficial to position inventories downstream if the demand decreased. In the Appendix J the results of these analyses in terms of inventory are showed.

5.4 Validation and Verification

The correctness and consistency of data is not only required to obtain good conclusions from the analysis. In the case of optimization analyses using multi-echelon tools and depending on the mathematics behind the model, data inconsistency of one echelon could originate the infeasibility of the optimization. This is produced by the fact that all the modeled echelons have direct or indirect links. As explained in Section 4, ChainScope is based on Synchronized Base Stock policies in which decision nodes are related with multiple items and vice versa. Consequently, special attention was given to the verification and validation of the model.

In order to verify and validate the correctness of the models and in view of the massiveness of the supply networks, the following procedure is used. Initially, data scan and assessment was performed in order to identify outliers and missing data. Additionally, the SKUs were categorized according to their impact on the supply chain and their relatedness to the research question. Subsequently, multiple meetings were maintained with GPC personnel for correcting inconsistencies. In addition, GPC agreed to re-verify the parameters for SKUs type A.

A tier approach was used to verify and validate the correctness of the model. In this tier approach, the supply network is assembled layer by layer in direction upstream-downstream. After each layer is assembled, an optimization run is performed. If the optimization is feasible, the next tier is assembled. In relevant tiers, key metrics are compared with reference figures. The reference figures were obtained from the Pipeline Visibility project of GPC and the current planning parameters for both supply chains.

The parameters that were assessed were: inventory levels, ratio of pipeline inventory and current target inventory, service level, and API Equivalence factors. With respect to the inventory levels, they were consistently in the range of current characteristics of the chain. This can be seen in the previous figures. In regard to the ratio pipeline inventory and target inventory, the figures were consistent with the Pipeline Visibility project. The verification of API equivalence factors guarantees the accuracy of BOM structure and the structure of the network structure up to finished products. These factors were equal. Finally, the behavior of the network was tested for different levels of stock and compared with the reference service levels. The values were relatively similar with the exception of the distribution stage in Omega. Nevertheless, when this stage was excluded, similar service levels were obtained. See Appendix K for further detail.

5.5 Limitations

The level of detail in the analysis is oriented to answer the research questions. Consequently, the analysis and recommendations are emphatic in the SKUs and aggregation levels driving the supply chains.

Due to the fact that ChainScope considers non-stationary demand, it is not possible to model the supply chain using just one model. The support of two additional models of subsystems is required. Consequently, the degree of synergies is lower than the optimal.

A number of discrepancies are found when determining the current average stock levels, specially, in the case of Omega. Even though this could change the relative difference of recommended and actual situation, the outcome of the analysis and relative difference with current targets remains identical.

Data corresponding to affiliates presents various discrepancies. Consequently, the results in the distribution stage are less accurate.

Demand and forecast information is not available for certain SKUs. Consequently, analogies are used. Nevertheless, information for the majority of SKUs is present.

6. Operational Validity

This section presents an analysis of required modifications – redesign - of a specific process related to the planning system in order to implement a multi-echelon technology. In order to develop this analysis Business Process Management (BPM) techniques are used. Consequently, the structure of the present section is aligned with the BPM cycle: Identification, Discovery, Diagnosis, Planning, and Designing. The phases of Execution and Control are not included in this analysis.

6.1 Identification

In order to identify the innovation scope and recognize related aspects with the present business process redesign, the following steps are followed: 1) enumerate major processes, 2) determine process boundaries, 3) asses strategic relevance of each process, and 4) define manageable process innovation scope.

6.1.1 Company Context

GPC GSCM is making several efforts to increase the global visibility, reduce the complexity, and optimize the inventory levels of its supply networks. Some of these initiatives are strongly related with the possible implementation of an Integral Planning System. Appendix L presents a list of all these initiatives. The process to be redesigned should be aligned with the initiatives of Integration, Pipeline Visibility and Risk Assessment. A description of these initiatives is presented in section 1.1.2.

6.1.2 Major processes

The general Supply Chain Planning process has the following general steps [GPC GSCM (2009)]. Based on the forecast provided by the marketing affiliates, APO provides independent requirements (finished goods), per month in a rolling schedule. In this step there is a reconciliation of the volume and allocation of a packaging site according to finished good country.

In addition, R/3-MRP generates derived dependent requirements in the form of planned orders for each production site.. Subsequently, the planned orders are scheduled manually and then frozen for various months. The next MRP run will not introduce changes. In this step the production is smoothed. A master plan is generated.

Taking into account this frozen period, orders are generated for the formulation step , for instance, twice per year for Omega. Based on this formulation plan, orders are generated to the raw materials suppliers with certain frequency. For example, the orders for raw materials are generated once per year in the case of Omega. In addition, each month the planned orders are verified. This verification constitutes the interface between the formulation and pharmaceutical stages.

The main aggregated operational functions related with supply chain planning for global pharmaceutical products and their main related tasks are described in the Appendix L.

6.1.3 Innovation Scope

The incorporation of a new technology such as a Multi-echelon Planning tool has an impact in different processes with various levels of importance. It has been considered important to define a process that fulfills with three conditions: 1) the process is contributing to one of the key initiatives of GPC GSCM, 2) the process has a systemic impact in the performance of the supply networks, and 3) the redesign is aligned with the available time frame.

It is considered that one of the processes that fulfills with these conditions is the Inventory Target Setting Process. This process is not only having the interaction of all the hierarchies in the organization and is part of one of the key initiatives, but also it represents one of the main coordination mechanisms to align different components of the supply network towards certain direction. In fact represents the relevant centralized variable control exposed in the section 1.

6.2 Discovery

For the discovery phase related to research questions 1 and 2, the recommendations of Sharp and McDermott (0658) have been followed. Various Interviews were carried out with personnel of GSC, Supply Chain Planning and Optimization (SCPO), Production Center Location Gamma, Production Center Location Epsilon, Involvation and CG.

6.2.1 Current Process

There is no standard procedure at the present time and the process varies among practitioners and supply centers. Nevertheless, a description of the main characteristics of this process is given.

In general, the procedure for setting inventory targets is a bottom up approach. This means that the lower hierarchical levels establish their targets according to their local optimization parameters. Subsequently, this lower hierarchy targets are aggregated into the next level, successively, until the top hierarchy is reached. For instance, this is the case of the Supply Center Location Gamma. See figure 6-1 for general bottom up process representation. The SKU level is represented by the lowest hierarchy H_{1n}, and the global target is represented by the highest hierarchy H_{m1}. The intermediate aggregation levels represent Supply Centers or Holding Companies, and GPC Groups from bottom to top, respectively.

In addition, there are few occasions in which a top down approach is used. In this case the inverse procedure occurs. The upper hierarchies determine a reduction in the inventory levels. This is not based on the behavior of the lower levels but in upper decision models, not necessarily related with the operation.

Less frequently, in certain supply centers there are types of interactions between the hierarchies before releasing a decision of target inventories. In addition, especially at SKU level, certain supply centers define levels within the hierarchy in order to set the target stocks. For instance, in the supply center Location Gamma used to be a common practice to categorize the SKUs according to the type of product. This categorization was not only dependent on financial considerations, e.g. products required for hospitals were priority and required a higher stock level. Moreover, according to GPC GSCM Supply Chain Planning & Optimization (SCPO), currently there are certain initiatives to categorize the products in coordination with the Commercial area of GPC. The objective is to define different service levels and based on this, different stock levels according to the segmentation.

The objective of GPC GSCM is to increase the frequency of global metrics control. One of this is the fulfillment of global target inventories. Consequently, tools enabling faster data aggregation and visualization have been recently implemented in order to execute the control and aggregation using the Bottom Up approach, more rapidly.

6.2.2 Assessment

It is clear that presently, there is not a standardized or documented procedure for setting stock targets. Different approaches are used across the organization.

In addition, the utilization of a Bottom Up approach for defining target stocks presents several disadvantages. A Bottom Up approach implies different levels of effort. Due to the fact that it is purely based on an aggregation of local optimums, all the possible synergies from a global perspective are lost.

Since information asymmetry is present among different hierarchies and even within different components of a hierarchy, lower levels of coordination are obtained.

Similarly, a Top Down approach is not optimal. In this case, a top hierarchy making a decision based on a high hierarchy model - without considering the base levels behavior - could have different levels of impact in the components. This could imply that the local restrictions are underestimated or overestimated. Consequently, reactive negotiations will be required. This implies lower levels of coordination.

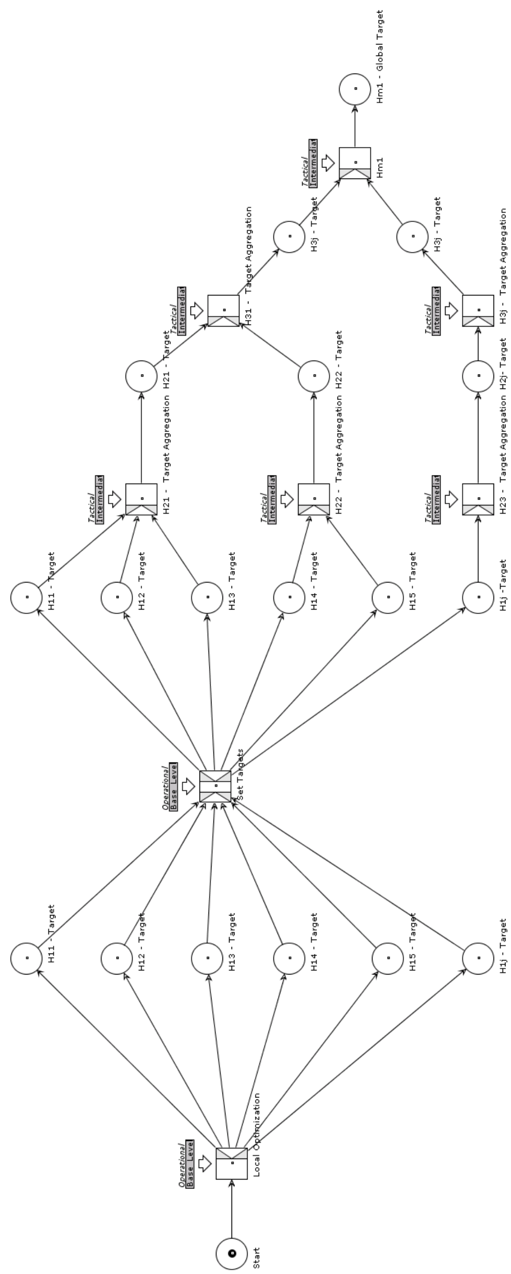

Figure 6-1 Inventory Target Setting Bottom Up Approach

6.3 Plan

In order to design the process, requirements obtained through interviews with GSCM, and Product Supply are considered as well as a reference decision model.

6.3.1 Requirements

Basically, the requirements for the process are: 1) the output of the process should be information that is meaningful for the hierarchies involved and represents the final decision of target stocks, 2) the process should include the interaction of an upper decision model and the behavior of the lower level behavior, 3) the process should take into consideration the organizational structure implications (See Appendix M for a discussion regarding organizational implementation restrictions of centralized decision models), 4) the process should be aligned with the initiatives of Integration, Pipeline Visibility and Risk Assesment.

6.3.2 Reference Model

Schneeweiss (2003) developed a complete conceptual framework on distributed decision making (DDM). This framework is primarily focused on the planning aspect and hierarchical relationships. This work distinguishes scenarios in which distributed decision making can be viewed as hierarchies' interactions. High levels of information asymmetry are stressed as a common characteristic of systems with a strong hierarchical character and multi-entity situation. This is the current case of GPC.

In his work, he characterizes classes of distributed decision making systems. This distinction is based on the symmetry of their information status. The information status comprises the information about the own internal and external situation, the information about the other's internal and external situation and the information about the other's information status. Constructional DDM systems are primarily characterized by the symmetry of their information status. Organizational DDM systems are primarily characterized by the asymmetry of their information status. Thus, different hierarchical levels do not have the same knowledge. Correspondingly, the decision system of GPC is characterized for different levels of knowledge among different decision levels and modules. The decision system in GPC could be catalogued as an Organizational DMM system.

In Schneeweiss' (2003) work, it is mentioned a key factor for designing a planning system: The distributed decision problem is not only defined as separating a system into partial subsystems. It is mainly related with the task coordination within the system. In this line, it is stressed the presence of three different stages of interdependence between hierarchies. The first of these stages is Anticipation, which involves the fact that in a first step, in finding a feasible decision, the higher level takes into consideration the relevant characteristics of the lower level. Once having anticipated the lower level, the higher level makes a decision that has an impact on the lower level. This corresponds to the second stage, and it is defined as Instruction. Finally, the third stage corresponds to a Reaction of the base level. With respect to the first stage, two major types of anticipation can be differentiated: reactive and non-reactive anticipation. Reaction and no reaction of the lower level are assumed in each case, respectively. Moreover, the reactive anticipation is further disaggregated based on the degree of precision of the representation of the lower level at the higher level. See figure 6-2.

Analyzing the decision structure of GPC for setting target stocks, it can be seen that the decisions are based on an aggregation of models of decoupled modules, and that there is not presence of a real Top-Level decision model related to the Base-Level behaviour. Thus, it has lower levels of integration. In order to solve effectively the decision making problem of setting target inventories a coordination mechanism that allows a step forward in the integration of the chain is required. In fact, a coordination mechanism involving a model anticipating the behavior of base levels would integrate the chain through planning activities and improve the decision making process.

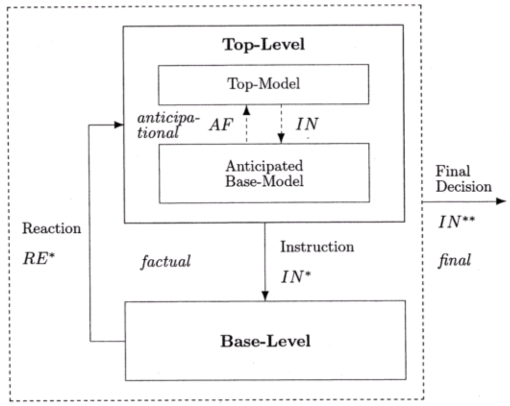

Figure 6-2 Interdependence of Hierarchical Levels [Schneeweiss (2003)]

6.4 Design

6.4.1 Proposed Process

This section describes the characteristics of the proposed process as well as recommendations related to it. Table 6-1 presents a comparative analysis of the current situation versus the requirements and characteristics of the proposed process. Figure 6-2 provides a representation of the proposed process. The following subsections explain, in parallel, the content of table 6-2.

Planning Integration and Interaction of hierarchies

Instead of using a Bottom Up approach, it is proposed to use of an "Anticipational Top Down" approach aligned with the model of Schneeweiss (2003).

The Base-Level corresponds to the decisions made at SKU level. The Top-Level corresponds to the decisions affecting one or various Supply Pipelines. As Anticipated Base-Model, any model describing the impact at SKU level when a decision of the Top-Level is made could be used. In this case, considering the project context, the Multi-echelon inventory model can be used as an Anticipated Base-Model. In fact, the multi-echelon model is built based on the current SKUs planning parameters. Thus, it represents the behavior of the Base-Level. In addition, specific restrictions of Intermediate Hierarchies such as shared resources for some pipelines could be represented through maximum stock levels per SKU or extended review periods.

If the level of accuracy of the multi-echelon model is enough, no reactive negotiation would be necessary, and the instruction will be executed. Nevertheless, if the model is not representing the system sufficiently, the Lower Levels will react. This implies a readjustment of the Multi-echelon model. This will be a continuous improvement process represented by a loop in the workflow model.

Organization Structure Alignment

The multi-echelon model should not be controlled by an operational hierarchy (Base-Level) or a strategic hierarchy (Top-Level). In the first case, the operational hierarchy would lack of a comprehensive perspective of the supply network and possibly, some conflicts of interest could arise. In the case of a strategic hierarchy, detailed figures necessary for building the model and operative process for running the model would not be meaningful for an upper hierarchy. Models are incomplete representations of the reality. This could be controlled in a better way for a lower hierarchy which knows the processes, exhaustively.

On the other hand, it is necessary to define a responsible entity of the model, and also assure that this entity has a comprehensive view of the network as well as an understanding of detailed figures. Consequently, it is considered adequate to assign the responsibility of the Anticipated Base-Model and the interactions between levels to a tactical hierarchy (Intermediate-Level).

Information

It is important to define meaningful information per hierarchy. The information that should be available per hierarchy for the initial instruction and final release of the decision is presented in table 6-1. The information for a feasible implementation of the new technology should be expanded and the level of precision increased. Availability and accuracy of Information related to network structure, inventories, reference stocks, and planning parameters should be expanded. Some discrepancies in the information of both supply chains were found.

Table 6-1 Hierarchies Data Requirements

Data Requirement	**Base**	**Intermediates**	**High**
H	H_{1n}	H_{mn}	H_{m1}
Planning parameters	x		
Supply chain investment as a function of service level		x	x
SKU target inventory [u.], [€], [gr API Equivalence]	x		
Pipeline target inventory [€], [gr API Equivalence]			x
Supply center target inventory [€], [gr API Equivalence]		x	
Holding company target inventory [€], [gr API Equivalence]		x	
Company Group target inventory [€], [gr API Equivalence]		x	
Target inventory breakdown (Safety, Dead, Remnant, Pipeline Stocks)	x	x	x
Target inventory breakdown (Stages, Tiers)		x	x

Metrics

With respect to the metrics, in the proposed process new pipeline indicators should be incorporated for increasing the visibility of the network. In fact, the inventory levels are the final consequence of various factors such as variability, lot sizes, review periods, and cost structure.

The service levels related to target stocks should be subjected to a segmentation analysis. Results of section 5.3 demonstrate that substantial benefits could be achieved through this segmentation. In the current situation, this is not a common practice, and this implies that all the SKUs are given the same importance.

Optimization

Regarding the optimization, interfaces between multi-echelon model and operational systems should be created for optimizing and implementing decisions. In fact, the new technology and current operational settings might not be working under the same logic or the definition of certain parameters could differ. Similarly, parameters required for the model need to be extracted and converted from the current operational systems. Consequently, it is necessary to define a conversion algorithm. Finally, multi-echelon models require a high level of information accuracy. Due to the fact that echelons are linked, in multi-echelon supply chain models, it is possible the inaccuracy of input data could cause an infeasible optimization. Moreover, even if the optimization is feasible, the stock positioning of various nodes could be affected by the inaccuracy of input parameters of a related echelon. In the case of a decoupled approach, the affectation would be local.

Table 6-2 As-Is Situation vs. New Process

Aspect	Sub-Aspect	As-Is	New Process
Integration	Global Optimization	One echelon approach	Multi-echelon approach
	Integration Level	Integration through reactive negotiations	Integration through planning activities
Organizational Structure	Factual planning	Base level and Top level	Implementation of an additional tactical level
	Business Models	Base-Level Model	Base-Level Model
		Top-Level Model	Anticipated Base-Level Model
			Top-Level Model
Information	Network Structure	Partially mapped, mostly incomplete in affiliates	Completely mapped according to SKU definition: Holding Company_Location_Material and relations predecessor-successor
		There is not actual data base containing the supply network structure. It has to be obtained from different sources and the information is not always easy to join or up to date.	Required process for data maintenance
	Inventories	Partially mapped	Completely mapped
			Required process for data maintenance
	Reference stocks	Snapshots are taken as a reference stocks	Average stock should be the reference stocks
			It is necessary to generate historical data (at least length of the chain)
	Availability of Planning Parameters	Partial accessibility	Complete accessibility
Metrics	Service Levels	Target service levels based on local optimization	Targets service levels based on global optimization
		Mostly no segmentation	Possible global segmentation
	Target Setting Approach	Mostly Bottom up	Anticipational Top down
		Occasionally Top down	
	Pipeline Indicators	Inventory levels along the pipeline	Inventory levels, service level, cost structure, lot sizes
Optimization	Model output	Localized	According to table 6-2
	Compatibility of Planning Parameters	Current Planning Parameters	Interface Planning System – Multi-echelon tool (Input Optimization)
			Interface Multi-echelon-tool – Planning System (Order Release)
	Degree of information accuracy	Medium-High	High. Optimization is not feasible when input parameters are not correct
		Opportunities of Improvement for distribution network	

Figure 6-3 shows a representation of the proposed process.

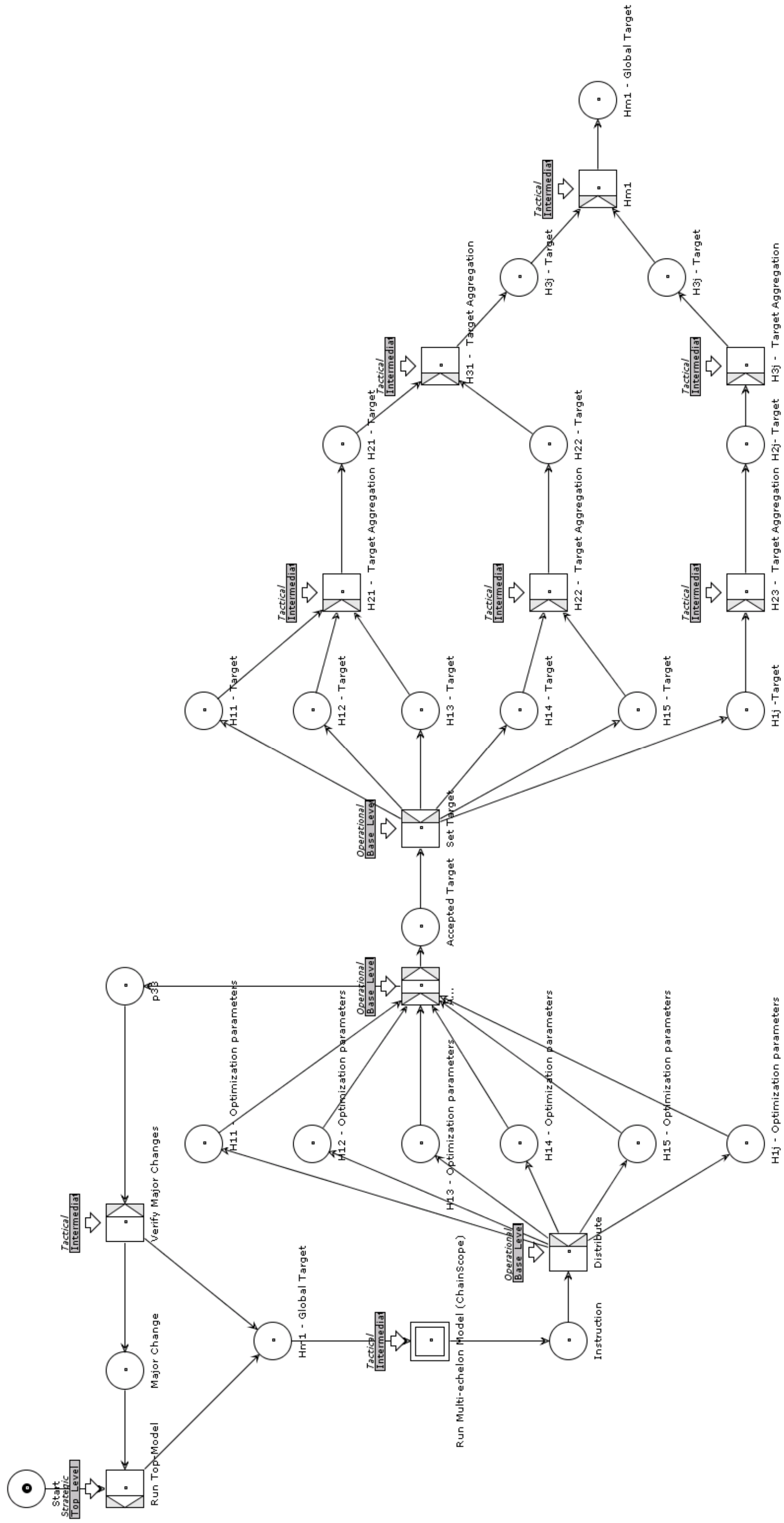

Figure 6-3 Proposed Target Stock Setting Process

6.4.2 Expected Impact

The expected impact of the implementation of a Multi-Echelon tool in the current Inventory Target Setting Process is described in this section. A graphical representation of this impact is showed in figure 6-4.

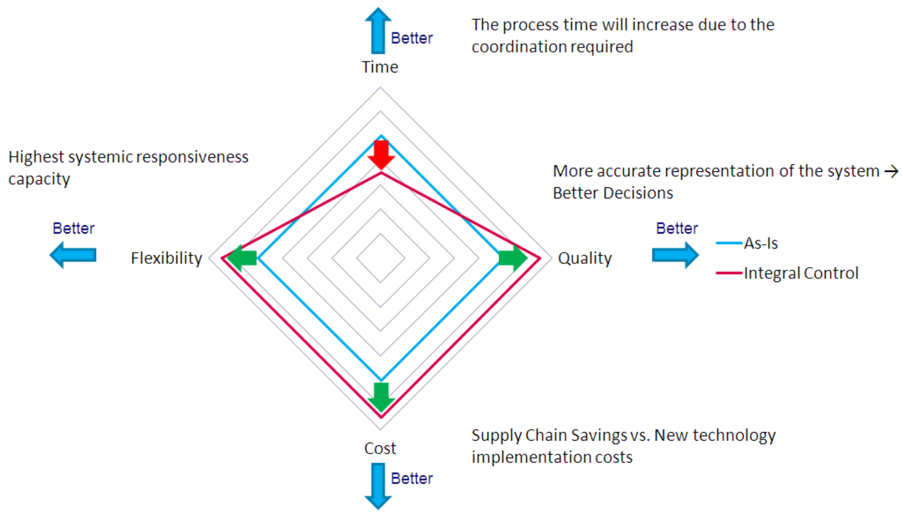

Figure 6-4 Multi-Echelon Technology Implementation Impact

Time

The time required for the planning process could be increased due to the required coordination mechanisms of a centralized decision, and the implicit asymmetric information in the decision process.

Cost

This new technology would imply a reduction in the stocks investments. However, "the purchase, development, implementation, training and maintenance efforts related to technology are obviously costly", Reijers and Liman (2005). A trade off of both components will determine the final impact. Nevertheless, it is considered that a positive impact will be the final outcome in view of the significantly high inventory investments involved in a pharmaceutical supply chain. In fact, according to the results of section 5, considerable reductions could be achieved in Omega and Aleph, respectively. This represents a significant quantity in the order of millions of euros in just 2 supply chains.

Flexibility

The concept of flexibility, in this context, can be defined as the responsiveness capacity of the planning process for becoming adapted to any possible change in the supply chain. Basically, a supply chain could have changes in its functional or structural attributes, as described in the AS-IS situation. In all these cases, the utilization of a coupled model would imply a faster adjustment to the new scenarios. In fact, only one coupled system would have to be adapted instead of multiple decoupled systems.

Quality

In this context, the concept of quality could be defined as the efficacy of the output of the model. Consequently, the planning process would have a higher degree of quality if a certain service level is obtained when using less stock. Clearly, this dimension is essentially related with the first research question of this study and with the first dimension cost. Taking into account that a centralized model would be more comprehensive, a higher degree of quality would be expected.

7. Conclusions and Recommendations

The research questions of the present study are:

1. Main question: Will the utilization of the integrated model for positioning stocks lead to a better optimization of capital investment in the system than the current decoupled-system approach, in terms of the cost related for achieving a specific service level?

2. Which would be a possible structure and coordination mechanisms, in a specific process of the planning system, necessary to incorporate such centralized model?

7.1 Methodology

It is concluded that the integral control of key variables reduces the inherent complexity of comprehensive models, and therefore, increases the operational validity of integral models. In this case, some variables, especially related to the scheduling process, were treated as given constants. Nevertheless, the consistency of the results, through different scenarios and through the comparison with the results of related projects in GPC, indicated that the integral control of key variables increases the level of coordination in the supply chain and maintain the degree of operational validity.

Using mono-equivalences along the chain reduces the complexity of the BOM structure and increases the mathematical tractability of models. Furthermore, it allows a standardized comparison of several attributes in the different stages. Consequently, it facilitates the visibility along the supply chain. However, the procedure developed in this project is applicable to supply networks composed by pure assembly systems and/or pure divergent systems.

For supply networks with varying forecast error, a procedure for incorporating this evolving forecast is developed. The results indicate that it is possible to represent stationary demand with non-stationary demand models as long as the relevant attributes and interactions are taken into account. In this case, the non-stationary forecast error was controlled through sub-models and scenario analyses. Due to the construction of sub-models certain degree of synergies was lost. Nevertheless, the models represented reasonably well the reality.

Despite of the fact that in the current project all upstream echelons were modeled explicitly, a numerical analysis intended to extend the aggregation procedure developed by Bisschop (2007) when using the synchronized base stock policy was performed. The study indicates that it is not necessary to have equal parameters for the aggregation but relatively similar parameters could be aggregated. Second, items with extreme differences in certain parameters could be aggregated as long as the dominant parameters remain similar. Third, even if some dominant parameters are very different between aggregated items, they could be aggregated if they have opposed effects over the cumulative lead times.

In massive supply chains, it is valuable to define certain level of aggregation. Based on it, it is useful to generate indicators of various attributes in order to understand the supply chain behavior and optimization results.

The present project makes an initial effort to link Operations Management with Business Process Management (BPM) in order to increase the operational validity of decisions and establish a framework for the research analysis. The use of BPM techniques allows the identification of different interactions for releasing decisions that cannot be identified by typical theoretical models of Operations

Management. Similarly, the framework of the BPM cycle which is typically applied to BPM related subjects demonstrates to be effective and applicable for other type of fields.

7.2 First Research Question

The analysis developed in the supply chains of Omega and Aleph demonstrated consistently that the integration through planning activities would imply lower capital investment. After the optimization, reductions were obtained for the total supply chain investment for both products.

After the incorporation of supply uncertainties obtained in the pipeline visibility project, the study suggested that the supply chain investment for Omega and Aleph should be increased and maintained, respectively. Nevertheless, again, this can be considered as a relative advantage because additional uncertainties that are not considered in the current situation were taken into account.

Regarding the Omega supply chain, it is recommended to relocate the inventories downstream of the chain. Specifically, it is recommended to decrease the current targets for API Production (Raw materials and Intermediate I) and increase the inventory targets for Pharma (Bulk). The optimization indicates that 5% of relative advantage could be achieved by implementing this recommendation.

The studies in Aleph's chain primarily suggested a reallocation of inventories from Synthesis VII to Synthesis III and balanced levels of inventories between Synthesis III and API. This implies a reduction of inventories in Raw Materials, Synthesis VIII and particularly in Synthesis VII and V. This also implies an increment in API Micro, Granulate and largely in Synthesis III. The optimization indicates that 7% of relative advantage could be achieved by implementing this recommendation.

Finally, it is concluded that through a segmentation of target service levels relevant decrements in inventory investment could be achieved. Furthermore, the study suggests that customers with higher levels of demand volume have lower related variability. This implies that for achieving higher service levels in the most relevant customers (based on volume) it is necessary to relatively invest less capital. Consequently, it is recommended to differentiate end customers using the variability of the products related to them as one of the reference variables and assign different service levels according to this segmentation.

7.3 Second Research Question

Concerning the requirements, it is fundamental to increase the coverage of available information if a pipeline is desired to be controlled, globally. In the new process, the SKU definition would acquire a higher degree of complexity, e.g. incorporation of new degrees of freedom with stock holding companies, locations, among others. Consequently, it is necessary to define a sort of BOM with the new SKU definition in order to define the network structure. In fact, at the present time, there is not actual consolidated data base containing the supply network or a process to maintain it. The information is obtained from different sources and the reliability or completeness is not assured. As a result, the implementation and maintenance of a data base - containing the predecessor SKU, the successor SKU and pipeline BOM numbers up to and including the distribution networks – is essential.

It is important to generate average pipeline inventory levels for reference using as a base historical data up to the length of the chain. Pipeline comparative scenarios with snapshots – currently used - are less relevant. In order to do this, it is also relevant to increase the current mapping degree of pipeline stocks. After analyzing the output of a stock generator developed by CG, it was concluded that several SKUs were not assigned and the stock levels were not always consistent with the levels from other sources.

Furthermore, to increase the accessibility to planning parameters for the SKUs contained in the supply network is fundamental. In the current situation, when developing the projects related with pipeline analysis, several parameters - especially in the case of affiliates – were subjected to assumptions. Moreover, the utilization of a multi-echelon tool would imply a higher level of information accuracy in order to be able to perform an optimization.

On the subject of metrics and target setting, first, an anticipational top-down approach is recommended to define the objectives. This approach implies that prior any decision released by a Top Level, an evaluation of the Base Level behavior through an Anticipated Base Level Model (Multi-echelon model) should be performed. Conversely, the current target setting process involves a bottom up approach and occasionally a top down approach. The utilization of this anticipational top-down approach would entail the consideration of the synergies along the pipeline as well as the specific local implications of any decision. The result of this is a higher degree in the quality of decisions released.

Second, it is necessary to increase the spectrum of pipeline indicators. At the present time, stocks levels are the only metric used for assessing the behavior of the pipeline. Nevertheless, inventory levels are the final consequence of other factors. Consequently, it is suggested to implement and maintain the following indicators per pipeline which are essential for having an accurate visibility: Service levels along the pipeline, variability along the pipeline, cost structure along the pipeline, and lot sizes in terms of API Equivalent along the pipeline.

Regarding the organizational structure, it is necessary to define a responsible entity of the model, and also assure that this entity has a comprehensive view of the network as well as an understanding of detailed figures. Consequently, it is suggested to assign the responsibility of the multi-echelon model to an Intermediate-Level responsible of controlling the entire pipeline.

Finally, it is recommended to define meaningful information in two aspects. First, it is suggested to generate meaningful figures for all the hierarchies involved in the releasing a decision over the pipeline. Data requirements per hierarchy exposed in section 6 could be used as an example. Second, it is necessary to define an interface which couples the current planning parameters and multi-echelon model input and output parameters.

7.4 Further Research

It is suggested to identify research opportunities in which the mono-equivalence approach, developed in this project, could be used. In view of the fact that this approach allows a standardized comparison of different aspects as well as an easier mathematical tractability, it could be extended to other type of industries besides the pharmaceutical industry. For future research projects in which general structures are present and the software cannot treat non-integer numbers, a possible solution is to divide the network in partial subsystems composed by pure assembly or/and divergent systems. The drawback of this approach is that it will be unavoidable to lose certain degree of synergies.

Further research is recommended in aggregation procedures. These procedures increase the tractability of complex networks. Specifically, is suggested further study in the formalization of the new conditions required for aggregation related to the procedure of Bischop (2007) and the numerical example developed in the present project.

It is recommended to develop additional research projects in which the techniques of Operations Management and Business Process Management are combined.

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Appendixes

A. Operations Planning and Control in the Pharmaceutical Industry

Shah (2004) proposed key issues and strategies for a supply chain optimization in the pharmaceutical industry focused on the large, research and development-based multinationals. According to this study, the single most important driver in the pharmaceutical industry is the time-to-market. The life-cycle of a pharmaceutical product is described, being the first phase of research, typically taking 10 years, the development phase with 6-8 years and finally, the manufacturing and distribution.

According to same study, a typical manufacturing and distribution chain in the industry is composed by primary manufacturing, secondary manufacturing, market warehouses/distribution centers, wholesalers and retailers/hospitals. The primary manufacturing site is in charge of the production of active ingredients (AI or API). This initial process implies multiple stages, and it is characterized by long task processing times, often rounded to multiple shifts. The traditional process technology involves batch equipment and flexible pipe-work. "*The typical mode of operation of the primary manufacturing is complex and not responsive and contributes significantly to some of the poor supply chain metrics exhibited by this industry*". In this stage, *the tendency of outsourcing is growing which implies more complexity and requirement of coordination methods*. The second manufacturing stage is concerned with taking the AI and adding inert materials and further processing and packaging. The outcome of this process is the final product, usually in SKU form. These secondary manufacturing locations are often geographically separate from the primary manufacturing locations. The number of the secondary is frequently bigger than the primary one. *Again here, the coordination is a key aspect*. Transportation between sites is of the order of 1,5 weeks. Finally, wholesalers are dominant in the sector. For instance, it is mentioned that in the United Kingdom, 80% of the demand flows through this channel.

With respect to the planning process, all major pharmaceutical companies operate ERP systems and relatively follow this process [Shah (2004)]: 1)demand management through forecasts, 2) inventory management and distribution requirements planning by an aggregation of demand, being the final outcome orders to the secondary manufacturing process, 3) secondary production planning and scheduling through MRP-II tools and APS tools, respectively, being the outcome orders to the primary process, and 4) primary manufacturing campaign planning and AI inventory management, where the demand will be satisfied in cascade. An important characteristic mentioned with respect to the decision process, is its distributed nature of decision making produced by the large scale and geographical span. According to Shah (2004), "Different nodes are not really aware of upstream nodes' resource constraints, and orders may be filled in order o receipt, rather than on an economic basis". This statement is very relevant because it demonstrates that different stages in the system are decoupled and without an effective integration. Importantly, it is mentioned that centralized planning would also imply some difficulties in this context.

The following supply chain performance measures are typical for the industry [Shah (2004)]: The pipeline stocks typically amount to 30-90% of annual demand in quantity, and there is usually 2-24 weeks' worth of finished goods socks. The turnover (annual sales/average stock) is typically between 1 and 8. Cycle times (elapsed time between material entering as raw material and leaving as product) are often between 1000 and 8000 h. The value-added time is of order 0,3-5%. Material efficiencies (the amounts of product produced per unit amount of total materials used) are 1-10%. As it can be seen, the amount of pipeline stocks is very significant.

To concluded, according to Shah (2004), the key issues in the pharmaceutical supply chain are uncertainty management, process development, capacity planning, network design, and plant design [Shah (2004)]. Nevertheless, taking into consideration the previous characterization, *it is necessary to lay emphasis on an additional key factor, which is probably the most important: The high degree of required coordination*.

Altrichter and Callet (2005) developed a Topology and Typology of the Pharmaceuticals Supply Chain and presented a case study based on a European pharmaceutical company. According to the case analyzed by these authors, the supply chain consists fundamentally of three main levels: chemical plants, pharmaceutical plants and customers. The chemical plants deliver certain active ingredients. These chemical plants can be either part of the same company or third party suppliers. Material necessities are planned considering the entire planning horizon.

With respect to the pharmaceutical plants, they produce an ample variety of product types: solids, liquids, biotech medicaments, medical devices, consumer, sterile products, patches, and "over the counter" products. There are 2 main processes: formulation, the product of which is the bulk material and packaging, the product of which is a package customized final product. As an example, the authors state that "as an order of magnitude, 50 active ingredients are formulated into 500 bulk materials, those are packed into 10.000 finished products". The customers are typically represented by marketing affiliates. Nevertheless, there are other types of customers such as tender business, small countries, whole-sellers, government agencies, and non-governmental agencies. The customers forecast their demand and this forecast are translated to orders according to certain Service Level Agreements. It is important to note here the complexity of the network interaction because, according to authors, "Demand assigned to one plant can also result from a dependent requirement of another plant. For example a bulk material is produced in one plant, but packed in a second plant.

In relation to the distribution centers and warehouses, they are mainly located close to the plants. There are two types of shipping scenarios. In the first case, and generally, products are directly shipped from the distribution centers and warehouses to the customers. In the other case, products are shipped from one manufacturing plant to another due to certain regulations and finally, the product is sent to the customer. It is stated that the distribution is not critical due to the high relative value of end products with respect to distribution costs.

Additionally, in this work, a typology of the pharmaceutical supply chain is presented. See table A-1. It is relevant the description of the relevant attributes of the case supply chain. In this description, the network structure is characterized as divergent being the major constraints the capacity of formulation lines and the manpower in packaging lines. With respect to the location of decoupling points, there is mentioned 2 cases: assemble-to-order (country specific) and deliver-to-order (standard export). It is stated that the type of information exchanged are forecasts and orders. Notably, the direction of the coordination is characterized as a "mixture". The initial state showed no central supply chain network planning and the planning process was developed in isolated subsystems. It is also interesting the characterization of power balance in this industry. According to the same authors, the balance of power is in the side of the customers.

Similarly Koh et al. (2003) developed a work aimed to secure the pharmaceutical supply chain in the United States. In this work, the organization of the production processes is also confirmed and an example of the pharmaceutical supply chain complexity with respect to the information flow is presented. It is emphasized the idea that traceability of all the units through the supply chain is done through registries in the package, and the idea of integration through information.

Table A-1 Typology for the pharmaceutical supply chain - Functional attributes [Altrichter and Caillet (2005)]

Functional attributes	
Attributes	**Contents**
number and type of products procured	few (Active Ingredients, AI)
	specific (Packaging Materials)
sourcing type	single (Active Ingredients)
	multiple (Packaging Materials)
supplied lead time and reliability	long, based on forecast (AI)
	short, reliable (Packaging Materials)
materials' life cycle	long
organization of the production process	two steps (formulation & packaging)
repetition of operations	batch production
changeover characteristics	sequence dep. Setup times & costs
bottlenecks in production	known, almost stationary
working time flexibility	frequently used, additional shifts
distribution structure	two stages
pattern of delivery	cyclic with specific country demand
	dynamic with standard export demand
deployment of transportation means	unlimited compared to
	cost of products & stock outs
availability of future demands	forecasted
demand curve	seasonal for medications linked to winter illnesses for example
	static for others
product's life cycle	several years
number of product types	several (solids, creams, liquids, sterile, patches, biotechs, medical services)
degree of customization	standard products (country specific)
bill of materials	divergent in formulation step
	divergent in packaging step
portion of service operations	tangible goods

Boulaksil (2005) in a study of rolling horizon simulation of a Supply Chain described the characteristics of a specific Supply Chain of a European pharmaceutical company. In this study, the structure of the planning system and the planning procedure are described in detail. It is stated that the production in the first part of the supply chain, up to bulk materials, is forecast driven, e.g. make-to-stock. The packaging process is based on the make-to-order principle. According to the description presented in this study, the structure of the planning system can be summarized as follows: "The packaging planning is controlled by an MRP system that is fed by orders from local companies. Local companies feed their sales data also in the forecasting system which is linked with the Advanced Planning System. The bulk production is planned and controlled by an Advanced Planning System (APS). Therefore it receives forecasts from the forecasting system and the actual inventory levels from local companies and production sites". In figure the most important control functions are presented. The structure is decoupled and the integration is based on data aggregation.

The APS is composed by 3 hierarchical levels: 1) The Long Range Plan that covers the allocation process of capacities generated by certain software. 2) The Supply Chain Plan that covers all production sites and all product groups that share capacities or materials. 3) The Operational Plan that covers one production site and all product groups that share capacities or materials. The planning procedure consists on an aggregation of plans from lower to higher hierarchy, in which each hierarchy has different planning horizons, being those planning horizons of 5, 2, and 1 year, with frozen periods of 24, 6 and 3 months, respectively. The most important feature is that the level of integration is low due to the fact that that the aggregation is based on local optimums and not considering interactions.

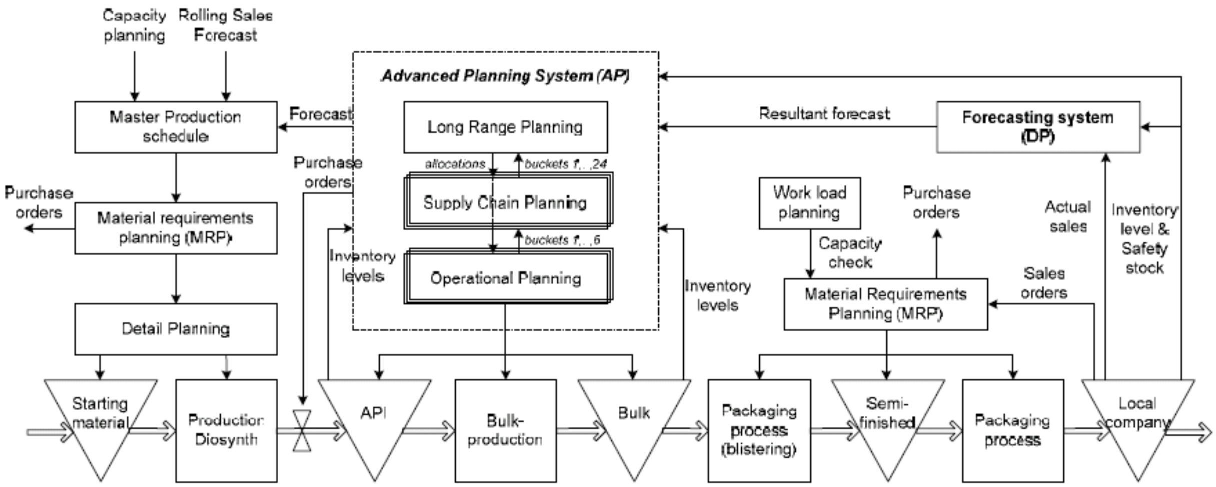

Figure A-1 Supply Chain Control Structure [Boulaksil (2005)]

To conclude, the pharmaceutical supply chain is a complex system requiring significant levels of coordination. In general, the levels of integration are low because the current planning systems are principally based on information integration and/or on the aggregation of local minimums, typically showing a reactive interaction between lower and higher levels. The upper echelons contribute the most to the relatively low performance of the chains.

B. Demand Analysis

Composition

Table A-2 Demand composition based on Class 1

Class 1	%
All	0,2%
Type Y	37,0%
Type X	62,8%
Grand Total	100,0%

Table A-3 Demand Composition based on Class 2

Class 2	%
API	0,2%
Finished Product	1,8%
Bulk	14,1%
Fp At LC	83,9%
Grand Total	100,0%

Table A-4 Demand ABC Classification

abc	Total products	Type Y	Type X	% of Total Demand
A	16	6	10	70%
B	38	9	29	20%
C	38	13	25	7%
D	92	28	64	3%
Total	184	56	128	100%

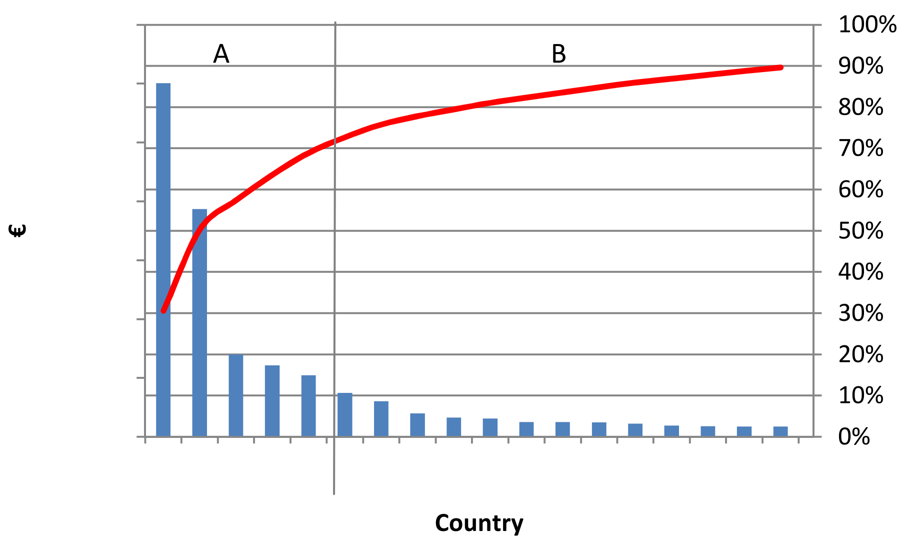

Figure A-2 Market ABC

Seasonality

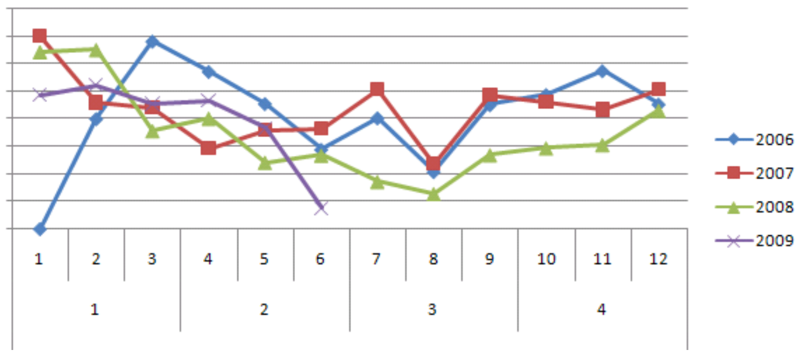

Figure A-3 Seasonality Type X

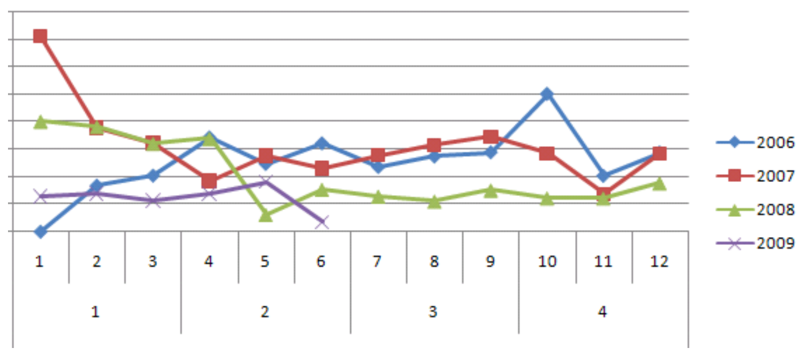

Figure A-4 Seasonality Type Y

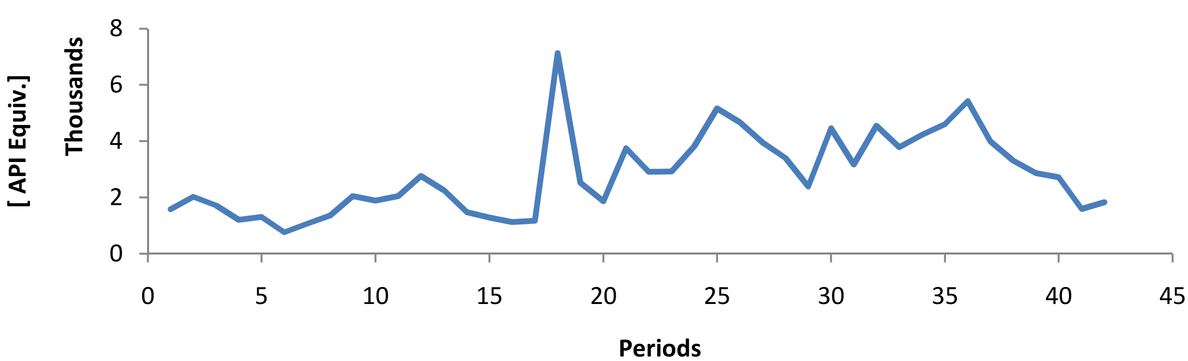

Figure A-5 Omega Main API Demand

C. Target Coverage

Table A-5 Coverage [months] Omega

Stage	june-09	Target
Raw Material	10,1	7,9
Intermediate I	0,1	2,7
Intermediate II	0,0	0,3
Intermediate III	0,0	0,3
API	7,4	5,1
Bulk	1,2	1,9
Finished Product	2,0	1,9
Fp At LC	2,7	2,4
Total	23,6	22,5

Table A-6 Coverage [months] Aleph

Stage	april-09	Target
Raw Material III	38,7	0,0
Raw Material II	31,9	0,4
Raw Material I	0,2	0,0
Synthese VIII	12,3	0,0
Synthese VII	42,5	0,0
Synthese VI	3,7	0,0
Synthese V	14,0	9,2
Synthese IV	8,4	1,8
Synthese III	0,2	7,2
Synthese II	9,8	3,7
Synthese I	2,5	0,4
API	1,8	13,0
API Micro	4,1	1,1
Granulate	0,5	0,7
Bulk	4,9	2,7
finished product at pack	2,8	1,2
finished product at loc	5,2	1,6
Total	183,5	42,9

D. Allocation Rules for Divergent Systems

Diks et al. (1996), developed a review of the most important results in this type of system. In their paper, they characterize the divergent multi-echelon systems by the property that a stock point is supplied by exactly another stock point, and supplies one or more stock points (See Figure 1), [Diks et al. (1996)].

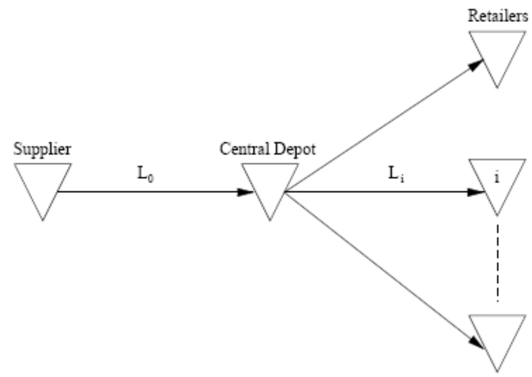

Figure A-6 Schematic representation of a divergent two-echelon inventory system [Diks et al. (1996)]

Most of the studies assume an infinite capacity of the supplier and consider the previous network supply (Two-echelon system). The retailers face stochastic customer demand, which is stationary and independent of other retailers. Several studies have been focused on this system. See De Bodt & Graves (1985), De Kok (1990), Federgruen (1993), Lagodinos (1993), Van Houtum et al. (1996), and Van der Heijden (1995), [Diks et al. (1996)].

The allocation models are those models in which, in addition to the ordering decision, there is an opportunity to allocate (operate on in a more general sense) the inventory on hand, [Eppen and Schrage (1981)]. Due to the large computational times, the studies of allocation models have been focused primarily on the approximate analysis of policies that have a simple structure [Van der Heijden (1995)], that is, the multi-echelon divergent system previously mentioned.

Among the previous mentioned policies, Eppen and Schrage (1981) developed a model of centralized ordering policies in a multi-warehouse system with lead times and random demand. The model considered a depot – warehouse system with independent normally distributed stationary demand, identical proportional costs of holding and backordering, and no transshipment. The study is motivated by the long lead times and highly random demand at downstream echelons in the network supply of certain industries. This would be aligned with the characteristics of the pharmaceuticals supply networks of healthcare commodities under analysis.

Their paper takes into account two models. In the first one, the depot orders items from the supplier and allocate them to the warehouses each period. In the second one, ordering and allocation are performed each number of periods. In addition, both models consider a pass-through system in which orders that arrive from the supplier are immediately allocated to the warehouses. To be precise, this pass-through system implies that the depot does not hold inventory but works as a (virtual) cross-docking facility. This kind of model would be suitable for a hierarchical planning structure in which a central authority has the role of system planner and coordinator. Explicitly, the central authority – the depot in the model of Eppen and Schrage (1981) -, would order the items from the suppliers and allocate the orders to the downstream echelons immediately after the order is completed. The allocation is based on equal stock-out probabilities for the warehouses, and it is called Fair Share (FS).

An additional feature of the work of these authors is that in the systems under study, a common order for all warehouses is placed. Consequently, the model takes into consideration the so called "joint ordering effect". These authors mention that the advantages of this joint ordering effect are first, to take advantage of quantity discounts offered by the supplier, and second, to reduce the system inventory due to a portfolio effect over the lead time from the supplier. Additionally to the advantages mentioned by Eppen and Schrage (1981), it is necessary to mention that the bargaining power of a party integrated different demand components in a common order becomes higher. Consequently, the capacity to influence positively in the party's interests increases. In a "real life" planning system, this common order could be executed by a central authority through a coordination mechanism.

Subsequently, the model of Eppen and Schrage (1981) was extended by Van Donselaar and Wijngaard (1987). In this extended version, the central depot is able to hold stock.

The most relevant extension is developed by De Kok (1990), in which the model considers arbitrary demand functions, arbitrary service criteria, non-stationary demand, different lead times between depot and retailers, and most important, different target service levels per retailer. In order to use the differentiated fill rate criterion, De Kok (1990) developed the Consistent Appropriate Share (CAS) rationing rule in which the allocation is based on safety stock ratios. Based on this work, De Kok at al. (1994), and Verrijdt and De Kok (1995) extended the study introducing the possibility of holding stock in the central depot and general N-echelon systems.

Lagodimos (1992) extended the analysis with a study of multi-echelon service models for inventory systems under different rationing policies. He introduced Priority Rationing (PR), in which the allocation to the retailers is based on an allocation list. Two rules are considered: assigning priorities at random (RAN), and assigning priorities in order of increasing order size (MIN). In general, this type of rules are the most used in practice.

Van der Heijden (1995) introduced the Balanced Stock rationing policy (BS). In this control rule, the rationing fractions are determined such that the (approximate) expected system imbalance is minimized. Subsequently, the order-up-to-levels are calculated such that the target fill rates are achieved. According to the comparative studies developed by Van der Heijden (1995) and Van der Heijden et al. (1996) of BS versus CAS, the BS rationing would be superior.

Kiesmuller, (2008), developed a case study in which different pooling scenarios are compared in a two-echelon divergent system. The base case considers the distribution of a single product through one supplier and several retailers with decentralized and non coordinated control. The ordering system uses an (R, S) policy. The initial planning and control system is modified considering different concepts - location pooling, virtual pooling, lead-time pooling, demand correlation between retailers and allocation rules - in order to analyze advantages and disadvantages of each planning model. One of the scenarios analyzed presents the inclusion of a distribution center between the supplier and retailers. It is assumed that a higher hierarchy is responsible for the distribution center and its replenishment orders, as well as for the retail outlets and their replenishments. In addition, the scenario considers that the distribution center is not allowed to keep stock and it is used as a cross-docking facility. The higher hierarchy places only one replenishment order at the supplier and allocates this order to the retailers when it arrives at the distribution center. In order to allocate the order to each retailer, rationing rules such as fair share, consistent appropriate rationing rule and balanced stock are used.

Basically, the main previous works treating this subject could be summarized as follows:

Table A-7 Rationing policies – Previous woks

Year	Author	Allocation rule
1981	Eppen and Schrage	FS
1987	Van Donselaar and Wijngaard	FS + stock central depot
1990	De Kok	AS/CAS
1992	Lagodinos	PR
1993	Federgruen	Models overview
1994	Inderfurth	Models overview
1994	De Kok et al.	AS/CAS + stock central depot
1995	Verrijdt and De Kok	CAS + N-echelon
1996	Verrijdt and De Kok	CAS + adjustment methods
1996	Diks et al.	Models overview
1997	Van der Heijden	BS
1997	Van der Heijden et al.	BS + N-echelon

E. ChainScope – Input and Output Parameters

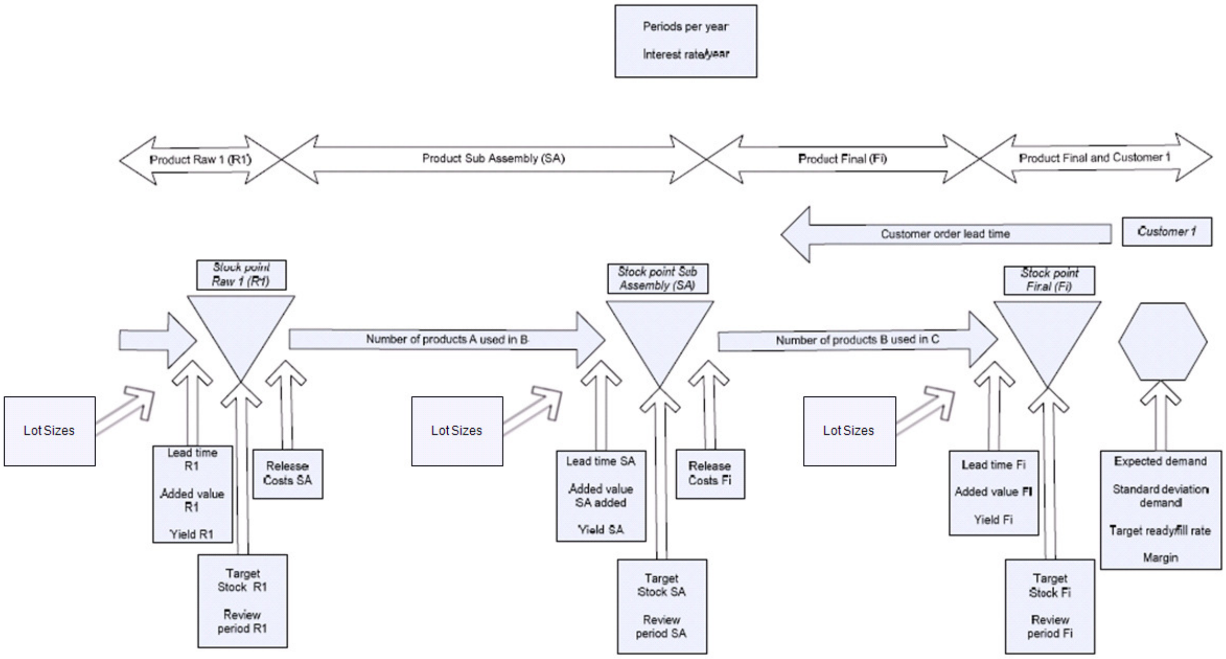

Figure A-7 ChainScope Input Parameters [De Kok (2009)]

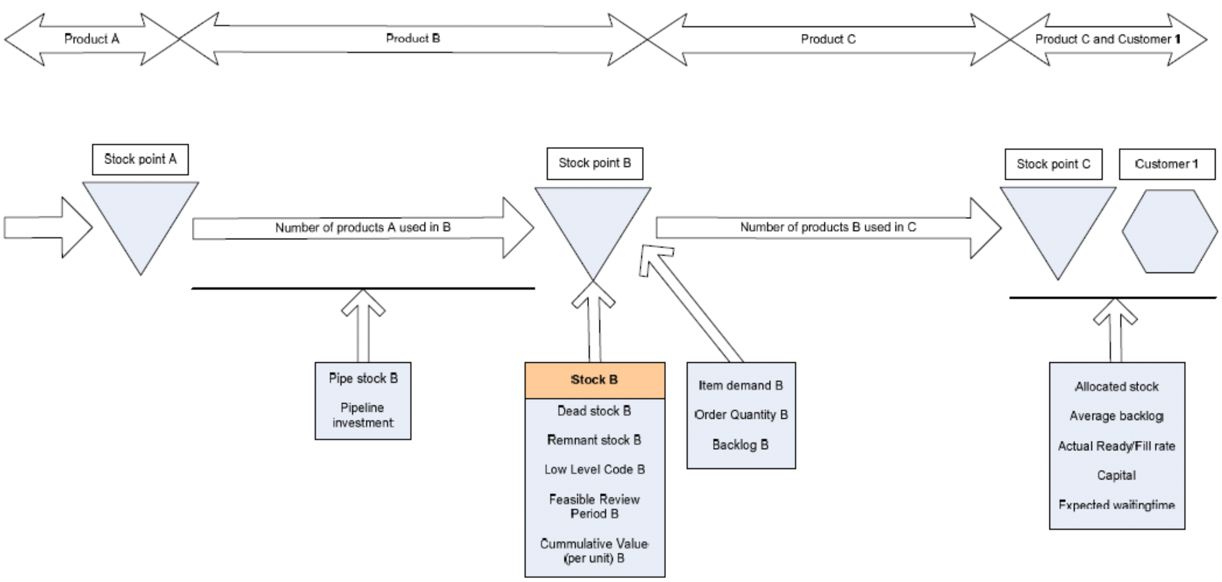

Figure A-8 ChainScope Output Parameters [De Kok (2009)]

F. BOM Error

Let's consider table A-8. In this case, aij = 0,792793 [u] of S1 are used to produce 1 [u] of S2:

Table A-8 BOM Error Example Data

Number	S1	S2	S3	S4	S5
aij	0,792793	0,916364	1,40398	0,97699	1
fij	8/10	92/100	14/10	98/100	1

The following table shows the conversion of 1 [u] S1 into S2. This implies that 1[u] S1 would be converted in (1*1)/0,792793 = 1,26 [u] S2.

1 [u] S1	1 [u] S2
	0,792793 [u] S1

If we use fij, then we have:

1 [u] S1	10 [u] S2
	8 [u] S1

Nevertheless, in ChainScope we cannot set a relation 8:10, but just 8:1. Consequently, we have to change the units of S2. In this case, the new unit [u'] has to be 10 times bigger than the old [u]. This implies that 1 [u] S1 would be converted in (1*1)/8 = 0,126 [10u] S2. This is correct because 1,26 [u] S2 = 0,126 [10u] S2.

1 [u] S1	1 [10u] S2
	8 [u] S1

For producing S3 we have that:

1 [u] S1	1 [10u] S2	100 [10u] S3
	8 [u] S1	92 [10u] S2

And again, due to the fact that the integer relation of S2:S3 in ChainScope has to be 92:1, we have to change the units of S3. In this case the new unit [u'] is 1000 (10*100) bigger than [u]. Basically, while we change the units downstream, consecutively, the units trend to be geometrically bigger.

1 [u] S1	1 [10u] S2	1 [1000u] S3
	8 [u] S1	92 [10u] S2

The same approach is followed for all the items of the chain. Due to the fact that the chain has up to 11 stages and in most of them there is a BOM correction factor, we get extreme units. For instance, a unit [u'] 1E+19 bigger than [u] is obtained in the case of the most downstream SKUs.

G. Supply Network Structure

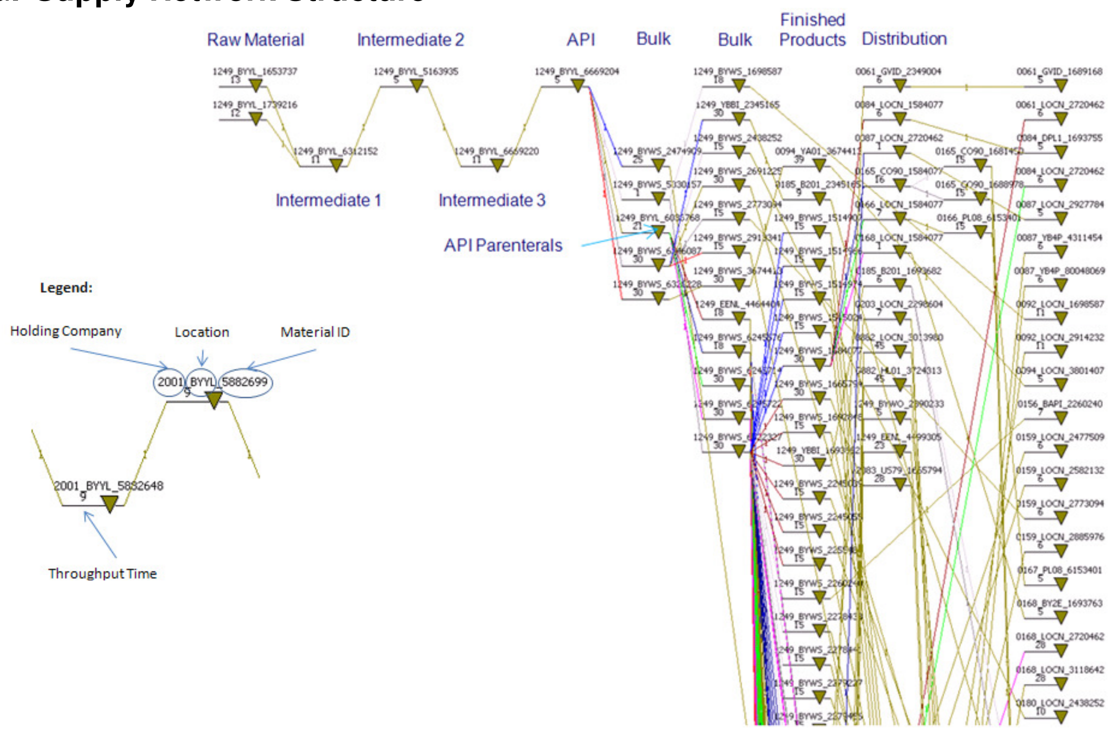

Figure A-9 Omega - General Supply Network Structure

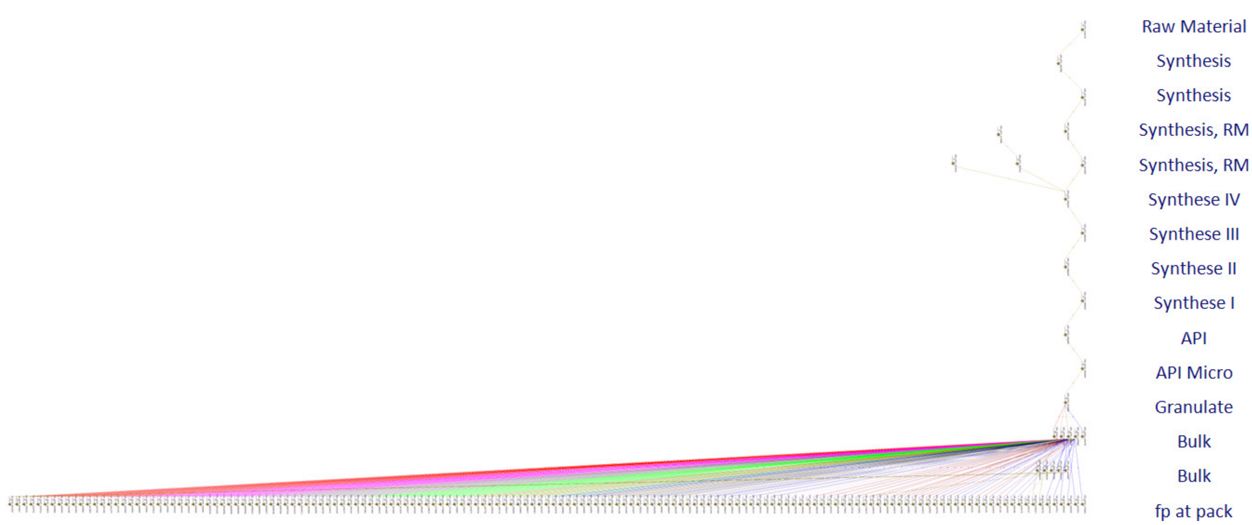

Figure A-10 Aleph – Complete Network

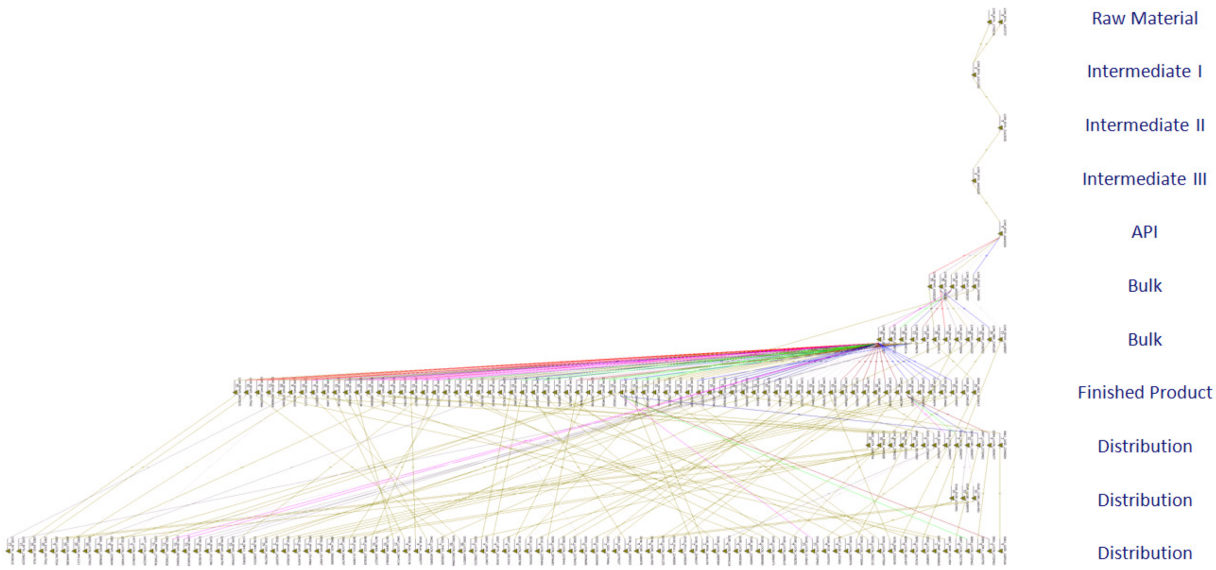

Figure A-11 Omega – Complete Network

H. Aggregation Conditions Numerical Example

The next figures represents the API production of Omega and the aggregation that we want to analize. We have a pure assembly system in which the raw materials n_1 and n_2 converge in the main API n_j. In this case the Mono-Equivalence conversion is based on n_j. The objective of this numerical example is to analyze under which conditions n_1 and n_2 could be aggregated in an item n_d.

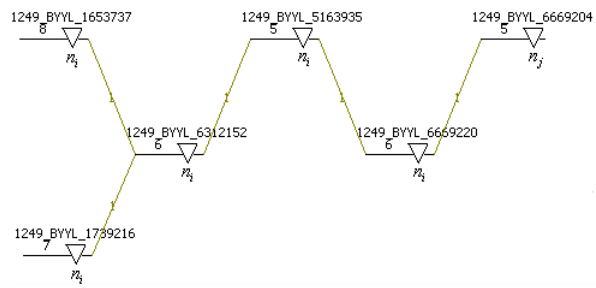

Figure A-12 Omega API Production - Pure assembly system

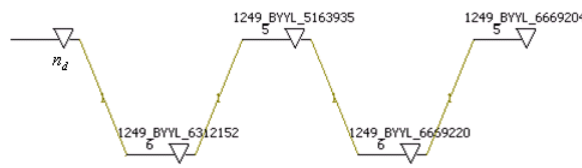

Figure A-13 Aggregation Raw Materials

In order to perform this analysis, we make a mono-equivalence conversion of the original network of API Production and model it explicitly. There are three aggregation conditions suggested by Bischop(2007): equal lead times, equal review periods and equal BOM level. In addition, equal lot size has been added in the previous section. Multiple scenarios have been created in which just the BOM level is maintained as a constant. The purpose of the scenario analysis is to determine in which scenarios the allocation of stocks is exactly equal to n_1 and n_2. Thus, aggregation of n_i is possible. The scenarios are defined in such a way that the parameters vary from equal to extremely different. For instance, if $\frac{L_1}{L_2} = 10$, this means that L_1 is 10 times bigger than L_2.

Table A-9 Aggregation – Parameters numeric example

Lead Time	L_1/L_2	1	2	10
Review Period	R_1/R_2	260	1	-
Lot Sizes	k_1/k_2	0,00000001	0,000001	1

Based on the previous parameters, different combinations are defined. The scenarios and results can be observed in table A-10, where S_i is the average stock allocated to the stock points of n_i. If S_1/S_2 = 1, the incorporation of all n_i in the model is redundant and therefore they could have been aggregated.

As it can be seen, there are 8 scenarios in which aggregation was feasible. In just one of them (scenario 3), the conditions established by Bischop (2007) are fulfilled. This has several interpretations. First, it is not necessary to have equal parameters for the aggregation but items but relatively similar parameter could be aggregated. Second, items with extreme differences in certain parameters could be aggregated as long as the dominant parameters remain similar (Scenarios 1, 2, 4, and 9). Third, even if some dominant parameters are very different between aggregated items, they could be aggregated if they have opposed effects over the cumulative lead times. For instance, in scenarios 8, 7, and 10, big differences in review periods or lead times in the side of one item balanced big differences in lot sizes in the side of the other item.

Table A-10 Aggregation – Scenarios and results numeric example

Scenario	R_1/R_2	L_1/L_2	k_1/k_2	S_1/S_2	Aggregation
1	1	10	1E+00	0,9999	Ok
2	1	2	1E+00	1	Ok
3	1	1	1E+00	1	Ok
4	260	1	1E+00	1	Ok
5	260	10	1E+00	0	Ng
6	260	2	1E+00	0	Ng
7	1	10	1E-06	0,9999	Ok
8	1	2	1E-06	1	Ok
9	1	1	1E-06	1	Ok
10	260	1	1E-06	1	Ok
11	260	10	1E-06	0	Ng
12	260	10	1E-06	0	Ng
13	1	10	1E-08	1,9368	Ng
14	1	2	1E-08	1,9051	Ng
15	1	1	1E-08	1,8897	Ng
16	260	1	1E-08	1,8897	Ng
17	260	10	1E-08	1,9368	Ng
18	260	2	1E-08	1,9051	Ng

I. Submodels

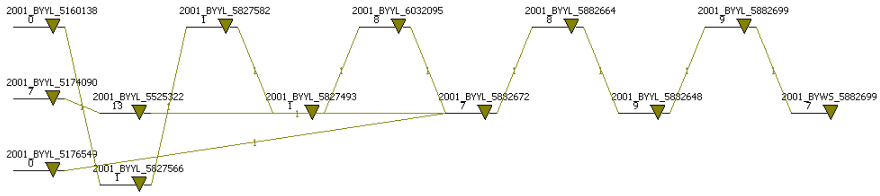

Figure A-14 Aleph – Submodel1: API Production

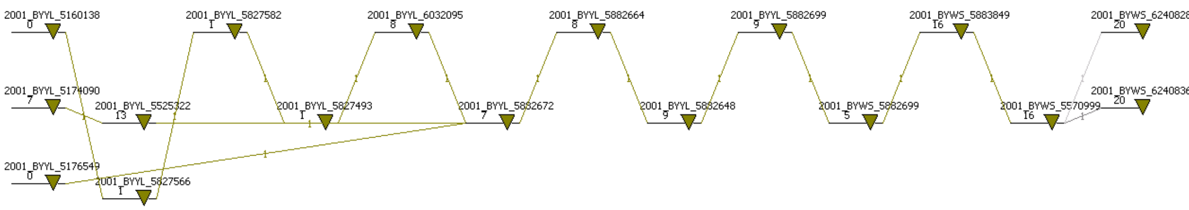

Figure A-15 Aleph – Submodel2: Bulk

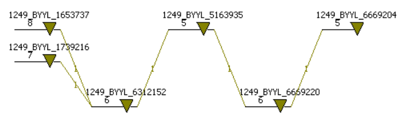

Figure A-16 Omega – Submodel1: API Production

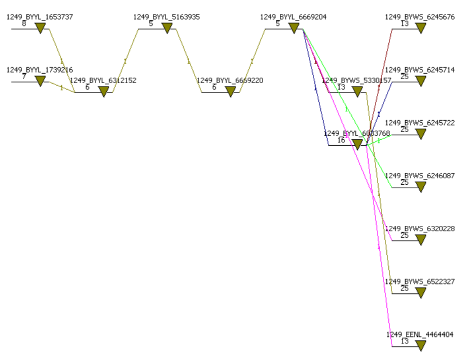

Figure A-17 Omega – Submodel2: Bulk

J. Service Level Segmentation and Demand Sensitivity Analysis

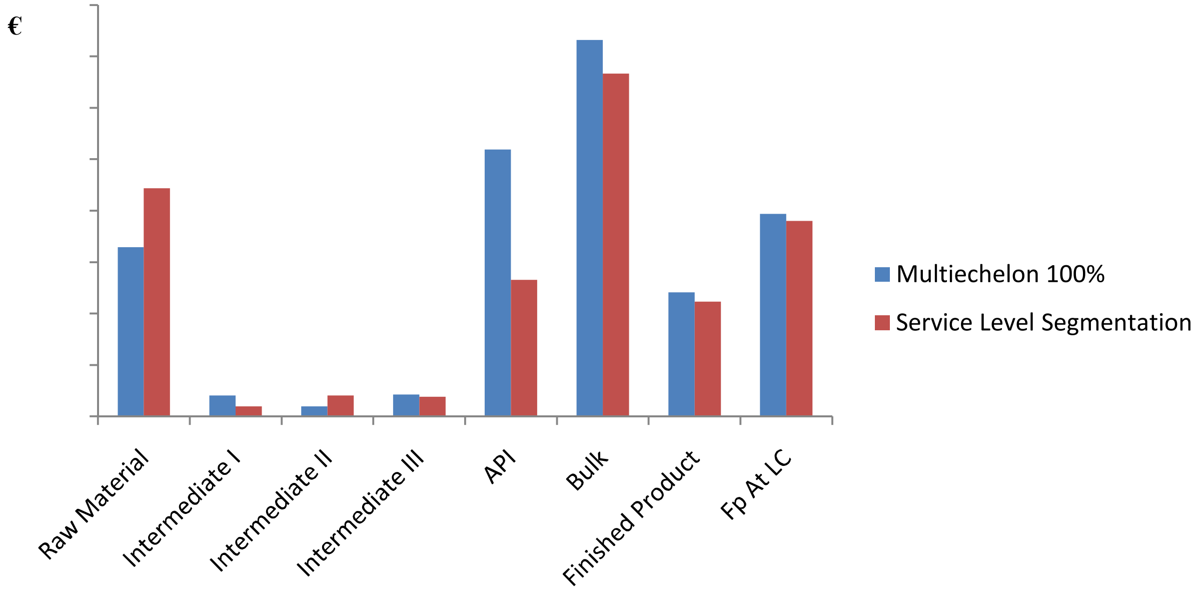

Figure A-18 Omega – Service Level Segmentation

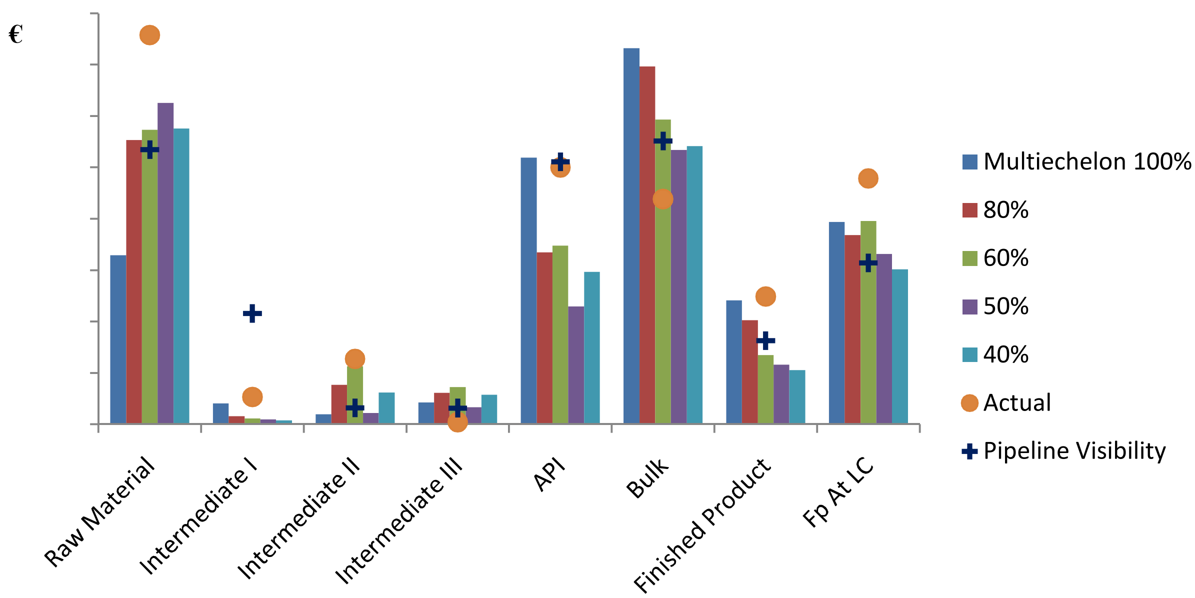

Figure A-19 Omega – Demand Sensitivity Analysis

K. Validation

In the figure A.20, a graphical representation of the tier approach for verification and validation is presented. In essence, the procedure consists on build the network in direction upstream-downstream step by step. For instance, in situation a, the demand after the fifth tier is aggregated according to the procedure described in section 4. An optimization run is performed and certain parameters are verified.

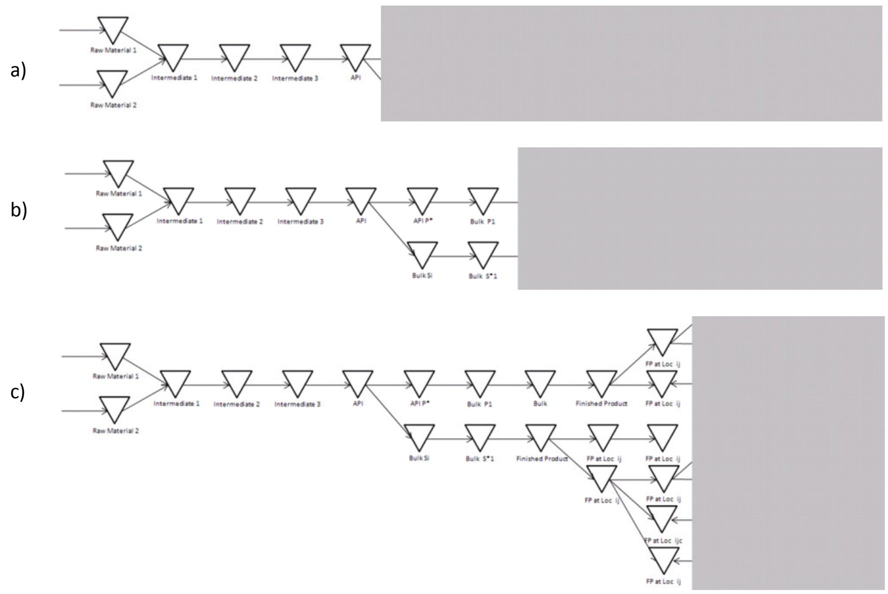

Figure A-20 Tier Approach

Table A-11 shows the deviation of the model characteristics with respect to the reference (pipeline visibility project or current planning parameters). The deviation is defined as follows: $\Delta_{v_y} = \left| v_{r_y} - v_{m_y} \right|$, where y is the tier in which the parameters are evaluated, v_{r_y} the reference parameter values, and v_{m_y} the model parameter values.

Table A-11 Model Deviation

	Product	Tier	Service Level	API Equivalence Factors	Ratio Pipeline/Total Target
Deviation	Omega	5	1%	0%	0%
		8	2%	0%	1%
		11	15%	0%	4%
	Aleph	9	5%	0%	1%
		15	3%	0%	0%
Reference	Omega	5	97%	-	8%
		8	97%	-	20%
		11	97%	-	20%
	Aleph	9	97%	-	6%
		15	97%	-	17%
Model	Omega	5	98%	-	8%
		8	99%	-	20%
		11	82%	-	23%
	Aleph	9	92%	-	7%
		15	94%	-	18%

The following tables show the ratio pipeline inventory/total target inventory for Omega and Aleph per different tiers.

Table A-12 Omega – Ratio Pipeline/Total

Tier	Model	Reference	Δ
5	8%	7%	1%
6	11%	10%	1%
7	16%	15%	1%
8	17%	16%	1%
9	19%	18%	1%
10	23%	20%	3%
11	23%	20%	4%

Table A-13 Aleph – Ratio Pipeline/Total

Tier	Model	Reference	Δ
6	5%	4%	0%
7	6%	6%	0%
8	10%	9%	1%
9	6%	5%	0%
10	7%	6%	1%
11	9%	8%	1%
12	11%	11%	1%
13	14%	13%	1%
14	14%	13%	1%
15	18%	17%	0%

L. Supply Network Optimization Initiatives and Main Operational Functions

Table A-14 Initiatives related to this project [GPC GSCM (2009)]

<table>
<tr><th>Initiative</th><th>Balanced inventory levels</th><th>Complexity reduction</th><th>Transparency</th></tr>
<tr><td>2</td><td colspan="3">Global Inventory Management</td></tr>
<tr><td>3</td><td colspan="2">S&OP Roll Out at BSP /Forecast Accuracy</td><td rowspan="3"></td></tr>
<tr><td>6</td><td>Pipeline Risk Assessment</td><td rowspan="2"></td></tr>
<tr><td>7</td><td>Inventory Target Setting</td></tr>
<tr><td>16</td><td colspan="2" rowspan="2"></td><td>GPC Supply Chain KPI</td></tr>
<tr><td>17</td><td>Pipeline transparency (API based)</td></tr>
</table>

The main aggregated operational functions related with supply chain planning for global pharmaceutical products and their main related tasks are [GPC GSCM (2009)]:

Demand Management:

- Demand forecast reconciliation (coherence, inventory, availability)
- Supply Network Planning

Purchasing

- Purchase requisitions for raw materials and packaging
- Toll manufacturers / subcontracted materials

Production Planning

- Rough-cut capacity planning
- Production planning: Master production schedule (MPS) and material requirements planning (MRP)
- Detailed sequencing and scheduling

Replenishment Logistics

- Sales order entry & processing, quantity allocation, order fulfillment

Inventory Management

- Finished and formulated bulk products, substance, raw materials and packaging
- *Target Stock Setting*

Logistics Services

- Forwarding, Export/Import Compliance Management, Shipping & Freight

M. Organizational implementation Restrictions

In this Section, the restrictions from an organizational perspective of a centralized model, presented by De Kok and Fransoo (2003), are discussed.

In terms of organization, there is no owner of the integrated model. Consequently, there is no responsible entity.

In this point, it has been stated that "Responsibilities within organizations tend to be dispersed over a number of people. The monolithic model assumes it is a single organizational unit deciding about a large number of details across the entire organization." Concerning this, it is true that a Top-Level hierarchy, feasibly, is not able to decide at any level of disaggregation. Nevertheless, it is possible to concentrate certain set o decisions in a Top-Level if the number of decisions is reduced and made meaningful through mechanisms of coordination between levels and the focus on critical variables. It is also important to reiterate the idea of Schneeweiss (2003), in the sense that a distributed decision making structure is mainly about mechanisms of coordination. This mechanism of coordination will not only reduce the number of decisions but also the complexity of them making possible the centralization of certain decisions.

In order to make more comprehensible this point, let's analyze the following example. The context is an automobile manufacturing plant. Looking backwards to the Hierarchical Features in Distributed Decision Making presented by Schneeweiss (2003), we have a scenario which presents a strong hierarchical character and multi-person situation. The Top-Level needs to make a decision based on a forecast of sales reduction. There is a Top Model, based on which an initial decision is made. The decision, e.g. the output of the model, is not concerned with all the downstream implications or responsibilities. The decision is just concerned with figures meaningful for the Top Level. Let's suppose in this example that the Top-level is just concerned with the Total Inventory Costs and the Structural Costs. This decision will be instructed to the Base-Levels 1 and 2 through an interaction/coordination mechanism. As initially mentioned, Schneeweiss (2003) differentiated at least four degrees of coordination from lower and higher levels of integration: Data integration, integrated systems through reactive negotiations, integration through planning activities and integration through leadership activities. Let's suppose that the one in this case is a reactive negotiation. In this case, the Base-Levels, through a mechanism, will disaggregate this initial decision, analyze the implications in the domain under the responsibility and react. In this example, the headcount, cost and damages lost, capacities will be verified by Base-Level 1 and safety stocks and transportation costs will be verified by Base-Level 2. They Base-Levels will react for example accepting the decrement in their budgets or request an addition. Finally, a closing decision will be made by the Top-Level.

As it can be seen in this example, even though there were 3 responsibilities involved and the integration level was low (reactive), first, the upper responsibility was just involved in the decisions meaningful for this level, and second, all the levels executed their decision responsibilities during the decision process. Consequently, the idea that a centralized model implies that a single organizational unit decides about a large number of details across the entire organization is not precise because it does not takes into account the coordination mechanism. The key is this coordination process. Here, it is necessary to reiterate the statement of Schneeweiss (2003), in the sense that the distributed decision problem is not only defined as separating a system into partial subsystems. In fact, it is mainly related with the task coordination within the system. The studies that consider an unfeasible implementation of a centralized control look at the decision problem just as separating into partial subsystems a system.

Even if an upper hierarchy would own the model. This would create several obstacles:

1.1. Detailed figures do not mean much to higher –level managers

1.2. Detailed figures of the model could be unreliable not only when they are describing future states of the system but also in the case of present states of the system. & 3.5. Models are just incomplete representations of reality. This incompleteness could be better controlled by a lower hierarchy directly involved in the process.

1.3. Centralized planning undermines the authority of lower hierarchies. As a result, the opposite effect –thus, a negative one - of empowerment is obtained.

3.4. Responsibility and decision authority are not aligned with the opportunity to control.

In relation to the first argument, the level of specificity is directly related to the requirements of information for performing certain task. In order to take decisions about relevant aspects of the entire supply chain, even the highest level would require certain level of exactitude. Nevertheless, it is clear that the Global Supply Director of a global company, in order to make a decision, will not precisely require knowing which is the stock of the piece A, in the rack B, of the warehouse C, in the small city D. Consequently, the level of aggregation of the information level should be the one that provides meaningful figures to the level. This can be achieved through another mechanism of coordination which will be treated below.

With respect to point 3.2, the same argument could apply to a decoupled model. Consequently, it would not imply an advantage of the decoupled over the centralized model. Now, if this point is related with the point 3.5, then, it could be argued that even if the figures are unreliable or the model is incomplete, this could be controlled by a lower level directly involved in the process. Nevertheless, here it could also be argued that a higher level, from a holistic perspective, could find some meaning in specific set of quantities that a lower level could not.

Regarding point 3.3, it is true that centralized planning under certain conditions could undermine the authority of lower hierarchies. Finally, under the assumption of a non-reactive lower level – which in general is not the case -, it could be considered the point 3.4 as true.

In order to overcome these difficulties, let's consider again the model of Schneeweiss (2003). Let's also suppose that we do have a centralized model in which the Top-Level hierarchy is the one controlling a specific variable V_{m3}, namely, safety stock. According to the model of Schneeweiss (2003), the Top-Level authority would take an initial decision, in this case, based on our one-significant variable COP model. This decision will not be implemented immediately, first because there is a lead time required for the implementation, but most important in this context, because the Base-Level will show certain behavior with respect to the decision according to the present coordination mechanism. This behavior will make the Top-Level to modify or hold the decision. Moreover, the Top-Level could determine the Anticipated Base-Model behavior based on certain model and reduce the divergence of perspectives between levels.

In the context of the previous example:

1. The Top-Level will take the decision of setting the safety stocks at certain level of aggregation meaningful for him based on a Top-Model. Let's suppose that for the Top-Level is meaningful

the total Safety Stock in a module in monetary units. The decision is that the Base-Level 1 will receive d1 as budget for safety stocks.

2. The Top-Level will expect certain behavior of the Base-Level based on an Anticipated Base-Model. The Anticipated model could be based in several factors but a rather simplified example could be:
    - If I assign a budget lower than d1 for the safety stocks of the Base-Model 1, the Base-Model 1 will deny the possibility of achieving a Service Level P1, carefully analyze his restrictions and will ask for d1.
    - If I assign a budget equal to d1 for the safety stocks of the Base-Model 1, the Base-Model 1 will deny the possibility of achieving a Service Level P1 and will ask for d2.
    - If I assign a budget higher to d1 for the safety stocks of the Base-Model 1, the Base-Model 1 will accept the decision.
3. The decision after applying the Anticipated Base-Model would be to assign to Base-Level 1 a budget slightly lower than d1.
4. The Base-Level would disaggregate the assignation for his analysis. Note that not only the low-level figures but also the high-level figures are meaningful for the Base-Level. The Reaction of the Base-level after analyzing its restrictions would be request d1.
5. The Final decision would be to assign d1.

Looking at this example, it can be seen that if a mechanism that works under the model of Schneeweiss is applied, first the restriction 3.2 and 3.5 would be overcome because the Base-Level is contributing with its expertise to build the decision. In case the Top Model fails, this would be corrected by the Lower-Level. In fact, in the example, the Top-Level “fails” on purpose and this is corrected by the Base-Level. In the same manner, points 3.3 and 3.4 would be undermined because the Lower level management would participate in the decision and it can relatively control which is the decision to be implemented. With respect to the point 3.1, the highest level model would work with aggregated figures meaningful for it. The decision could easily be disaggregated in figures tractable for the Base-Levels.

However, there is an important factor to take into account: the fact that the factual implementation of a decision has certain lead time. There are some strategies to reduce this lead time. One of them is to improve the Anticipated Base Model behavior so that the reaction lead time and final decision lead time could be shorter. Other could be to reduce the number of decision levels, so that the number of interactions is reduced. Another strategy, and probably the most relevant, is to generate mechanisms that produce a short lead time when both levels are interacting. For example, in our example again, the decision could be negotiated between Top-level and Base-levels in a planning sessions in which the Base-Levels should accept or present counterproposals. After the planning session, the decision is sanctified. In fact, usually, this is the way in which sales numbers are set, actually, based in rather inferior models than those used in Operations. There could be other options, but the main idea would be to generate mechanisms of agile interaction.

In conclusion, a comprehensive model is definitely feasible considering that: 1) Organizational restrictions can be overcome when implementing agile mechanisms of coordination between levels, 2) Its complexity can be substantially reduced when centralizing just relevant variables, and 3) A comprehensive model or at least partially comprehensive model with respect to a main variable could lead a better optimization of the capital investment in a system. This will be further supported by the analysis of certain models in the next section.