A Dissertation

entitled

Essays on Biopharmaceutical Supply Chains

by

Marouen Ben Jebara

Submitted to the Graduate Faculty as partial fulfillment of the requirements for Doctor of Philosophy Degree in

Manufacturing and Technology Management

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An Abstract of

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An emerging trend in the pharmaceutical industry is the *high level of personalization* of medicines that firms offer today. Such medications are expected to account for 50% of the amount spent on drugs by 2018. In conjunction with the growth of this new class of medications, firms are also continuing to serve markets for traditional (or small molecule) medications, which are often standardized or mass customized for consumer markets. Managing the diverse portfolio of medications can require different supply chain structures, specifically with respect to distribution channels. For example, the prostate cancer vaccine involves a reverse flow of raw material in the form of patient blood cells from the hospital/physician clinic to the pharmaceutical firm processing centers – a characteristic that is often not seen with traditional medications that are dispensed at the pharmacy or hospital. This has led to a new trend in the distribution channel practices for such medication, i.e. *supply chain disintermediation,* where the firm engages in a direct sales model, which means that the medication is shipped directly to the patient or the administrating facility (e.g. the physician's clinic/hospital) instead of being distributed through the traditional channel of wholesalers. In summary, firms today have a choice of

structuring their supply chains to have a traditional intermediated distribution channel, a direct disintermediated distribution channel, or combination thereof. However, little research exists that can guide managerial decisions with respect to the appropriate supply chain structure given the portfolio of the firm's medication offerings. The firm's choices for product portfolio and supply chain structure for distribution channels raise a critical question of *'what is the most appropriate supply chain disintermediation strategy given the firm's product portfolio?'* Therefore, in this dissertation, the research objective is to address this central question. In addressing this research objective, the dissertation is composed of four distinct essays.

The *first essay* is aimed at answering the above question conceptually. It maps the evolution of the pharmaceutical product paradigm along a continuum of standardized/mass customized/mass personalized products as well as discusses the evolution of the supply chain structure in terms of disintermediation for pharmaceutical firms. Drawing on literature in operations management in the areas of mass customization and supply chain disintermediation, as well as industry practices, the study presents a framework which identifies the appropriate supply chain structure (intermediated vs. disintermediated) given the level of personalization of pharmaceutical products.

Additionally, a critical characteristic of personalized (biologics) medicine is its time sensitive nature and consequent market mediation costs that make logistical design a critical issue. To understand how management science tools can guide managerial decision making, the *second essay* investigates this location decision problem for highly personalized products under a total disintermediation strategy assumption. Results based on the analysis of a case study are presented.

In addition to the time sensitivity and consequent market mediation costs that result from the short shelf life of personalized (biologics) products, firms also face varying levels of demand uncertainty for such products, making the disintermediation strategy decisions crucial. Therefore, the *third essay* aims to understand the behavior of the total market mediation costs, given the level of demand variability and the firm's supply chain disintermediation strategy. An evaluative study based on a scenario approach is presented. The results from a scenario approach analysis and a large scale numerical study provide insights about the appropriate supply chain disintermediation strategy given the pharmaceutical firm's product characteristics. The results shows the dominance of demand variability in shaping the total market mediation cost. High demand variability favors intermediated distribution channels, whereas disintermediation strategy is preferred when the shortage cost ratio is high. The contrast analysis provides evidence of the area of distribution strategy indifference.

Finally, recognizing that a pharmaceutical firm's choice regarding its product portfolio (standardized/mass customized/mass personalized products) and supply chain disintermediation strategy (intermediated/hybrid/disintermediated) has implications for its financial performance, the *fourth essay* aims to empirically assess the financial performance consequences of the fit between the firm's product portfolio and its supply chain disintermediation strategy. This essay empirically examines the relationship between disintermediation, product portfolio strategy, and financial performance. The results show that supply chain disintermediation positively impacts the firms' financial performance. Additionally, the alignment between product portfolio and supply chain disintermediation has positive effects on return on assets and gross margin.

This dissertation contributes to operations management literature in terms of conceptually, analytically, and empirically assessing how a firm's choices for product personalization and supply chain disintermediation individually and collectively influence its performance. It aims to provide actionable guidelines that can help firms match their supply chain disintermediation strategy with their product portfolio characteristics.

In Loving Memory of my Mother

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List of Abbreviations

SCD: Supply Chain Disintermediation

SL: Service Level

SC: Shortage Cost

WHO: World Health Organization

PSC: Pharmaceutical Supply Chain

DSP: Drug Shortage Program

FDA: Food and Drug Administration

CAS: Complex Adaptive System

CAGR: Compounded Average Growth Rate

R&D: Research and Development

PBM: Pharmacy Benefit Managers

CV: Coefficient of Variation

GM: Gross Margin

ROA: Return on Assets

ATurn: Assets Turnover

Chapter 1: Introduction

The pharmaceutical industry has evolved over the past century to become one of the biggest global industries, with sales exceeding 1 trillion dollars in 2013 and expected continued growth in 2014 (IBIS, 2014). The pharmaceutical industry is both a capital and labor intensive industry with high emphasis on research & development and innovation as critical success factors. The pharmaceutical industry represents an evolving innovative environment where organizations are competing over the exclusivity to provide a cure to patients. The drugs developed are then distributed to patients via a variety of outlets. Over the past few decades, the industry has experienced several structural changes that have impacted the pharmaceutical business model and its supply chain configuration.

The pharmaceutical product paradigm is shifting from more standardized and mass-produced goods to a highly customized product with a focus on serving one patient's specific needs. Pharmaceutical companies are not only offering standardized medication but are also providing more customized medication. Scientific evolution and the mapping of the human genome has enhanced the development of personalized medication. This new advancement has led to a more evolved type of medication scientifically referred to as Biologics (large molecule drugs). Unlike the traditional medicine (small molecule drugs), biologics represent highly customized products with high value proposition to patients. In some extreme cases, biologics are personalized and aimed at serving a patient's unique needs. Biologic medication can be distributed to patients via multiple distribution channels.

The pharmaceutical supply chain shows a strong influence of distributors and wholesalers on the distribution channels. Over 90% of the traditional medication is sold via distributors and wholesalers (Fein, 2012). Wholesalers provide the pharmaceutical supply chain with a higher level

of service by insuring the availability of the medication. The role of the distributor seems less relevant in a case of more personalized medication with a shorter shelf life. The current pharmaceutical supply chain is showing a shift to more direct distribution channels where the drug is shipped directly from the firm to the patient or the hospital. This new distribution trend is fueled by both product characteristics and quality concerns. This phenomenon is also known as supply chain disintermediation. Supply chain disintermediation (SCD) proved its attractiveness in retail and electronics, among other industries. While supply chain disintermediation represents an alternative for certain industries like electronics, it represents a unique choice for personalized products. For instance, Vista Print products are solely sold via direct distribution channels. However, the use of disintermediated distribution channels in the pharmaceutical field is gaining more importance from practitioners, especially with the emergence of more personalized medication.

1.1 Problem Statement

The pharmaceutical industry is moving away from a blockbuster business model to a more collaborative configuration based on innovation (Cooper, 2008). Biologic drugs represent an example of an innovative product with strong value proposition. Biopharmaceutical medicines are characterized by a high level of customization and personalization with greater focus on service as part of the product bundle value proposition. In many cases, a patient's inputs are part of the production process providing this particular industry with a unique setting. This unique setting has shaped the evolution of the pharmaceutical supply chain. Despite this debated attractiveness, biologics firms are not generating large profits and are, in many cases, failing to compete with larger corporations (Grabowski, Cockburn, and Long, 2006). Moreover, biopharmaceutical firms experience a high cost of goods sold due to the complexity of the production process as well as the

logistics cost. In fact, biologic medications require special handling and are time-sensitive. The biologics processing facility location becomes a critical factor that has an impact on the cost of goods sold and the quality of the service delivered. Additionally, biopharmaceuticals are characterized by a short shelf life and high demand variation. On one hand, the short shelf life combined with the high product value increases the perishability cost. On the other hand, the high demand variability impacts the shortage cost. The tradeoff between the perishability cost and the shortage cost will determine the supply chain configuration strategy. Unlike traditional medication where there is a clear answer for the supply chain distribution channel configuration, biologics firms are not able to crack the code for the optimal distribution strategy. While a disintermediated model will reduce the lead time and reduce the perishability cost, intermediated configuration will reduce the product variability effect and minimize the shortage cost. The adoption of newer distribution channels is fueled by high financial risk, varying demand, quality concerns, and special handling requirements.

1.2 Research Objectives

The dissertation work aims at analyzing the evolutionary changes of the pharmaceutical industry and supply chains configuration in the context of personalized medicine and its influence on biopharmaceutical firms' performance. First, the conceptual part of the study explores the evolution of the pharmaceutical supply chain and its interaction with the new paradigm of personalized medication. To provide more generalizable understanding, the conceptual part addresses the product paradigm shift and supply chain evolution in general context first and then apply it to the pharmaceutical industry's purpose. The research study aims at providing an original mapping of the evolution of the pharmaceutical products paradigm with more focus on personalized medication and the emergence of biologic medicine as a more personalized product.

The study also attempts to link the impact of product paradigm evolution to pharmaceutical supply chain distribution. The dissertation reconciles product personalization level with supply chain disintermediation for pharmaceuticals. Second, the study addresses the case of highly personalized medication with high disintermediation level configuration. Based on a case study, the study explores the strategic decision of the location problem for the case of highly personalized medication where the patient is a raw material supplier. Third, the dissertation explores the impact of the disintermediation level on the total market mediation cost. Using a scenario approach simulation and numerical analysis, the study aims at identifying the best disintermediation configuration for different demand patterns and shortage cost structure. Finally, the dissertation investigates the interaction of product personalization level and supply chain disintermediation and how it impacts firms' financial performance. Based on secondary data, the dissertation develops an empirical model to test for the fit between product configuration and supply chain configuration and how it influences a firm's performance.

The study contributes to the existing literature in supply chain and management research by providing a novel conceptualization of product paradigm. It draws on Kumar's (2007) work on personalization by providing a personalization level continuum and applying it to the pharmaceutical product context. The study also provides an extension of supply chain disintermediation studies and develops a novel reconciliation of product paradigm and supply chain disintermediation. Moreover, the study is among the few studies to address the problem of disintermediation using large numerical analysis. Finally, the study contributes to the work on disintermediation and alignment literature by empirically addressing the role of supply chain disintermediation on pharmaceutical firms' financial performance. This work elaborates on the conceptual foundations in order to empirically test for the impact of product paradigm and supply

chain structure on a firm's performance. This work develops and tests for a novel product paradigm and supply chain reconciliation.

The dissertation work contributes to the practice by providing more insights about some of the unexplored areas and delivers a clear and practical mapping of some of the theoretical concepts relating to personalization paradigm and supply chain disintermediation. Practitioners will find the answer to some of the critical problems relating to distribution strategy and will determine the most adequate distribution channels to use. Finally, the study is relevant to practice as it provides some insights about the impact of product structure and supply chain disintermediation strategy on a firm's current and potential future financial performance.

The dissertation is structured into four self-contained essays that will address the different problems discussed in the introduction. Chapter 2 presents the conceptual foundation of the study. Chapter 3 is a case study based on real data that addresses the location problem in highly personalized medication with totally disintermediated distribution channels. Chapter 4 is a numerical study that discusses the impact of the disintermediation level on the total market mediation cost. Finally, chapter 5 empirically addresses the interaction of product personalization level and disintermediation.

Chapter 2: Evolution of Pharmaceutical Industry: Product Paradigm and Supply Chain Configuration

2.1 Introduction and Research Objectives

The global pharmaceutical industry reached the key milestone of 1 trillion dollars in 2013, with a growth rate of 4% between 2007 and 2012 (IMS_Health, 2014). The pharmaceutical industry represents a major player in the healthcare landscape, as it provides patients with the appropriate medications. This industry was marked by several structural changes that have an impact on pharmaceuticals firms' value proposition and supply chain structure. The pharmaceutical business model is shifting from the blockbuster model, where a company will hold the exclusivity of a product for a long time via a patent, to a more collaborative integrative business model. The integrative model suggests that pharmaceutical firms will need to collaborate with different supply chain members such as suppliers and customers, as well as other competitors, to achieve and sustain a competitive advantage. Both the relaxing of regulations and the advancement of technology have facilitated the changes in the business model. The current regulations in the United States are reducing the barrier to entry by favoring generic medication production. The pharmaceutical industry has followed the manufacturing paradigm from crafted production to mass production, and then from mass customization to personalization (Hu, 2013). In fact, the pharmaceutical industry has witnessed the emergence of a new product segment called specialty pharmacies, which are mainly biologic medications. Biologic products have vague product specifications and, therefore, are hard to patent. The recent structural changes in the pharmaceutical industry have impacted the product paradigm and the supply chain configuration. Figure 2-1 provides a timeline of the pharmaceutical industry evolution.

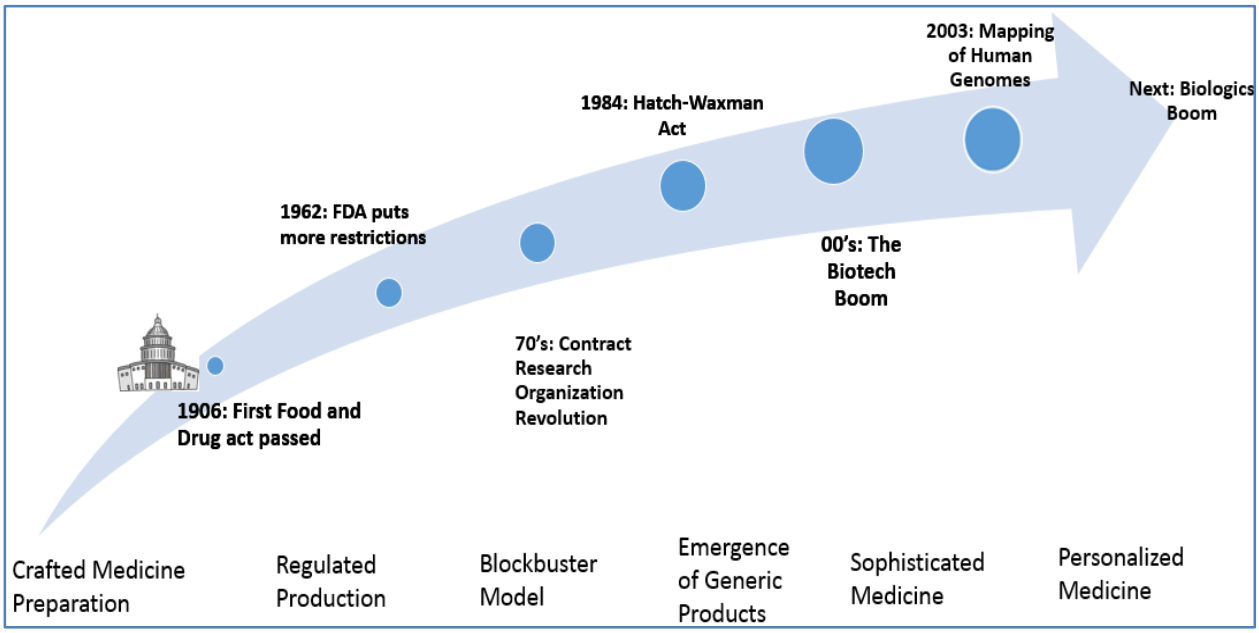

Figure 2-1: Pharmaceutical Industry Evolution

2.1.1 Evolution of the Pharmaceutical Product Paradigm

The evolution of the pharmaceutical industry and the emergence of specialty medication has shaped different product paradigms. The pharmaceutical industry has shifted from a crafted industry with its focus on production capabilities as the main competitive edge. The regulation of the pharmaceutical industry at the beginning of the 20th century marked the establishment of the blockbuster model. The pharmaceutical firms had engaged in mainly research contracts as a unique collaboration mechanism during the 1970s and 1980s. The Hatch-Waxman Act in 1984 reduced the barriers to entry by allowing generic medicine producers the license to replicate medicine. The beginning of the 21st century is considered to be the biotechnology boom in the pharmaceutical industry. More focus was accorded to highly sophisticated treatment with a strong emphasis on service as a value proposition. The mapping of the human genome in 2003 inside

Celera Corporation provided the pharmaceutical industry with an opportunity to develop new medication based on genetic material.

As noted above, and like many other industries, the pharmaceutical industry is moving towards a paradigm focusing on the one-to-one-marketing. In essence, the pharmaceutical industry is providing more personalized medication, creating significant implications for the way firms operate today. Biologics represent an example of a personalized medication with high value proposition. Pharmaceutical companies are offering more personalized products that meet specific patients' needs. Indeed, some biologic medications are highly personalized, requiring the patient input as part of the medication. This paradigm shift has been fueled by technological advancements enhancing customer input and making the patient a medicine co-creator, not simply an end consumer. The topic of personalization is gaining more interest as pharmaceutical firms seek new ways to deliver products and services and remain competitive. However, there is a lack of research attention addressing the issue of mass-personalization, especially in the context of the pharmaceutical industry. The emergence of new specialty medication has added more complexity to the supply chain configuration by increasing the level of financial risk and by creating closed looped physical flows. Specifically, the higher level of personalization creates additional complexities for the supply chain configuration from the perspective of distribution. In summary, the new product paradigm that calls for a higher level of personalization has impacted the pharmaceutical business model by requiring firms to re-evaluate their supply chain configurations.

2.1.2 Evolution of the Pharmaceutical Supply Chain

The pharmaceutical supply chain configuration represents an interesting area of investigation for practical and academic ends. The pharmaceutical supply chain has been following a traditional flat material flow (often referred to as a serial supply chain) with a strong emphasis on the distributors

and wholesalers as a major node in the network. The emergence of specialty medication (referred to as large molecule medication) has added a level of complexity that has significant implications for a firm's supply chain configuration. In fact, the specialty medications (such as biologic medication) are very expensive, have a short shelf life, require special handling, and necessitate prior approval from the payer (insurance, in most cases). These factors significantly increase the risk of perishability for the biologic medications. The higher levels of risk of perishability, as well as the higher level of customer inputs that are required for production of personalized medication, have significant implications on the structure of the downstream aspects of the firm's supply chain (i.e. the distribution channel). Specifically, this required firms to evaluate their strategy for going direct or for using disintermediation in their supply chain[1]. The topic of the pharmaceutical supply chain has been extensively studied in the field of operations and supply chain management (Koh et al., 2003; Papageorgiou, Rotstein, and Shah, 2001). Most of the studies addressed the security issues in pharmaceutical supply chains and the role of technology, as well as the pharmaceutical supply chain optimization (Shah, 2004a). Other studies also showed some interest in the pharmaceutical supply chain distribution channels (Muller et al., 2009). However, to the best of my knowledge, no prior study has addressed the structural changes to distribution channels of the pharmaceutical industry in the context of highly personalized specialty biologic medications. This represents a research opportunity and an area of study that this dissertation is aiming to address.

2.1.3 Key Research Questions

Business viability is highly tied to the firm's value proposition and its ability to provide unique value to its customers (Drucker, 2013). To cope with the structural changes of the industry,

[1] Given that the most significant supply chain configuration changes that can result from personalization of products would reside in the distribution channels (downstream supply chain), for the purpose of this dissertation proposal, supply chain configuration is used interchangeably with distribution channel configuration.

pharmaceuticals are now providing a different set of personalized products targeting specific types of patients. These products are distributed via traditional distribution channels as well as via alternative avenues. The new product paradigm which calls for highly personalized medication also calls for a strong emphasis on delivery of the medication (i.e. service) as a significant part of the value proposition. In essence, the highly personalized biologic products may be viewed as a product-service continuum. Researchers have extensively studied the product-service continuum (Vargo and Lusch, 2004; Zeithaml, 1981) and mass personalization (Kumar, 2007; Wang et al., 2011). The interaction between the product-service continuum and the personalization level represents an area of investigation that has received little attention in previous studies. There is some existing literature which has looked into aspects of pharmaceutical supply chain concepts (Pedroso and Nakano, 2009; Stadtler and Kilger, 2000). However, this literature does not investigate the role of personalization of medication and how it can shape the distribution channel configuration. Given that personalization of medication leads to a significant increase in complexity in the downstream supply chain (i.e. entities involved between the product manufacturer and customer), it is critical to lay emphasis on the distribution aspects of the supply chain configuration. Indeed, the involvement of the customer in the production process as well as the time sensitivity of medication perishability noted above make it critical for pharmaceutical firms to understand potential disintermediation opportunities that may exist for them as well as develop a strategy that can help them match their product portfolio with the appropriate supply chain configuration from the perspective of distribution. To the best of my knowledge, the current literature does not provide firms with an appropriate framework that can guide managerial strategies for distribution channel configuration to align with their product portfolio, thus representing a gap in existing literature.

In order to address this gap in literature, the current chapter aims to investigate a specific research question: What is the appropriate distribution channel strategy (with respect to disintermediation) given the level of personalization represented in the product portfolio of firms? Distribution channel strategy for disintermediation refers to the firm's choices with regard to maintaining intermediaries for the product flow from their manufacturing facilities to the customer (or hospital). Such a choice may be represented along a continuum of completely intermediated (traditional serial supply chain) to completely disintermediated (going direct). The level of personalization in a firm's product portfolio refers to the potential mix of medication in the firm's product portfolio along a continuum of highly standardized medication (at times referred to as small molecule medication or generic medication) to highly personalized medication (large molecule medication such as biologics).

In investigating the research question, the aim of this chapter is to provide a conceptual framework that links the level of personalization with the appropriate distribution channel configuration. Such a framework can guide managerial thinking as they assess the firm's distribution channel strategy, keeping in mind their product strategy. To develop such a framework, this chapter first provides a conceptualization of the customization-personalization and the product-service continuum. Second, the study presents an overview of the supply chain distribution channels configuration of small (standardized) and large (personalized) molecules medication. Third, a conceptualization of disintermediation continuum is developed. Finally, the chapter provides the framework that links the product standardization-personalization continuum to the disintermediation continuum.

The rest of this chapter is organized as follows: First, a synthesis of the relevant literature related to mass-customization & personalization and pharmaceutical supply chain is provided. In

the following section, the study provides a conceptualization of product paradigm and pharmaceutical supply configuration. The conceptual foundations also serve as guidelines for the following chapters. Finally, the chapter provides a framework that maps the two main paradigms under investigation: the pharmaceutical product personalization continuum and the supply chain disintermediation continuum.

2.2 Literature Review

The following section provides a summary of the literature review that relates to mass customization & personalization and pharmaceutical supply chain. The aim of this section is to summarize the most relevant work to the study and emphasize the gap in the literature that this chapter is addressing. The literature review section addresses the mass customization & mass personalization and pharmaceutical supply chain.

2.2.1 Mass Customization and Mass Personalization

The area of mass customization and mass personalization has been of interest to scholars as a new product paradigm. The following subsection provides an analysis of the literature review and comparison analysis between the concepts of personalization and customization.

2.2.1.1 Mass Customization

In his book Future Perfect, Davis (1987) first introduced the term "mass customization." The book did not put a large emphasis on mass customization (MC). Marketing researchers were among the first to adopt the concept of mass customization and study it more in depth (Kotler, 1989). Mass customization started gaining some interest in Operations Management in the mid-90s (Pine and Davis, 1999; J. Pine, 1993). Pine (1993) defined MC as a firm's ability to deliver individually customized products at low-cost with minimum required quality at a large volume. Mass

customization corresponds to "producing goods and services to meet individual customers' needs with near mass production efficiency" (Moser, 2007). Mass customization should be seen as a process for aligning an organization with its customers' needs through the development of a set of certain capabilities such as process design (Salvador, De Holan, and Piller, 2009). This alignment suggests that the mass customization happens across different levels of the supply chain players.

Levels of Mass Customization: Mass customization can occur at various levels of the value chain. Mass customization can be viewed in a continuum where the product/service can be purely standardized to purely customized (Lampel and Mintzberg, 1996). A product is designed, produced and finally distributed. The purely customized product will have customization activity at each stage of the value chain (Gilmore and Pine 2nd, 1997; Lampel and Mintzberg, 1996). Pine (1997) proposes five stages of modular production: customized services (standard products are tailored before the delivery process), embedded customization (standard products are changed by customers during use), point-of-delivery customization (more work is performed at the point of sale), delivery customization (short time delivery of products), and modular production (wide configuration of products and service) (B. J. Pine, 1993). Mass customization can be also divided into four types based on the focus of the customization: customized packaging, customized services, additional custom work, and modular assembly (Spira, 1993). The levels of mass customization are among a large set of work from an operations management perspective.

Mass Customization in Operations Management: In the context of Operations Management, Mass Customization refers to the ability to rapidly produce customized offerings with quality and costs similar to those achieved by the mass production approach (MacCarthy, Brabazon, and Bramham, 2003). Mass customization has interested the core of research in the past decade with an increased number of research and studies focusing on mass customization. Tu et

al. (2001) addressed the role of mass customization as a capability. In fact, while facing dynamic product and process change, firms would have to develop a higher level capability to maintain a competitive advantage (Tu, Vonderembse, and Ragu-Nathan, 2001). Organizations have utilized multiple operational practices such as Time Based Manufacturing Practices as mass customization enabler (Koufteros, Vonderembse, and Doll, 1998; Tu et al., 2001). The impact of information technology on mass customization capability has been the subject of very few empirical examinations (Peng, Liu, and Heim, 2011). Peng et al. (2011) addressed the theoretical relationship between four types of IT applications with MC capability. Moreover, scholars have looked to the impact of work design on mass customization capability based on sociotechnical system theory (Liu, Shah, and Schroeder, 2006). Organization learning scholars showed some interest in investigating the impact of organization learning and mass customization capability development (Huang, Kristal, and Schroeder, 2008). Huang et al. (2008) investigated the role of learning and effective process implementation in the development of mass customization capability. More recently, scholars started focusing on service mass customization (Moon et al., 2011). Moon et al (2011) developed a method for designing customized families of services using game theory to model situations involving dynamic market environments. The designing process was inspired by the manufacturing modularity to provide customized services.

2.2.1.2 Mass Personalization

The recent business trend is shifting from the mass customization to profitably serving one market (Kumar, 2007). Kumar (2007) emphasized the strategic shift from mass customization to mass personalization, where companies will position themselves in the "personalization spectrum." This transformation is feasible because of the development of the Web 2.0, modern manufacturing systems, and modularity and delayed differentiation (Kumar, 2007). In fact, companies that

employ Web 2.0 succeed in productive customer integration enabling personalization (OReilly, 2007). Second, flexible manufacturing cells, modularity, and delayed differentiation increase the firm's potential to develop mass customization capability (Kumar, 2004; Lee and Tang, 1997).

Personalization Process: The marketing literature offers foundations for addressing personalization issues. The body of literature proposes mainly three frameworks of the personalization process (Vesanen and Raulas, 2006). Even though the three approaches appear different, each model suggests customers as a starting point with a minimum level of interaction to determine the customer's personalized need. The data is then processed to create a customer profile. Finally, the personalized product/service is delivered to the customer. The model suggests the creation of loops to guarantee the quality of the personalized product/service (Adomavicius and Tuzhilin, 2005; Murthi and Sarkar, 2003; Pierrakos et al., 2003). In fact, the customers' feedback represents the main point that separates customization from personalization. The mass personalization process suggests different dimensions aside from the customer inputs and feedback.

Dimensions of Mass Personalization: The concept of mass personalization is still under investigation by researchers. While there is no consensus on the main dimension of mass personalization, recent studies have attempted to provide some insights about the matter (Zhou, Ji, and Jiao, 2013). First, mass personalization reflects the market for one customer, which requires the product fulfillment to be changeable, adaptable, and configurable (Wiendahl et al., 2007). The second dimension relates to mass efficiency by bringing more value to both customers and producers in a cost effective way (Zhou et al., 2013). Third, mass personalization involves intensive interactions with customers from the product/service design as well as a total life cycle involvement (Jiao, 2011). This is referred to as co-creation. Finally, mass personalization is

characterized by a particular user's experience. Mass personalization goes beyond exploring market potential; it addresses customers' latent needs (Zhou, Xu, and Jiao, 2011). The four dimensions explained emphasize the difficulty that companies are facing to successfully shift to more personalized products and services.

Implementation Issues in Mass Personalization: The process of product/service personalization is challenging and requires some technical work, such as providing specific personalization algorithms and patterns of actions within personalization systems (Fang and Salvendy, 2003; Fink et al., 2002). While the personalization issues were not addressed yet to a great extent in the operations management literature, the marketing field and, specifically, the e-commerce related body of literature has been investigating personalization for over a decade (Adolphs and Winkelmann, 2010). The personalization process as described previously requires customers' and users' inputs, data processing, and customer feedback. In the context of ecommerce, more issues need to be addressed mainly related to recommender systems and mass customization. Recommender systems or comparison shopping systems will provide customers with suggestions that will reflect the customers' personal preferences and profiles (Ricci and Werthner, 2006). The customer input for ratings, recommendations, and reviews are very critical to the performance of the personalization process. Moreover, Adolphs and Winkelmann (2010) emphasized the importance of achieving mass customization as a gateway to realizing personalization. Mass personalization is perceived as a high level capability that is achieved through mass customization, a lower lever capability. The study, however, did not provide any empirical proof to support this statement. The literature had also addressed other issues related to personalization such as data analysis and data processing. These parts are highly technical and address different algorithms for data mining and profile processing (Schubert, 2003). The set of

challenges have evolved into more specific constraints that organizations are facing and scholars have identified.

Classifying Personalization Constraints: The adoption of a personalization strategy is marked by a series of constraints that make the process more challenging. First, some constraints are related to the process of adoption itself (Adomavicius and Tuzhilin, 2005; Vesanen and Raulas, 2006). These problems relate to implementation dynamics. Second, firms are limited by the technology available when collecting and processing the data and delivering the product/service (Harnisch, 2013). Finally, organizational capability represents a major restriction to the personalization success. Harnisch (2013) classified the constraints into three dimensions: origin (internal, external), subject (technological, organizational), and time (data collection, matchmaking, delivery). Despite this set of constraints and challenges, some organizations were able to achieve mass personalization and put serving the market of one customer as their main strategy. Several examples from manufacturing contexts are identified.

Personalization in Manufacturing: Numerous examples can be provided dealing with personalization in the manufacturing industry. Personalization is widely used in clothing industry. Nike Inc. was among the pioneers in the industry to provide personalized shoes. In 2001, Nike offered its customers the opportunity to add a personal message on their shoes. The personalization level has increased since then, reflecting a higher level of manufacturing capabilities and engaging more advanced manufacturing systems. Customers can participate in 3D garment design by choosing particular components to construct their own garment. Additive manufacturing is another technical definition of the 3D printing. Additive manufacturing is a disruptive manufacturing technology that revolutionized the production of mass personalized clothing (Reeves, Tuck, and Hague, 2011; Wang et al., 2011). Vista Print and other online printing service providers achieved

the capability of delivering unique products to their customers. The website capabilities allow the customer to make a variety of selections to personalize the product. Vista Print also suggests some personalized related products when placing an order of business cards or event invitations.

2.2.1.3 Mass Customization vs. Mass Personalization

The concept of personalization was the subject of extensive research in the area of marketing (Allen, Yaeckel, and Kania, 1998; Coner, 2003). While some researchers consider personalization as a higher level priority than customization (Hanson and Kalyanam, 2007), others argue that customization is a form of personalization performed by the customers (Roberts and Zahay, 2003). The following Table 2-1 summarizes the difference between customization and personalization.

Table 2-1: Personalization vs. Customization

Personalization Vs. Customization			
Personalization	**Customization**	**Interrelationship**	**Reference**
A specialized form of product differentiation, in which a solution is tailored for a specific individual	The combining of individual-level information and flexible product design	Customization is part of personalization and different levels of personalization create a continuum	(Hanson and Kalyanam, 2007)
Customizing some feature of a product or service so that the customer enjoys more convenience, lower cost, or some other benefit	Treating a particular customer differently based on what that customer said during an interaction	Not important to distinguish between personalization and customization	(Peppers and Rogers, 2012)
The ability of a company to recognize and treat its customers as individuals	Customization includes individualization of features, e.g., Web-site content, by customers	Customization is part of the personalization concept	(Allen et al., 1998)
Personalization can be initiated by the customer or by the firm	Customization further developed into customerization while the business strategy is customer centric	Customerization is a more advanced form of personalization	(Imhoff et al., 2001)
Personalization is performed by the company and is based on a match of categorized content to profiled users	Customization is performed by the user	Customization is a form of personalization which is done by the customer.	(Coner, 2003)
The process of preparing an individualized communication for a specific person based on stated or implied preferences	The process of producing a product/service to the exact specifications/desires of the purchaser	Customization is more in-depth individualization than personalization	(Roberts and Zahay, 2003)

The mass customization & mass personalization literature section identified the major work in that area and had emphasized the dynamics of the shift of the new product paradigm. While the literature review showed a rich content exploring the dynamics of mass customization in the context of operations and supply chain management, the study of the mass personalization is still lacking some extensive work in the manufacturing context despite the attractiveness of the concept (Zhou et al., 2013). The mass customization & personalization paradigm represents an opportunity

for an investigation from the operation and supply chain angle. While some conceptual and empirical work attempted to study mass customization and personalization in a manufacturing context (Jiao, 2011; Tu et al., 2001), very few studies have investigated the paradigm in a service oriented context. A recent study pointed out the managerial impact of mass personalization in the healthcare context. Very few studies have looked at personalization in healthcare service delivery (Chaudhuri and Lillrank, 2013). The healthcare field represents an interesting area of management studies, which is relevant in both academia and practice. The pharmaceutical industry represents a major segment of the healthcare field. The pharmaceutical supply chain represents an area of research that can be linked to mass customization & personalization paradigm.

The following subsection provides a literature review of the pharmaceutical supply chain. The literature review subsection is intended to identify the major findings relevant to both the evolution of the pharmaceutical supply chain and how it can relate to the mass customization & personalization paradigm.

2.2.2 Pharmaceutical Supply Chain

Several studies from the operations management field have investigated different aspects of the pharmaceutical supply chain. For over two decades, the financial performance of the pharmaceutical firms has interested several empirical studies by exploring profitability, research intensity impact, and the role of mergers and acquisitions in financial viability. These studies have explored the dynamics of the pharmaceutical supply chain and have explored the role of certain factors such as Information Technology. More recent studies have addressed the structural changes in the pharmaceutical industry and how it can shape the future of pharmaceuticals.

2.2.2.1 Pharmaceutical Supply Chain Dynamics

Profitability and Optimization: The pharmaceutical industry is considered to be among the most profitable industries, as measured by return on investment in R&D. The return on R&D expenditure is relatively high due to extensive innovation (Grabowski, Vernon, and DiMasi, 2002). The crucial role of innovativeness urged researchers to investigate the new product development key success factors as well as the role of environmental factors. Older studies addressed research productivity and a firm's size impact on new product success (Henderson and Cockburn, 1996). More recent studies have developed a new product cost analysis by determining the cost of the different stages of the product development (DiMasi, Hansen, and Grabowski, 2003). Optimizing the supply chain configuration remains among the ultimate goal for firms in general and for pharmaceuticals in particular. Shah (2004) proposed a list of issues to take into consideration while optimizing the pharmaceutical supply chain. These issues are related to facility location and design, inventory and distribution planning, capacity and production planning, and detailed scheduling. Supply chain "debottlenecking and decoupling strategies" and inventory management are crucial for the viability of the firm in a rapidly changing market (Shah, 2004a). To my knowledge, no prior studies have addressed the pharmaceutical profitability and product paradigm issues.

Security Issues in Pharmaceutical Supply Chain: Because of the critical nature of the pharmaceutical industry and the high regulation, security issues in the supply chain are extremely important. The main issue related to security is the risk emerging from counterfeit products. In fact, The World Health Organization (WHO) estimates that between five and eight percent of the worldwide trade in pharmaceuticals is counterfeit (Koh et al., 2003). In a more global environment, and with the development of new distribution channels such as online, patients have access to

counterfeit medicine. For example, the amount of counterfeit drugs in the European market increased enormously in the past years (Schweim and Schweim, 2009). Moreover, motivated by quality concerns and pressured by regulatory directives, pharmaceutical firms are urged to address this issue. The security issues have created more possible distribution channels such as direct sales in an attempt to minimize the health risk and guarantee high quality for patients.

Most of the solutions that pharmaceutical firms were using rely on quality control and manual inspection of the medicine. These techniques are considered "static" and inefficient to prevent counterfeit practices from happening (Koh et al., 2003). New techniques were proposed by some scholars and for the most part, they call for the use of information technology systems as a major enabler. First, the use of a unique medicine identifier powered by an information system database was proposed as a solution to reduce the counterfeit risk (Muller et al., 2009). The study proposed a simulation model showing the evolution of a product with a unique identifier in the supply chain. More effort should be done at the regulators' side to minimize the distribution of counterfeit medicine in non-authorized distribution channels. In fact, according to the WHO, more than 50% of the medicines purchased from illegal websites are counterfeit. Second, RFID tags are another alternative to track the medicine and guarantee that it is not counterfeit (King and Zhang, 2007; Koh et al., 2003). RFID tags are more appropriate in the context of a pharmaceutical supply chain given the complexity level and the amount of information a package can contain.

Information Technology in Pharmaceutical Supply Chain: Information Technology (IT) is a crucial factor in supply chains but more so in the pharmaceutical industry. In fact, pharmaceutical companies have used IT to prevent counterfeit products (Koh et al., 2003). After that, the use of IT developed into a more integrative and decision making role in the supply chain. Scholars have investigated the importance of the use of RFID as a new IT tool in addressing PSC issues (Kumar,

Kadow, and Lamkin, 2011). RFID technology is a critical success factor for creating a more effective pharmaceutical supply chain (Yue, Wu, and Bai, 2008). Moreover, IT improved the negotiation process in the supply chain in order to maximize the value to customers (Konstantinos, Vrassidas, and Dimitra, 2008). Konstanitos et al. (2008) have also proposed a supplier selection framework emphasizing the role of IT as the connecting element. Finally, the shift in the pharmaceutical industry from revenue-centered to value- and collaboration-focused relies on IT as an important factor (Cooper, 2008). In fact, health 2.0, which is the use of a specific set of Web tools by actors in healthcare, including doctors, patients, and scientists, in order to personalize healthcare, collaborate, and promote health education, will be the new trend in healthcare in general and the pharmaceutical industry specifically (Cooper, 2008; Hughes, Joshi, and Wareham, 2008).

The emergence of IT in the business landscape in general and the pharmaceutical industry in particular is promoting a major paradigm shift. The health 2.0 initiative will constitute an enabler for a more personalized health care delivery system. The body of literature has emphasized the importance of IT in the pharmaceutical industry without addressing how it can enable the shift to more personalized medication and direct sales strategy. Even though the role of IT is outside the scope of this study, it was judged important to point it out because it represents an important piece of the personalization enabling tools in pharmaceuticals. Moreover, IT is a major component of the pharmaceutical direct sales model, as it helps patients order their medication.

2.2.2.2 Structural Change in the Pharmaceutical Supply Chain

The changes in U.S. regulations and the Medicare/Medicaid reimbursement process have changed the impact of some external players, such as third party logistics providers (Reisman, 2002). This change in regulation is endangering the role of wholesalers in the pharmaceutical

supply chain (Mullin, 2003). Shah (2004) emphasized the important role of the immerging distribution channels such as direct shipping and mail order as cost savers. Furthermore, the Hatch-Waxman Act, which encouraged the manufacturing of generic medicine has also changed the landscape of the pharmaceutical industry and impacted the pharmaceutical supply chains. Figure 3 shows the evolution of the brand/generic drugs mix. The transition to generic products means lower profit margins, higher stock keeping units, and higher demand variation.

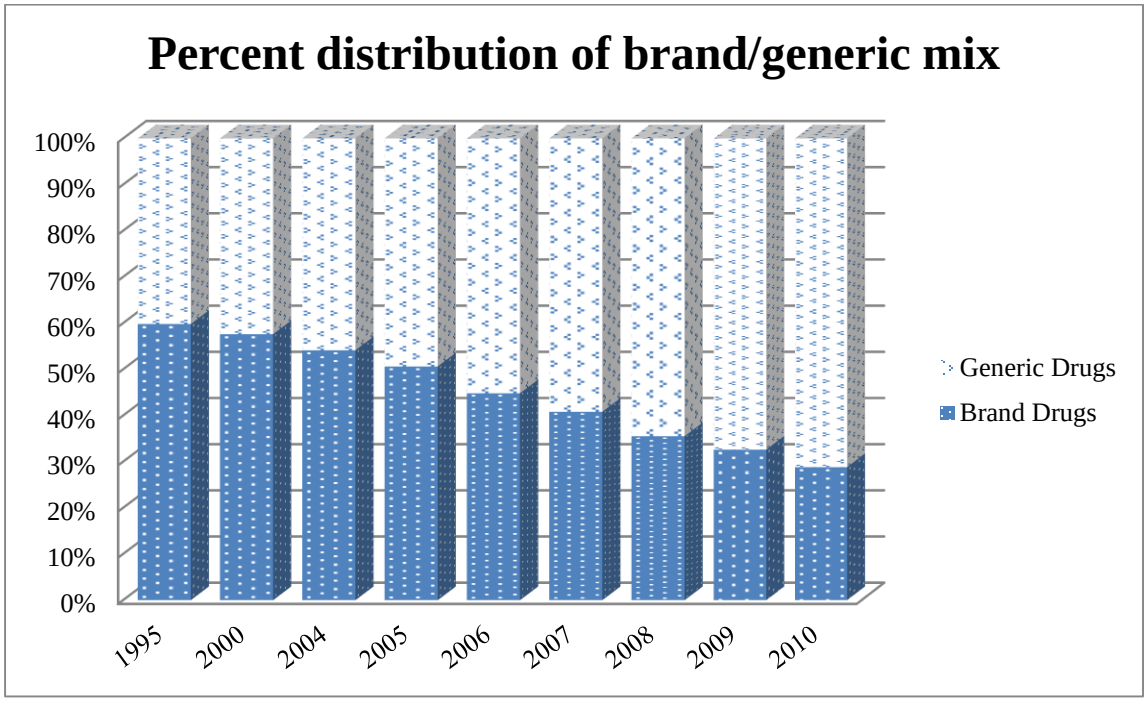

Figure 2-2: Brand vs. Generic Drugs

Moreover, biologics and biotechnology products in particular represent now a major product in the pharmaceutical industry. In 2012, the biological products accounted for 19% of the total pharmaceutical industry, and it is expected to grow substantially in the next years (Yang, 2013). Biotechnology pharmaceuticals are characterized by higher contingencies and interdependencies, which makes the application of the traditional supply chain models harder (Goetschalckx, Vidal, and Dogan, 2002). The pharmaceutical industry is becoming more global, diverse, and complex. This has an impact on the pharmaceutical value chain from the development

of a new drug to the marketing of the products (Papageorgiou et al., 2001). Given the high cost of R&D and the reduced profit margin, pharmaceutical companies are required to optimize the introduction of a new product given the existing capacity and the required investments. Papageorgiou et al. (2001) proposed a mixed integer programming aiming to optimize the problem and provide the most adequate configuration.

Finally, the changes in the regulations and the effect of the different players in the supply chain make the conceptualization of the PSC more complicated. Rossetti et al (2011) identified three main forces: compensation forces, channel forces, and product and regulatory forces. The pharmaceutical supply chain is conceptualized as "a complex adaptive system (CAS) (Choi, Dooley, and Rungtusanatham, 2001) whereby agents (participants) in the PSC are coupled in a value chain of production, and any agent's actions can potentially affect any other agent" (Rossetti, Handfield, and Dooley, 2011).

Challenges Facing Pharmaceutical Supply Chain: The standard Supply Chain strategy models are not easily applied to the PSC. First, the industry is shifting toward a higher personalization level of product with high shortage cost and strict expiration rules. Second, the separation of consumers (patients) and the customers (insurance companies and government) makes the application of traditional SC practices more challenging (Rossetti et al., 2011; Teisberg and Porter, 2006). Finally, the longer lead time, the high unpredictability demands, and the large number of intermediaries contribute to more uncertainty in the PSC (Goetschalckx et al., 2002).

The literature of the pharmaceutical supply chain had also emphasized the new pharmaceutical firms' practices as another challenge. Distribution strategy was proposed as one of the prominent challenges that the pharmaceutical industry is dealing with. Despite the domination of indirect distribution modes (via wholesalers and distribution centers), about 13 percent of orders

are shipped directly to chain stores (Gautrin, 2002). This change in the distribution mode will represent a supply chain configuration issue (e.g. ordering, storing, and logistics). Moreover, the current pharmaceutical business model is focusing on securing and protecting the Intellectual Property. The "Blockbuster Model" will ensure the firm's financial viability. However, with most of the blockbusters' medicine patents already expired or expiring soon, pharmaceutical firms will need to revise their strategy and give up the profit alone model (Cooper, 2008). In fact, the profit alone model can be described as "A model where you are guaranteed to lose your entire book of business every 10 to 12 years," according to J.P. Garnier, former chief executive of GlaxoSmithKline. Pharmaceutical viability will depend on the firm's ability to develop a collaborative business model.

Financial performance is an indicator of the business model viability. Although the pharmaceutical firms are showing one of the highest profit margins among the industries (Teisberg and Porter, 2006), the recent trends are not showing positive results. Between 1985 and 2000, the top 15 pharmaceutical and biopharmaceutical firms were able to generate high returns to their shareholders, measured by the compounded average growth rate (CAGR). In fact, eleven out of fifteen firms had a CAGR higher that S&P 500. The same firms, between 2000 and 2010, however, were unable to outperform the market. Only 3 firms had a CAGR higher than the market and ten firms had a negative CAGR (Ajay, Matthias, and Martin, 2012). This is mainly due to the high cost of R&D, the long process of new drug approval, and the fact that most low-hanging fruit had already been picked.

The literature review of the two main concepts investigated (pharmaceutical supply chain and mass customization and personalization) informs us about the relevance of the matter. It also

shows a gap in the literature that is addressed in the chapter research questions. The following section addresses the various areas of investigation.

2.3 Conceptual Development

The literature review section has identified the major findings and areas of research related to mass personalization. The current section expands the existing literature review by providing an investigation of the new product paradigm (more personalized product with higher service level) in the context of pharmaceutical products.

2.3.1 Customization and Personalization Continuum

The issue of mass customization and mass personalization in the area of pharmaceutical industry is not as recent as it appears to be. While very few academic researchers have investigated mass customization in a pharmaceutical context, practitioners have been calling for mass customization and mass personalization as the new trend in the pharmaceutical industry for over a decade. Mass customization in medicine will allow pharmaceutical companies to build a competitive advantage and customer allegiance (Fitzgerald and McLaughlin, 2001). With a reduced profit margin and less productive R&D activities, pharmaceutical firms are required to customize their products while keeping the cost of production low. Specialized journals in the medical field have emphasized the role of personalized medicine as an emergent practice in the pharmacogenomics area (Mette et al., 2012; Xie and Frueh, 2005). The concept of mass personalized medicine was investigated in the area of cancer treatment, dental medicine, and pain medicine. (Eng et al., 2012; Kim and Dionne, 2009; Xie and Frueh, 2005).

The mass-production and mass-customization continuum as developed by Salvadore et al. (2009) illustrates how firms can move along the continuum and what different capabilities are required. The current chapter proposes to extend the existing continuum by adding the

personalization paradigm. The extended continuum will be referred to as the personalization continuum. The continuum varies from purely standardized products and services to highly personalized ones. Firms will position themselves along their value proposition. In a manufacturing context, a firm can decide to provide a standardized product that aims to serve a large customer base with no preference differences. Many products are standardized and do not require any changes. This type of product is usually mass produced and delivered to customers. On the other end of the continuum, highly personalized products aim at serving a unique customer. This type of products portfolio is highly competitive and critical to manage. Very few firms have captured the power of mass personalization and were able to provide a set of products that vary along the spectrum (e.g. Vista Print, Nike). The personalization continuum is easier to assimilate in a product paradigm where the market has showed a variety of examples along the continuum. The personalization continuum can also be applied in the healthcare context. The literature review section has discussed mass customization & personalization in the healthcare delivery context.

The healthcare industry is among the most complicated and labor & capital intensive segments. The variety of products and services provided are in some parts standardized, yet need to meet some unique patient specifications. Hospitals, for example, provide some standardized procedures such as weight check and blood pressure as well as more personalized ones that addresses the patient's particular case. The pharmaceutical industry represents a major player in the healthcare landscape with different products paradigms. While some medications are purely standardized, where all patients take the same medication regardless of gender, age, blood type, on the other side of the personalization continuum, some medications are prescribed based on patient specifications, thereby making it more personalized. The pharmaceutical industry is now

offering extreme customized medication, where there is one exact medication for each patient. This type of medication, like the products, are critical to administer.

The personalization continuum illustrates an organization's value proposition and how firms could determine their product portfolio. In the context of healthcare management, a strong emphasis on service is provided as part of the value proposition. In fact, the healthcare industry is highly service oriented. Even pharmaceuticals, which represent highly goods-focused organizations, are providing service as part of their value propositions. The next section focuses on the service product continuum.

2.3.2 Product-Service Continuum

The new value proposition requires an organization to provide combined products and service components. Most of goods today are a combination of products and services (Bateson and Hoffman, 1991). The goods/service continuum was first introduced by Johnson in 1969. Products are perceived as a goods-service bundle, and the consumer choice is based on evaluation of these criteria (Johnson, 1969). Several studies since then have attempted to measure the level of service component vs. the goods one on the bundle (Murray and Schlacter, 1990; Parasuraman, Zeithaml, and Berry, 1985). Operations management scholars have shown an interest in the product-service continuum as important to better understand supply chain dynamics (Jacobs and Chase, 2010). Most of the studies have identified four segments within the continuum: pure goods, core goods, core services and pure services. Pure goods, such as commodity products, have a minimal service element where the purchase decision is based purely on product assessment. Pure services, such as legal consulting, have a minimal product component, except for a documentation or a report. Most of the value derives from the service. Most of the products have a combination of goods and service such as restaurants or car service.

Many studies have investigated the continuum by looking into more aspects. Murray et al. (1990) have looked into the risk and reliability aspect of the product service continuum. They found that the intangibility aspect of service makes consumers more risk averse to evaluating the value of services. Customer satisfaction is impacted by the position of the product within the continuum as the consumer perception of reliability of the product (Anderson, Fornell, and Rust, 1997). More recent studies have attempted to map the continuum across other variable. For example, the goods-service continuum has been investigated across possession utilities for retail industry (Winsor, Sheth, and Manolis, 2004).

The next subsection will provide a new mapping of the product-service continuum across the personalization level spectrum. To my knowledge, no prior study has attempted to conceptually reconcile the two concepts. This chapter attempts to link the mapping to the essence of this study by applying the mapping to the healthcare concept.

2.3.3 Mapping the Personalization and Product/Service Continuum

The product/service continuum can be combined with the level of personalization continuum. The following subsection will map the continuum for both general cases and the healthcare context.

2.3.3.1 General Context Mapping

Figure 2-3 has mapped the two different continuums for the general product/service context. Commodity products are 100% standardized with no service component as part of the value proposition. Sugars, wheat, and other commodities represent a typical standard product. Moving along the personalization continuum, more customized products will reflect customers' choices and specifications. Personalized shoes and other gadgets will represent an example of highly personalized products. The mapping will also combine the service level. Make to measure clothes

are more customized products with a service component since there is a strong interaction between the customer and the service provider. In the extreme personalization level, bespoke, which are a type of clothes that are designed for only one person, represents an evolution of the made to measure clothes in the personalization continuum. Other relevant examples in the product/service mix can be derived from the food industry. Fast foods, for example, tend to be more standardized in comparison to restaurants. Despite a difference in the level of service provided by restaurants and fast food, they are both located at the service/product mix with a different personalization level. Finally, on the high service level extreme, high school education is, in general, standardized in order to allow the students access to colleges. More customized services are consulting services, such as legal and taxation, among others. The service provided will depend on the customers but will have some standardized component. Website ads are highly personalized services provided to computer users. In fact, when a user is browsing on the internet, information is stored regarding preferences and needs. Web ads will be displayed according to these specifications. For example, when an internet user searches for a hotel in a city or a treatment for a skin problem, a list of relevant advertisements will be showing when he is surfing the website. The emergence of these web ads is now amplified by the use of smart phones and their capabilities to capture and follow users' preferences.

The mapping for the general goods/service context is shown in figure 2-3.

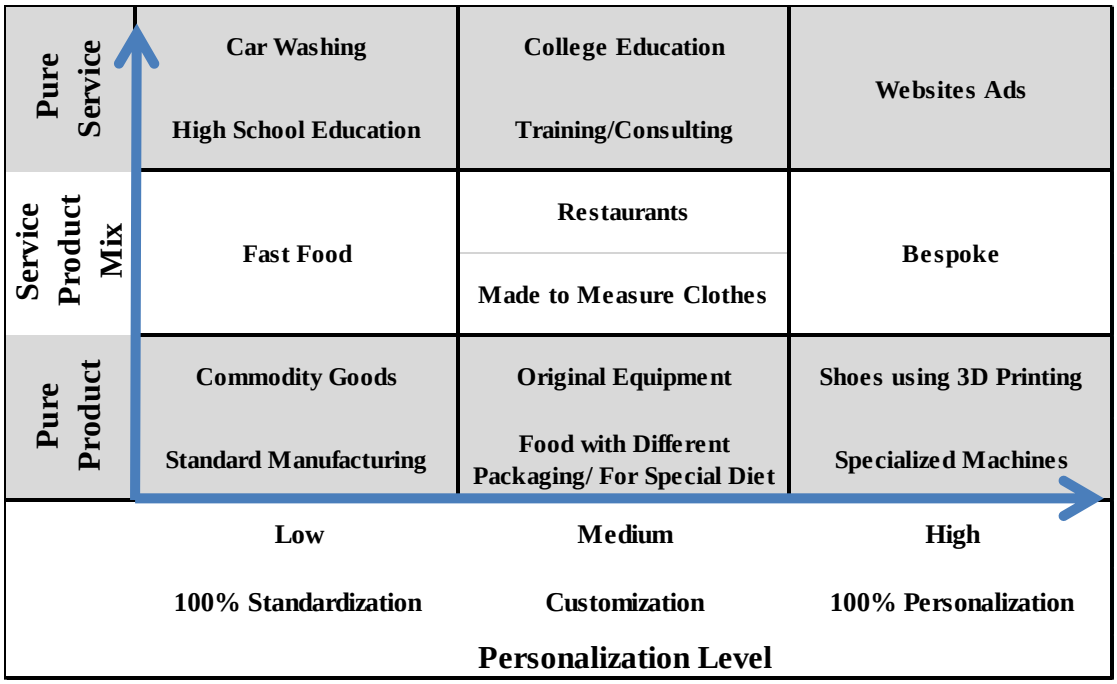

Figure 2-3: Standardization-Personalization Continuum

2.3.3.2 Health Care Context Mapping

The product-service continuum with regard to personalization level is replicated in the pharmaceutical product context in figure 2-4. The healthcare industry and pharmaceuticals, in particular, are providing a multitude of products and services that can be standardized targeting the mass population or can be more personalized. Most of the over the counter products are a perfect example of pure product 100% standardized. Some of the over the counter products are customized with specific packaging or to meet the need of patients with special diets. Highly personalized products would be some biologic polypills that are designed for particular cases and patients with specific conditions. In the case of prescribed medication, the service level is higher as the patient interacts with the pharmacist and might get some advice as how to use the medication. The prescribed medication is still standardized to a very high level. Compounding pharmacy products such as Arthritis gels are customized for specific patients' needs. The treatment

also has some service component associated with it as the patient interacts with the healthcare provider to prepare the medication. The biologic vaccines segment occupies the highly personalized part of the matrix with product service value proposition. In fact, cancer vaccines are administrated at a doctor's office or infusion center, making the biologic vaccine an example of product-service mix. Moreover, biologic vaccines are made partly from patient inputs. The patient inputs will make the medication very unique and, therefore, highly personalized. Finally, at the top of the product-service continuum, blood work is an example of a pure service healthcare related component. Blood work is standardized and is prescribed for particular cases. Dental cleaning is a purely customized service. In fact, dental services are customized to the patient needs with some standard facts. Dialysis is considered a highly personalized service. The setting of the dialysis service will be adjusted to the patient's specific case, blood type, and diabetic conditions, among other factors. This will place dialysis service at the upper right corner of the matrix. The detailed mapping of the continuums is presented in figure 2-4.

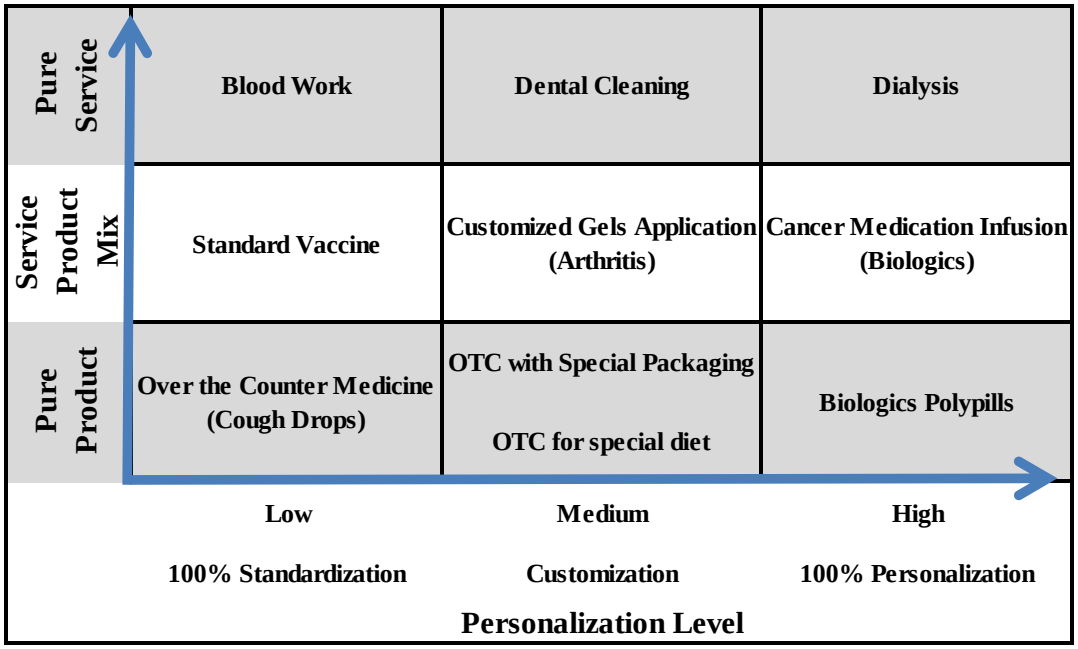

Figure 2-4: Pharmaceutical Standardization-Personalization Continuum

2.3.4 Mapping the Pharmaceutical Supply Chain Evolution

According to the Kaiser Family Foundation report (2005), the Pharmaceutical Supply Chain (PSC) is identified as the means through which prescription medicines are delivered to patients. PSC represents the different flow of transferring the medicine to the patient. The process includes the procurement of raw material, the manufacturing of the drugs, marketing and logistics functions (Horton, 2010; Shah, 2004a). The pharmaceutical supply chain includes three main flows: physical, financial, and information flows. The physical flow consists of the drugs travelling along the value chain and from a raw material to the patient. The information flow represents the exchange of information that happens along the supply chain among the different participants in the supply chain (manufacturer, suppliers, patient, doctor, hospital, insurance, pharmacy benefit managers). Finally, the financial flow is the payments made between and among the different players within the supply chain. The consumer, who is the patient, will receive the service/product and the customer, who is the payer, will be in charge of making the payment. The customer in most of the cases is the patient, the insurance, the government or a combination of these.

2.3.4.1 Mapping the Small Molecules Pharmaceutical Supply Chain

The pharmaceutical supply chain is conceptually composed of five key echelons: (a) drug manufacturers, such as biotechnology research institutes, pharmaceutical companies, and medical suppliers; (b) medicine delivery intermediaries, such as wholesalers, distributors, logistics companies, and group purchasing agencies; (c) healthcare providers: hospitals, clinics, and physicians; (d) medicine payers, such as insurance companies, government, employers; and (e) medicine consumers: patients (Burns, 2002; Pedroso and Nakano, 2009).

Pharmaceutical Manufacturers: The pharmaceutical industry is a consolidated industry with relatively few large, multinational firms. Pharmaceutical manufacturers have the most

influence over pharmaceutical prices, assessing expected demand, future competition, and projected marketing costs to establish the wholesale acquisition cost (WAC), which is the baseline price at which wholesale distributors purchase drug products. The pharmaceutical manufacturing industry is highly consolidated with a decreasing number of brand name manufacturing firms in the United States over the past 10 years (Yang, 2013). In fact, the top six firms account for almost 50% of the market share as shown in figure 2-3 (Yang, 2013). The consolidation is mainly caused by high barriers to enter. The large investment required, the high governmental regulations, the advanced research and investment capabilities, and the product time to market make very hard the success of new entrant in the market.

Wholesale Distributors: The wholesale distribution industry has consolidated in the last 30 years, with the number of wholesale distributors in the U.S. declining from approximately 200 in 1975 to fewer than 50 in 2000 (Alazraki, 2011). The top 3 wholesale distributors account for almost 90 percent of the wholesale market. Wholesale distributors typically sell drugs to pharmacies at WAC plus some negotiated percentage. Three major companies generate about 85% of all revenues from pharmaceutical wholesaling in the United States (AmerisourceBergen, Cardinal Health and McKesson). The total revenue generated by the big three wholesalers is $290 billion in 2011 (Fein, 2012). The wholesaler's main role is to guarantee the timely distribution of the medicine, especially for the high value density drugs. Moreover, through their network of representatives, the wholesale distributors will ensure the geographical distribution of the drugs to smaller retailers and pharmacies.

Pharmacies: In 2010, The United States accounted for approximately 63,000 pharmacies. More than half (37,615) are part of big chain (SK&A, 2012). The graph below summarizes the pharmacy ownership in the United States.

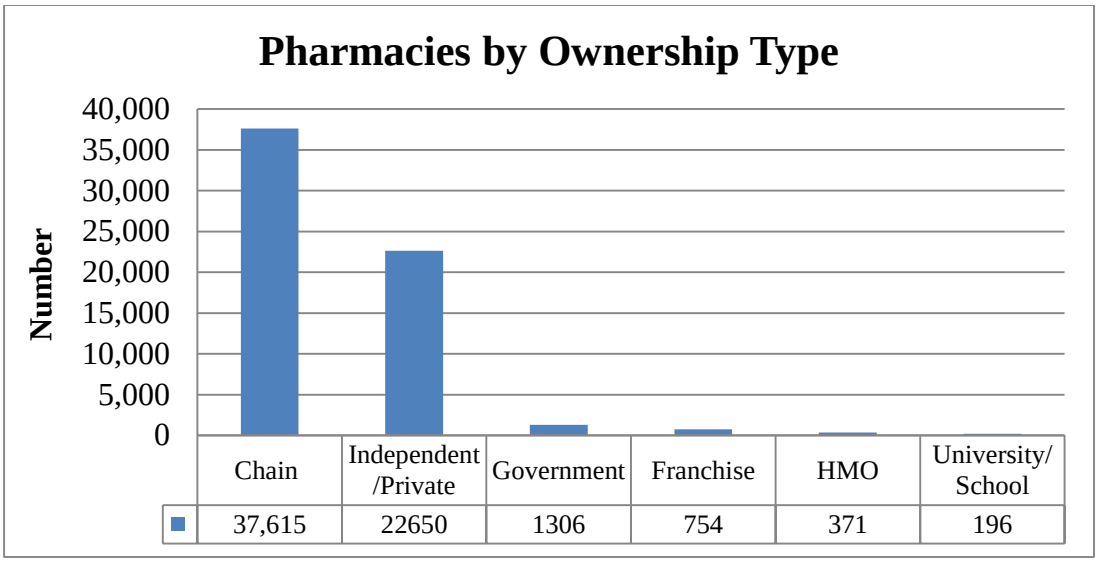

Figure 2-5: Pharmacy Ownership

The new trend in pharmacies' practice is the mail order technique. Although it accounts for only 6.1% of the total filled prescriptions, mail-order pharmacy sales were the fastest growing sector of the U.S. prescription drug retail market in 2004, increasing by 18 percent over the previous year (Dietz, 2004).

Pharmacy Benefit Managers (PBMs): Pharmacy benefit managers, or PBMs, act as an intermediary between the entity paying for the medicine and everyone else in the healthcare system. Pharmaceutical benefit managers process prescriptions for the groups that pay for drugs, which are typically insurance companies or corporations (Robison and Vernachio; Sroka, 2000). Approximately two-thirds of all prescriptions written in the U.S. are processed by a PBM (Welborn, 2005). PBMs may achieve savings for their customers by negotiating discounts and through cost containment programs, including use of formularies and cost sharing.

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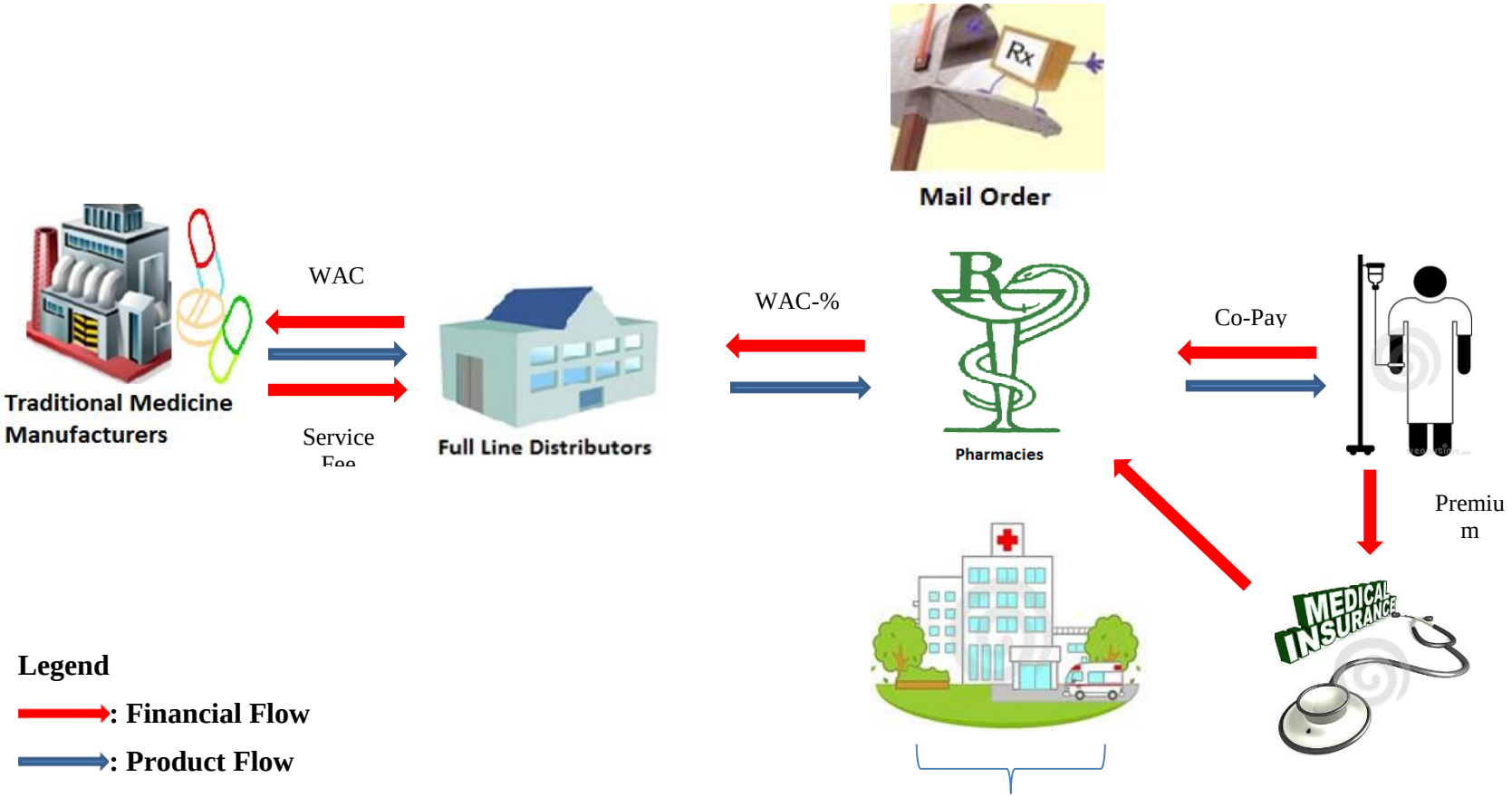

Figure 2-6: Pharmaceutical Supply Chain

2.3.4.2 Mapping the Large Molecules (Biologics) Pharmaceutical Supply Chain

The current section will provide an overview of the biologics pharmaceutical supply chain with a focus on the changes related to the different flows (physical, financial, and information) and the role of each entity in the supply chain.

The shift in the pharmaceutical industry paradigm from the blockbuster model to a more innovation-based business model pushed pharmaceuticals to look for more areas of research. Pharmaceuticals are investing more in the market of specialty drugs. Specialty Drugs are prescription medications that require special handling and administration (Cuttler et al., 2009). Specialty drugs are projected to have the highest growth and account for the most costly therapeutics over the next three years. In fact, by 2014, specialty drugs are estimated to account for 40% of the total US drug spending (Lipsy, Schapiro, and Prostko, 2009). In 2012, the U.S. pharmaceutical market leveled $325.8 billion in total sales volume with $86.1 billion accounting for specialty pharmacies.

Specialty Pharmacies are characterized by unique production processes and distinguished supply chain configurations. While the influence of pharmaceutical distributor giants is limiting the specialty pharmaceutical industry's ability to shift from the standard distribution model, medicine personalization, financial risk, and short product shelf life are inspiring manufacturers, pharmacies, and healthcare facilities to attempt a new supply chain configuration.

Biologic medicine accounts for the most prominent segment within the specialty drugs. Biologic medicine has enhanced the patient situation and revolutionized disease treatment. The main difference between standard drugs and biological medicine relates to the size of molecule. Biologic drugs are large and complex molecules. According to IMS Health, specialty medicine is the most growing sector in the pharmaceutical sector with a growth rate about four times the

growth rate of the traditional pharmaceutical sector. This trend is expected to continue for the next years with an increased dollars spent. Figure 2-6 illustrates the growth trends for between 2008 and 2012.

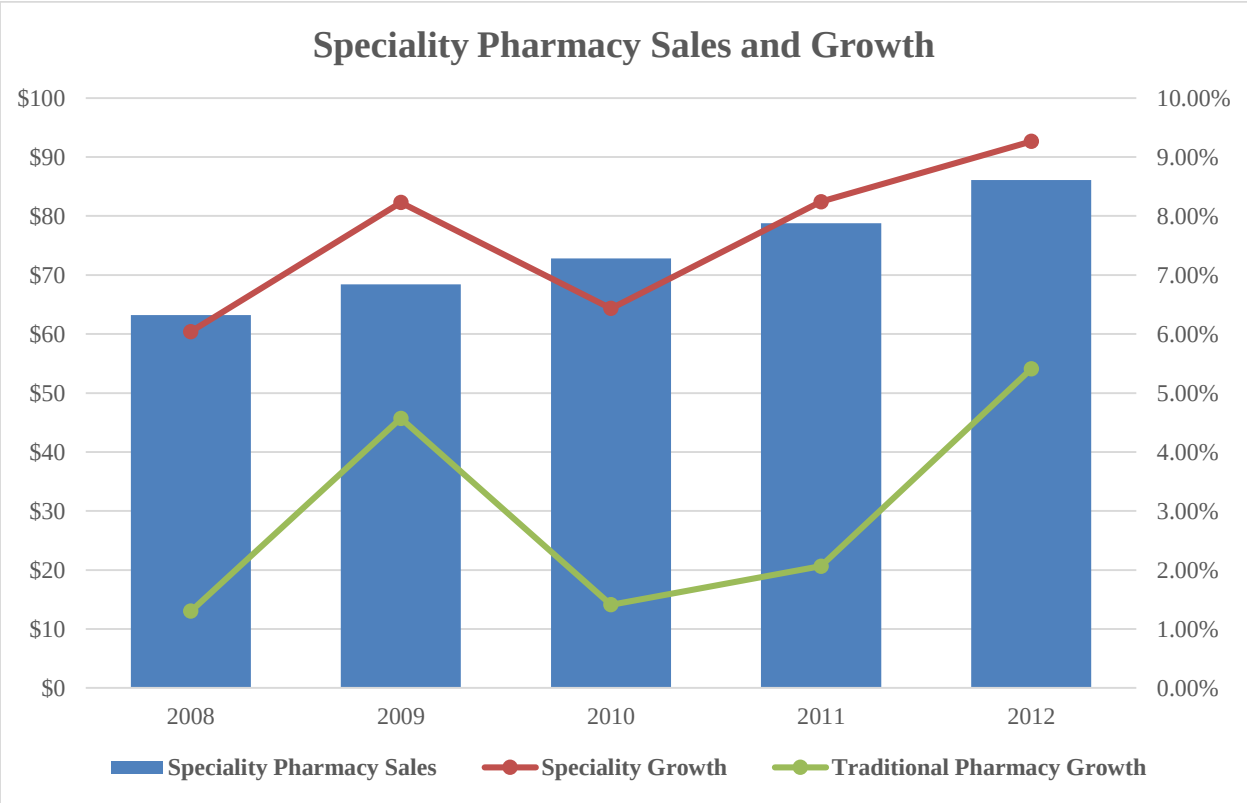

Figure 2-7: Specialty Pharmacy Growth

Biologics Production Process: Biologic medicines are prepared in living organisms to produce proteins aiming at the cure of multiple diseases. In most of the cases, pharmaceuticals will use DNA technology to improve the efficiency of the medicine. First, the process will begin with cell cultures where large numbers of human cells are collected. The cell is placed in a seed bioreactor to multiply. The "grown cells" will move to the production reactor. The second phase consists of the recovery of the cells for cell separation. Third, the cells will be purified for impurities and treated according to the situation. Finally, the biologic medicine will be ready for

storage and administration. Figure 2-8 provides a visualization summary of the biologics manufacturing process.

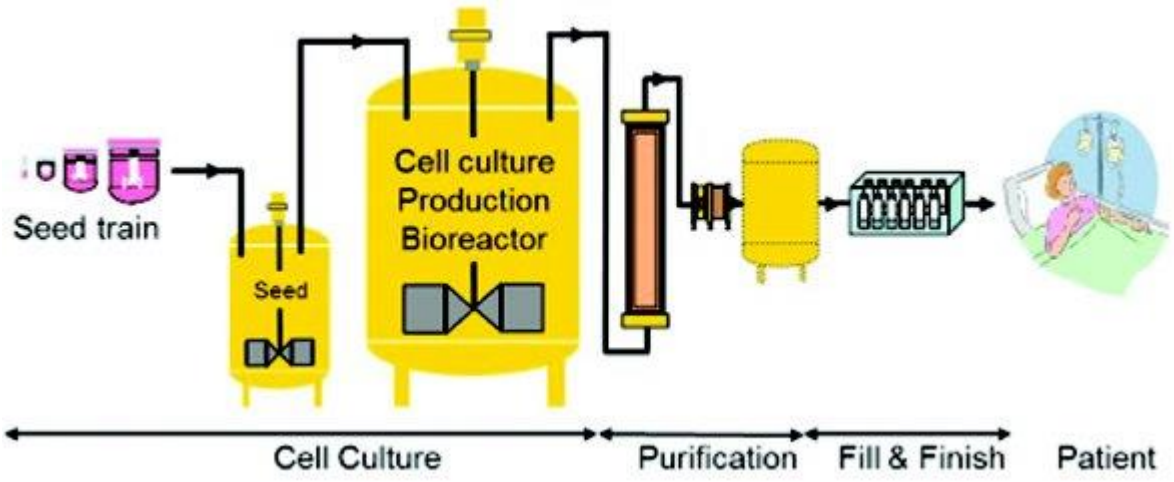

Figure 2-8: Biotechnology Manufacturing Process

Material Flow: The material flow in the case of biologics can be unique and interesting. First, the concept of product in the case of biologics is confusing. In many cases, there is no special product with specific characteristics and particular chemical composition. In fact, the medicine is the result of the process interaction. The inputs' (whether DNA, blood cells or any other components) interaction when infused with other components will determine the drug's output. Second, in many cases, patient inputs are part of the production input. The patient is the supplier and the product consumer. Finally, in a more classical configuration, the medicine will go from the manufacturer to the distributors, then to the specialty pharmacy, and finally to the care center or the patient. The product flow will be influenced by other factors, such as risk factors, handling and storage requirements, and product shelf life.

Financial Flows: The high financial risk for specialty drugs developed alternative distribution channels. Unlike regular medication where the insurance's role is clear, biologic medication offers multiple alternatives. The financial risk can be carried by either the patient or

the care giver (Clinic or doctor's office), or in rare cases shared. The jargon used in the industry is white bagging and brown bagging. In white bagging, the specialty pharmacy ships the drug directly to the clinic or doctor's office just in time for the patient's scheduled treatment. On the other side, brown bagging, the patient will buy the product directly from the pharmacy and take responsibility for the storage and transportation. White bagging represents more of a financial risk for doctors because they might not get reimbursed entirely for the drug cost. Moreover, small doctors' offices will have some obstacles with handling and storing the medication, as it adds more cost. On the other hand, brown bagging puts the financial risk at the patient's end, where the patient will have to get reimbursed for the medication. However, many doctor's offices do not accept this alternative because of the drug mishandling issues and dosage problems. In fact, in many cases, doctors have to change the medication dosage or reschedule the appointment because the patient either lost weight or is not in a good condition to receive the treatment. The brown bagging distribution channel does not provide enough flexibility to the doctor to make changes to the doses.

The financial flows in the biologics supply chain are mainly influenced by the level of risk sharing which determine who is accountable for what. For large doctors' offices, "the buy and bill" model is common, where the doctor purchases the medicine directly from the distributor and takes a full financial risk. The other alternative will require the involvement of specialty pharmacies and more risk taking from the patient.

Pharmaceutical Closed Loop: The biologics supply chain represents the uniqueness of having the patient input as part of the raw material. In many biologic medications (e.g. cancer vaccine, blood products, tissue product), the patient will provide a sample from his/her body to be treated and developed into personalized medication. In this case, the material will flow first from the doctor's office back to the manufacturing processing location and then back to the doctor's

office for treatment. This represents a unique closed loop where the initial flow starts at the product's consumer and will be shipped to the processing facility and, after that, shipped back to the medication consumer.

Biologics Supply Chain: The biopharmaceutical supply chain is more elaborate than the classical medication supply chain. Figure 2-9 shows the different product flows that are dictated by the nature of the product and the risk sharing options. Biologics distribution channels are characterized by direct sales favoring a disintermediated supply chain configuration. The medicine can be shipped directly to the specialty pharmacy or the care provider (clinic or doctor's office or hospital). In more extreme cases, the medication will be shipped directly from the patient to the processing facility. This is a case of highly personalized medication. Figure 2-9 illustrates the biologics supply chain with an emphasis on the physical flow. The graph provides an estimate of the percentage of material flow across the different supply chain echelons. The numbers are computed from a previous study and from compilation of BLOOMBERG financial database results.

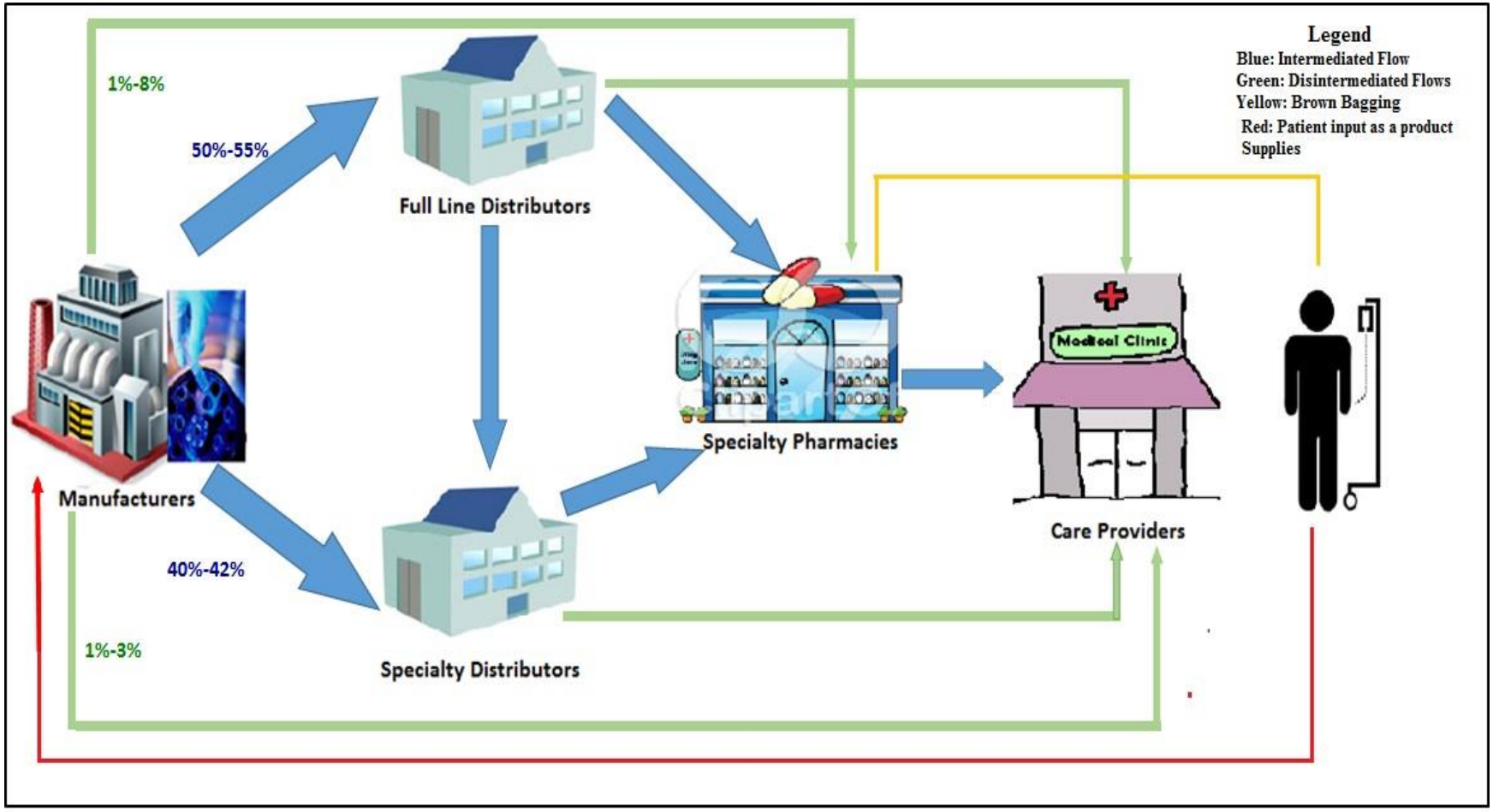

Figure 2-9: Biologics Supply Chain

2.3.5 Disintermediation Continuum

The choice of a distribution channel represents a strategic decision that will shape the firm's long-term commitment with its supply chain partners. The pharmaceutical supply chain as explored in the previous section is evolving from a more traditional flat supply chain distribution model where the medication moves down the supply chain and is distributed through wholesalers and distributors to a more complex configuration. The drugs in the case of biologic medications can be shipped directly to the hospital or the end consumer. Such practice is referred to as supply chain disintermediation. Disintermediation refers to the elimination of the middle entities between the product/service provider and the end customer (Chircu and Kauffman, 1999). The concept of disintermediation is a popular practice in many industries such as retail, where customers will buy their products and services directly from the manufacturer or the service provider. The organization will have the option to select the distribution channels configuration. Some organizations will decide to be fully intermediated, fully disintermediated, or have a mix strategy by balancing disintermediated and intermediated distribution strategies. The distribution strategy is therefore conceptualized as a disintermediation level continuum.

The level of disintermediation in the distribution channels will dictate the organization's supply chain strategy. Many companies decide to be fully intermediated. The main purpose of intermediation is to facilitate product/service diffusion by utilizing the intermediaries' networks, the customers base, and know-how (Chiang, 2012). A fully intermediated distribution strategy is a common practice in functional and commodities products. For example, the sugar supply chain is totally intermediated. A customer cannot buy the sugar directly from the sugar producer. This is due, in fact, to the level of standardization and the low variable cost. Sugar producers are better off pushing their products through the distributors and wholesalers. Paper-related products are

another good example of a totally intermediated industry. With a stagnant demand and high set up costs, paper mills sell their products to the wholesalers and distributors. Other organizations would prefer to have a mixed strategy where the firm will attempt to capture the benefit of both strategies. From one end, the intermediated distributed channels will enable more market access for the firm and push the products and services in the pipeline. On the other end, a disintermediated strategy will enable the organization to have more customer input and provide more customized products. According to Apple Inc. reports, the firm maintained a more disintermediated strategy before 2010 when its products were mainly sold online and through its Apple store network. Today, Apple products are available in a variety of distribution channels, outlets such as Best Buy and Walmart, among others. Electronics products, in fact, represent a good example of a hybrid disintermediation distribution strategy. Clothes products are also sold direct to customers or can be distributed through wholesalers. Adidas, for instance, is selling its products directly online as well as through some retailers such as Macy's stores. Finally, a fully disintermediated strategy is popular among certain products. For example, Vista Print, Shutterfly, and Zazzle are selling their products exclusively through direct sales. This type of product is, in general, customized and requires customers' input. The disintermediation continuum is also applicable in the healthcare context with its stronger focus on product as part of value proposition. In fact, the disintermediation level relates to the physical flow.

The pharmaceutical supply chain presents a variety of disintermediation levels. First, standardized medicines such as over the counter medication which are characterized by a long shelf life are sold through distributors and wholesalers. Pharmaceutical firms use push strategy to sell some of its medication by using the middleman as a buffer to maximize the service level. Other examples of disintermediated pharmaceutical products are vaccines which are distributed through

wholesalers and organizations. In fact, the World Health Organization is responsible for the distribution of certain vaccines to doctors' offices and hospitals. Second, a hybrid distribution strategy will be characterized by a mix of direct and intermediated distribution channels. Compounding pharmacy represents a hybrid model where the wholesaler is eliminated, but the medication still needs to go through some intermediation. In fact, the doctor will prescribe the medication and the patient will get it from the pharmacy. The delayed differentiation in the medicine preparation calls for a certain level of disintermediation. Moreover, today's practice suggests that some drugs are sold both directly and through distributors. In fact, Pfizer is selling Viagra online directly. The emergence of this alternative distribution outlet is the result of risk and safety concerns from Pfizer due to counterfeiting. Finally, a total disintermediated model suggests that the medication is sold directly from the manufacturer to the patient. The previous section discussed a case of biologic vaccines that are sold directly from the manufacturer to the patient. Cancer treatments and highly personalized medication are disintermediated.

2.3.6 Mapping the Disintermediation Personalization Continuum

The previous discussion showed an interaction between the disintermediation level and the degree of personalization. This subsection reconciles the supply chain distribution channels as reflected by the disintermediation level and the product personalization level.

2.3.6.1 General Context Mapping

The product paradigm will dictate the type of distribution strategy. Fisher (1997) addressed the idea of product type (functional vs. innovative) and the type of supply chain (efficient vs. responsive). This section represents an attempt to map the type of product from personalization precept and the supply chain distribution strategy as measured by the level of disintermediation. Figure 2-10 shows an example of different products and the level of disintermediation.

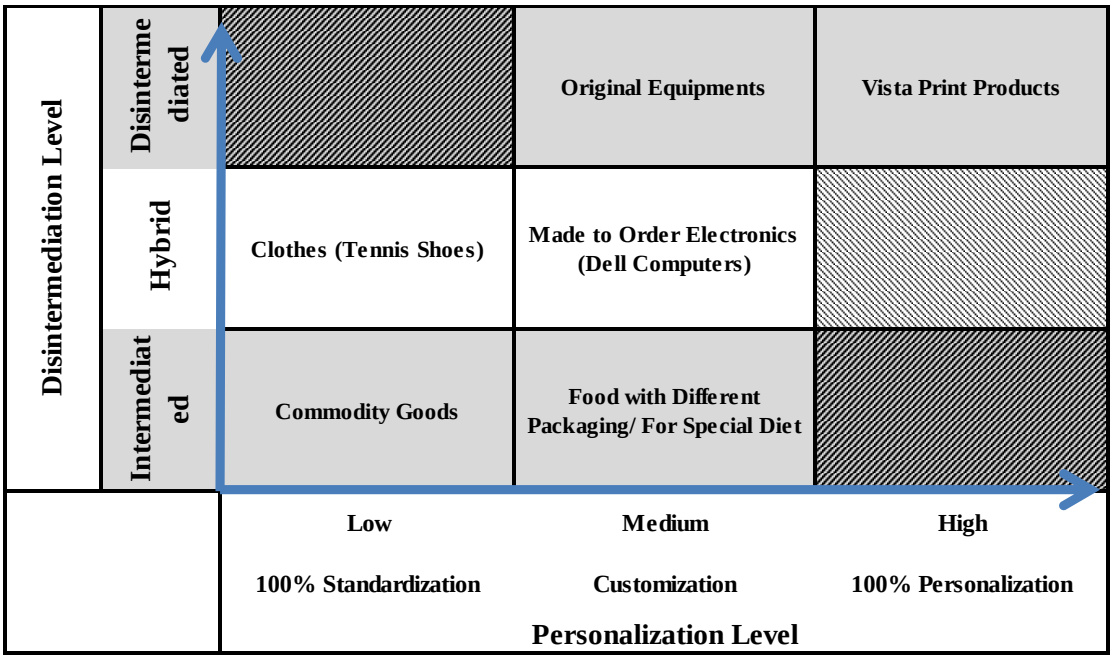

Figure 2-10: Personalization and Disintermediation Mapping

Intermediated distribution strategy suggests that the product flow will be shipped from the manufacturer to the wholesaler/distributors. The product is then shipped to the retail stores to be available for the end consumer. Standardized product like commodity products (e.g. sugar, rice, and aluminum) have an intermediated supply chain configuration. In fact, the commodity products are produced and then sold to the wholesalers which will be responsible for the distribution of the product to the local distributors or the large retail stores. A consumer cannot buy basic products like a pack of sugar or coal directly from the producer. The main driver of this traditional distribution channel is the cost minimization and consolidation of the distribution function. These basic products are now available in more customized forms. For example, a consumer has the opportunity to buy food for a special diet from the store. For example, gluten-free pasta or low sodium soy sauce are available at the local retail stores. Foods, including commodity products like sugar, are available in a variety of packaging and with added flavor. The increase in the level of customization has not impacted the distribution channels. The products are still sold mainly via

traditional distribution channels (intermediated). While the producer can charge a premium price for these personalized products, the demand for these products is not stable. To cope with this variation, the adequate strategy consists of using the distributor as a demand variation buffer.

The hybrid distribution channel model is very common in the field of clothing. A customer has the option today to buy tennis shoes directly from the producer (Puma, for example) or from the mall at some retail store. Tennis shoes are a typical example of standardized products that can be purchased through a variety of distribution channels. More customized products such as electronics can also be purchased through a variety of distribution channels. For example, the new customized tablets by Dell and HP can be sold through direct distribution channels from the producers and are also available via retailers such as Best Buy. Best Buy is now attempting to provide more customized products and provide alternatives to the direct sales business model. The hybrid distribution model for customized products is also available in the travel service. A recent study showed that travel agencies (the middleman in this context) are providing more customized holidays packages that fit tourists' particular interests. The customized holiday packages are also available via direct distribution channels where hotels will provide customized packages (Law, Leung, and Wong, 2004).

A total disintermediation distribution channel happens when a product is exclusively sold through direct sales. The direct sales model is not common in the case of highly standardized products. The products' value proposition and the universality of the item makes direct distribution channels financially not feasible. For more customized products, the disintermediation phenomenon is observable. Some of the original manufacturing equipment is sold directly to the customer. For example, when Ford Motor Company buys parts to assemble a particular product line, it will purchase them directly from its supplier, not from a distributor. The part is customized

to fit Ford's particular specification. The part, in most cases, can be used for other car models, making it highly customized but not personalized. Highly personalized products such as Vista Print wedding invitations or personalized t-shirts are sold exclusively through direct sales. When a customer connects to Vista Print and designs business cards or wedding invitations, the product is then shipped directly to the customer. This represents an example of a disintermediated supply chain structure. The high level of customization eliminates the middleman contribution.

The personalization level impacts the supply chain distribution channels structure. As the level of personalization decreases (high standardized products), the product demand variability decreases and the middleman contribution is more relevant. Moreover, standardized products' value proposition is low in general and, therefore, they are sold exclusively through intermediated channels. On the other hand, highly personalized products aim to serve one person. In this case, the distributor's added value to the supply chain is negligible. Therefore, the product is sold directly to the customer, leading to higher disintermediation level.

2.3.6.2 Pharmaceutical Context Mapping

In the context of healthcare, the pharmaceutical supply chain configuration and the type of products can be reconciled. As shown in previous sections, pharmaceutical products present different levels of personalization which are distributed differently (direct sales, disintermediated, hybrid). Figure 2-11 shows the mapping of personalization and disintermediation levels.

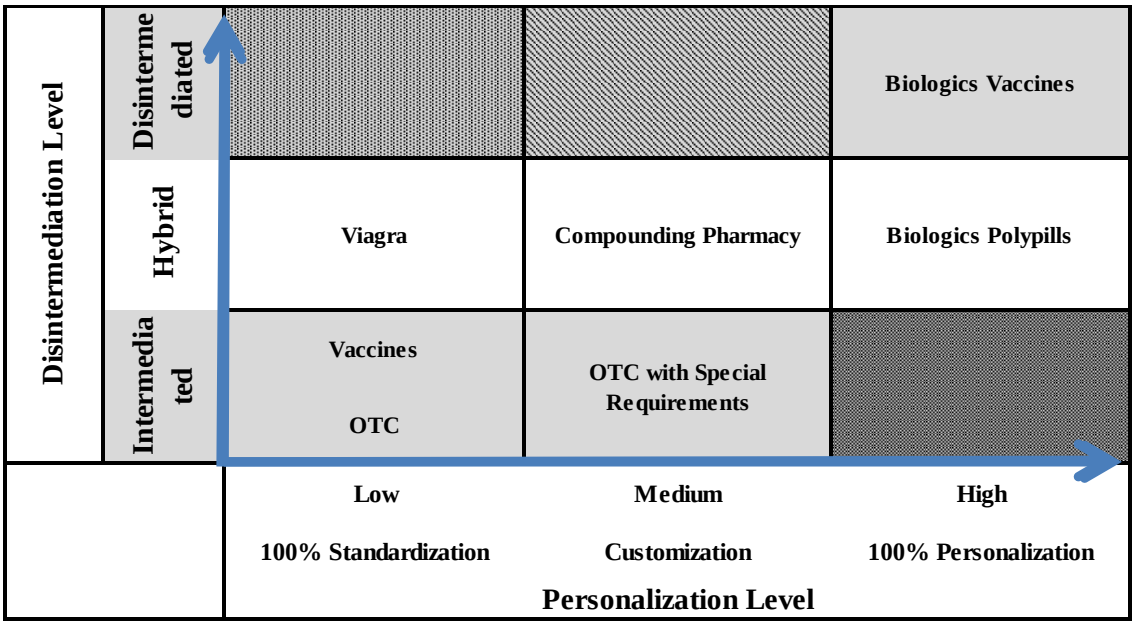

Figure 2-11: Pharmaceutical Personalization and Disintermediation Mapping

Intermediated distribution channels for pharmaceuticals suggest that a medication is sold through wholesalers and retail pharmacies. Over the counter medications, highly standardized drugs, are sold through the disintermediated model. Aspirin (Bayer, for example) is available at the retail pharmacies which obtain it from the distributors and wholesalers. Because of the simplicity of the product and its low cost, the aspirin is not sold directly by Bayer to patients. More personalized over the counter products such as Tylenol for a special diet or with specific doses are also sold through traditional distribution channels. Despite the increase in the personalization level, this class of medication does not provide enough variety and value proposition to make alternative distribution channels profitable. The pharmaceutical supply chain structure does not experience a configuration with highly personalized products that are exclusively sold through classical distribution channels.

Hybrid disintermediation models are marked by products that can either be sold directly to the customer or via traditional distribution channels. Viagra, a highly standardized product, is available via direct sales and through intermediaries. Pfizer was not motivated by the high value

proposition of the product or the personalization level to adopt the direct sale model. The main reason was related to safety and quality issues. With counterfeit problems, Pfizer decided that direct sales might be a good alternative to deal with safety problems. More personalized products that can derive from compounding pharmacy are sold via intermediated and disintermediated channels. When ordering a medication at a compounding pharmacy, the product can be available for direct shipping to the patient or can be managed through regular distribution channels. Finally, more personalized products such biologic polypills are available through a variety of options. The drug can be sold directly to hospitals and dispensed to patients. Also, some of the specialty distributors carry a significant amount of polypills which are then shipped to different hospitals according to the hospital needs.

The case of extremely disintermediated configuration suggests that the medication is only available via a direct sales option. The most common example is the biologic vaccine. This type of medication which deals with very complicated cases such as cancer and genetic issues is highly personalized. In many cases, the medication is unique to the patient's characteristics (genes, weight, and blood type). In this case, the medication is shipped directly to the patient or the hospital to be administrated. In an earlier section, a discussion was provided about the example of the cancer vaccine as an example of a highly personalized product with a disintermediated distribution strategy. The pharmaceutical industry does not experience, to my knowledge, any configuration for low personalized medication that is sold exclusively through direct sales models.

The personalization and disintermediation mapping is showing some patterns. As the level of personalization increases, there is a higher tendency to more direct distribution channel opportunities. At one extreme, standardized medication is totally intermediated. Highly

personalized medication is distributed directly to the patient or doctor's office where the drug is administrated.

2.4 Conclusion

The pharmaceutical industry's landscape is experiencing an evolutionary change for both the product paradigm and the supply chain configuration. The current chapter intends to provide a better understanding of the evolution of pharmaceutical industry and how it shaped the development of the pharmaceutical supply chain and the emergence of the new product paradigm. With more emphasis on the market of the one customer, the product paradigm has shifted from mass produced goods to more personalized products with higher attention to the service component as part of the value proposition. The pharmaceutical industry has followed the same evolution with much slower pace due to less consumer involvement in the product design.

The change of the product paradigm has influenced the supply chain configuration. First, the level of medicine personalization has created more direct sales opportunities and disintermediated distribution channels. This has an impact on the physical flows. In fact, the pharmaceutical practices are offering more direct sales opportunities, making the medication flow directly from the manufacturers to the patient and/or hospitals. The product flow has even evolved to a more complex closed loop flow. The drug production process starts at the doctor's office where inputs from the patient is part of the raw material input. The patient's inputs will be shipped to the processing facility and then sent back to the patient to be administrated. Second, the financial flows are more complex in the case of more personalized medication. The practices have shown newer flows known as brown and white bagging. The risk sharing level has an impact on the financial flow. Finally, the financial performance structure is different according to the level of product personalization. On the other side, the evolution of the pharmaceutical supply chain has enhanced

the emergence of more personalized medication. The direct sales distribution channels and the development of the third party logistics service firms are improving the financial performance of personalized medication. In fact, personalized medicines are suffering from a low profit margin despite the fact that it is more innovative and provides a unique value proposition.

The following table will cross the level of personalization with some of the major supply chain attributes. The reconciling attempt intends to provide a perspective of the interaction among product paradigm and supply chain characteristics.

Table 2-2: Personalization Level and Supply Chain Attributes

		Personalization Continuum			
		Mass Production	**Mass Customization**		**Mass Personalization**
Examples	**General Example**	Commodity Products (Salt)	Original Equipment		Personalized Shoes
	Pharmaceutical Examples	Over the Counter Medicine (Aspirin)	Customized OTC (Customized Tylenol)	Customized Gels Application (Arthritis)	Biologics (Provenge)
Supply Chain Characteristics	**Product/Service**	Pure Product	Product/Service mix		Product/Service mix
	Disintermediation Level	Intermediated	Hybrid Distribution Channels		Disintermediated (Direct Sales)
	Competitive Capability	Cost	Quality and Delivery		Quality and Delivery
	Type of Supply Chain	Efficient	Hybrid		Agile
	Physical Flow	Standard Forward Physical Flow	More Complex Standard Forward Flow		**Closed Loop Physical Flow**
	Information Flow	Order Quantity and Production Forecast	Order Quantity, Production Forecast, Customer Preferences		**Customer Feedback and Customer Input as part of product inputs**
	Financial Flow	Classical Reverse Flow of Cash	More Elaborate Financial Flows with the more influence from of Insurance and PBM		More Complex because of the high Cost. Financial risk sharing influences the financial flows
	Profit Margin	High	Moderate		Low
	Risk Level	Low	Moderate		High

The current chapter attempts to creatively conceptualize the interaction of personalization as a new product paradigm and supply chain configuration. An original reconciliation of product paradigm measured by the level of personalization across other continuums was developed. The personalization represents the new product paradigm that aims at increasing customer satisfaction

and improving profitability. First, the chapter mapped the personalization spectrum with the service/product continuum. Despite extensive work on the product-service continuum for over four decades, very few studies have attempted to reconcile the continuum across different dimensions. The conceptualization provides an innovative mapping to the product-service continuum across the personalization level. With no loss of generalization, the framework has applied the general finding to the healthcare context, the main focus of this study. Second, the study addressed the structural change of the pharmaceutical supply chain. The extensive literature review showed rich exploration of the pharmaceutical supply chains, yet no major works have addressed the recent evolution of pharmaceutical supply chains. The emergence of a new type of medication which is highly personalized, expensive, and with low shelf life has provided a new type of distribution channel. The pharmaceutical supply chain has shown new distribution practices marked by disintermediation and direct sales. The chapter provided an attempt to assess the new distribution channels and quantify the physical flows. Based on observations from pharmaceutical firms' annual reports and data collected from secondary sources, an estimation of different physical flows for the large molecules (specialty pharmaceuticals) supply chains was provided. The finding showed a relatively higher level of disintermediation for large molecule drugs in comparison with traditional small molecule medication. The pharmaceutical industry is still, however, under the pressure of traditional distribution channels through the distributors. Finally, the study has mapped the main two concepts addressed in this chapter: product paradigm and pharmaceutical supply chain. While the product paradigm was measured by the personalization level, the supply chain configuration was conceptualized by the disintermediation level. Certain patterns of personalization and supply chain disintermediation interaction were identified. The observations showed that large molecule medication (biologics) have a higher personalization level. Biologic

drugs are also distributed in more direct distribution channels promoting disintermediation. On the other hand, small molecule drugs (traditional medicine) are more standardized and are sold using classic distribution outlets, emphasizing a more intermediated model.

Chapter 3: Strategic Location Consideration in Biopharmaceuticals: A Case Study

3.1 Introduction and Research Objectives

Facility location represents a strategic decision that has an impact on the organization performance. Facility location is critical in manufacturing as well as service industry to minimize logistical cost and improve customer service level. In the healthcare context, the location decision is even more critical because the level of liability goes beyond the loss of profit to involve patients' lives.

The literature review had addressed the location problem for pharmaceutical companies (Ruane and Zhang, 2007). The decision variable in the pharmaceutical case can be a warehouse location decision or manufacturing site. However, the importance of location problem for traditional pharmaceutical modulated by the high value density of the products and the high operating margin. As discussed in chapter 2, the traditional (small molecules) pharmaceutical supply chain relies on the intermediaries to insure the product availability at the pharmacies. The location problem is more critical in the case of biologics. Biologics are expensive medication that requires special handling and are time sensitive. The case are even more critical in the case of extremely personalized medication where the patient input (blood cells, DNA material…) are part of the input into the production process. In this case, the processing location facility is critical because of the cost of transportation and the product perishability.

Prior literature addressed the location problem in the context of healthcare facilities for over forty years (Fitzsimmons, 1973; Toregas et al., 1971). Several problems were investigated and multiple solution methodologies and heuristics were proposed (Klose and Drexl, 2005; Melo, Nickel, and Saldanha-da-Gama, 2009). Other work addressed the problem on non-business context

such as disaster management (Altay and Green III, 2006; Mete and Zabinsky, 2010). The problem can be more interesting in the case of biologics where the transportation cost is high and time is critical constraints. The biologics (personalized medication) provide the uniqueness of bidirectional flows — from the doctor's office to the processing facility, and back to the doctor office for infusion. This setting represents an opportunity to practically investigate the location problem in a case of biologics medication. While the research in location problem in the context of healthcare medical field is rich, few practical studies have addressed this issue using real data. This will represent an opportunity to test some of the well-grounded facility location techniques in practical situations.

The location configuration problem represents an important strategic decision that can reduce the cost of goods and increase customer satisfaction. The problem is more relevant in the case of pharmaceutical biologics medication. This chapter provides an application of the location problem using case study. This chapter aims at investigating the location problem in the case of highly personalized medication with totally disintermediated distribution channels using Dendreon Corporation, a prostate cancer vaccine manufacturer. The use of publicly available data allows us to determine the problem parameters and provide the organization's current approach and compare it with the theoretical optimal solution. This chapter aims at emphasizing the role of location using a real case study. We will provide an optimal location decision based on cost minimization tools. The results are then compared to the results obtained from optimal configuration.

The rest of the chapter is organized as follows: first, a summary of the literature review related to location problem with an emphasis on the health care applications is provided. Second, the case study is presented and Dendreon Corporation problem is identified. Third, a methodology

to address the location problem is provided and analyzed. Summary of results, limitations of the study and future area of improvement will be discussed.

3.2 Literature Review

The location problem has been extensively investigated for long period leading to multiple formulations and heuristics to solve the different problems (Brandeau and Chiu, 1989; Maranzana, 1964; Nagy and Salhi, 2007). The location models were then applied in the healthcare context. The literature review related to the location problem in the healthcare context presents three main models: the location set covering model, maximal covering model and P-median model (Daskin and Dean, 2004).

The location set covering models aims at minimize the location costs or the number of facilities to be located while maintaining certain coverage level (Toregas et al., 1971). Covering 100% of the location can result in high cost and large number of facilities. The model then was modified to include the demand level at the different nodes. The problems consists of maximizing the demand covered under the constraint of a number of facilities (Church and Velle, 1974). The two previous models do not consider the distance factor in the location. The final main mathematical model, known as the P-median model, aims at minimizing the demand weighted total distance (Christofides, 1975). The P-median model has been implemented in many practical cases where the optimal healthcare facility location has been identified (Jia, Ordóñez, and Dessouky, 2007).

The application of the location problem in the healthcare context aims at improving the accessibility, availability and adaptability. Accessibility refers to the patient's ability to reach the healthcare facility and vice-versa. Accessibility models are adequate in a case where the problem has static parameters such as demand, cost and distance. Availability addresses location problems

that process uncertainty in one or more of the problem parameters. This family of problems is mostly used when the system experiences short term changes. For example, an ambulance at certain facility might be busy. The system will find an alternative ambulance that will perform the work (Daskin and Stern, 1981). Finally, the case of long term decision with uncertainty is referred to in the literature as adaptability. Adaptability problems are relevant when deciding about building new hospital under uncertainty conditions. Once the hospital is built, it is prohibitively expensive impossible to relocate it. To address the problem, the literature suggested the use of minimax and minimax regret scenarios (Jia et al., 2007).

The main three locations problems methodology discussed earlier provide the grounding for the development of more customized problem formulations that target particular problems. The case of service facility location problem represents an interesting application of the location problem. The service location problem suggests that the service provider will identify the service location configuration that maximizes the number of customers captured (Gas stations location for example). This model is referred to as the "flow capturing location problem" (Berman, Larson, and Fouska, 1992; Hodgson, 1990). The research in location problems has evolved to add more complexity to the problems with emphasis on variability, capacity, and number of locations among other considerations. More emphasis is given by scholars on the application of location methodologies in real case situations (Hall et al., 2006).

The following section will address a service location problem for a blood processing facilities from the perspective of investigating bi-directional material flows. The analysis is based on real data retrieved from secondary sources.

3.3 Case Study

3.3.1 Dendreon Corporation

Dendreon was established in 1992 by Drs Edgar Engleman and Samuel Strobber in Mountain View, California. At the beginning, company's main activity consisted of isolating hematopoietic stem cells from blood for use in patients with cancer who require transplantation. The firm later started developing therapeutic products that fight cancer by manipulating aspects of the immune system. Dendreon went public in 2000 with shares listed at 10$. In April 2010, the Food and Drug Administration sent the approval letter to Dendreon for its prostate cancer treatment medicine (Malarkey and Witten, 2010). Dendreon is mainly focusing on cancer treatment development.

3.3.2 Dendreon Product: Provenge

Provenge is the only FDA-approved vaccine treatment for advanced stage prostate cancer. It is the first drug of its kind to use the body's own immune system to fight cancer (Plosker, 2011). A patient prescribed Provenge must have a sample of their white blood cells extracted. These cells are then sent to a processing factory where they are incubated to create the vaccine. From there, the vaccine must be transferred to doctor facility or to the infusion center to be infused into the patient (Kantoff et al., 2010). Provenge medication has no defined chemical structure as it is considered as autologous product (Tsao et al., 2013).

Provenge is the main product and the major source of Dendreon revenue. Revenues from Provenge accounted for 283 millions in 2013 more than 80% of the total revenue. The remaining revenue was generated from grant and collaboration with other firms. The treatment costs $93,000 to receive three phased treatment (Begley, 2012). According to Dendreon former CEO, Mitch Gold, the high price is creating a "price density" phenomenon (Winslow, 2011). Dendreon is

attempting to address this issue by emphasizing the long-term cost of other treatment that can equal or exceed the $93,000. The high cost represents a major obstacle to Provenge sales.

3.3.3 Production Process

Dendreon supply chain represents a unique configuration. The patient's input, which is the white blood cells, represents the major component of the production cycle. The production and delivery of the medicine is done in three stages. On day one, the patient will go through standard blood collection process. The blood sample will next be shipped to one of the manufacturing locations for Provenge preparation. The process of preparation lasts 40 hours. The vaccine is then shipped back to the doctor's office for infusion. The treatment requires three infusions and can be achieved in 30 days. Figure 3-1 illustrates the production cycle.

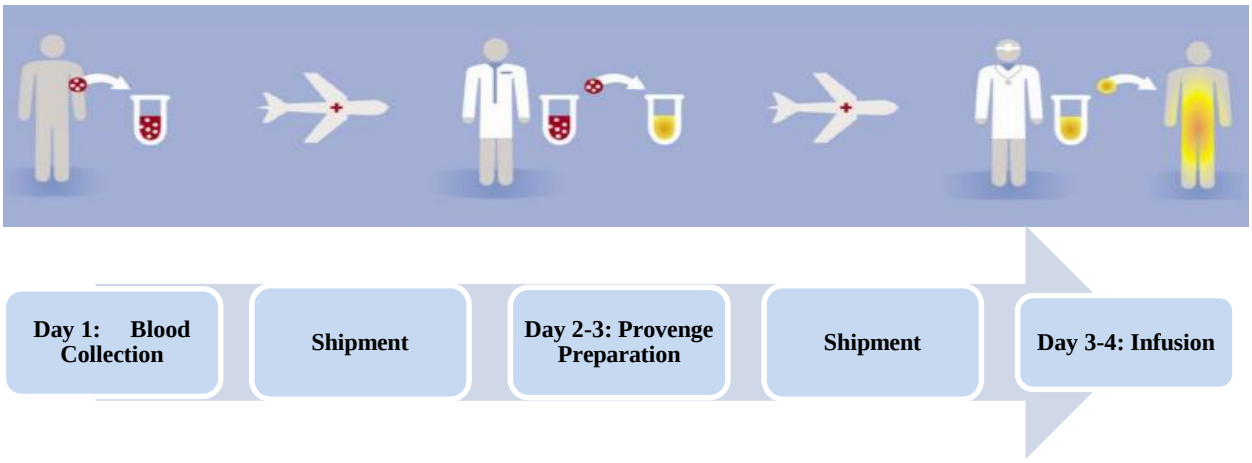

Figure 3-1: Prostate Vaccine Service Process

Dendreon supply chain configuration represents a unique configuration and relevant topic. The healthcare supply chain is part of the legacy supply chains. The vaccine is time sensitive as it requires an infusion within 48 hours and therefore requires rapid transportation. These factors increase the cost of medication. Dendreon is using third party logistics to ensure the transportation of the medication from the doctor's office to the processing facility and back to the infusion center.

The third party logistics is an emerging trend in the healthcare industry and is of importance to both healthcare and logistics firms.

3.3.4 Processing Locations Network

Dendreon is outsourcing most of its activities. Vaccine preparation represents the unique component of the supply chain that is insourced. Dendreon operates the manufacturing facilities and control the production process. Dendreon had three facilities— New Jersey, Atlanta, and Los Angeles. The three locations serve the potential U.S. market. Figure 3-2 shows the map with the three existing manufacturing locations. The figure also provides an illustration of the potential market. The market size for each state is represented by a circle located at the state capital. The capital coordinates of each state capital is identified.

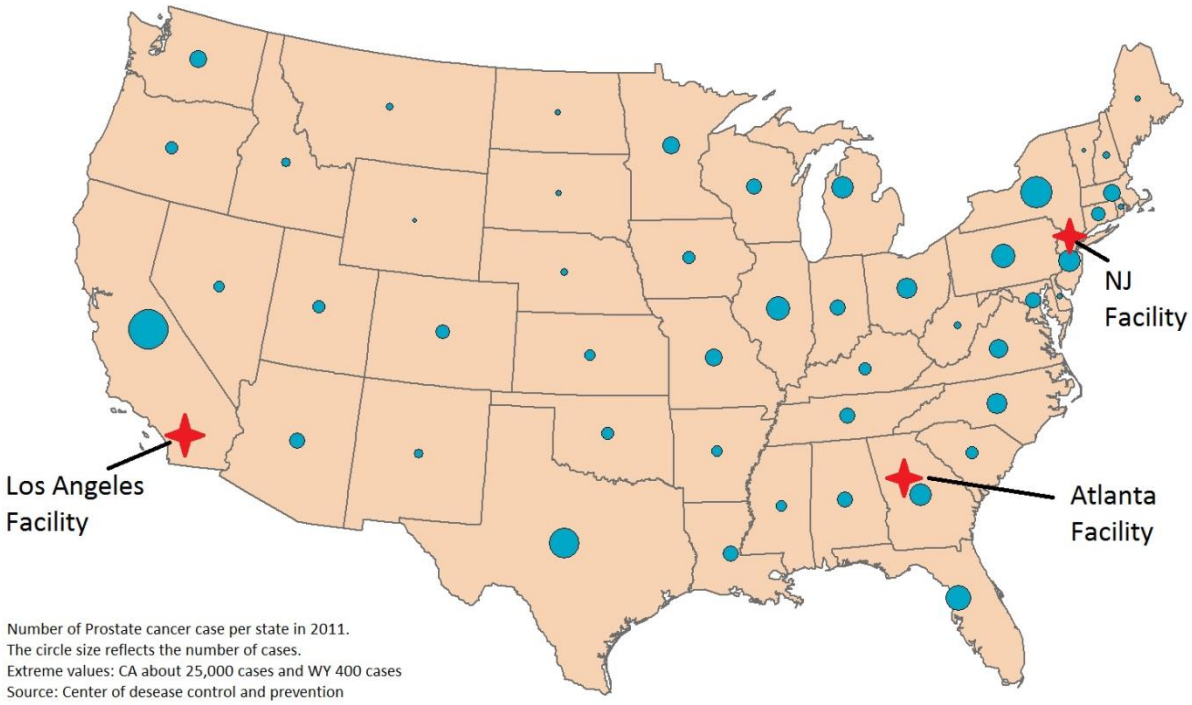

Figure 3-2: Dendreon Processing Facility Location Problem

3.4 Problem Definition

Dendreon faced financial problem and its capacity was underutilized. Despite a steady income between 2011 and 2013, Dendreon Corporation experienced increasing losses. The top management decided to shut down one location among the three existing facilities. With only two locations, Dendreon will save operating costs and will free up more cash for future operations requirement and marketing campaigns.

This section analyzes the configuration issues, solve the location problem. From location decision standpoint of view, the Dendreon goal consists of minimizing the total transportation cost. First, the problem is modeled using the well-known load-distance method. This method is intuitively appealing, and is widely used as pedagogical tool (Kuo and White, 2004). This will provide an idea about the location to close that will provide the least volume-traveled distance. Second, we will provide a solution of the problem using non-linear programming. The non-linear programming will provide an optimal two location solution.

3.4.1 Methodology 1: Load-Distance

Load distance methodology is a common technique used to solve location problem.

3.4.1.1 Load Distance Model

The problem can be solved using spreadsheet based methodology since it is among the most widely used software in business field. The load distance problem will be modeled to determine the best alternative. Dendreon will have the choice to shut down one of three existing locations (California, Georgia, and New Jersey). We will compute the total load-distance of each alternative. The option showing the least amount of load-distance will be the best solution. This methodology requires projecting the United States maps in 2D plan to determine the distance as well as identifying the travelling volumes.

- Step 1: Projection the USA map in 2 D plan

This example is analyzing only the contiguous states in the USA. To be able to compute the Euclidian distance, the states latitudes and longitudes are projected longitude and latitude in a 2D plan. Several tools are available in Geographic Information Systems software. Several applications and software are available. The Woods Hole Oceanographic Institute online resources provides free online application able to translate any longitude and latitude into a Cartesian coordinates . Briefly, the web application asks for origin latitude and longitude to compute the X and Y coordinate of the projected location (NDSF, 2014). The selection of the origin's coordinates is arbitrary. For an easy computation, the origin could be at the southwest of the United States Map. This will make all the capital states coordinates positive. For example, the origin latitude and longitude can be chosen as be 25N and -125E[2]. The coordinates of each state capital will be determined and projected in a 2 D plan. Figure 3-3 provides the coordinates of the 48 states capitals of the contiguous states. The coordinates of each state capital will be used to compute the Euclidian distance. The distance between city A and B is computed as the following:

$$[(X_A - X_B)^2 + (Y_A - Y_B)^2]^{.5} \qquad (3\text{-}1)$$

[2] http://www.whoi.edu/marine/ndsf/utility/NDSFutility.html

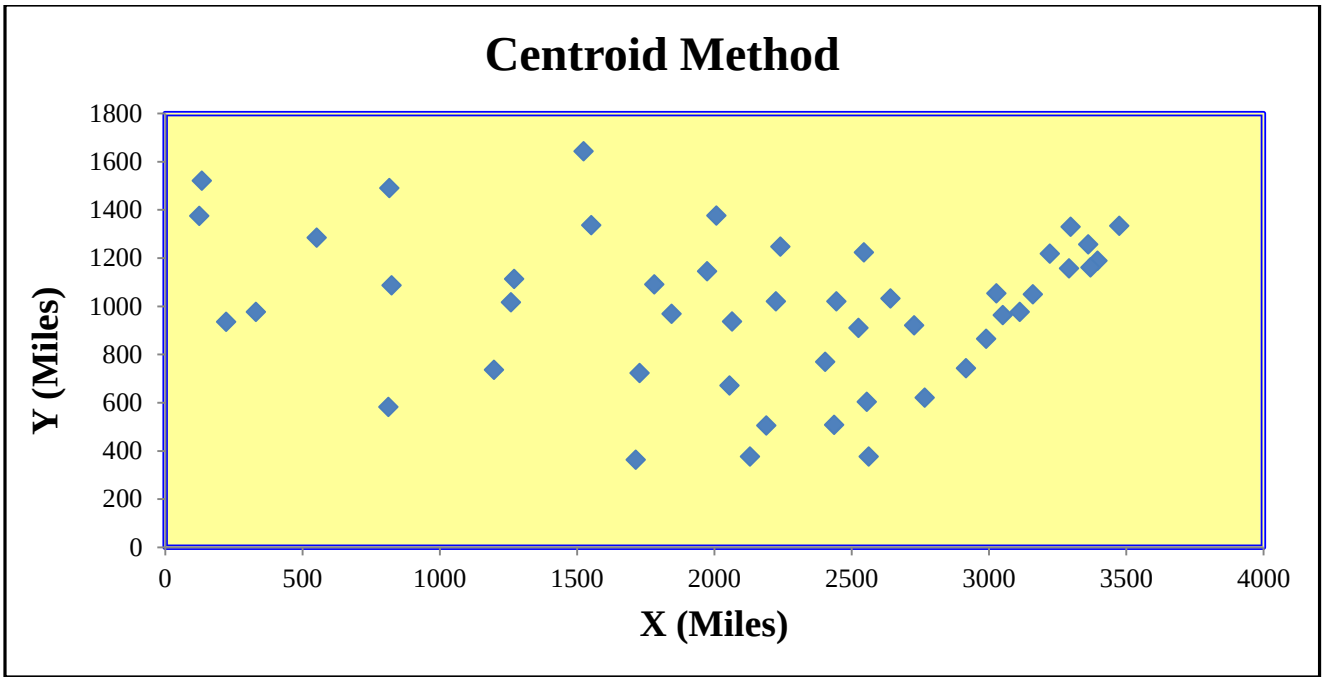

Figure 3-3: Location Problem 2D Mapping

- Step 2: Determine the load of each State

Advanced prostate cancer patients (stage IV-castration resistant metastatic cancer patients) represent potential customers for Dendreon Corp. The number of cases per state represents the load (volume) that will be transported from the doctor's office to the processing facility. To determine the number of cancer cases per state, we first researched the number of male population for each state. Then, the prostate cancer rate per state is retrieved. The exact number of cases per state is not available. However, the Center of Disease Control and Prevention provides an interval estimate of number of cases per 100,000 males. The interval median is used as an estimate for the cancer rate[3]. Provenge, Dendreon's medication, is intended for stages 3 and 4 prostate cancer. The data collected are for all types of cancer. The number of stage 3 and 4 cancer cases will be a percentage of the total cases. Prostate cancer does not discriminate among the states! Therefore,

[3] http://www.cdc.gov/cancer/prostate/statistics/state.htm

the location problem will remain the same and the data collected for all phases of prostate cancer is used as a proxy for the potential population.

- Step 3: Computation

The table below shows some of the States data. Dendreon is facing three alternatives where one location among the three existing will be closed: shutting down New Jersey, California, or Atlanta location.

Table 3-1: Dendreon Problem Data Collection

	States	Latitude	Longitude	X (mile)	Y (mile)	Cancer Rate # per 100,000	Male Population (1,000)	Number of Cases
1	AL	32.3615	-86.279118	2435	508	166	2,281,612	3787
2	AZ	33.4485	-112.0738	813	583	112.8	3,306,841	3730
3	AR	34.7360	-92.3311	2055	672	134.1	1,415,500	1898
4	CA	38.5556	-121.4689	222	936	134.1	18,505,202	24815
18	MD	38.9729	-76.5012	3050	964	145.8	2,763,806	4030
19	MA	42.2352	-71.0275	3395	1189	134.1	3,204,983	4298
20	MI	42.7335	-84.5467	2544	1224	166	4,902,854	8139
21	MN	44.95	-93.0940	2007	1377	166	2,620,570	4350
46	WV	38.3495	-81.6333	2728	921	112.8	892,120	1006
47	WI	43.0747	-89.3844	2240	1247	140	2,809,066	3933
48	WY	41.1455	-104.8020	1270	1114	145.8	277,040	404

The problem will have three different alternatives. For example, if the processing facility in Atlanta is shut down, a patient's from Arizona will have his blood cells processed at either New Jersey or California. With no capacity constraints on both locations, the patient of the state of Arizona will be served by the closer location which is in this case California. For each state, the patient medication will be processed at the closer opened location. The total distance load-distance traveled is computed for the three different alternatives.

3.4.1.2 Results

The results are computed for the three alternatives and the best solution is determined. The results from the excel computation are summarized on the table 3-2.

Table 3-2: Load Distance Results

	Total Load-Distance (patient-miles)		
Alternatives	Closing NJ	Closing CA	Closing GA
Results	**122,984,904**	166,098,109	137,092,310

From the previous analysis, it is apparent that shutting down New Jersey is the option with the lowest load-distance travelled. In case Dendreon decides to one more location, and based on location decision criterion, it will be New Jersey. Closing California location will be the worst decision in term of total load distance. The load distance methodology provides an understanding of the best alternative given the current Dendreon processing network configuration. Non-linear mathematical programing approach listed below will provide the theoretical optimal solution.

3.4.2 Methodology 2: Non Linear Programming

In this section, Dendreon still have to select the best two locations that will minimize the load-distance. The purpose of this section is mainly to assess the effectiveness of the current facility location configuration. The problem is modeled as a non-linear program where the decision variable will be the X and Y coordinates of the facility locations. To solve the problem, we are using excel solver package.

The objective function is given by the equation 3-2.

$$\text{minimize} \sum_{i=1}^{48} \min_{j=1,2} \left\{ \left[\left(X_i - \bar{X}_J\right)^2 + \left(Y_i - \bar{Y}_J\right)^2 \right]^{.5} * \mathrm{V_i} \right\} \qquad (3\text{-}2)$$

$$X_i, Y_i \in \mathbb{R}$$

Where

$\bar{X}_J, \bar{Y}_J$ *represents the corrdinate of optimal two location,* $j = 1,2$

X_i *and* Y_i *represents the coordinate of the states capital,* $i = 1..48$

Formulation can vary easily to extend for more than two locations.

3.4.3 Analysis

Given the size of the problem, there was no need to involve any specializing non-linear programming software to solve the problem. The optimal solution is developed using excel solver. Results are shown below.

Table 3-3: Optimal Solution Coordinates

	X (Miles)	**Y (Miles)**
Location 1 Coordinate	**222**	**936**
Location 2 Coordinate	**2593**	**905**

The current solution provided a total of 102,006,203 load-distance. This represents a 17% improvement over the existing location. While location 1 coordinate indicate the capital of California, we looked up the second location by transferring the X,Y coordinates into latitude and longitude and using google map, we found that the second optimal location will be in Owingsville, Kentucky.

3.5 Methodology Comparison

This section compares the results obtained from the two methodologies. The graph below summarizes the two methodologies. This emphasizes the level of inefficiencies of Dendreon configuration from logistics perspective. The graph also illustrates the impact of adding extra location which can be useful to perform cost benefit analysis.

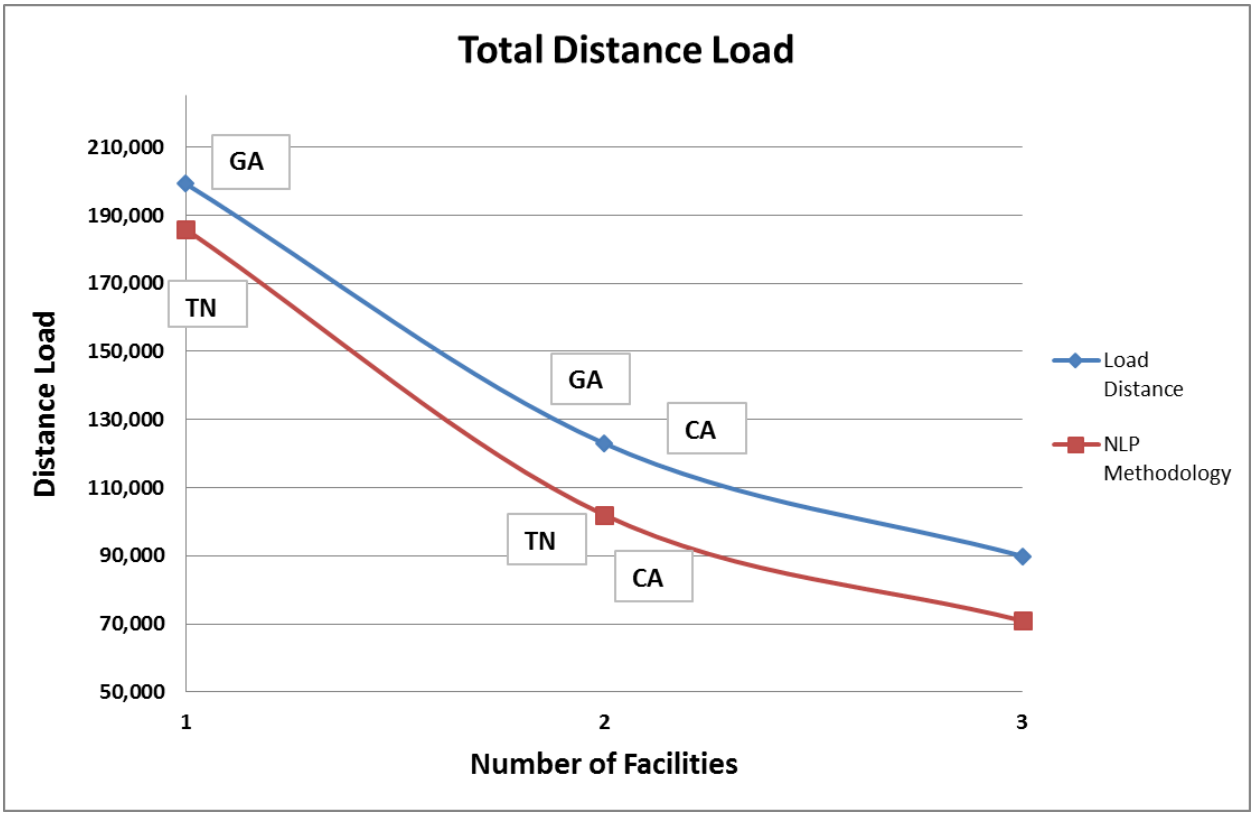

Figure 3-4: Results Comparison

3.6 Conclusion

The current chapter aimed at investigating the strategic decision in the case of processing facility location in service oriented pharmaceutical supply chains. In the case of biologics, time is a sensitive factor and therefore logistic configuration is crucial. This study also illustrates the imperative for disintermediation where the pharmaceutical supply chain involves bi-directional flows and the patient is both a supplier and a customer.. The case study developed in the current

chapter represents a real word application of highly personalized medicine with total disintermediated distribution channels. The case study development represents a practical application of using basic decision science tools in supply chain context. First, the projection of longitude and latitude coordinates represents an approximation for distance approximation that can be used in pedagogical context as well as in business decision context. The solution methodology is modeled using widely available spreadsheet based tools. The case study will make such tools more relevant in business environment and provide an opportunity to apply it in real cases.

Chapter 4: Disintermediation Problem in Biopharmaceuticals Supply Chain: Numerical Study

4.1 Introduction and Research Objectives

The journey of medicine from the manufacturer to the patient involves many entities: wholesalers, distributors, pharmacies, healthcare providers, and payment agencies. As discussed in chapter 2, the pharmaceutical industry has shown some structural changes favoring direct sales (supply chain disintermediation). For example, Pfizer started selling Viagra online in 2013 (Isidore, 2013). The study of distribution channel networks in general and the supply chain disintermediation in particular, has interested researchers. The supply chain disintermediation (elimination of the middleman) has shown its attractiveness in several industries (e.g. insurance, electronics, garments & apparel) where the supply chain configuration eliminates the double marginalization and allows the users to have a better price for the same product and service. Supply chain disintermediation was almost exclusively applied to retail and service fields with far less emphasis on the healthcare industry (Hesse et al., 2011). The disintermediation phenomenon has become a common practice, especially in the case of personalized goods (customized Nike shoes, business cards, etc.). In the case of pharmaceuticals, the emergence of biologics in general, and personalized drugs in particular calls for disintermediation. Supply chain disintermediation is gaining more attention in the pharmaceutical context from managerial and practical perspectives (Enyinda and Tolliver, 2009).

4.1.1 Supply Chain Disintermediation in Biologics

The topics of supply chain disintermediation in the context of pharmaceutical industry in general and biologics in particular is of interest to practitioners who are attempting to find alternatives to

better serve their customers (Danzon and Nicholson, 2012). Chapter 2 provided a discussion of the relevance of supply chain disintermediation in the context of biologics. The biologics industry provides a unique situation: short product shelf life, high demand variability, and high financial risk. The product's short shelf life makes disintermediation attractive as it increases the product's useable time and therefore it reduces the perishability cost. In fact, in the case of biologics and because of the higher production cost, the perishability cost becomes a critical factor. The high demand variability at the hospitals will impact both the stock out and excess inventory levels. A disintermediation decision will influence the shortage and perishability costs. The disintermediation level will have an impact on the total market mediation cost: the sum of perishability and shortage cost.

Direct distribution channels intend to reduce the perishability cost by providing longer shelf life for products. The direct sales reduces the total product lead time from the manufacturer to the hospital in comparison with intermediated configuration. Therefore, it is expected that the shorter lead time will minimize the total perishability cost (Deniz, Karaesmen, and Scheller-Wolf, 2010). On the other hand, intermediaries provide the opportunity to reduce the impact of the supply chain variability via pooling effect. The demand variability at the hospitals will be mitigated by the distributor's pooling effect which will reduce the shortage cost. The disintermediation level will impact the tradeoff between perishability cost (overstocking) and shortage cost (under stocking) and the total market mediation cost.

Despite the possible benefits deriving from direct distribution channels, the findings in chapter 2 showed that about 85% of the biologics' physical flows is intermediated by specialty distributors and/or wholesalers. The non-intuitive existing practices represent a motivation to study the different factors influencing the material flows and the disintermediation level. Based on the

different arguments provided in chapter 2, it was expected that specialty pharmaceutical supply chains will witness a greater level of disintermediation. Moreover, the novelty of the supply chain disintermediation practices in the area of pharmaceuticals represents another source of motivation to further explore the alternative distribution channels and determine some of the factors that influences this decision. Finally, the practical aspect of the disintermediation problem and its relevance to healthcare practitioners provides more incentives to explore this topic.

4.1.2 Research Objectives

The current chapter aims at providing a better understanding about supply chain disintermediation dynamics from a market mediation cost perspective. While excess inventory at the hospitals and the distributor will increase the perishability cost, it will at the same time reduce the shortage cost by providing a demand variability buffer. The tradeoff between the perishability cost and shortage cost will dictate the supply chain disintermediation level (intermediated, disintermediated, or hybrid). The demand variation and the shortage cost structure will influence the total market mediation cost. The current chapter aims at answering the following research questions:

What's the best disintermediation strategy that will minimize the total market mediation cost measured by the sum of perishability and shortage costs?

What are the most influential factors that impact the total market mediation cost?

The current chapter uses scenario approach to gain an understanding of the problem. Analytical complexity of the problem does not lead itself to easy interpretation of the disintermediation level sensitivity. The level of disintermediation, which is the decision variable, is determined by the ratio of medication that is directly delivered to the hospital to the total

delivered medication. The inventory and the shortage level at the end of each period will determine the amount of perishability and shortage cost.

As a first step, a scenario approach simulation was designed with 10 hospitals, one distributor, and one manufacturer. The demand is generated at the hospitals and pulled from the distributor and the manufacturer. The disintermediation ratio varies between 0% (all the medicine is sold via the distributor) and 100% (direct sales). The model parameters will be the demand variability at the hospital expressed by the coefficient of variation. The other parameter will be the shortage cost ratio expressed as the ratio of the shortage cost to the perishability cost. The adoption of standardized parameters provides a better generalization of the problem. The scenario approach will serve as an exploratory study of the supply chain disintermediation problem. In a second step, a large scale numerical study is developed. The numerical study will analyze the different influence of different factors on the total market mediation cost. Using a three factor Anova analysis, the numerical study will investigate the importance of demand variability, shortage cost structure, and supply chain disintermediation in shaping the total market mediation cost. Finally, the numerical study will be extended to include the impact of service level on total market mediation costs.

The current chapter is organized as follows: first, a literature review of disintermediation in general and in the context of pharmaceutical supply chain will be provided. The literature review will emphasize the relevance of the topic, and highlight some of the research gaps. The following section will address the scenario approach which represents an exploratory analysis of the study. Next, a large scale Anova experiment is designed to determine the most influential factors affecting the total mediation cost structure. Finally, a summary of the results and findings as well as areas of future research is provided.

4.2 Literature review

The following section will provide major findings in literature linked to the supply chain disintermediation. First, an overview about the fundamentals that relates to supply chain disintermediation is provided. The subsequent section will address the major findings in an attempt to show some research gaps that this chapter is addressing.

4.2.1 Supply Chain Disintermediation

4.2.1.1 Definition

Intermediaries have an important role in distributing products, using promotions and offering special offers for customers. They also provide services for customers and help the manufacturers better understand the market and the customer behavior. Intermediaries help facilitate transactions between buyers and manufacturers and improve the value of the product/service by insuring product quality and providing warranty services (Choi, Stahl, and Whinston, 1997). For example, Microsoft and Samsung have recently signed a deal with Best Buy to promote and demonstrate the features of their products. For manufacturers, the decision to disintermediate is challenging.

The term disintermediation was first used in financial sector to describe the trend for small investors to invest directly and avoid using traditional intermediaries such as brokers (Gellman, 1996). The terminology of disintermediation then was adopted in the field of supply chain management. Disintermediation is the action of cutting out the middlemen by direct transaction between the service/product provider and the end customer (Hoffman, 1995). This aims at reducing the role played by the intermediaries. Disintermediation is also defined as the elimination of an intermediary from the business process when the cost of adding the intermediary exceeds its value added (Chircu and Kauffman, 1999; Pinto, 2000). Companies will reach customers directly instead of going through the traditional supply chain venues (distributors, wholesalers…). The idea of

disintermediation emerged from the persistent customer's demand for lower cost (Shunk et al., 2007). To remain competitive, firms had to flatten their supply chain, favoring more direct contact between the firm and its customers (Pinto, 2000). Moreover, customers are requesting more personalized products and services which might not be available in the traditional supply chain pipeline. Therefore, the customer will directly interact with the product manufacturer/service provider to place the order. Direct channels of communication between the customer and the product/service providers have created multiple disintermediation mechanisms.

4.2.1.2 Supply Chain Disintermediation Advantages and Disadvantages

The need for disintermediation in some cases implied the mechanism of Supply Chain disintermediation. Six main ways of SC disintermediation emerged from B2B business practices: (i) strategic partnering, (ii) mergers and acquisitions, (iii) organic growth, (iv) communication and training, (v) incentives, and (vi) information and communication technology (Nordin, Brozovic, and Holmlund, 2013). Nordin et al. (2013) proposed different ways of eliminating the middleman and collaborating directly with the customer in business to business (B2B) context. Disintermediation techniques involve working closely with the middleman and serve together the final customer. The direct distribution channels have shown some benefit from a customer's perspective. However, the complex nature of these different mechanisms provides insights about the challenges facing disintermediation strategy.

On one side, supply chain disintermediation provides several advantages. First, it allows a closer relationship between the product/service provider and the end customers. This will increase the interaction and improve the coordination level, leading to higher customer satisfaction (Nissen, 2000). Second, customer input represents a great source of knowledge and an alternative for improvement (Davenport and Klahr, 1998). Disintermediation promotes knowledge sharing by

increasing the level of interaction. Third, organizations adopting supply chain disintermediation have experienced a higher level of product innovation based on the customer input, and also attained greater control over product innovation (Coe and Hess, 2005). Moreover, disintermediation can provide more agility to manufacturers by responding quickly to changes in the market. This also helps firms better manage their inventories (Erengüç, Simpson, and Vakharia, 1999). Finally, the cost benefit to both customers and product/service providers remains the most prominent advantage.

On the other hand, supply chain disintermediation is a complex issue. First, when a firm decides to eliminate the middlemen, it has to replicate intermediaries' core competencies. In many cases, the wholesalers/distributors have a greater distribution knowledge and can achieve high sales levels (Atkinson, 2001). Second, the management of the different flow in the supply chain (physical, information, financial and knowledge) becomes more difficult. In some cases, the focal company will lose its focus on its core competency (Halbert, 2006). Third, in case of physical goods, disintermediation will increase the level of stock on hand for the focal company. Instead of pushing its products on the supply chain pipeline, manufacturers should rapidly respond to customers' demand by maintaining an inventory buffer in house. This will require a higher level of investment.

The literature review shows recent trends toward investigating supply chain disintermediation. A large number of conceptual studies have addressed the problem of disintermediation. However, very few studies have attempted to empirically or analytically assess the issue of disintermediation (Rossetti and Choi, 2008). The conflicting signals that disintermediation strategy is showing and the pressure that exists from existing distribution channels provides relevance to research on this topic further. This chapter addresses the

disintermediation problem in the context of the pharmaceutical supply chain. The next subsection provides an overview of the disintermediation practices in the field of pharmaceuticals.

4.2.1.3 Supply Chain Disintermediation in Pharmaceutical Industry

The disintermediation strategy is not widely used in the pharmaceutical industry despite its attractiveness evidence from other industries (Niziolek, Chiam, and Yih, 2012). In fact, the direct-ship sales strategy in the pharmaceutical context represents some challenges due to the number of influential players in the supply chain. The complex relationship linking the consumer/customer/decision-maker triad is unique to the prescription pharmaceutical context. The decision maker (doctors, in most cases) is different from the consumer (the patient) as well as the customer (Insurance, Pharmacy Benefit Management, and Government). Moreover, pharmaceutical firms strive to enhance the availability their products (Burns, 2002). Pharmaceutical firms use distributors as a buffer to guarantee a certain service level at the pharmacies. Additionally, disintermediation requires a large investment in information technology to guarantee smooth functioning of the supply chain and make up for the intermediaries' roles. In the case of pharmaceuticals, firms tend to invest more in production assets, R&D, and patient care instead. Therefore, pharmaceutical supply chains are behind other industries in term of disintermediation configuration (Niziolek et al., 2012).

The complex nature of the pharmaceutical industry did not stop companies from attempting disintermediation. The mail order prescription represents a way of partial disintermediation where the order is placed directly at the pharmacy and shipped to the patient's home. In 2007, Pfizer started selling its medicines directly to pharmacies in the United Kingdom. Today, Pfizer offers some of its medicine online for direct sales. Recent studies have addressed the issues of supply chain disintermediation from a cost benefit perspective and inventory analysis (Jetly, Rossetti, and

Handfield, 2012; Niziolek et al., 2012). The result showed that mixed disintermediation strategies, where 55% of the revenue are generated from sales, are direct-shipped, providing better financial results and a smaller inventory level. The analytical study did not consider the nature of the product.

4.3 Supply Chain Disintermediation in Biologic Pharmaceuticals: Scenario Approach

Computer simulation methodology is gaining more popularity in social and organizational science research (Dooley, 2001). Simulation allows researchers to address the complexity of a system and help develop a "what if analysis." The current section provides a scenario approach to the problem by providing general formulation.

The previous studies in the simulation showed three main practices:

- System dynamics, which consist of determining the "key state variables" that determine the system behavior. The other system parameters are related to one another (Karnopp, Margolis, and Rosenberg, 2012).
- Discrete event simulation, which involves modeling the operations of a system as a sequence of events evolving over time. The system behavior will be influenced by the organization's resources and other trigger events (Zeigler, Praehofer, and Kim, 2000).
- Agent-based simulation, which consists of simulating of the action and interaction among different autonomous agents in order to maximize the system utility (Railsback, Lytinen, and Jackson, 2006).

The current chapter uses scenario approach simulation in order to provide an approach to the problem. First, decision rules will be established. Then, a mathematical model will be

developed to address the problem. Finally, the problem will be analyzed using simulation techniques.

The illustrative example aims to show the cost behavior at different disintermediation levels for biologics supply chains. In this study, it is assumed that one manufacturer will produce and sell a biologic product. The manufacturer will have the production shipped directly to the hospital or sell the medicine via the distributor which will then sell it to the hospital. The level of disintermediation will be determined by the percentage of medicine that will be sold directly to the hospital. In this example, there is one manufacturer targeting one region with 10 hospitals and one distributor. The hospitals are the decision makers and will decide to buy from the distributor or from the manufacturer (Figure 4-1). Therefore, the hospital's procurement policy determines the level of disintermediation. As an assumption, all hospitals will have the same disintermediation policy and are served by the same distributor.

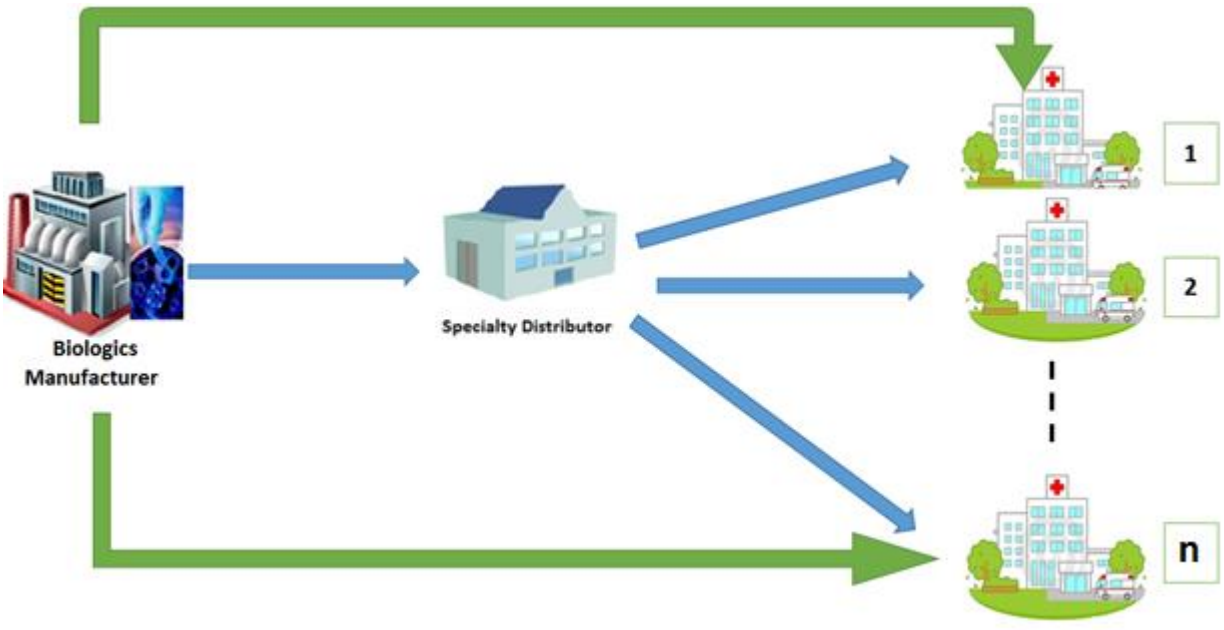

Figure 4-1: Illustrative Example

4.3.1 Simulation Scenario

Scenario analysis approach suggests setting up different steps for the scenario (Hsia et al., 1994).

Step 1: Each Hospital will generate its daily demand. There are n hospitals that are served by one single distributor/wholesaler. It is assumed that all hospital have independent and identical demand distributions. Demands are uncorrelated.

Step 2: The hospital will determine the purchasing strategy: the percentage of demand that will be satisfied directly from the manufacturer and the percentage of demand that will be purchased from the distributor (the disintermediation level).

Step 3: The demand from the hospitals placed on the distributor will be pooled at the distributor which will determine the demand at the distributor level.

Step 4: Each hospital will place an order from the manufacturer. Orders are placed on a weekly basis. The order placed aims at satisfying the weekly demand. The hospital aims at maintaining a certain service level. The service level will determine the order up-to level quantity.

Step 5: The distributor, based on the weekly pooled demand, will place an order from the manufacturer to satisfy a certain service level as well. The service level will determine the order up-to level quantity.

Step 6: The daily demand will be satisfied with the existing inventory. At the end of each replenishment period, the quantity of expired (perished) or shortage quantity will be determined at the hospitals and the distributor.

Step 7: An up-to level inventory replenishment will be used at the hospitals and at the distributor.

4.3.2 Simulation Set-up

The main goal of simulation is to find the supply chain network configuration as reflected by the disintermediation level that will minimize the total cost. Biologic medicine is experiencing a growing demand with high variability (American Cancer Society, 2013). The high demand variability at the hospital's end increases the risk of shortage. Moreover, biologic medicines are characterized by a short shelf life (Pitts and Stark, 2012). The short shelf life increases the risk of

perishability. The illustrative example will focus solely on the tradeoffs existing between shortage cost and perishability costs. On one end, the distributors provide the pooling effect, which will minimize the risks of shortage by improving the service level. On the other end, the direct sales model to the hospitals increases the product's useful life, which will reduce the perishability cost. The objective function is to minimize the sum of the perishability and shortage cost at the hospitals and the distributor, which is referred to as the total cost in this example.

Decision Variables: In this model, the hospital represents the decision maker. The hospital decides the quantity to be ordered directly from the manufacturer and the quantity to be ordered at the distributor. The ratio of medicine ordered directly from the manufacturer over the total demand will determine the disintermediation level. The disintermediation level will dictate the inventory levels at the hospital and the distributor, which will impact the total cost at the supply chain. Let's define X: $The\ disintermedaiation\ Ratio$. It is defined as the ratio of the quantity ordered directly by the hospital from the manufacturer to the total hospital demand.

$$0 \leq X \leq 1 \qquad (4\text{-}1)$$

Demand Variation: The medicine demand is generated at the hospital level. The model uses a daily demand that follow a normal distribution.

$$d_h \sim N(\mu_h, \sigma_h) \qquad (4\text{-}2)$$

In the supply configuration with n identical hospitals being served by one distributor, the pooling effect at the hospital will provide the following parameters for distributor's demand:

$$\mu_d = n * (1 - X) * \mu_h \qquad (4\text{-}3)$$

$$\sigma_d = \sqrt{n} * (1 - X) * \sigma_h \qquad (4\text{-}4)$$

Service Level: The service level represents a measurement of the system performance. It refers to the extent to which a service meets or exceeds customer expectation (Parasuraman et al., 1985). Service level is defined in inventory management policy as the probability that the demand of a product in a specific period is less than or equal to the inventory on hand (Tempelmeier, 2000). The literature review related to service level and inventory management is rich. In the context of a single period stochastic model, the newsvendor model is the most popular approach. In the newsvendor model, based on the critical fractile ratio, the inventory policy will be determined. This policy aims at minimizing the tradeoff between the overstocking and under-stocking costs. This ratio will also determine the optimum service level for the organization. When the overstocking cost is high, companies will tend to have a lower service level. In other cases, if the under-stocking cost is high, organizations will have an extra inventory which will increase the service level.

For hospitals and distributor, the rational behavior based on the newsvendor model suggests that each entity will order the quantity that will minimize the total inventory cost. However, research in the area of healthcare management did not make the rational choice of finding the optimal service level (Gebicki et al., 2013). It actually considered the service level as a target or a minimum level that healthcare entities should maintain (Möllering and Thonemann, 2010). In these cases, the service level becomes a constraint that will affect the shortage structure and relevance. Therefore, in many cases, hospitals will not follow the newsvendor model to determine their replenishment policy.

The determination of the required service level at the hospital and the distributor is based on previous studies. Healthcare officials have provided a set of instructions regarding the medication service level at hospitals and distributors. However, no specific minimum service level

or suggested target is provided. The medication service level requirements emphasize patient risk minimization and providing the best healthcare. Gebicki et al. (2013) analyzed 4 different inventory policies at hospitals and compared the results for 3 different service levels: 95%, 97.5% and 99%. Because of the nature of the problem on hand (high priced medication and relatively low shortage cost), the newsvendor model suggests that the service level will be relatively low. In this chapter, 90% and 85% service level policies are selected for hospitals and distributors.

Replenishment Policy: In this scenario, the replenishment happens at a weekly frequency using a FIFO policy. The medicine will arrive at day 1 and will serve to satisfy the cumulative demand for the periods until the next the shipment arrives. Let T be the length of the replenishment cycle. Let $Q_{hi} and\ Q_{di}$ be the quantity of medicine replenished at the hospital and the distributor at the beginning of the cycle. Let $I_{hi}\ and\ I_{di}$ be the inventory level at the hospital and the distributor at period i. Finally, we assign l_1 to be the lead time from the manufacturer to the distributor and the hospital. We also assign l_2 to be the lead time from the distributor to the hospital.

The hospitals and the distributor will assess the existing inventory at the time to place the order from the manufacturer and will place an up-to service level order. The adjustment of the order placed will take into consideration the average daily demand.

$$Q_{hi} = F^{-1}\ (Service\ Level)\ ) - max\ \ (0, I_{i-l1} - l1 * X * \mu_h) \qquad (4\text{-}5)$$

weher the demand distribution at the hospital follows $\mathrm{N}(\mathrm{X} * \mathrm{T} * \mu_{\mathrm{h}}, \sqrt{\mathrm{T}} * \sigma_{\mathrm{h}})$

$$Q_{di} = \mathrm{F}^{-1}\ (\mathrm{Service\ Level})\ ) - max\ \ (0, \mathrm{I}_{\mathrm{i-l1}} - (\mathrm{l1} + \mathrm{l2}) * \mu_{\mathrm{d}}) \qquad (4\text{-}6)$$

weher the demand distribution at the hospital follows $\mathrm{N}(\mathrm{T} * \mu_{\mathrm{h}}, \sqrt{\mathrm{T}} * \sigma_{\mathrm{h}})$

Inventory Level: The inventory level at period i in a given replenishment cycle for the hospitals and the distributor will be given by:

$$I_i = Q - \sum_{j=1}^{i} d_j \qquad (4\text{-}7)$$

In a case of perishable goods, inventory can be seen as a vector of items with different age stages. Let $\overleftarrow{Y_t}$ represent the inventory vector at the date t.

$$\overleftarrow{Y_t} = (y_1, y_2, .., y_m) \qquad (4\text{-}8)$$

Where m represents the medicine shelf life. At the end of the t^{th} day, a quantity qt+1 will be delivered. Let w_t represent the quantity that will expire at the end of the period t.

$$w_t = y_m \qquad (4\text{-}9)$$

The cumulative expired medicine in D period problem will be expressed by

$$W = \sum_{i=1}^{D} w_i \qquad (4\text{-}10)$$

The recurrence formulation of the inventory level at period i will be identified as following:

$$y_j = y_{j-1} - d_i \qquad (4\text{-}11)$$

And the general formulation of the inventory at period i is given by:

$$y_j = max(\sum_{n=i-m+l}^{i} Q_n - \sum_{n=i-m+l}^{i} d_n , 0) \qquad (4\text{-}12)$$

The inventory formulation as shown does not allow any negative inventory. In this case, any unsatisfied demand will be considered as lost sales (no backlog orders).

Shortage Cost: The shortage cost is the most challenging component to estimate, especially in the healthcare context. The shortage cost is the cost incurred when the demand cannot be fully and immediately satisfied due to a stock shortage (Oral et al., 1972). The Drug Shortage Program (DSP) at the Food and Drug Administration defines a drug shortage as "a situation in which the total supply of all clinically interchangeable versions of an FDA regulated drug is inadequate to meet the current or projected demand at the user level" (Center for Drug Evaluation and Research, 1998). Shortage cost has been operationalized in several different ways in the literature. It can be estimated as: (i) a fixed cost per stock-out and independent of the units and duration, (ii) a specified charge per unit per period of time , and (iii) a multiple of the unit value and independent of the number of period (Peterson and Silver, 1979). The current study will use the latter operationalization which is judged most adequate to the healthcare context. When a patient is scheduled for a medication and the drug is not available, the hospital will suffer from a shortage cost during that period. Because of the critical aspect, the patient treatment will be administrated somewhere else and therefore, it is considered as lost sale.

The drug shortage cost estimation is more challenging in the context of biologics with less available substitutes (Mellstedt, Niederwieser, and Ludwig, 2008). An investigation of 228 hospitals showed that 89% of hospitals suffer from shortage (Cherici, Frazier, and Feldman, 2011). Drug shortage is costing U.S. hospitals more than 200 million dollars annually, not including the labor cost to manage the shortage (Cherici et al., 2011). The drug shortage has an impact on the quality of healthcare and the overall cost of healthcare delivery (Ventola, 2011). The determination of the exact shortage cost is, however, arbitrary and will depend on the nature of the product and its value (Leng and Parlar, 2009). In the case of biologics, because of the lack of substitute

products, a hospital suffering from cost shortage will reschedule the patient for the following period.

In this illustrative example, the shortage cost will be experienced at both hospitals and distributors. The shortage quantity is the difference between the daily demand and the inventory in hand. Let S_k be the total shortage quantity at replenishment cycle j.

$$S_j = \sum_{n=1}^{T} \max(d_n - Q_k - I_{n-1}, 0) \qquad (4\text{-}13)$$

Where $Q_k$represents the quantity received at the beginning of cycle k.

The shortage cost will be equal to:

$$Shortage\ Cost = SC * \sum_{k=1}^{K} S_k \qquad (4\text{-}14)$$

Where SC represents the shortage cost per unit.

Perishability Cost: Scholars have been investigating perishable goods under different conditions of production and demand conditions for over four decades (Nahmias, 1982). Most of the studies have looked to the problem from a cost minimization perspective (Raafat, 1991). The determination of the perishability cost depends on the nature of the product and the type of buying contract. In some cases, the perishable products will require a special disposal treatment that can be costly. This concern arises in the case of pharmaceuticals where the expired products can be toxic. To determine the perishability cost at the distributor and the hospital, the product cycle life needs to be investigated when the product is delivered to the distributor and in case it is dispensed directly to the hospitals (Figure 4-2 and 4-3).

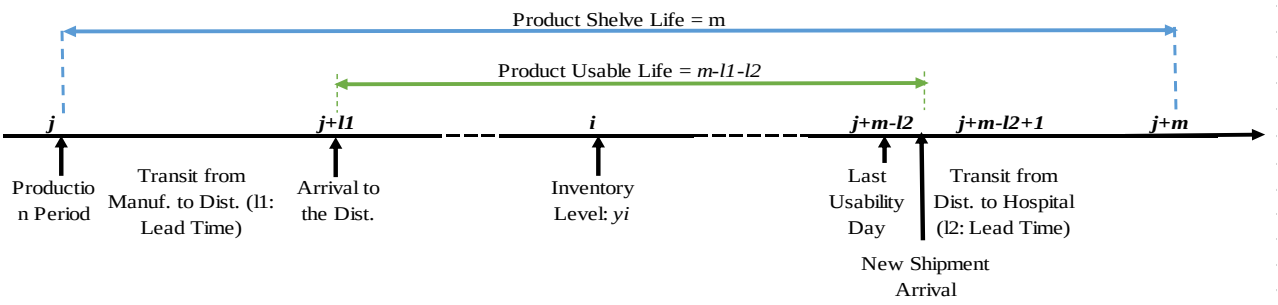

Figure 4-2: Medicine Life Cycle at the Distributor

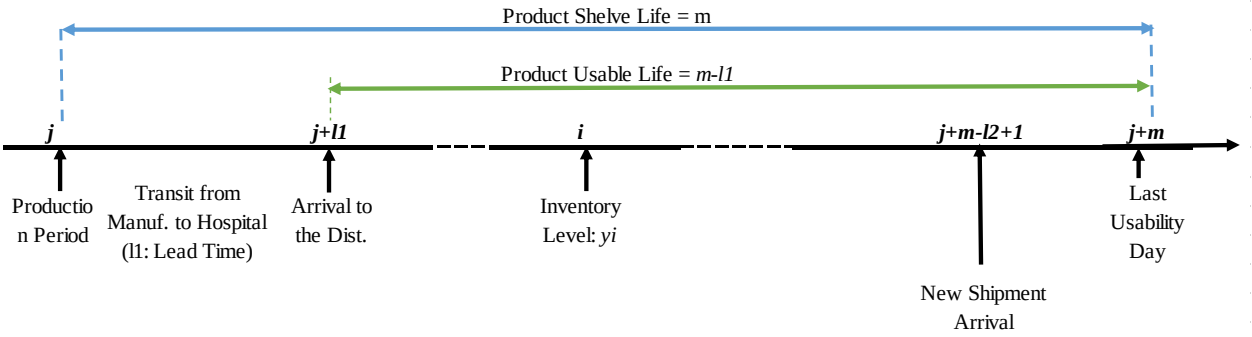

Figure 4-3: Medicine Life Cycle at the Hospital

The perishable items for the single period replenishment will be identified by the inventory level on the last day of the usability life. Using the general formula of inventory, the perishable items can be determined for both distributor and hospital at the end of the cycle.

The total perishable quantity at the distributor for a replenishment cycle j is determined by w_{kd}:

$$w_{jd} = \max\left(\sum_{n=j}^{j+m-l2} Q_n - \sum_{n=j}^{j+m-l2} d_n, 0\right) \qquad (4\text{-}15)$$

The total perishable quantity at the hospital for a period j is determined by w_{jh} :

$$w_{jh} = \max\left(\sum_{n=j}^{j+m} Q_n - \sum_{n=j}^{j+m} d_n, 0\right) \qquad (4\text{-}16)$$

For a K cycle problem, the total perishable cost will equal to

$$Persishability\ Cost = P * \sum_{k=1}^{K} w_k \qquad (4\text{-}17)$$

Where P will represent the perishable cost (a different perishability cost for the hospital and the distributor).

Objective Function Formulation: As shown at the beginning of the section, the objective function consists of minimizing the total market mediation cost. The total mediation cost will be the sum of the perishability and shortage cost at the hospitals and the distributor. The objective function will depend on the level of disintermediation.

$$\min\left(\sum_{k=1}^{K} P_h * w_{hk} + \sum_{k=1}^{K} P_d * w_{dk} + \sum_{k=1}^{K} SC_h * S_{kh} + \sum_{k=1}^{K} SC_d * S_{kd}\right) \qquad (4\text{-}18)$$

The disintermediation level, which is the model decision variable, will influence the inventory level. Based on the inventory level at both distributor and hospitals, the number of perishable and shortage items at the end of each cycle will be determined.

Both hospitals and distributor procurement policies satisfy certain structural properties. The service level constraint is shown in the replenishment policy as shown in equation (4-5). The second main constraint relates to the cost structure. Both hospitals and distributor will suffer from either shortage cost or perishability cost or none of them at each period. These properties are shown in equations (4-19) and (4-20).

$$w_{hk} * S_{hk} = 0, \quad k = 1..K \qquad (4\text{-}19)$$

$$w_{dk} * S_{dk} = 0, \quad k = 1..K \qquad (4\text{-}20)$$

4.3.3 Simulation Analysis

The current chapter uses simulation analysis to gain an understanding of the disintermediation levels and its effects on the market mediation cost. In fact, the other works of disintermediation have used the simulation technique due to the complexity of the problem (Chiang, 2012; Niziolek et al., 2012). To address the complexity level, this section uses simulation analysis to address the problem. In this chapter, @Risk Excel companion software is used. @Risk software provides more sophistication to Excel spreadsheets by adding more functionality. @Risk is used to generate the daily demands at the hospitals. The software also provides the descriptive statistics of the simulation outputs. This section develops the results of the different Monte Carlo simulation models. Two variables will be manipulated: variability and shortage cost structure. The demand variability will be measured by the coefficient of variation. The cost structure is assessed by the shortage cost ratio. The shortage cost is the ratio measured as the shortage cost to the perishability cost.

4.3.3.1 Model Parameters

The scenario approach requires decisions about the parameters values. The scenario approach models and parameters are determined based on literature investigation and secondary data. Table 4-1 provides the model parameters estimates. The product shelf life and the lead times can be used or modified based on values determined at the industry level for specific instances.

Table 4-1: Parameters Notation

Notation	Description	Value
μ_h	Hospital daily demand	40 units
σ_h	Hospital daily standard deviation	10 units
N	Number of hospitals	10
C	Manufacturing cost	\$200 per unit
c_h	Transportation cost from the manufacturer to hospital	\$0.25 per unit
c_d	Transportation cost from the manufacturer to distributor	\$0.10 per unit
P_h	Hospital perishability cost	$P_h = C + c_h$
P_d	Distributor perishability cost	$P_d = C + c_d$
SC_h	Hospital shortage cost	Variable
SC_d	Distributor shortage cost	Variable
k	Shortage cost ratio	$k = \frac{S_h}{(P_h + S_h)} = \frac{S_d}{(P_d + S_d)}$
$l1$	Manufacturer lead time	2 days
$l2$	Distributor lead time	1 day
m	Medicine shelf Life	10 days
SL_h	Hospital service level	90%
SL_d	Distributor service level	85%

Clearly, the transport cost to the hospitals is assessed to be greater than the transportation cost to the distributor. In fact, because of transportation economy of scale, distributors will experience lower transportation cost per unit than hospitals Also, it is reasonable to expect perishability cost at the hospital level to be higher than that incurred at the distributor.

$$c_d \leq c_h \qquad (4\text{-}21)$$

$$P_d \leq P_h \qquad (4\text{-}22)$$

4.3.4 Results

In this illustrative example, two different variables will be manipulated (demand variability, shortage cost ratio). First, the demand variability is measured by the coefficient of variation. Higher coefficient of variation will favor the use of distributors who will provide the pooling effect. Second, the shortage cost effect will be the ratio between the shortage cost and the perishability cost. In this model, the perishability cost will be fixed at the landing cost for both distributor and the hospital.

4.3.4.1 Demand Variability Model

The first study illustrates the impact of the demand variability. This is accomplished through varying standard deviation of daily demands. With all other parameters remaining the same, the variation of the coefficient of variation will impact the best disintermediation strategy. Figure 4-4 provides a demand variability analysis for a particular value of shortage cost ratio. For example, for a shortage cost of 0.45, a set of market mediation costs were developed by varying the coefficient of variation. The results in figure 4-4 show that for high variation($CV > 0.25$), the total intermediation provides a lower cost. In fact, at high variations, the distributor pooling effect becomes very critical. At the other end, for a lower variation configuration($CV < 0.2$), the total disintermediation provides a lower cost. In fact, at high variation level, the shortage cost will be significantly higher. Therefore, the distributor's contribution will be important for buffering the demand variation. The risk pooling effect will minimize the total market mediation cost, making the intermediated model a better alternative (Schwarz, 1989). On the other hand, a low level of variation is expected to minimize the shortage cost. Therefore, direct distribution channels will be more profitable.

The discussion above shows a trade-off between the perishability and the shortage cost. The variability level will have an impact on the total cost. For a fixed level of shortage cost, the coefficient of variation variable will determine the optimal disintermediation strategy. Based on the previous discussion, it is expected to observe the following:

High level of product demand variation suggests that disintermediated distribution channels will lead to higher market mediation cost in comparison to intermediated distribution strategy.

Low level of product demand variation suggests that disintermediated distribution channels will lead to lower market mediation cost in comparison to intermediated distribution strategy.

To address the previous observations, a set of one way Anova experiments was set up. For different combinations of levels of coefficients of variation and shortage cost, a set of 500 replications of total market mediation cost was simulated for the five different levels of disintermediation (0%, 25%, 50%, 75%, and 100%). For example, a CV of 0.2 and a shortage cost ratio of 0.6, the Anova analysis shows that total disintermediation has provided a significantly different total cost. To be able to perform the mean difference test, it is suggested first to test for the variance homogeneity, also known as Levene's test (Olkin, 1960). Table 4-2 shows that the Levene's test is significant and, therefore, the analysis of variance is possible.

Table 4-2: Test of Homogeneity of Variances

Total Cost

Levene Statistic	df1	df2	Sig.
71.579	4	2495	.000

Table 4-2 presents the Anova analysis results. It shows that there is a statistically significance difference across the five disintermediation levels. A highly disintermediated strategy provides a

statistically lower market mediation cost when the coefficient of variation is low in comparison with the shortage cost ratio. The data used for the Anova test is large and suggests a high level of random variation. In cases like this, the Levene test might not be appropriate to ensure the homogeneity of the variance (Montgomery, 1984). More tests such Welch and Brown–Forsythe can be used to assess the robustness of the results (Brown and Forsythe, 1974). The results in table 4-3 show a strong robustness of the results and support the fact that higher variation leads to a more intermediated model in comparison with low variation.

Table 4-3: ANOVA Analysis

Total Cost

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	4.071 E+11	4	1.018 E+11	59.436	.000
Within Groups	4.272 E+12	2495	1.712 E+09		
Total	4.679 E+12	2499			

Table 4-4: Robust Tests of Equality of Means

Total Cost

	Statistic [a]	df1	df2	Sig.
Welch	54.527	4	1233.509	.000
Brown-Forsythe	59.436	4	1936.780	.000

a. Asymptotically F distributed.

In these two extreme configurations of demand variability (high and low coefficients of variation), the cost function is steep and favors one extreme configuration or another (Intermediation or Disintermediation). The figure also shows an intermediate variability area where the total cost function appears to be more flat.

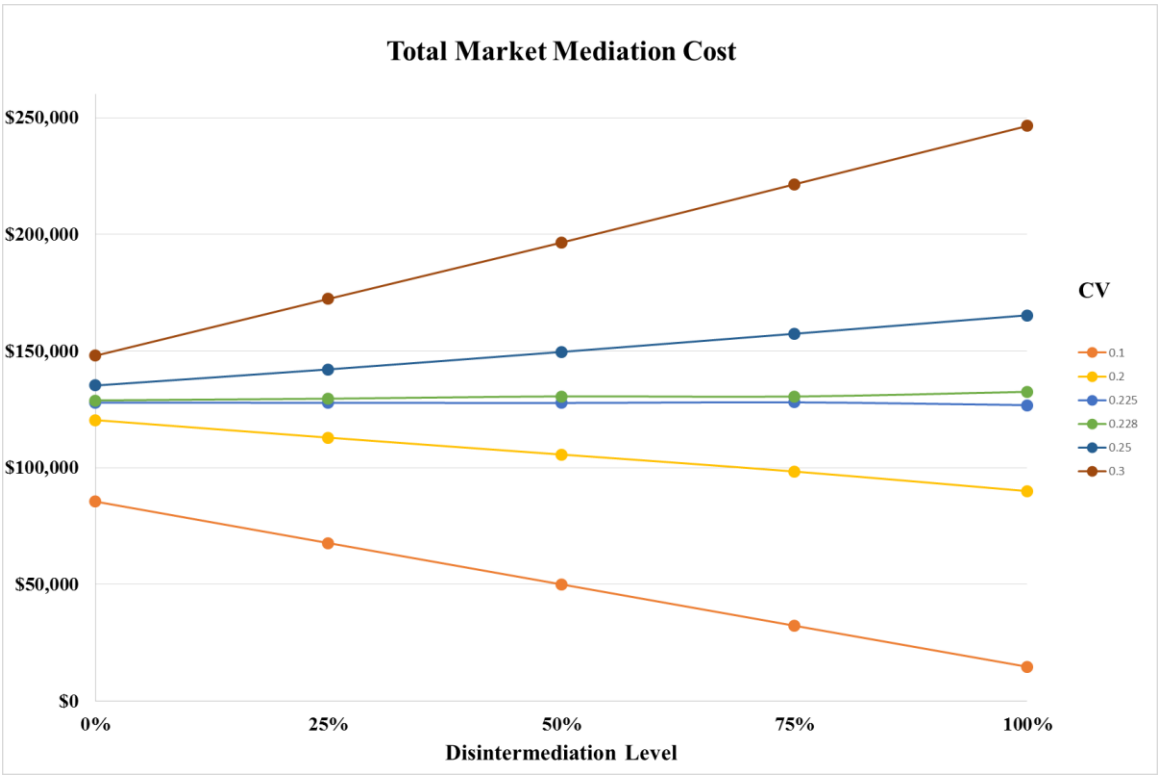

Figure 4-4: Total Cost for Demand Variability Model

A detailed analysis of the flat area will provide a better understanding of the total cost behavior. Figure 4-5 shows the total cost as function of the disintermediation level for a coefficient of variation equal to 0.225 and a shortage cost ratio equal to 0.45. The total cost function shows an "optimal" level of disintermediation that requires more investigation. In fact, the difference between the maximum and the minimum cost in the middle variability range is small. To determine whether there is a significant difference in the total cost function, a one-way Anova test was performed with the total cost as the dependent variable and the disintermediation levels (0%, 25%, 50%, 75%, and 100%) as factors or control variable.

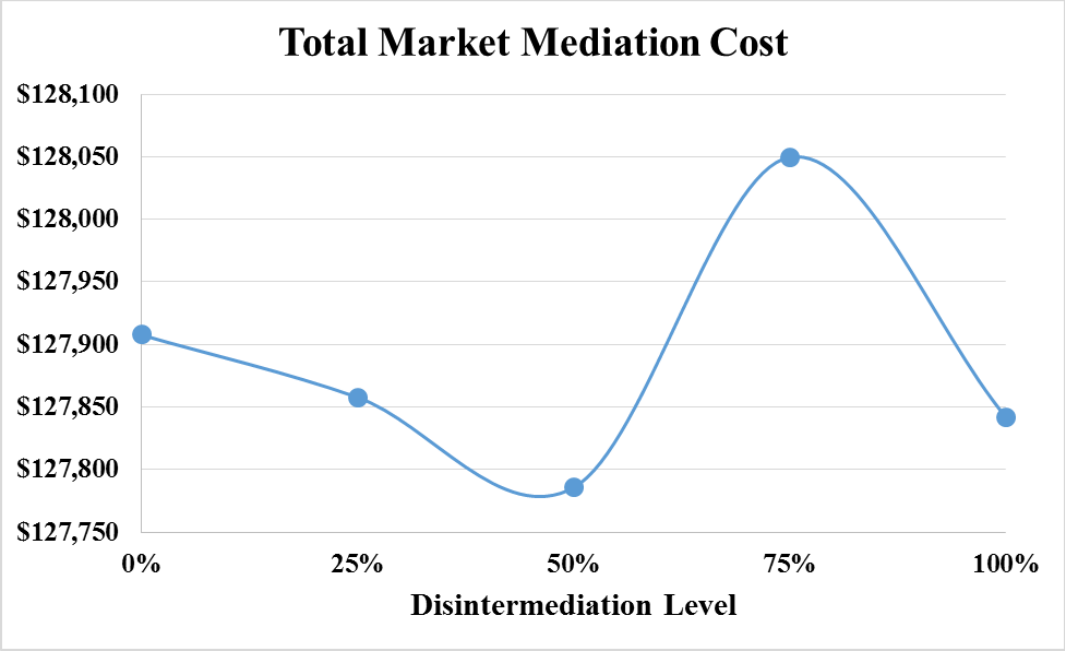

Figure 4-5: Total Cost for "moderate variability"

The results from the one-way Anova analysis are shown in table 3. The one-way Anova analysis suggests that there is no significant difference in the total cost structure for that particular demand variability configuration (F=.138, not significant). Therefore, there is no preferred disintermediation configuration that will minimize the total mediation cost. This finding represents an interesting fact showing that certain combinations of coefficients of variation and shortage cost ratio will make a disintermediation configuration irrelevant.

Table 4-5: One-Way ANOVA Cost Difference Analysis

Total Cost

	Sum of Squares	Df	Mean Square	F	Sig.
Between Groups	1.558 E+11	4	3.961 E+8	.138	.968
Within Groups	1.431 E+12	4995	2.866 E+8		
Total	1.992 E+12	4999			

The finding from the first variation model showed the existence of "optimal disintermediation strategy" for various combinations of shortage costs ratio and the coefficient of variation. Interestingly, the optimal configuration is an extreme solution (100% disintermediated

or 0% intermediated). The demand variation analysis showed a combination of coefficient of variation and shortage cost with no preferred disintermediation level.

4.3.4.2 Shortage Cost Variability Model

The second model consists of investigating the role of shortage cost in the total mediation cost structure. To provide more generalizable results, the shortage cost ratio will be manipulated. For this part, the perishability cost of the product will remain constant at the landing cost (no disposal or handling costs after expiration date). Figure 4-6 provides a set of total market mediation costs as a function of disintermediation levels for multiple shortage cost ratios. The analysis is developed for a constant level of demand variability (0.228 in this particular case).

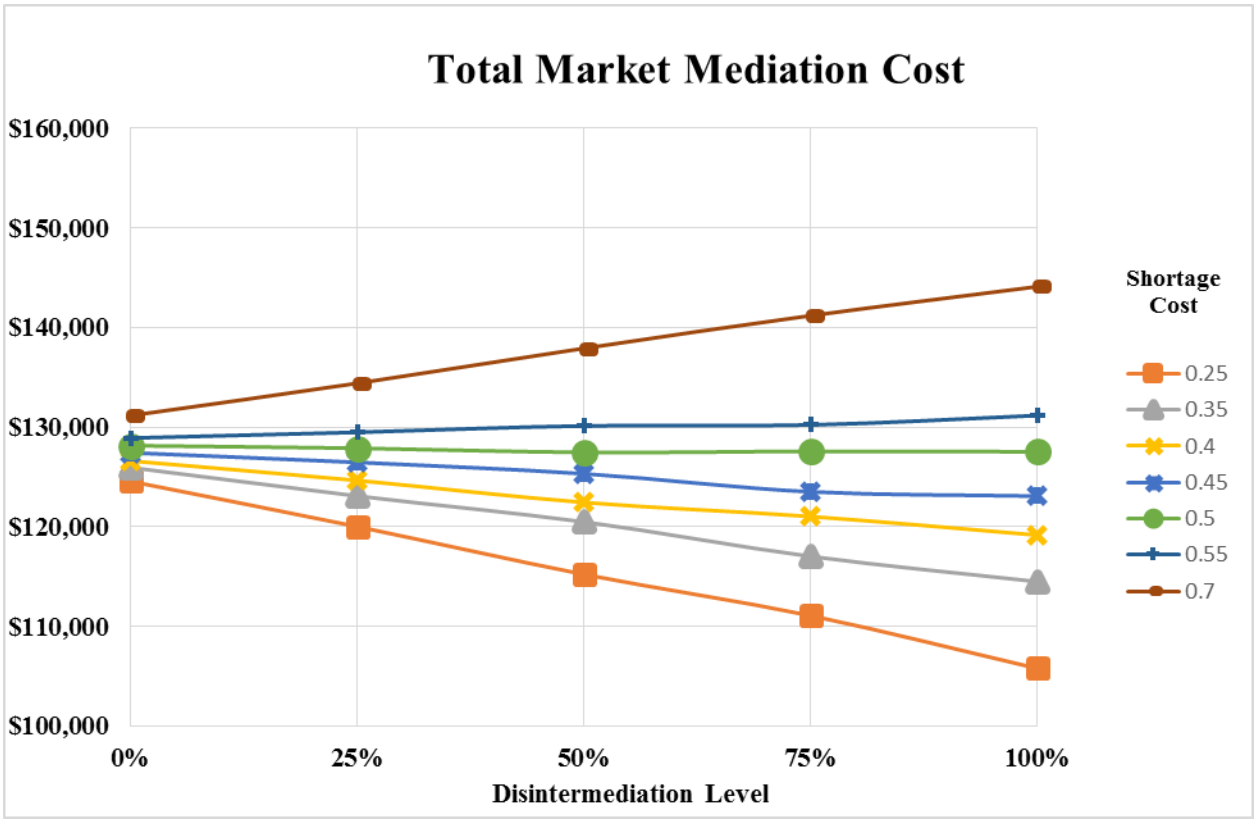

Figure 4-6: Total Cost for Shortage Cost Variation Model

The results from the shortage cost variation model showed that for high shortage cost ratios (Shortage Cost Ratio >0.7), the total intermediated model provides a lower market mediation cost.

Therefore, the use of a distributor provides a better performance and reduces the total cost. On the other end, a small shortage cost ratio (Shortage Cost Ratio < 0.25) will favor total disintermediation cost. Figure 4-6 shows a middle region where the total mediation cost curve is flat. To better understand the behavior of total cost, we will zoom in on that area to explore the cost structure.

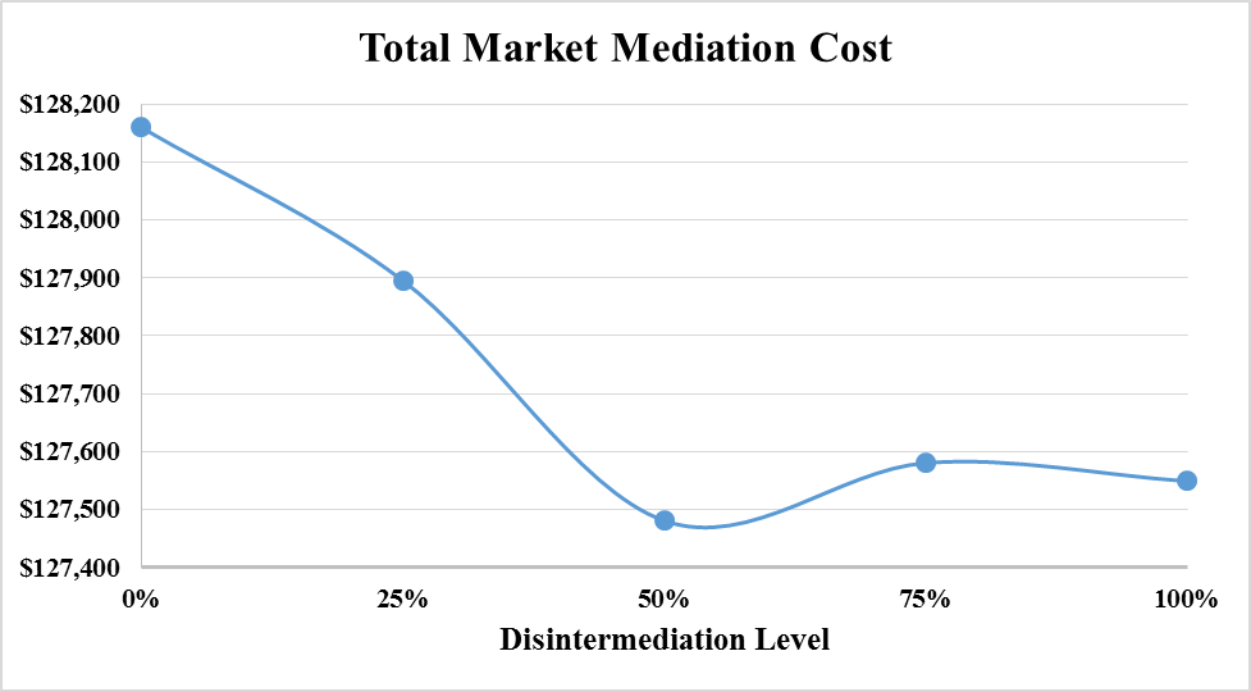

Figure 4-7: Total Market Mediation Cost for the Flat Region

To test for cost variation, a large scale Anova analysis was performed based on 1,000 cost iterations and showed that the disintermediation level does not have an impact on the cost level. The results are similar to the findings from the demand variability section. In fact, for this particular combination of shortage cost and demand variability, there is no preferred disintermediation strategy that will minimize the total market mediation cost.

The results provide interesting, yet counterintuitive results. While it was expected to find a best disintermediation strategy, the findings suggested that an extreme strategy will be beneficial

in some cases. The results suggest further analysis to address the combination of both variation models (demand and shortage cost).

4.3.4.3 Combined Model

In the previous two sections, one variable has been modified at a time. The results showed some preferred strategy (totally disintermediated or intermediated) depending on the parameters. This section will combine both parameters into one general model that addresses the impact of both demand variability and shortage cost structure on the total market mediation cost. First, a set of coefficients of variation is generated, varying from 0.01 to 0.3 with 0.01 increments. Also, multiple shortage cost ratios are generated between 0.05 and 1.5 with 0.025 increments. Therefore, a total of 30*59=1,770 combinations are created. For each combination, a total of market disintermediation cost is determined by the five disintermediation levels. The cost is determined based on large scale Monte Carlo simulation. For each combination, an optimal disintermediation strategy, if it exists, was determined. The disintermediation configuration optimality was performed using Anova analysis similar to the one performed on the demand variability and shortage cost models. The analysis has identified three main optimality levels: a total intermediated strategy, a total disintermediated strategy, and a no-optimal strategy.

The total disintermediation strategy suggests that the total market mediation cost is minimized when the direct sales strategy from the manufacturer to the hospitals is applied. This happens when the level of demand variation impact is lower than the shortage cost factor. Total disintermediation strategy is possible when the shortage cost ratio is too high, making the intermediated distribution channels inappropriate. Second, totally intermediated distribution channels are appropriate when the demand variation is too high compared to the shortage cost ratio. In this case, the distributor's pooling effect will reduce the shortage cost. Intermediated

configuration is optimal when the shortage cost is very high making the direct sales alternative more lucrative. Finally, the results have shown that no preferred distribution strategy exists for some combinations of shortage cost ratio and coefficients of variation.

This subsection illustrates the results in 3D representation: the x and y axis represent the coefficients of variation and the shortage cost ratio respectively. The z axis will be represented by the best disintermediation level. Disintermediation level is divided into three different levels: level 0 represents a pure intermediated strategy, 0.5 level reflects a hybrid strategy, and level 1 is a pure disintermediated strategy. For each combination of coefficient of variation and shortage cost ratio, a best strategy is identified. Figure 4-8 provides 3D illustration of the findings.

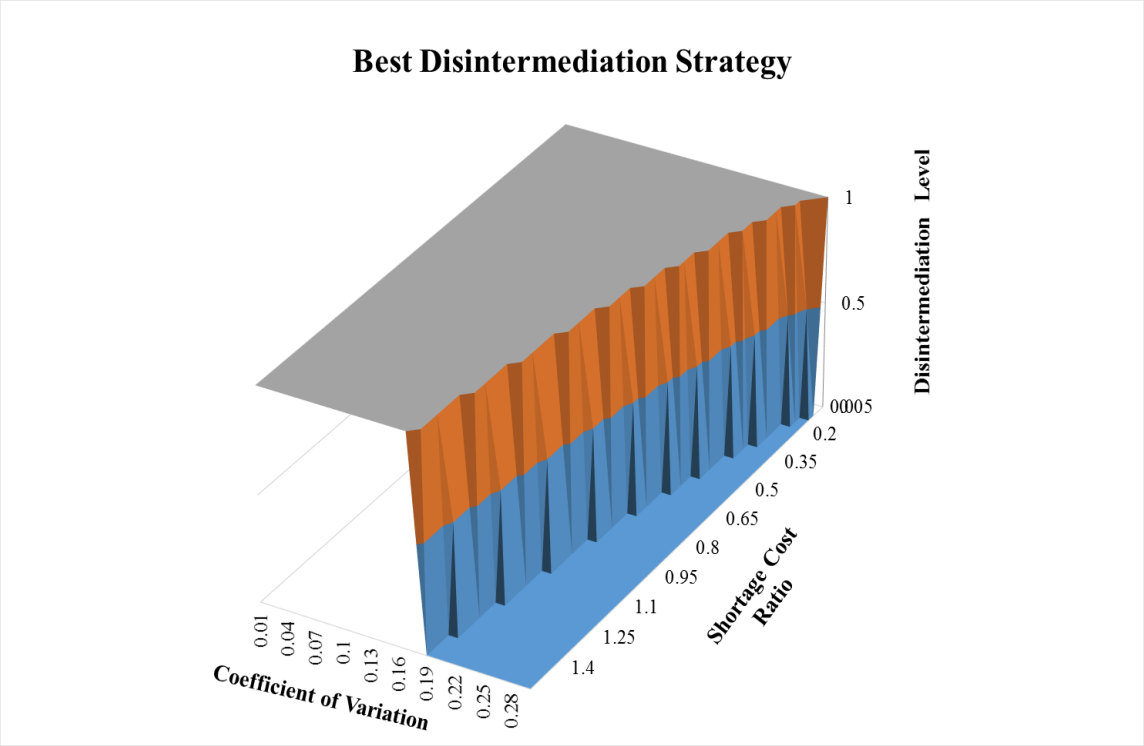

Figure 4-8: 3D Optimal Distribution Strategy

The results as shown in the 3D graph do not provide enough information about the different combinations and the most appropriate disintermediation strategy. To better illustrate the findings of the exploratory analysis, the 3D graph is projected into a 2D plan by eliminating the

disintermediation level. Figure 4-9 shows three areas: two symmetric areas where either direct sales or intermediated distribution strategy will provide the best solution and a median band (in the middle of the graph) where there is no dominant distribution strategy exists. This area reflects a distribution strategy indifference region. For a demand variation and shortage cost ratio combination existing inside the indifference region, there is no best alternative for distribution strategy. The disintermediation level does not have any significant impact on the total market mediation cost.

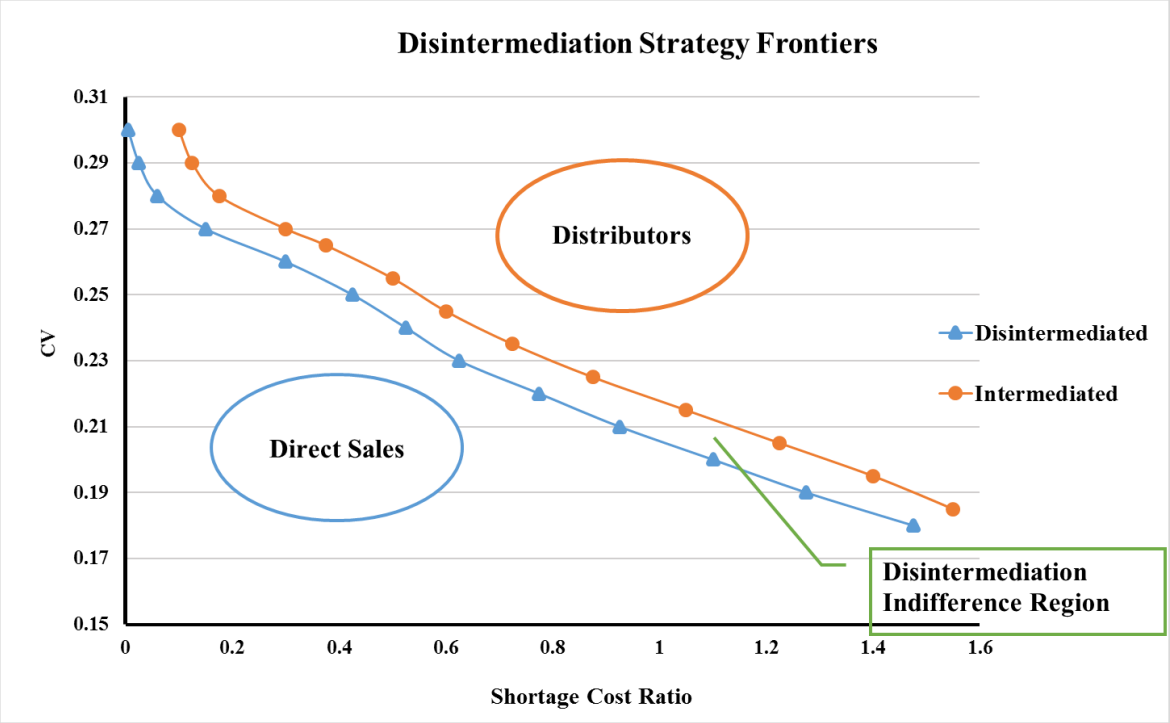

Figure 4-9: Optimal Distribution Strategy Frontiers

The results from the scenario approach emphasized the importance of supply chain disintermediation in the context of biologic medications. The tradeoff between perishibility, cost, and demand variability will determine the most adequate distribution channel strategy. High variability suggests a more intermediated model, and higher shortage cost structure calls for disintermediated distribution channels. The scenario showed a region where neither the variability

nor the shortage cost structure is prominent. In this case, no preferred distribution channel is recorded.

4.4 Total Market Mediation Cost: Numerical Study

The scenario approach represents an exploratory study of the supply chain behavior and how demand variability and shortage costs impact the total mediation cost. The findings from the exploratory study revealed three zones in order to identify the most adequate supply chain distribution strategy.

This section aims at exploiting the results from the exploratory part and identifying the most influential factors on the total mediation cost. This section will expand on the scenario approach to provide a more general analysis of the total mediation cost (shortage cost plus perishability cost). To conduct the analysis, a multi-factor Anova analysis will be performed. The dependent variable is the total market mediation cost, and the total cost will be a function of 3 factors: demand variability, shortage cost structure, and disintermediation level. Table 4-6 identifies the different factors and the levels. Two extreme values for each factor are identified, and then the intermediated levels of the factors are computed.

Table 4-6: Anova Factors

Factors	**Factor Index**	**Levels**
Demand Coefficient of Variation (CV)	$i = 1..5$	0.05, 0.1125, 0.175, 0.2375, and 0.30
Shortage Cost (K)	$j = 1..5$	0.1, 0.575, 1.05, 1.525, and 2
Disintermediation Level (SCD)	$k = 1..5$	0%, 25%, 50%, 75%, and 100%

4.4.1 Three Way ANOVA

The three-way Anova analysis is focused on the coefficient of variation (CV), shortage cost ratio (k), and supply chain disintermediation (SCD) as the independent variables. The experiment is

balanced with 5 levels for each of the three factors. The three-way Anova analysis suggests that a certain number of replications is necessary to perform the analysis. It also suggests that the sample size should be large enough to provide enough statistical data. Researchers in the psychology and biomedical fields have suggested that an a priori power analysis is preferred in these situation in order to best determine the required size replications (Faul et al., 2007).

4.4.1.1 A priori Power Analysis

An a priori G-Power analysis aims at determining the number of replications needed to ensure a certain power analysis level and contrast among the factors. This type of analysis is common in numerical studies to avoid the noise of having large sample sizes. In an a priori analysis, a sample size is the computed function of the desired power (1-β) and a specified significance level α, and the size effect (Cohen, 2013). The a priori power analysis is an efficient technique to control the sample size before setting up the study, thereby impacting the resources needed to perform the analysis (Hager, 2006). The a priori power analysis will determine the replication size needed.

Cohen (1998) provided the guidelines for the power analysis. He suggested that desired power should be between 0.8 and 1. In a three-way Anova analysis context, power of 0.95 is a common level (Aberson, 2011). Cohen (1998) also suggested an effect size of 0.25 to be moderate and 0.1 to be small. Many studies have adopted a low effect size when there are many factors involved. The low effect size suggests that some of the factors won't have a strong impact on the dependent variable and will ensure that these factors are fairly represented. In this study, the disintermediation level is not directly linked to total market mediation cost formulation and, therefore, the size impact of this variable is expected to be small. Consequently, a small effect size of 0.1 is proposed. Finally, the significance level α of 0.05 is commonly used in these kinds of analyses. In addition to the three main factors identified by Cohen (power, size effect, and

significance level), the Anova analysis also involves the number of degree of freedom and the number of groups. In a balanced Anova design with *m* factors and *l* levels within each factor, the following formula is provided:

$$Degree\ of\ Freedom = (l-1)^m \qquad (4\text{-}23)$$

$$Number\ of\ Groups = l^m \qquad (4\text{-}24)$$

To determine the required sample size, multiple software can be used. Many researchers have suggested using GPower 3.1, as it is an open source software and is easy to use, is accurate, and has the capability to provide a sensitivity and post hoc analysis (Faul et al., 2009). Therefore, this study used this software as well. The results showed a total size of 4788. Since the number of groups is 125, the number of replications will be $\left\lceil \frac{4788}{125} \right\rceil = 39$.

To assess the role of size on power, an F test power analysis was performed to measure the effect of sample size on power. Graph 4-10 shows the power explained as a function of the total sample size. The graph shows the sensitivity of the power to the sample size, and it can be determined that for a number of replication equal to 39 (the minimum number of replications determined), the model will have a power of .97.

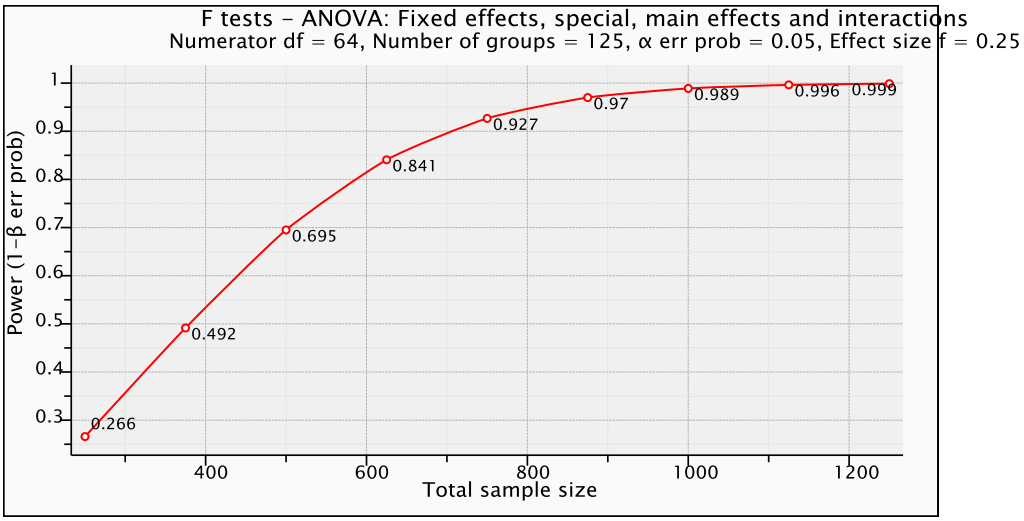

Figure 4-10: Power Level

4.4.1.2 Analysis of Variance

The three-way Anova analysis will be performed for a moderate service level structure. The following section will add service level as a new factor.

Let Y_{ijkl}: $the\ total\ cost\ obeservation\ for\ replication\ l, l = 1..39$

$$Y_{ijkl} = \mu_{ijk} + \varepsilon_{ijkl} \qquad (4\text{-}25)$$

Where μ_{ijk} represents the expected value of all observations in cell ijk and ε_{ijkl} is the error measure for the l^{th} iteration in cell ijk.

The Anova analysis suggests that the error and the dependent variables are normally distributed and are independent.

$$\varepsilon \sim N(o, \sigma) \qquad (4\text{-}26)$$

$$Y_{ijkl} \sim N(\mu_{ijk}, \sigma) \qquad (4\text{-}27)$$

The factor effect model for a three-factor Anova analysis is modeled as follows:

$$Y_{ijk} = \mu + \alpha_i + \beta_j + \gamma_k + (\alpha * \beta)_{ij} + (\alpha * \gamma)_{ik} + (\beta * \gamma)_{jk} + (\alpha * \beta * \gamma)_{ijk} + \varepsilon_{ijkl} \qquad (4\text{-}28)$$

Where:

μ: the overall mean of all observations,

$\alpha_i, \beta_j, \gamma_k$: the main effects of factors CV, k, and SCD,

$(\alpha * \beta)_{ij}, (\alpha * \gamma)_{ik}, (\beta * \gamma)_{jk}$: the two-way first order interactions, and

$(\alpha * \beta * \gamma)_{ijk}$: three-way second order interactions.

Researchers have suggested a template to use in three-way factor analysis (Wuensch et al., 2002). The methodology is summarized in figure 4-11.

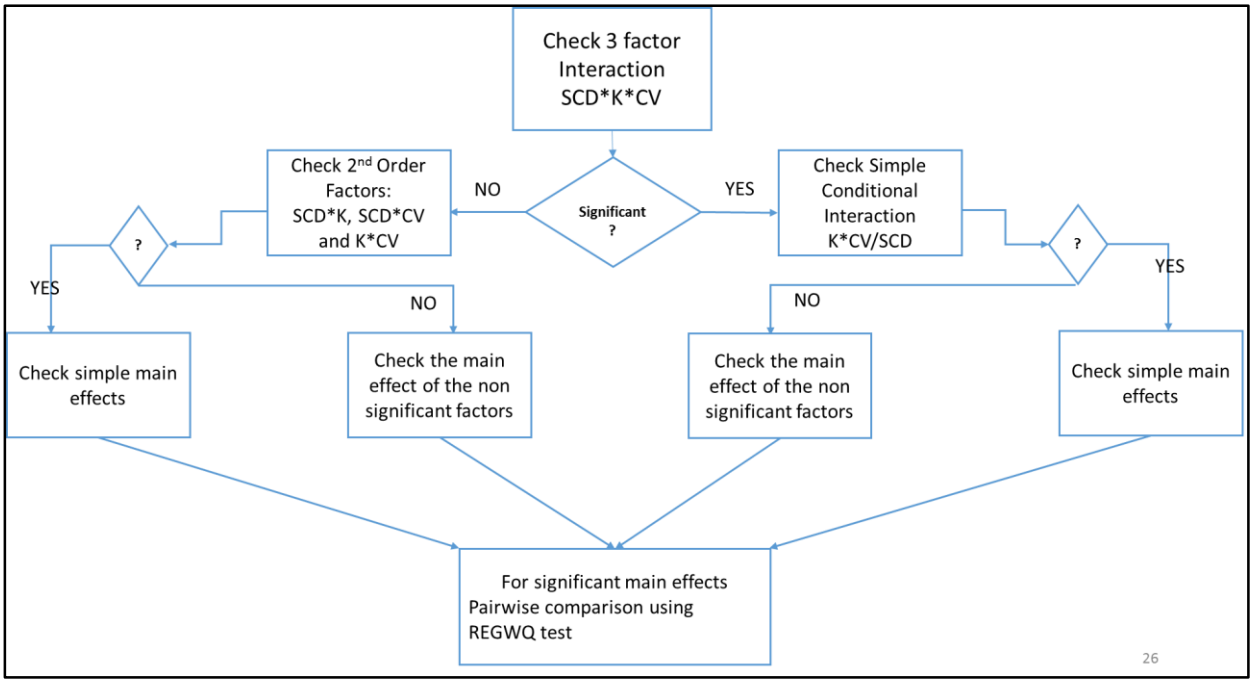

Figure 4-11: Anova Analysis Plan

4.4.1.3 Results

The three-way Anova analysis is performed using SPSS 21. A random sampling of 39 observations is selected from the simulation data for each of the 125 combinations of coefficient of variation, shortage cost ratio, and disintermediation levels. The results from the three-way Anova analysis are summarized in table 4-7.

Table 4-7: Anova Analysis Results

Tests of Between-Subjects Effects

Dependent Variable: Total Cost

Source	Type III Sum of Squares	Df	Mean Square	F	Sig.	Partial Eta Squared	Noncent. Parameter
Corrected Model	42,396,337[a]	124	341,906	63.125	0	0.622	7827.558
Intercept	111,828,858	1	111,828,859	20646.758	0	0.813	20646.758
CV	33,668,652	4	8,417,163	1554.045	0	0.567	6216.182
SCR	1,479,334	4	369,834	68.282	0	0.054	273.127
Dist	45,384	4	11,346	2.095	0.079	0.002	8.379
CV * SCR	369,342	16	23,084	4.262	0	0.014	68.191
CV * Dist	4,596,290	16	287,268	53.038	0	0.152	848.605
SCR * Dist	1,887,968	16	117,998	21.786	0	0.068	348.572
CV * SCR * Dist	349,364	64	5,459	1.008	0.459	0.013	64.503
Error	25,727,384	4750	5,416				
Total	179,952,580	4875					
Corrected Total	68,123,721	4874					

a. R Squared = .622 (Adjusted R Squared = .612)

b. Computed using alpha = .05

The general rule is that the analysis of the results should start at the highest interaction level (figure 4-12). However, the output table should be processed holistically across the different interactions levels. The three-way factor analysis will assess whether each of the two-way analysis depends on the third factor. In this case, the study will assess the impact of the different level of disintermediation on the various coefficients of variation and shortage cost ratios. The three-level factor analysis has an F value of 1.008 ($p<0.459$), showing that all factors combined do not have

a statistically significant effect on the total market mediation cost. Despite the non-significant level of the three-factor analysis, one should take a look at the different graphs and assess if there is any pattern changes on the two-way Anova across the different levels of the third factor. In this case, the study looks at different levels of Dist and its interaction with CV and SCR. The three-way effect can be identified in the interaction plot. For example, for a Distribution variable equal to 50%, figure 4-13 shows the interaction among the different factors.

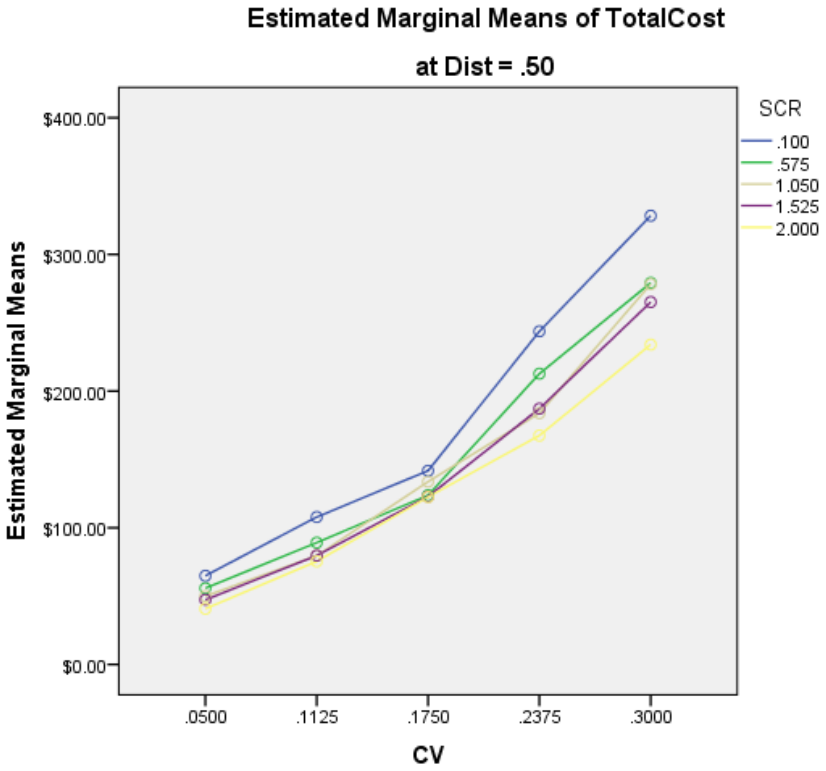

Figure 4-12: Three-Factor Anova Analysis

The three-factor analysis suggests that the Coefficient of Variation and the Shortage Cost Ratio interaction will differ based on the disintermediation level. The five plots of the three-factor interaction are shown in appendix A. The graphs in appendix A show a regular ascending pattern of the total market mediation cost.

First, at a level of no disintermediation, the total mediation cost is high at a low shortage cost ratio. This shows the dominance of the perishability cost. As the disintermediation level increases, the gap among the different graphs shrinks and the dominance of the perishability cost reduces. At a 100% disintermediation level, though, the total market mediation cost shows a remarkable change of pattern. At a low coefficient of variation, as the shortage cost ratio increases, the total cost will increase as well. The pattern is the opposite at a high disintermediation level. This shows that the disintermediation level impacts the total market mediation cost at certain levels. Second, as the disintermediation level increases, the range of total market mediation cost will decrease among the different combinations of CV and shortage cost ratio. In fact, the gap among the different total cost graphs will decrease also. Finally, the different graphs from the 5 disintermediation levels did not show any apparent change on the slopes. More details about the three-factor Anova plots are available in appendix A.

The Anova analysis framework recommends assessing the second order factor analysis. The shortage cost ratio is a factor that has a direct implication in the total market mediation cost as the dependent variable formulation. The three-way Anova analysis suggests three sets of two factors analysis.

Coefficient of Variation and Shortage Cost Ratio: The two-factor analysis evaluates the total market mediation cost for these two factors. The results in Table 4-7 show that the two-factor Anova was significant at the .001 level. The results in figure 4-12 show that as the coefficient of variation increases, the total cost will also increase. On the other hand, a shortage cost ratio increase will decrease the total market mediation cost. Moreover, the graph does not show any change in cost patterns as both the coefficient of variation and the shortage cost increased. Finally,

the increase of the coefficient of variation will increase the gap among the various shortage cost levels.

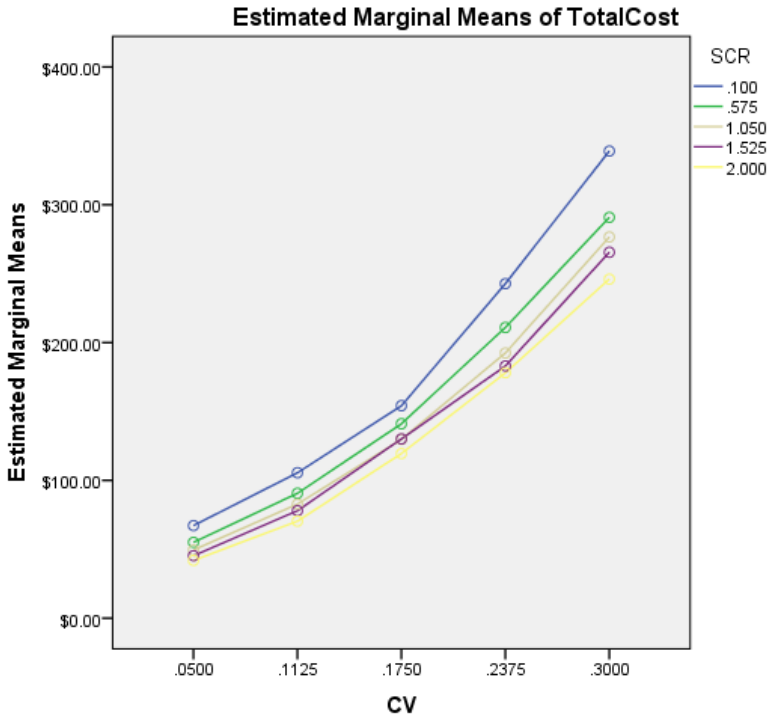

Figure 4-13: Coefficient of Variation and Shortage Cost Anova

Coefficient of Variation and Disintermediation: The two-factor Anova analysis is significant at the .0001 level with the F value equal to 53.038. The cost graph in figure 4-15 shows a change of pattern in the cost functions. As the coefficient of variation increases, disintermediation strategy becomes less attractive. In fact, at a low coefficient level, total disintermediation results in low cost. On the other hand, at a high coefficient of variation level, intermediated distribution channels provide lower market mediation cost. Moreover, as the coefficient of variation increases, the total cost graph's slope will increase for a high disintermediation level. In contrast, for small disintermediation levels, the increase of coefficient of variation will decrease the graph's slope. The two-factor Anova graphs show that all the graphs' intersection points are close. A zoom on the intersection area shows that the points do not coincide. In fact, a more refined analysis was developed to address the impact of disintermediation and coefficient of variation on total market

mediation cost around the intersection area. The results showed the total market mediation cost for the different disintermediation levels to be close but not the same. The closeness results from the fact that the factor levels are equidistant and the cost graphs are extrapolated around that area. The detailed analysis is shown in appendix B.

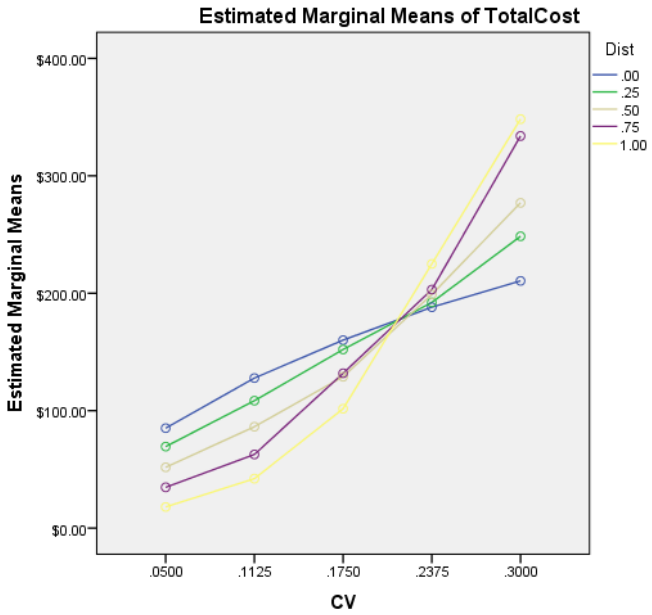

Figure 4-14: Coefficient of Variation and Disintermediation Anova

Shortage Cost Ratio and Disintermediation: The last two-factor Anova analysis relates to shortage cost ratio and disintermediation level. At a high shortage cost ratio level (dominance of shortage cost over perishability), no disintermediation provides a lower market mediation cost. On the other hand, a low shortage cost ratio level favors total disintermediation strategy.

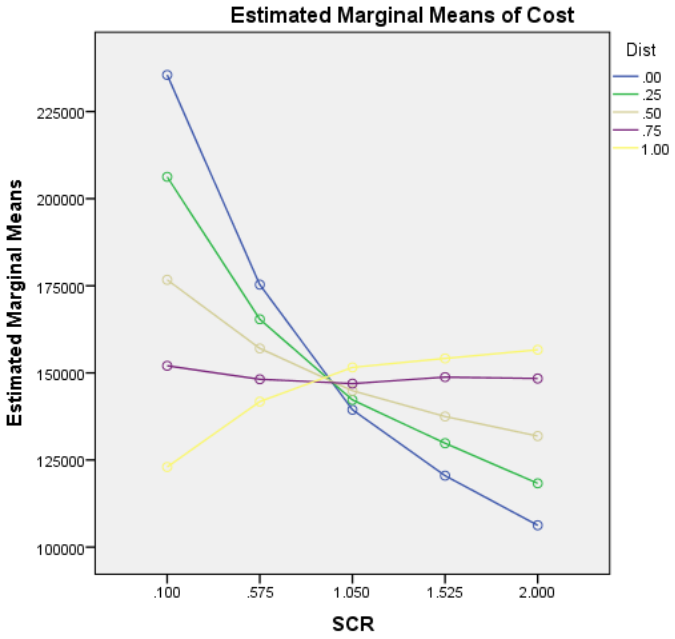

Figure 4-15: Shortage Cost Ratio and Disintermediation Anova

4.4.1.4 Effect Size

The effect size in Anova reflects the degree of association between the different factors of effect (e.g., a main effect and the various interactions) and the dependent variable. The effect size is similar to the correlation between an effect and the dependent variable (Kirk, 1982) . When the effect size value is squared, the value can be interpreted as the percentage of variance in the dependent variable and is explained by the different factors. Researchers in experimental design have outlined four of the commonly used measures of effect size in AVOVA: Eta squared (η^2), partial Eta squared (η_p^2), omega squared (ω^2), and the Intraclass correlation (ρ_I) (Tabachnick and Fidell, 2001). On one hand, Eta squared and partial Eta squared are estimates of the degree of association for the sample. On the other hand, Omega squared and the Intraclass correlation are estimates of the degree of association in the population. This study uses the Eta squared and omega squared as they are more appropriate for the present experiment design.

Eta Squared (η^2): Eta squared is the proportion of the total variance that is attributed to an effect. This procedure represents the first step in size effect analysis (Levine and Hullett, 2002). It is assimilated to R squared and is calculated as the ratio of the effect variance (SS_{effect}) to the total variance (SS_{total}).

$$\eta^2 = {SS_{Effect}}/{SS_{Total}} \qquad (4\text{-}29)$$

$$SS_{Total} = \sum_{i=1}^{N} SS_i + SS_{Error} \qquad (4\text{-}30)$$

Where SS_i is the sum squared of effect *i* and SS_{error} is the sum squared of the error term.

When performing the Anova, SPSS does not provide the Eta Squared (it provides the partial Eta Squared instead). The table below provides the results from the Partial Eta computations. The partial Eta is expressed in a percentage.

Table 4-8: Eta Squared

Factors	Eta Squared
CV	49.423%
SCR	2.172%
Dist	0.067%
CV * SCR	0.542%
CV * Dist	6.747%
SCR * Dist	2.771%
CV * SCR * Dist	0.513%
Error	37.766%

The results from the Partial Eta show that about 50% of the cost variation is explained by the coefficient of variation. The disintermediation level accounts for less than 1% of the variation. Shortage cost ratio and disintermediation account for almost 3% of the cost variation. The Eta Squared is sensitive to the number of factors existing in the model. As the number of factors

increases, the magnitude of the different factors gets modified. The Partial Eta Squared represents another alternative to assess the size effect (Tabachnick and Fidell, 2001).

Omega Squared (ω2): Despite its popularity, Eta statistics provides a biased estimation of the size effect, which is often overestimated (Peters and Van Voorhis, 1940). Omega Squared represents another alternative to calculate the effect size. Omega Squared is calculated by using variance estimators corrected to the design parameters.

$$\omega^2 = \frac{[SS_{Treatment} - df_{Treatment} * MS_{Error}]}{(SS_{Total} + MS_{Error})} \qquad (4\text{-}31)$$

Equation 4-31 is not appropriate for repeated experimental design (Kirk, 1982). A more generalized equation for computing Omega Squared is posed by Olejnik and Algina (2003). The generalized formulation accounts for the treatment levels and the degrees of freedom.

$${\omega_G}^2 = \frac{[SS_{Treatment} - df_{Treatment} * MS_{Error}]}{[SS_{Treatment} + (N - df) * MS_{Error}]} \qquad (4\text{-}32)$$

Table 4-9 shows the results from the Omega Squared size effect. The Coefficient of variation effect is the most dominant with about 50% of the variation explained.

Table 4-9: Omega-Squared Size Effect

Factors	Omega-squared ω2
CV	56.03%
SCR	5.23%
Dist	0.09%
CV * SCR	1.06%
CV * Dist	14.59%
SCR * Dist	6.39%
CV * SCR * Dist	0.01%

4.4.2 Contrast analysis

Anova analysis provides an F-test which reflects all possible differences between the means of the groups (or factors). The results provided by the Anova analysis do not provide insights about the factors behind the experimental manipulation (Salkind, 2010). Therefore, contrast analysis has the capability to provide accurate conclusions about the factors' behavior. The contrast analysis compares the different factor levels via linear combinations of the treatment levels. Orthogonal contrast is the most widely used technique and is characterized by a sum of a coefficient equal to zero (Casella, 2008). The contrast analysis can be planned (a priori) or done post hoc (a posteriori). An a priori contrast is selected before conducting the analysis to validate the hypotheses. An a posteriori is conducted after the design is set to ensure that the unexpected results are reliable (Abdi and Williams, 2010).

4.4.2.1 Multiple Contrast

For a one-factor analysis, the assignment of different coefficients is relatively simple as it is imminent of the null hypothesis. For example, for a 3 treatment level, if the goal is to compare the mean of one level to the average of the two remaining treatments, the coefficients will be 2, -1, and -1 respectively. However, in a case of a two or more factor comparison, the designation of the coefficient is more challenging (Maxwell and Delaney, 2004). In the case of the current study, the interest is to address the behavior of the disintermediation level.

The contrast analysis accounts for multiple comparisons across different factors. The current study aims at comparing the impact of different disintermediation levels, the coefficient of variation, and the shortage cost ratio. SAS software has the capability to perform the multiple comparison using the least squares means (LSMEANS) procedure. Least squares means are

computed for each of three effects (Dist, CV, and SCR). The LSMEANS statement performs multiple comparisons on interactions as well as main effects. LSMEANS "are *predicted population margins"* (SAS Manual, 2009**).** The Disintermediation level is the reference factor. In order to contrast a given level of disintermediation against a certain level of coefficient of variation and shortage cost ratio, SAS constructs a row vector. Because of the balanced nature of the design, Sum Square Type I and Type III are equivalent (Littell, Freund, and Spector, 1991). The results from the contrast analysis are shown in table 4-10.

Table 4-10: Contrast Analysis Results

CV*SCR*Dist Effect Sliced by CV*SCR for Cost						
CV	**SCR**	**DF**	**Sum of Squares**	**Mean Square**	**F Value**	**Pr > F**
0.05	**0.1**	4	1,003,290	250,823	45.68	<.0001
0.05	**0.575**	4	410,852	102,713	18.71	<.0001
0.05	**1.05**	4	204,201	51,050	9.3	<.0001
0.05	**1.525**	4	115,240	28,810	5.25	0.0003
0.05	**2**	4	68,138	17,035	3.1	0.0146
0.1125	**0.1**	4	2,223,965	555,991	101.25	<.0001
0.1125	**0.575**	4	785,349	196,337	35.76	<.0001
0.1125	**1.05**	4	292,343	73,086	13.31	<.0001
0.1125	**1.525**	4	121,940	30,485	5.55	0.0002
0.1125	**2**	4	41,291	10,323	1.88	0.1109
0.175	**0.1**	4	1,963,028	490,757	89.37	<.0001
0.175	**0.575**	4	440,388	110,097	20.05	<.0001
0.175	**1.05**	4	78,603	19,651	3.58	0.0064
0.175	**1.525**	4	822	205	0.04	0.9973
0.175	**2**	4	17,666	4,417	0.8	0.5222
0.2375	**0.1**	4	461,971	115,493	21.03	<.0001
0.2375	**0.575**	4	10,056	2,514	0.46	0.7667
0.2375	**1.05**	4	108,893	27,223	4.96	0.0005
0.2375	**1.525**	4	330,785	82,696	15.06	<.0001
0.2375	**2**	4	694,711	173,678	31.63	<.0001
0.3	**0.1**	4	25,025	6,256	1.14	0.3359
0.3	**0.575**	4	842,870	210,717	38.37	<.0001
0.3	**1.05**	4	1,950,095	487,524	88.78	<.0001
0.3	**1.525**	4	2,172,833	543,208	98.93	<.0001
0.3	**2**	4	2,511,468	627,867	114.34	<.0001

The shaded rows in table 4-10 are the combinations that are not significant and, therefore, have no predominant factors. This provides a statistical evidence of the indifference frontier area shown in the exploratory section (figure 4-9).

4.4.2.2 Predetermined Contrast

The disintermediation level is the center of this study. One interesting contrast to assess is how different the middle level of disintermediation is from the extreme disintermediation levels. In other words, this contrast aims at comparing moderate disintermediation strategy to a pure disintermediation strategy or middle level of disintermediation to 100% disintermediation.

$$H_o: \sum_{j=1}^{5} Y_{1j} + \sum_{j=1}^{5} Y_{5j} = \sum_{j=1}^{5} \sum_{i=1}^{3} Y_{ij}$$

To run the contrast analysis, a designation of coefficient needs to be provided for in the various treatments. Maxwell et al. (2004) suggested that without a valid rational in the experiment design, all "homogenous treatments" should have an equal weight. In the case of comparing the middle level of the coefficient of variation treatment, the following graph illustrates the coefficients' assignment rationale. The sum of the coefficient in row 1 and 5 should be equal to 1. With an equal weight for each of the treatments, the appropriate coefficient is 1/10. For the remaining 15 treatments, the sum of the coefficient should be equal to -1. With the same weight assumption, the coefficient for each combination is -1/15.

Table 4-11: Contrast Analysis Coefficient Assignment

		Coefficient of Variation				
Disintermediation Level		0.05	0.1125	0.175	0.2375	0.3
	0%	1/10	1/10	1/10	1/10	1/10
	25%	-1/15	-1/15	-1/15	-1/15	-1/15
	50%	-1/15	-1/15	-1/15	-1/15	-1/15
	75%	-1/15	-1/15	-1/15	-1/15	-1/15
	100%	1/10	1/10	1/10	1/10	1/10

The contrast analysis was performed using SAS. The program as formulated was adapted to assess other contrasts. To avoid rounding problems, the coefficients are multiplied by 15. The results for the contrast analysis showed that a hybrid supply chain distribution strategy (a mix of direct and intermediated) is statistically significant from pure strategies.

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	124	104501603	842754.9	153.48	<.0001
Error	12375	67951968	5491.1		
Corrected Total	12499	172453571			

R-Square	Coeff Var	Root MSE	Cost Mean
0.605969	49.2902	74.10174	150.3377

Contrast	DF	Contrast SS	Mean Square	F Value	Pr > F
cv vs dist	1	67638821	67638821	12318	<.0001

Parameter	Estimate	Standard Error	t Value	Pr > |t|
cv vs dist	2252.3125	20.293598	110.99	<.0001

The results from the previous contrast analysis suggest that a hybrid disintermediation strategy provides a lower market cost mediation compared to the total disintermediation and no disintermediation strategies.

4.4.3 Post Hoc Analysis

Post Hoc analysis is designed to test for more insights than the Anova analysis. The Post Hoc analysis aims at assessing the different levels of supply chain disintermediation strategy and the impact on the total market mediation cost.

4.4.3.1 Least Significant Difference (LSD)

The first suggested post hoc analysis aimed at exploring all possible pairwise comparisons of means comprising a factor using the equivalent of multiple t-tests (Hayter, 1986). The results from the LSD test for disintermediation are shown in table 4-12.

Table 4-12: LSD Post Hoc

(I) Dist			Mean Difference (I-J)	Std. Error	Sig.
LSD	.00	.25	182	3333	.956
		.50	5719	3333	.086
		.75	1054	3333	.752
		1.00	7305.13*	3333	.028
	.25	.00	-182	3333	.956
		.50	5537	3333	.097
		.75	871	3333	.794
		1.00	7122.89*	3333	.033
	.50	.00	-5719	3333	.086
		.25	-5537	3333	.097
		.75	-4666	3333	.162
		1.00	1586	3333	.634
	.75	.00	-1054	3333	.752
		.25	-871	3333	.794
		.50	4666	3333	.162
		1.00	6252	3333	.061
	1.00	.00	-7305.13*	3333	.028
		.25	-7122.89*	3333	.033
		.50	-1586	3333	.634
		.75	-6252	3333	.061

The results from the LSD analysis show that most of the differences at the 50% and 75% disintermediation levels are not significant. For a difference to be significant, the level of disintermediation has to be at least 75% or more (between 100% and 25%, for example). This suggests that the total market mediation cost is not very sensitive to the disintermediation level.

4.4.4 Service Level Impact

Service level is a critical decision in the healthcare field and more so in the pharmaceutical industry (Shah, 2004b). Previous studies have adopted a targeted service level rather than finding the optimum service level in the drug inventory studies (discussed in section 1.3.1). In the numerical analysis, the service level was selected at a moderate level. This section addresses a higher service level target (95% for hospitals and 90% for distributors). The results from the "high service level" were identical to the previous analysis. This section will illustrate some of the impact of an increased service level and the role of disintermediation.

First, the Anova analysis has shown similar results at the lower service level. The increase in the service level has improved the total variation explained by the model. In fact, the adjusted R squared for the model has increased from 0.612 to 0.734. This indicates that the increased service level has reduced the level of fluctuation among the dependent variable. Additionally disintermediation level impact on market mediation cost has increased. In fact, the disintermediation level has a higher level of significance and the partial Eta squared has doubled (from 0.2% to 0.4%). This shows that as the service level increases, the disintermediation level impact on market shortage cost also increases. Moreover, the coefficient of variation impact has increased. The Partial Eta has increased, showing more information to be explained by the coefficient of variation. Finally, the shortage cost ratio influence has been reduced, showing that

at a high service level, shortage cost ratio is not very relevant. The detailed results are shown in table 4-13. The comparison of plots patterns is provided in Appendix C.

Table 4-13: High Service Level Anova Results

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Corrected Model	85094795[a]	124	686248.347	109.428	0.000	.741
Intercept	189064958	1	189064958	30147.913	0.000	.864
CV	62598332	4	15649583	2495.451	0.000	.678
SCR	8908387	4	2227097	355.128	.000	.230
Dist	116276	4	29069	4.635	.001	.004
CV * SCR	2436845	16	152303	24.286	.000	.076
CV * Dist	8708539	16	544284	86.790	.000	.226
SCR * Dist	1956113	16	122257	19.495	.000	.062
CV * SCR * Dist	370302	64	5786	.923	.651	.012
Error	29788415	4750	6271			
Total	303948168	4875				
Corrected Total	114883210	4874				

Second, the service level has an impact on the total market mediation cost. As the service level increases, the total market mediation costs also increase. These results are expected, as an increase in the service level calls for more investment in inventory in order to respond to the demand fluctuation. Moreover, the rate of increase of the total market mediation cost for the different disintermediation level remains relatively constant. The detailed comparison is shown in table 4-14.

Table 4-14: Service Level and Disintermediation Impact on Total Market Mediation Cost

Dist Level	Service Level	Mean	Cost Increase	Increase Percentage
0%	Low	155.405	47.92	30.83%
	High	203.322		
25%	Low	152.401	48.04	31.52%
	High	200.440		
50%	Low	149.593	47.93	32.04%
	High	197.519		
75%	Low	148.863	46.69	31.36%
	High	195.548		
100%	Low	145.426	45.60	31.35%
	High	191.022		

Third, a higher service level will provide a shift in the disintermediation strategy indifference area. As discussed in sections 4.3.4 and 4.2.4, the disintermediation strategy has shown an indifferent region where there is no best disintermediation strategy. At a higher service level, the disintermediation indifference area will experience a shift, favoring more of an impact of disintermediation and coefficient of variation. In fact, at a high service level, there is only a small indifference area when both coefficients of variation are at a moderate level (.175). At the extreme points, pure distribution channel strategy (disintermediated or intermediated) will provide a lower market mediation cost. The results are obtained using a contrast analysis at a high service level (Table 4-15).

Table 4-15: Contrast Analysis for High Service Level

CV*SCR*Dist Effect Sliced by CV*SCR for Cost						
CV	**SCR**	**DF**	**Sum of Squares**	**Mean Square**	**F Value**	**Pr > F**
0.05	**0.1**	4	1,991,438	497,859	76.61	<.0001
0.05	**0.575**	4	884,765	221,191	34.04	<.0001
0.05	**1.05**	4	460,716	115,179	17.72	<.0001
0.05	**1.525**	4	268,081	67,020	10.31	<.0001
0.05	**2**	4	173,852	43,463	6.69	<.0001
0.1125	**0.1**	4	4,179,166	1,044,791	160.77	<.0001
0.1125	**0.575**	4	1,639,430	409,858	63.07	<.0001
0.1125	**1.05**	4	759,775	189,944	29.23	<.0001
0.1125	**1.525**	4	416,656	104,164	16.03	<.0001
0.1125	**2**	4	237,713	59,428	9.14	<.0001
0.175	**0.1**	4	2,430,339	607,585	93.49	<.0001
0.175	**0.575**	4	672,722	168,180	25.88	<.0001
0.175	**1.05**	4	187,490	46,872	7.21	<.0001
0.175	**1.525**	4	50,906	12,726	1.96	0.098
0.175	**2**	4	11,787	2,947	0.45	0.77
0.2375	**0.1**	4	154,819	38,705	5.96	<.0001
0.2375	**0.575**	4	107,273	26,818	4.13	0.0024
0.2375	**1.05**	4	354,176	88,544	13.62	<.0001
0.2375	**1.525**	4	554,759	138,690	21.34	<.0001
0.2375	**2**	4	612,188	153,047	23.55	<.0001
0.3	**0.1**	4	1,299,627	324,907	50	<.0001
0.3	**0.575**	4	2,037,211	509,303	78.37	<.0001
0.3	**1.05**	4	2,609,451	652,363	100.38	<.0001
0.3	**1.525**	4	3,027,580	756,895	116.47	<.0001
0.3	**2**	4	3,644,494	911,123	140.2	<.0001

Finally, the service level and the coefficient of variation level will have an impact on the total market mediation cost. At a high level of coefficient of variation, high service level will always provide a higher cost when compared to low service level. At a low coefficient of variation (.1125 or less), the disintermediation level is critical, depending on the service level. For a low service level target, an intermediation strategy is more beneficial. When hospitals shift to a higher

service level configuration, disintermediation is a more adequate distribution strategy. These results are shown in figure 4-16.

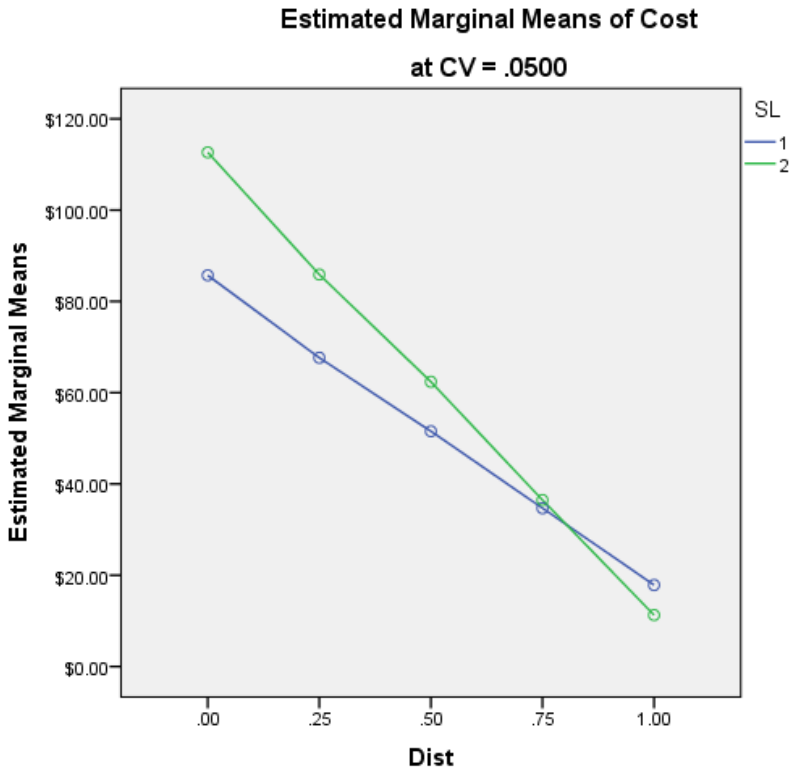

Figure 4-16: Low vs. High Service Level Costs at Low Coefficient of Variation

4.5 Conclusion and Managerial Implications

The current numerical studies aim at addressing the various influential factors on total market mediation cost for biopharmaceutical companies. Biopharmaceutical drugs are expensive, have shorter a shelf life, and are highly personalized. In such circumstances, the distribution channel configurations become critical and crucial to the health care supply chain performance. Biologic drugs can be distributed via traditional channels using distributors or they can be shipped directly to the end consumer, eliminating the middle-man.

This essay addresses the problem from a hospital perspective, simplifying the supply chain to three echelons (manufacturer, distributor, and hospital) and the hospital, being the end

consumer, and the decision maker. First, the essay provided a scenario approach analysis to assess the impact of disintermediation level, coefficient of variation, and shortage cost ratio on the total market mediation cost. While direct sales provide longer product usage time, which reduce the perishability cost, an intermediated strategy will use the middle-man as a buffer, thereby utilizing the risk pooling effect to reduce the shortage cost.

The numerical analysis performed aimed at comparing the different factors shaping the total market mediation cost. First, a three-way Anova showed that coefficient of variation is the most impacting factor in determining the total market mediation cost. The second order factor analysis has also shown the importance of coefficient of variation as the strongest factor to define the total market mediation cost. The results were validated via a size effect analysis. Moreover, the findings have shown that, overall, disintermediation will reduce the total market mediation cost. Disintermediation has a stronger effect on cost when the coefficient of variation is low. In fact, when the product has a predicted demand, the direct sales model is the most adequate. At a high coefficient of variation, however, intermediated distribution strategy is more appropriate. These results support the assumptions that have been developed regarding the various distribution strategies.

Second, a contrast analysis provided a significant statistical analysis for the area of supply chain distribution indifference region. In fact, for the various levels of the three factors used in the study (coefficient of variation, shortage cost ration, and disintermediation level combinations), the contrast analysis tested for the market mediation cost differences. The contrast analysis determined the distribution strategy frontier area. At low coefficient of variation, direct sales provides the lowest market mediation cost. As coefficient of variation and shortage cost increase, the

distribution channels strategy will change. At middle coefficient of variation range, the results showed a distribution strategy indifference area.

Third, the post hoc analysis addressed the impact of supply chain disintermediation, as the main subject of interest, on the total market mediation cost. The post hoc analysis also showed that the hybrid supply chain distribution strategy (a mix of direct and intermediated sales) does not provide statistically significant different results compared to (pure strategy) in most cases. The results, however, showed that there is a statistical significance when hospitals adopt one of the pure distribution strategies (disintermediated or intermediated). Therefore, based on the product characteristics, the total market mediation cost can be reduced by modifying the distribution strategy.

Finally, the service level at a hospital represents an interesting area of research, given the critical factors associated with healthcare industry. The problem addressed in this essay could be assimilated to a news vendor problem, with finding the optimal service level given the combination of excess (perishability) cost and shortage cost. However, hospitals do not operate this way. In fact, hospitals target service level first, and then they determine the most appropriate distribution strategy. The last section of the essay investigated the impact of service level on the disintermediation strategy. Taking two service level points (moderate and low), the results have shown that as the service level increases, the impact of disintermediation becomes more important. Moreover, at a high service level, a higher disintermediation strategy will provide a better market mediation cost performance.

Chapter 5: Supply Chain Disintermediation and Product Portfolio Strategies: An Empirical Study

5.1 Introduction and Research Objectives

The role of the supply chain strategy is very crucial to a firm's operational and financial performance. Skinner (1969) has emphasized the role of the organization's manufacturing strategy and its positive impact on organization outcomes. The operations and supply chain strategy has evolved from research on competitive priorities in operations management, configurations of operations and manufacturing strategy, supply chain configuration, and the successful alignment between supply chain strategy and organization output characteristics (Boyer, Bozarth, and McDermott, 2000; Ward, Bickford, and Leong, 1996). The seminal work by Fisher (1997) provided a research agenda focused on the fit between product characteristics and supply chain strategy. An organization should consider its product characteristics such as demand patterns and identify the best supply chain strategy that fits the most (Fisher, 1997). Recent studies have attempted to empirically investigate the Fisher's (1997) model by testing the fit existing between product type and supply chain strategy (Lee, 2002; Lo and Power, 2010; Selldin and Olhager, 2007; Wagner, Grosse-Ruyken, and Erhun, 2012). While some studies have used a simplified taxonomy to determine the type of supply chain (efficient vs. responsive), other studies have built on the existing literature to provide a more comprehensive supply chain strategy taxonomy (Frohlich and Dixon, 2001; Zhao et al., 2006). These studies have primary investigated the fit between the supply chain strategy and the products' demand characteristics.

Product typology and specification represents an area of research that has been the subject of several studies in the area of management and marketing (Day, 1977; MacMillan, Hambrick,

and Day, 1982; Wind and Mahajan, 1981). The topics have been then introduced to the operations management literature in terms of investigating product characteristics such as variety, modularity, type of demand, uncertainty, and complexity (Fisher, 1997; Jacobs and Swink, 2011; Rothaermel, Hitt, and Jobe, 2006; Zamirowski and Otto, 1999). The previous chapters discussed product paradigm in the context of product customization-personalization continuum. The first essay expanded on the product paradigm to define a product portfolio structure based on the level of personalization. The emergence of biologics (large molecule medication) calls for a higher level of personalization. The product portfolio structure with regard to personalization remains an area of investigation that has not received much research attention. The personalization level paradigm elaborated on was extrapolated to the field of the pharmaceutical industry. The current study investigates the product portfolio structure based on the personalization level of medication that exists within the pharmaceutical firms' products. As such, the current study adds to the literature by providing a better understanding of under researched area of product personalization in the operations management.

With regard to supply chain strategy, existing literature has identified a multitude of typologies. The first set of typologies relates to the type of supply chain as developed by Fisher (1997) and other studies. An organization's supply chain can be responsive, efficient, agile, risk hedging, or leagile (Mason-Jones, Naylor, and Towill, 2000). Another set of taxonomy addresses the supply chain focus: supply chain integration; Just-In-Time; and supply chain relationship (Narasimhan, Kim, and Tan, 2008). The supply chain focus taxonomy evolved into a competitive advantage (Mckone-Sweet and Lee, 2009). The body of literature has shown vast studies related to supply chain strategies at the macro level. More emphasis was provided to supply chain distribution channels, as it falls under the strategic supply chain configuration. Organizations have

multiple distribution channel opportunities that can impact the firm's operational and financial performance (Stock, Greis, and Kasarda, 2000). The research on distribution channels configuration has evolved from the marketing to operations management to involve concepts related to supply chain. The traditional distribution channel configuration suggests that the product is sold to the customer through retailers. The retail store will purchase the product from the wholesalers or distributors. The business landscape suggests more direct sales opportunities aiming at eliminating the middleman. This practice is also known as supply chain disintermediation.

The previous chapter provided a conceptualization of the supply chain disintermediation as a distribution strategy that organizations will decide to adopt. The level of disintermediation is determined by the extent to which an organization will sell its products directly to the end consumers. The research on supply chain disintermediation is lacking extensive empirical investigation and strategy effectiveness validation (Rossetti and Choi, 2008). Few studies have addressed supply chain disintermediation as a distribution channel strategic decision, attempting to assess its outputs (Rossetti and Choi, 2008; Tay and Chelliah, 2011). This represents a clear area of opportunity for investigation to better understand the mechanisms of disintermediation and how it relates to a firm's performance. The previous studies from the area of marketing and sales have shown some conflicting results to the benefit of disintermediation and its impact of firm value proposition and competitiveness. While many studies have looked into the customer benefit and cost reduction deriving from the double margin (Davenport and Klahr, 1998; Nissen, 2000), other studies have pointed out the complexity of disintermediation and how it can limit the firm's potential sales and growth (Atkinson, 2001). These conflicting signals represent another area of investigation and emphasize the relevance of the topic.

Additionally, it is critical to note that product customization/personalization has significant implication for distribution channels configuration (direct or indirect). Often, customer inputs are needed for the firm to deliver personalized products to customers, like in purchasing a holiday package (Nicolau, 2013). In these cases, it is more appropriate for the firm to sell its products directly to the consumers. For products with low personalization level, firms could sell the product directly to its customers or distribute it via regular distribution channels. However, the low level of personalization obviates the need for direct distribution channels. The existence on most adequate disintermediation strategy for a certain level of product personalization raises the critical question of fit between product characteristics (personalization level) and supply chain strategy (disintermediation level). This represents an area that needs further investigation.

The current chapter aims to add to the above literature gap addressing the stated research objective. First, it investigates the impact of distribution channels on a firm's financial performance. In fact, the chapter empirically tests for the relationship between the level of disintermediation and the pharmaceutical firms' financial performance. Second, the study addresses the relationship between the product portfolio (in term of level of biologic products) and pharmaceutical's financial results. More precisely, since biologic products are more personalized, it serves as a proxy to test the influence of the level of personalization in products at a pharmaceutical organization and the firm's financial performance. Finally, the chapter proposes that there exist a fit between the product portfolio and supply chain disintermediation strategy and investigates its relationship with financial performance. In doing so, this section provides a novel application and empirical test of the Fisher's (1997) model from two new paradigms inspired by product characteristics (personalization level) and supply chain configuration (disintermediation level).

The current chapter is organized as following. First, a literature review provides the relevant work to the area of disintermediation, product portfolio, and financial performance. Second, a conceptual development provides the hypotheses for the empirical model. Finally, the research methodology section proposes how the study is conducted.

5.2 Literature review

Chapter 4 had discussed the literature related to supply chain disintermediation and showed some of the research gaps. In this current chapter, a literature review specifically oriented toward empirical work in supply chain disintermediation is provided.

5.2.1 Supply Chain Disintermediation in the Literature

The supply chain disintermediation involves the interaction between a buyer and supplier and therefore can be viewed as a contracting problem. The decision of whether to disintermediate or not can be analogous to a make-or-buy decision. In a make-or-buy configuration, the focal company will make the decision based on the minimum transaction cost (Eisenhardt, 1989). The concept of agency theory can be applied in the context of supply chain intermediation, where the decision is based on evaluating a cost benefit analysis of a disintermediation decision. Table 5-1 summarizes the most relevant studies that address the benefit of disintermediation.

Table 5-1: Motivation for Disintermediation

Condition	Source	Methodology and comment
Intermediaries increasing buyers cost	(Benjamin and Wigand, 1995; Prahalad, 1998)	• Used case study from the electronic industry. • Showed the saving of eliminating wholesalers and wholesalers and retailer to the end customer cost. • The role of discontinuities
Increased cost by the middle man	(Sarkar, Butler, and Steinfield, 1995)	• Conceptual work
The use of IT to reduce the inter-firm coordination cost	(Malone, Yates, and Benjamin, 1987)	• Conceptual work: the shift from hierarchal structure to market structure leads to more disintermediation
Internet Role in lowering the transaction cost	(Bakos, 1998)	• Conceptual work
The irrelevance of intermediary service	(Chircu and Kauffman, 2000)	• Case study of the electronic industry
Improvement of logistical capabilities	(Cort, 1999)	• Conceptual work
Sustain IT enabled innovation	(Clemons and Row, 1991)	• Conceptual work
3PL firms as intermediaries substitutes	(Delfmann, Albers, and Gehring, 2002; Lewis, 2001)	• Conceptual work showing how 3PL capability can facilitate disintermediation

The list of work in table 5-1 shows a great interest in supply chain disintermediation. However, none of these studies have empirically tested the importance of disintermediation. The conceptual and case oriented nature of existing studies highlight the nascent state of the literature and provide an opportunity for making empirical contribution.

The most relevant empirical study related to supply chain disintermediation was done by Rossetti & Choi (2008). In their paper, the authors investigated the different incentives to

disintermediate in the aerospace context. The study used disintermediation as an outcome to buyer supplier congruence and the impact of secondary market. The study was inspiring and shed light on some supply chain disintermediation concepts. The authors have called for future research assessing how disintermediation could impact a firm's configuration. Two other major works scientifically addressed the concept of supply chain disintermediation. Dutta et al. (2010) mathematically tested the impact of supply chain disintermediation on market equilibrium in the Indian tea market. The findings showed that complete disintermediation will shift the market equilibrium (Dutta, Sarmah, and Goyal, 2010). The second paper, analytical as well, assessed the price sensitivity & demand consideration and its impact on disintermediation and centralization configurations (Chiang, 2012).

The literature review of supply chain disintermediation demonstrates a continuing interest in investigating the supply chain configuration. The body of literature also shows a gap in evidence suggesting that supply chain disintermediation does impact an organization's financial performance. Most of the existing studies are conceptual in nature. The few studies that have empirically and analytically addressed supply chain disintermediation focused on disintermediation as an outcome and the result of buyer supplier congruence or market demand. Supply chain disintermediation can be considered as a strategic decision that will impact the distribution channels and the firm's operating and financial performance. In the context of the pharmaceutical industry, the current study *defines supply chain disintermediation as the extent to which a pharmaceutical firm is selling its products directly to the patients, retail pharmacies, and hospitals without distributing the products through wholesalers and distributors hereby identified as middlemen.*

5.2.2 Product Portfolio

Product portfolio refers to the set of products a company sells to its customers (McGrath, 2000; Meyer, 1997). In more competitive markets, many firms are obliged to diversify their product portfolio and provide a variety of products to maintain their competitive advantage (Fixson, 2005). The research of product portfolio management has emerged in the field of marketing, finance, and strategic management field. A firm's goal consists of optimizing its product portfolio to maximize the organization's value (Cooper, Edgett, and Kleinschmidt, 1999; Fernhaber and Patel, 2012). Studies suggest that the diversification level in the product portfolio requires an organization's higher capabilities to leverage the diversification and generate more value to customers and businesses (Eggers, 2012). Earlier studies in the area of marketing have identified product portfolio classification and diagnosis. The classification focused on determining the product portfolio that aims to serve different markets and how it should be designed and managed effectively (Wind and Mahajan, 1981; Wind, Mahajan, and Swire, 1983). Organizations should use their resources effectively to design the best value added portfolio (Day, 1977).

Scholars from operations and supply chain management showed interest in the product portfolio strategy. Fisher (1997) has classified products into functional and innovative. Fisher's work did not provide insights about how to manage the product portfolio; it did, however, define a product's taxonomy, which can be used to identify portfolio characteristics. More recent studies have addressed product portfolio management from a complexity angle. Scholars have measured the product portfolio complexity and assessed its impact on a firm's performance (Closs et al., 2008). As the complexity increases, organizations will require more resources to manage these complexities (Jacobs and Swink, 2011). Product portfolio was also assessed from a configuration point of view. Researchers studied the impact of product portfolio configuration in terms of

functionalities and design on firm performance. The finding showed that product portfolio functionality optimization is driven mainly by gross margin and pricing strategy (Chen, Vakharia, and Alptekinoğlu, 2008).

The research in the field of product portfolio has shown a great emphasis on product portfolio design, optimization, and management. Very little interest was awarded to product portfolio classification despite some earlier studies which identified different product classification such as Fisher (1997). Product portfolio can be classified according to different taxonomies such as the product characteristics. The lack of studies focusing on the product portfolio characteristics and its impact on organization performance represents an opportunity of investigation. As discussed in chapter 2, the current chapter is conceptualizing product portfolio from a personalization level perspective. In the context of the pharmaceutical industry, one may map the level of personalization to the type of medication. In general, biologic medicine tends to require higher level of personalization (Ginsburg and Willard, 2009) compared to traditional medication. In line with this, keeping in mind the pharmaceutical context, a portfolio with only biologic products would have a higher personalization level. A portfolio with only traditional medication would have a low personalization level. *In the pharmaceutical context, the current study defines product portfolio based on the biologic products that exist within the pharmaceutical firm products portfolio*. As such, portfolios that are composed of only biologic products are considered to have high level of personalization while those that are composed of only traditional medication are considered as having a low level of personalization, with ones containing both as hybrid portfolios having a moderate level of personalization.

5.2.3 Financial Performance

The research on financial performance in the operations management field in interesting a large number of researchers (Chen, Frank, and Wu, 2005). Several studies have used multiple financial performance measures in the operations management context. Return on Assets represents a commonly used performance measure to evaluate the firm's productivity and assets utilizations. Liu et al. (2014) investigated the impact of innovative products on the firm's return assets. As a firm adopts a strategy favoring more innovation, the firm's return on assets is expected to improve (Liu et al., 2014). Moreover, firms are expected to have higher return on assets when engaged in higher quality products (Terjesen, Patel, and Covin, 2011). Other studies looked at the fit existing between the product characteristics and the return on assets. Organizations that align the adequate supply chain strategy to the product characteristics showed better financial performance or, more precisely, return on assets (Wagner et al., 2012).

Gross margin represents another financial measure that is used in the operations management literature (Gaur, Fisher, and Raman, 2005). The gross margin reflects the firm ability to provide products at competitive price. Gross margin reflects both the firm's inbound and operations processes and its capability to deliver products and services effectively. Firms who adopt IT-based supply chain strategy are experiencing higher gross margin (Dehning, Richardson, and Zmud, 2007). Gross margins are influenced by product characteristics and are different at manufacturers, distributors, and retailers levels (Steiner, 2001). In line with the operations management literature investigating the financial performance implications of operations resources and decision *the current study refers to the firm's financial performance as reflected in the measures of return on assets (the ratio of the firms' income before extraordinary items to the*

firm's total assets) and gross margin (the difference between the total revenue and the cost of goods sold normalized by the total revenues).

Table 2-5 provides a summary of the constructs definition.

Table 5-2: Constructs Definition

Constructs	Definition
Supply Chain Disintermediation (SCD)	SCD is defined as the extent to which a pharmaceutical firm is selling its product directly to the patients, retail pharmacies and hospitals without going through wholesalers and distributors.
Product Portfolio	Product Portfolio is defined as the level of biologic products that exist within the pharmaceutical firm products portfolio.
Fit	Fit is defined as the extent to which a pharmaceutical firm is aligning its SCD level (distribution strategy) with its product portfolio structure.
Financial Performance (FP)	FP is defined as the firm's performance as reflected by its return on assets and gross margin.

5.3 Conceptual Development

The operations management body of literature has been showing a keen interest in the area of disintermediation in recent years, as indicated by the increasing number of research addressing this supply chain configuration issue. As discussed in the introduction, the body of literature in the operations management field lacks a substantial work on supply chain disintermediation and its impact on a firm's performance. Moreover, the literature that looks into the concept of disintermediation and how it relates to firm performance and customer satisfaction has been primarily conceptual work from the management and marketing field. The results based on conceptual foundations have shown some attractiveness for direct distribution channels and how they improve the consumer's experience (Bakos, 1998). Other studies, however, have expressed the challenges that disintermediation faces and how direct distribution channels can impact a firm's

performance (Brabazon, Winter, and Gandy, 2014). The following subsection addresses the conceptual development.

5.3.1 Supply Chain Disintermediation and Financial Performance

The operations management and financial performance interface is gaining attention from academic researchers (Chen et al., 2005; Hendricks and Singhal, 2003). Supply chain disintermediation represents a strategic distribution channel decision that can impact the firm's financial performance. Pharmaceutical manufacturers have the option of selecting a supply chain disintermediation strategy by selling directly to the hospitals, the retail pharmacies, and individual patients. This can influence their financial performance positively for the following reasons.

First, when engaging in direct sales, an organization will have the opportunity to reach a broader customer base. The broad market access will help the pharmaceutical firm generate more revenue. In fact, a high disintermediation level will stimulate closer relationships with customers, which will lead to repeated purchasing and, therefore, higher level revenue (Raymond and Tanner Jr, 1994). Moreover, Reichheld and Schefter (2000) discussed the role of loyalty as the "secret weapon" of the web and direct sales strategy. Direct sales will ensure a higher level of loyalty, leading to more sales (Reichheld and Schefter, 2000). From a practical standpoint, the results achieved by Dell Inc. in the late 1980s, when it adopted its direct sales strategy, was reflected in Dell's revenue and efficiency (Kraemer, Dedrick, and Yamashiro, 2000). In fact, Dell Corporation's return in 1998 was 26%, more than three times that of Apple Inc. and IBM Corp.'s performances.

Second, the traditional supply chain configuration (intermediated) suffers from the problem of double marginalization, where the profit margin will be split between the manufacturer and the distributor (Jeuland and Shugan, 1983). The double marginalization phenomenon suggests

that successive parties along a distribution channel price a product to maximize individual profits (Spengler, 1950). When double marginalization occurs, the distributor and retailer order propositions independent of each other, focusing only on maximizing their own company's profits (Chopra and Meindl, 2007). Double marginalization favors individualism and opportunistic behavior in the supply chain. Opportunism and individual consideration will have a negative impact on a firm's performance (Koppenjan and Klijn, 2004). In fact, double marginalization will reduce the manufacturer's profit margin and income (Heese, 2007). A supply chain disintermediation strategy will improve the firm's profit margin by allowing them to charge a slightly higher cost instead of sharing the total gross margin with the intermediaries (Coughlan et al., 2010). This will also improve the firm's profitability and efficiency, especially the return on assets and gross margin.

Third, disintermediated distribution channels promote a pull production system and just-in-time supply chain (Gehani, 2000). Pull production systems are more efficient and have the capability to provide better performance. Companies adopting pull and just-in-time are lean and, therefore, are expected to have better performance (Koufteros, 1999). More precisely, lean manufacturing systems enable firms to produce at lower prices, which will impact a firm's profitability and its cost of goods sold (Kinney and Wempe, 2002). In the context of pharmaceuticals, pull system allows firms to meet the existing demand to the production level and avoid any loss of sales risk and cost of goods sold by reducing potential waste and perishability cost.

Based on the above discussion, supply chain disintermediation provides opportunities for higher sales, capturing higher margins, and reducing cost of goods sold. Therefore, the following hypotheses are proposed:

H1a: Higher level of supply chain disintermediation will be positively associated with the firm's return on assets, ceteris paribus.

H1b: Higher level of supply chain disintermediation will be positively associated with the firm's gross margin, ceteris paribus.

While the above discussion points to the positive effect of supply chain disintermediation on a firm's financial performance, there may also be valid arguments which indicate that supply chain disintermediation could hurt financial performance.

First, supply chain disintermediation in the pharmaceutical context suggests that the firm will sell its products directly to the hospital and the end-patient. When engaging in a direct sales strategy, pharmaceutical firms lose the risk pooling effect. Risk pooling suggests that demand variability is reduced when the demand is aggregated at the distributor level (Levi, Kaminsky, and Levi, 2003). The risk pooling effect is a critical success factor for pharmaceutical firms to deal with diversification and demand variability (Hill and Hansen, 1991). Engaging in direct sales distribution channels may hurt the pharmaceutical firm as it could suffer from higher cost due to the incapability to deal with demand variability. In fact, the demand variability will result on both higher shortage and excess inventory costs. This will reduce the firm's profitability. Moreover, to cope with the product demand variation, the pharmaceutical firm will hold an excess inventory to satisfy the demand. This will also result in a higher level of asset requirements at the firm, which would also lower financial performance.

Second, a disintermediated channel, where the firm engages in direct sales, suggests that an organization will serve a broader range of customers. A broader customer base typically would require the firm to deal with a larger number of customers. Research indicates that a higher number of elements is an indicator of more complexity (Jacobs and Swink, 2011). As such, going direct

exposes a firm to a more complex customer base. The large and complex customer base would require a higher level of investment in assets by the firm to successfully meet customer demand (Homburg, Steiner, and Totzek, 2009). Moreover, a disintermediated distribution channel implies that the firm will manage each customer individually. Management of a large customer base requires specific efforts in order to manage the trade-offs between scale economies and lifetime customer value. Direct sales distribution channel is known to result in diseconomy of scale, as the firm will need to individually manage its customer (Johnson and Selnes, 2004). Hence, the disintermediation distribution channels will lead to a higher cost of goods sold, which will impact the firm's performance.

Based on the previous discussion, supply chain disintermediation requires higher investment on assets and will lead to higher cost of goods sold, which is expected to negatively impact the pharmaceutical firm's performance. Therefore, the following hypotheses are proposed:

H1a': Higher level of supply chain disintermediation will be negatively associated with the firm's return on assets, ceteris paribus.

H1b': Higher level of supply chain disintermediation will be negatively associated with the firm's gross margin, ceteris paribus.

5.3.2 Product Portfolio and Financial Performance

Product portfolio structure represents a strategic decision that could also impact a firm's financial performance. Specifically, offering more personalized products would require different investments and offer varied opportunities compared to offering less personalized (more standardized) products. A pharmaceutical firm can provide standardized products (small molecules drugs), personalized specialty drugs (biologics), or a combination of the two categories. As

discussed in chapter 2, biologic medications are characterized by a higher level of personalization. High level of personalization within the pharmaceutical product portfolio is expected to have a positive effect on the firm's financial performance for the following reasons.

First, personalized medication represents a high value added medication that aims at serving unique patients' needs. Firms will charge premium prices for highly customized products (Dewan, Jing, and Seidmann, 2000). Customers are willing to pay premium prices for personalized products and services (Moon, Chadee, and Tikoo, 2008). Moreover, personalized products call for value based pricing and, therefore, higher prices (Riemer and Totz, 2003). In fact, the value based pricing argument suggests that customers are willing to pay premium prices for products perceived as high value (Varian and Farrell, 2004).

Second, biologic drugs are innovative products targeting a specific patient's health problems (Roughead, Lopert, and Sansom, 2007). In general, innovative products are more expensive and their specialized nature enables firms to charge premium prices for such products (Fisher, 1997). More specifically in the context of the pharmaceutical industry, biologics represent personalized and innovative products that are high value and more expensive products (Stein, Pearce, and Feldman, 2005).

In summary, a product portfolio with a focus on biologics (personalized) are expected to generate more revenue and higher income since such products represent higher value to the customer and are more innovative. Higher revenues and income suggest higher return on asset utilization and gross margin. Based on the previous discussion, the following hypotheses are proposed:

H2a: Higher level of biologic products in a pharmaceutical product portfolio will be positively associated with firm's return on assets, ceteris paribus.

H2b: Higher level of biologic products in a pharmaceutical product portfolio will be positively associated with firm's gross margin, ceteris paribus.

A product portfolio focused on biologic (personalized) medication represents a challenging task which could impact the pharmaceutical firm's financial performance. One could expect that the product portfolio structure could have a negative impact on financial performance for the following reasons.

First, biologic products are characterized by a higher level of complexity in both the production process and the product structure (Declerck, 2012). Higher complexity level in the product portfolio can lower the firm's financial performance. In fact, as complexity increases, organizations will experience more challenges to achieving higher operational efficiency (Ameri and Dutta, 2005). As the operational efficiency is reduced, the pharmaceutical gross income will diminish, which will have a negative impact on financial performance.

Second, biologic products are costly medications with high financial risks. Biologic products are characterized by high production cost due to process complexity and time constraints (Simpson, 2011). The variable cost per unit for a biologic medication can cost several thousands of dollars in many cases (Simpson, 2011). Moreover, the biologics' production requires skilled labor. Skilled labor, in general and specifically in the medical field, tends to be more expensive compared to unskilled labor and, therefore, may impact the firm's labor costs (Murray and Gerhart, 1998).

Third, biologic medicines are highly personalized and, therefore, are produced in low quantities, often single or dual units of production (Shukla and Thömmes, 2010). This hampers firms from enjoying the corresponding cost effectiveness that can derive from mass-production. In fact, the nature of the biological medication does not favor economies of scale. It is well known

that as a firm engages in an economy of scale, the total product cost per unit will decrease (Silvestre, 1987). Therefore, it is expected that biologic medicines will suffer from a higher cost of goods sold.

In summary, a product portfolio with a focus on biologics (personalization) is expected to have a higher cost of goods sold, which will impact the firm's financial performance. This will suggest lower return on assets utilization and gross margin. Based on the previous discussion, the following hypotheses are proposed:

H2a': Higher level of biologic products in a pharmaceutical product portfolio will be negatively associated with firm's return on assets, ceteris paribus.

H2b': Higher level of biologic products in a pharmaceutical product portfolio will be negatively associated with firm's gross margin, ceteris paribus.

5.3.3 Supply Chain Disintermediation and Product Portfolio Fit

A firm's performance is influenced by the level of consistency between the strategy adopted and the environment. This consistency, also referred to as fit or alignment, has a positive impact on performance (Alexander and Randolph, 1985; Doty, Glick, and Huber, 1993). The study of fit has also interested scholars from operations management literature for a long time. Manufacturing configurations should be consistent with the firm's strategic vision (Skinner, 1969). More recent studies have attempted to test alignment configurations and address a firm's performance (Burton, Lauridsen, and Obel, 2002). Fisher's (1997) paper addressed the idea of fit in the supply chain management and the type of product. The study has inspired scholars to empirically test whether an organization will achieve a better performance when it aligns its supply chain configuration with the type of product (Wagner et al., 2012).

In line with the base notion proposed by Fisher (1997) that a firm's supply chain strategy must align/fit with its product characteristic for the firm to be competitive, this research suggests that a high level of personalization would call for a disintermediated supply chain distribution channel strategy. The earlier discussion in chapter 2 highlighted the details about the product paradigm and the supply chain configuration. Briefly, pharmaceutical firms' product portfolio consists of biologics and non-biologics. Pharmaceutical firms can sell exclusively biologic drugs, traditional medication, or a combination of both. Further, the drugs can be sold directly to the end user (patient or hospitals), thereby adopting disintermediated configuration or, alternatively, the drugs can be sold using traditional distribution channels (intermediated configuration) or a combination of methods (hybrid configuration).

Biologic products, highly personalized medication, are most effectively distributed through direct distribution channels as such a product portfolio with biologics is most appropriate via disintermediated modes. In fact, the high level of personalization and higher value proposition suggests that direct distribution channels are most suitable. Moreover, because of their shorter shelf life, biologic pharmaceuticals will benefit from supply chain disintermediation by improving the product's useful life span. Finally, because of the uncertain demand in biologic medication, a pull strategy is more appropriate to manage the demand requirements. Pull strategy is more effective in a direct sales distribution configuration. On the other hand, traditional medications are characterized by a high standardization level. Higher product standardization obviates the need for direct distribution channels and suggests that traditional distribution channels are most adequate. In fact, over the counter medication and other non-biologic products are distributed using wholesalers. Selling non biologic products via direct distribution channels is inappropriate and

represents a misfit between product portfolio and supply chain disintermediation. This is mainly due to the level of product sophistication and the drug's cost.

The current chapter identifies supply chain fit as the alignment between product portfolio characteristics (biologics vs. non-biologics) and supply chain disintermediation level. For biologic products, firms will generate higher performance when selling the product directly. For traditional medication, the fit suggests that firms will have better performance when the drug is sold through traditional distribution channels. Organizations are expected to achieve higher performance when their competitive capabilities and supply chain configuration match their product characteristics (Hayes and Wheelwright, 1979).

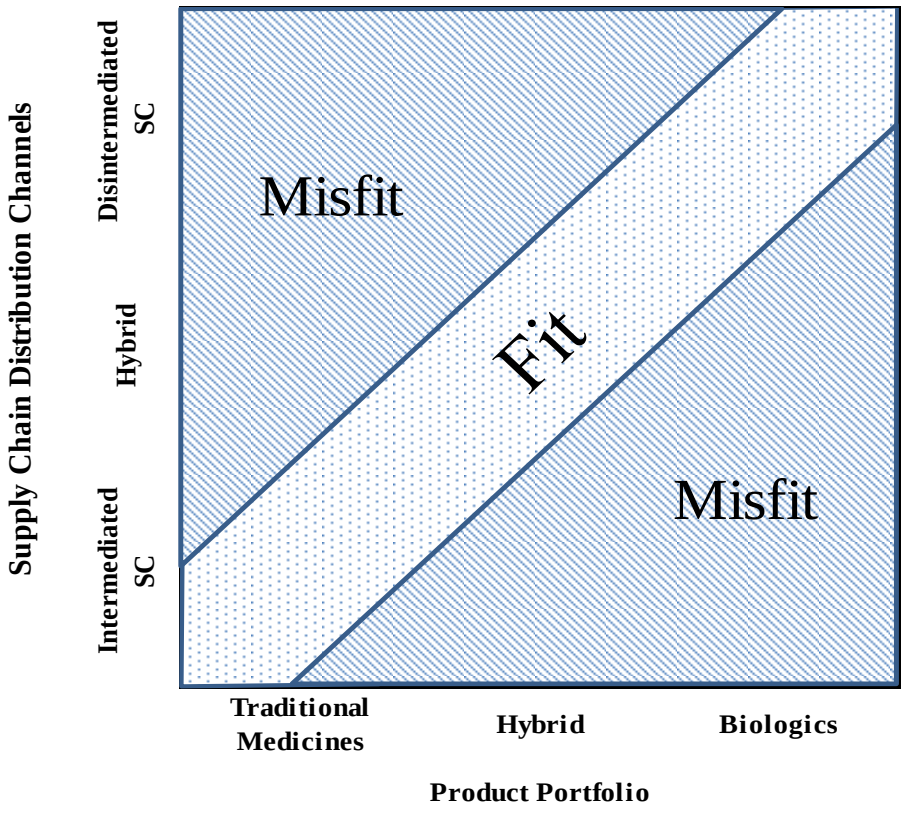

Figure 5-1: Supply Chain Disintermediation and Product Portfolio Fit

Figure 5-1 illustrates the supply chain disintermediation and product portfolio fit conceptualization. Based on the previous discussion, the following hypotheses are provided:

H3a: A fit between the firm's product portfolio and supply chain disintermediation will be positively associated with the firm's return on assets, ceteris paribus.

H3b: A fit between the firm's product portfolio and supply chain disintermediation will be positively associated with the firm's gross margin, ceteris paribus.

5.3.4 The Hypothesized Model

The current study will draw from the existing literature in supply chain disintermediation, product portfolio, and fit to develop a set of definitions for this study. The hypothesized model shows a set of three main hypotheses. The first two sets address the impact of disintermediation and product portfolio on financial performance. The final set investigates the fit between the distribution channels and the type of products and how it relates to a firm's financial performance.

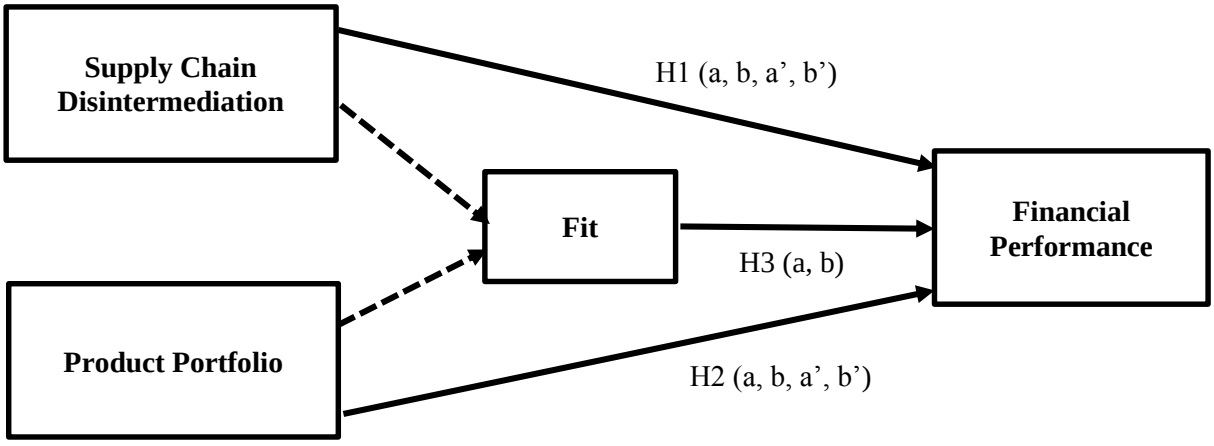

Figure 5-2: Hypothesized Model

5.4 Research Methodology

The following section discusses the research methodology used in this essay. First, the dependent, independent, and control variable operationalization is presented. Then, the empirical model is developed to test for the hypothesis and a plan of study is discussed.

5.4.1 Variable Operationalization

This section discusses the conceptualization of the variables as well as the sources of data collection.

5.4.1.1 Dependent Variables

The study uses two measures to assess a firm's financial performance: Return on Assets (ROA), and Gross Margin (GM). The paragraphs below provide more details about how to capture each variable.

Return on Assets (ROA): ROA is an accounting-based measure that provides information on the profitability of a firm and how its assets have been used efficiently (Fullerton, McWatters, and Fawson, 2003; Modi and Mishra, 2011). The data to compute ROA is obtained from the COMPUSTAT database. The ROA for company i in year t is obtained in the following manner:

$$ROA_{it} = \frac{IBEI_{it}}{TA_{it}} \qquad (5\text{-}1)$$

where, $IBEI_{it}$ = income before extraordinary items of firm i in year t, and TA_{it} = total assets of firm i in year t.

Gross Margin (GM): GM is a major business and financial performance indicator and an indicator about a firm's performance. It is also a typical indicator of industries' behavior and dynamics (Farris et al., 2010). The data to measure the gross margin is obtained from COMPUSTAT. The gross margin is calculated as follows:

$$GM_{it} = \frac{TS_{it} - GOGS_{it}}{TS_{it}} \qquad (5\text{-}2)$$

Where TS_{it} = total sales of firm i in year t. and $GOGS_{it}$ = cost of goods sold of firm i in year t.

5.4.1.2 Independent Variables

The model discussed in the previous section has two independent variables: supply chain disintermediation and product portfolio structure.

Supply Chain Disintermediation (Dis_Level): As discussed in the conceptual development section, the supply chain disintermediation (SCD) represents the level of material flow that is shipped directly to the end customer. In this chapter, the SCD is conceptualized by the level of medicine that is sold directly to the patients, hospitals, and retail pharmacies. When the drug is shipped through the regular distributors and wholesalers, the product is considered intermediated. To determine the level of disintermediation, the Bloomberg database terminal is used. The database provides data on many public firms' supply chain relationships, including pharmaceuticals and biopharmaceuticals. The data maps a company to its suppliers, customers, and competitors and gives an indication of the strength of the relationship, marked by the relationship transaction numbers. For each of the companies in the pharmaceutical industry, a supply chain network is developed with a list of customers and suppliers. The Bloomberg terminal has information about the quantified relationships where it provides the exact level of operation. For example, the database reports that in 2013, 1.5 billion dollars of Pfizer's sales were generated from McKesson Corporation. Also, the database provides some estimates about non-quantified relationships where Bloomberg analysts, basing it on mathematical modeling, have provided an estimate of the existing relationships (Steven, Dong, and Corsi, 2014). The Bloomberg database has the data available in "real time" and does not provide an option of historical data compilation.

To determine the relationship magnitudes, more data was extracted from Bloomberg and the firm's financial reports. The supply chain disintermediation level is assessed as a percentage of the goods that are shipped from the manufacturer directly to a hospital or the drug stores. The Bloomberg data base provides an estimation of the financial flows that relate the manufacturers to their clients. Based on the estimates, the disintermediation level is estimated for each firm. The disintermediation level in this case is a continuous variable and is computed as follows:

$$Dis\_Level = \frac{\sum Sales\ to\ end\ customers}{Total\ Sales} \qquad (5\text{-}3)$$

The use of the Bloomberg database provides an indication about the types of relationships and its magnitude. For each firm, a list of customers' 6 digit NAICS and 4 digit SIC code has been developed to identify the supply chain's tier positioning. Based on the firm's customer base positioning within the supply chain and the dollar value of the physical flow, the supply chain disintermediation code is determined. The SCD variable is coded as follows: 1, 2, and 3. Code 1 reflects a totally disintermediated distribution strategy. A code 1 for SCD is given to a firm that sells the majority of its product through direct distribution channels. A code 3 reflects a totally intermediated distribution channel. When the majority of the drugs is sold to distributors and wholesalers, a level 3 SCD is assigned. In some cases, firms will have a hybrid distribution strategy: the customers will be a mix of wholesalers & distributors (intermediated) and patients, hospitals, & drug stores (disintermediated). In these cases, a code 2 is assigned. For example, Pfizer's customer list includes McKesson, Cardinal, Express Script, Walgreen, and Rite Aid, among others. The NAICS and SIC codes for each client determine if it is an end customer or an intermediary. McKesson's NAICS is 424210 (Drugs and Druggists' Sundries Merchant Wholesalers), positioning McKesson as an intermediary. Walgreen and Rite Aid's NAICS codes are 446110 (Pharmacies and Drug Stores), distinguishing them as end customers. The SCD code

for Pfizer is 2. The cutoff used to determine the disintermediation level is 80%. If a firm sells over 80% of its product via intermediated channels, it is considered an intermediated firm and is assigned a code 3. The same methodology is used to assign code 1 for a disintermediated firm. For all other firms, the SCD is assigned a level 2. The assumption of an 80% cutoff level for disintermediation is relaxed, and sensitivity analysis is conducted using 90%, 85%, 75%, and 70% cutoffs. The details are discussed in the robustness check section.

The current study uses the continuous variable to test for the impact of disintermediation level on financial performance. The coded disintermediation level is used to determine the firm's distribution strategy and assess the fit.

Product Portfolio: Pharmaceutical firms sell a set of drugs and medicine which make up its product portfolio. The discussion section above addressed the product portfolio and its impact on the firm's performance. To assess the product portfolio, data is collected from Bloomberg and organization annual reports. For each period (2010, 2011, 2012, 2013), the list of products is determined. Based on the product description, it was determined to be either a biologic or traditional drug. Biologics are large molecule medications characterized by a higher level of personalization. The product portfolios are coded as 1, 2, or 3. Code 1 denotes a biologic product portfolio and code 3 represents a traditional medication portfolio. Code 2 represents a hybrid product portfolio.

Product Portfolio and Supply Chain Fit: The fit between the product portfolio structure and supply chain is measured by matching two variables: product portfolio and supply chain disintermediation. High fit or alignment suggests that an organization will adopt a disintermediation level that is consistent with its product portfolio structure. The concept of fit was conceptualized by Venkatraman's (1989) seminal work where he provided a list of measurement

techniques to assess fit in business research. Depending on the degree of variable specificity and the anchoring test, six fit techniques were provided: i) moderation, ii) mediation, iii) matching, iv) gestalts, v) profile variation, and vi) covariance (Venkatraman, 1989). The variables used in the study have moderate specifications with three levels. The matching degree between the two variables is expected to have an impact on the firm's performance. According to Venkatraman, matching by deviation appears to be the most appropriate fit technique to use. For example, to measure the alignment between IS strategy and business strategy in a 3*3 matrix, Sabherwal and Chan (2001) used fit by deviation. A distance measurement between the business strategy and the IS strategy was then developed (Sabberwal and Chan, 2001).

5.4.1.3 Control Variables

A set of control variables are included in the empirical analysis. Control variables provide more insights about the model.

R&D intensity: Research and Development intensity reflects a firm's innovative capability and may have an impact on the firm's financial performance, especially in the pharmaceutical industry. It is expected that R&D intensity has a positive impact on financial performance. It is measured by a firm's R&D expenditure and normalized by sales. The *R&D intensity will be calculated as follows:*

$$RDI_{it} = \frac{RD_{it}}{Sales_{it}} \qquad (5\text{-}4)$$

The second control variable used in the model relates to the *firm size*. Firm size is a common control variable in empirical studies, as it impacts the firm's performance (Hendricks and Singhal, 2003). On one end, it is expected that a firm's size has an impact on the firm's profitability measures, such as ROA. However, prior studies have found that a firm's size has a negative impact

on both a firm's growth and Tobin's Q (Bharadwaj, Bharadwaj, and Konsynski, 1999). The firm's size is measured by the natural log of total assets.

Third, to account for industry concentration, the model uses *Herfindahl-Hirschman Index* (*HHI*). The HHI index is used as a proxy for industry competitiveness. This study has only two industries. However, because of the paneled nature of the data, the use of HHI for the different years of the study will provide more insights about the results. The HHI is calculated as follows:

$$HHI_{It} = \sum_{i=1}^{N} (MKS_{lt})^2 \qquad (5\text{-}5)$$

Where: HHI_{it} represents the *Herfindahl-Hirschman Index for industry I in year t and* MKS_{lt} is the market share of firm *l* in year t.

Finally, *Market Share* (*MKS*) is calculated for each firm and is expected to impact a firm's performance. Organizations with higher market share enjoy more comfortable situations and are expected to have stronger performance (Modi and Mishra, 2011). MKS for firm i for industry I in period t is computed as the firm's total sales in period t divided by the total sales of all the firms within the industry I.

$$MKS_{it} = \frac{Sales_{it}}{Total\ Industry\ Sales_{It}} \qquad (5\text{-}6)$$

5.4.2 Data Collection

This study uses multiple sources to collect the different variables. First, the Bloomberg database is used to collect the data related to the independent variables. Both supply chain disintermediation and product portfolio structure are collected from that database. Bloomberg provides data regarding the focal company's supply chain network and the dollar value of the relationships. The

data is collected for the pharmaceutical related industries with NAICS of 315412 and 325414. The Bloomberg database also provides the firm's product portfolio and the type of revenue sources. In the pharmaceutical industry, typical revenues are generated from sales of products, services, grants, subcontracting, and royalties, among others. In this study, the focus is on firms that provide at least one product. Firms that have exclusively non-product revenue streams have been eliminated because the intent of the study is to address the supply chain disintermediation, and that requires the existence of physical flows. The supply chain disintermediation results from Bloomberg are then validated using the Mergent Horizon database. Mergent Horizon provides a list of the main customers and suppliers. The product portfolio results are checked across the firms 10k reports. A key word search looks for biologics-related words within the products' characteristics. Based on the key word search results, the pharmaceutical product portfolio typology is determined. Table 5-3 provides a summary of the variables operationalization.

Table 5-3: Variables Operationalization

Variable	Description	Source
Return on Assets (ROA)	The ratio of income before extra-ordinary items to the total assets.	Compustat
Gross Margin (GM)	The ratio of the gross margin to the sales	Compustat
Supply Chain Disintermediation (SCD)	A three level dummy variable the represents the level of product that is sold directly to the end users.	Bloomberg database, Mergent Horizon, and Financial reports
Product Portfolio (PP)	A three level dummy variable that reflects the level of biologic medication in the firm's product portfolio	Bloomberg database and Financial reports
Market Share (MKS)	The firm's sales divided by the total industry sales	Compustat
Herfindahl-Hirschman Index (HHI)	The sum of squared shares of firm's market shares in the industry defined at the 6-digit NAICS code.	Compustat
Firm Size (LnTA)	The natural log of total assets	Compustat
R&D intensity (RDI)	The ratio of the R&D expenditure to the total sales	Compustat

5.5 Empirical Model Formulation

The data was collected from the years from 2010 through 2013 from firms with NAICS of 315412 and 325414. A total of 353 firms were identified across the four years. Entries with no recorded revenue were eliminated. In fact, many firms were operating at clinical stage. Additionally, firms that specialize in discovery and development were eliminated. Finally, a few firms specialized in animal medication, and, therefore, were outside of the study's scope. Ultimately, 216 unique firms were identified across the 4 years, resulting in 772 observations. The nature of the problem suggests using a panel data. However, the panel is short (4 years) and unbalanced, as some of the firms have four years of observations while others have fewer years of observations. This is due mainly to acquisition and merger activities common in the pharmaceutical industry. Moreover, some companies went public after 2010 and, therefore, no observations were available for certain years. In order to deal with such a short and unbalanced model, an option was to combine all the data into one single pool (Park, 2005). To do so, first, a poolability test was required.

5.5.1 Poolability Test

The poolability test checked whether the different slopes would vary across the groups or over time (Baltagi, 2008). The null hypothesis of a poolability test assumes homogeneous slope coefficients. An F value calculation compares the different slopes of the regressions model and tests for differences (Chow, 1960). Some statistics packages such as R and Stata can perform the test in less computational steps. The test can also be conducted manually using the results from the SAS regression.

The SAS manual (2009) for panel data procedure suggests the following. First, for the unrestricted model, the user should run a regression for each cross section and save the sum of squared residuals as SSE_u. Second, for the restricted model, run the regression and save the sum

of squared residuals as SSE_r. The model that is tested does not apply to the constant variable (only the slope); therefore, the restricted model is the fixed one-way model with cross-sectional fixed effects. Let's denote N and T as the number of cross sections and time-periods. The total observation n will be equal to N*T. In this study, the panel data is unbalanced, with some missing observations from certain years. However, the number of observations is determined in the study. Let's call k the number of "regressors" (independent variables and control variable in the exhaustive model). The degree of freedom for the unrestricted model is $df_u = T * (N - k)$ and the number of restrictions is given by $q = (N - 1) * k$. Based on that, the F statistics is given as the following:

$$F = \frac{(SSE_r - SSE_u)/q}{SSE_u/df_u} \sim F(q, df_u) \qquad (5\text{-}7)$$

For this study, the number of unique observations (N) is 216. The number of total observations n=772, and the number of regressors k= 6. The SSE_u is obtained using SAS for the four different years of observations. SSE_r is derived from the pooled model. To test for poolability, the analysis was first performed for Return on Assets as the dependent variable. The detailed results from the poolability test are presented in appendix D. A summary of the results is shown below.

Variable	**Comment**	**Value**
SSEr	The error from the pooled model	143,771
SSEu	The sum of error from the years observation	138,995
Q	The degree of freedom of the numerator $q = (N - 1) * k$	1,290
df_u	Degree of freedom on the denominator $df_u = T * (N - k)$	840
F Statistics	$\frac{(SSE_r - SSE_u)/q}{SSE_u/df_u}$	0.022

The p_value for the F(1,290, 840) is equal to one. The small F statistic does not reject the null hypothesis in favor of poolable panel data with respect to time (p<1.00). Therefore, it can be concluded that the data can be pooled with respect to the time horizon.

5.5.2 Estimated Model

To estimate the model parameters, an ordinary least squared (OLS) model is developed. The OLS regression model contains the independent and control variables.

$$ROA_{it} = \beta_0 + \beta_1 Dis\_Level_{it} + \beta_2 Prod\_Prot_{it} + \beta_3 Fit_{it} + \beta_4 MKS_{it} + \beta_5 HHI_{it} + \beta_6 Ln(Total\_Assets) + \beta_7 RDI_{it} + \varepsilon_{it}$$

$$GM_{it} = \beta_0 + \beta_1 Dis\_Level_{it} + \beta_2 Prod\_Prot_{it} + \beta_3 Fit_{it} + \beta_4 MKS_{it} + \beta_5 HHI_{it} + \beta_6 Ln(Total\_Assets) + \beta_7 RDI_{it} + \varepsilon_{it}$$

Where ROA_{it} and GM_{it} are the model's independent variables and they represent the return on assets and the gross margin for firm *i* in year *t,* respectively. Dis_Level_{it} represents the disintermediation level for firm *i* in year *t.* $Prod\_Prot_{it}$ is the firm's *i* product portfolio structure in year *t.* $MKS_{it}, HHI_{it}, Ln(Total_{Assets}), and\ HHI_{it}$ are the firm's control variables, identified in the variable operationalization section. Finally, ε_{it} is the disturbance term.

5.6 Analysis and Results

This section presents the analysis to estimate the above models for testing the hypotheses.

5.6.1 Data Descriptive Statistics

The data collected from the Bloomberg database and Compustat identified 216 unique firms for the 4 year span. At the end, 772 usable observations where identified. Tables 5-4 and 5-5 summarize the financial performance across the two independent variables.

Table 5-4: Disintermediation Level Descriptive Statistics

Dis_Level	N	Variable	Mean	St. Dev.
1 **Disintermediated**	134	ROA	-0.047	3.407
		GM	-0.0067	1.338
2 **Hybrid**	377	ROA	-0.337	0.910
		GM	-0.4158	3.241
3 **Intermediated**	261	ROA	-0.269	1.289
		GM	-0.31	4.988

Table 5-5: Product Portfolio Descriptive Statistics

Product Portfolio	N Obs	Variable	Mean	Std Dev
1 **Biologics**	247	ROA	-0.349	2.605
		GM	-1.614	5.823
2 **Hybrid**	281	ROA	-0.209	0.781
		GM	0.300	0.983
3 **Traditional**	244	ROA	-0.240	1.366
		GM	0.311	2.437

Tables 5-6 and 5-7 present the frequency distribution of the variable across the main two independent variables (disintermediation and product portfolio). The two tables also provide the mean and the standard deviation of the financial performance. The results show that disintermediated biologics firms have the highest return on investment (45%). Pharmaceutical firms that sell traditional drugs and use disintermediated distribution channels experience the lowest return on assets (-187%). Gross margin performance was at its highest for traditional

product portfolio with intermediated distribution channels (40%). Biologic products that are distributed through direct sales showed the lowest gross margin (-365%). Both return on investment and gross margin improved as a firm shifted from intermediated distribution to more direct channels. Moreover, traditional and hybrid product portfolios have a higher gross margin when compared to the biologic drugs.

Table 5-6: Two Way Frequencies, Mean, and Standard Deviation for ROA

		ROA			
		Product Portfolio			
Disintermediation		1 Biologics	2 Hybrid	3 Traditional	Total
1 Disintermediated	Freq	82	43	9	134
	Mean	0.45	-0.62	-1.87	
	St. Dev.	4.07	1.12	3.29	
2 Hybrid	Freq	126	175	76	377
	Mean	-0.74	-0.06	-0.3	
	St. Dev.	1.19	0.49	0.87	
3 Intermediated	Freq	39	63	159	261
	Mean	-0.76	-0.35	-0.12	
	St. Dev.	1.38	1.02	1.34	
Total Frequencies		247	281	244	

Table 5-7: Two Way Frequencies, Mean, and Standard Deviation for Gross Margin

		Gross Margin			
		Product Portfolio			
Disintermediation		1 Biologics	2 Hybrid	3 Traditional	Total
1 Disintermediated	Freq	82	43	9	**134**
	Mean	-0.03	0.25	-0.99	
	St. Dev.	1.51	0.67	1.65	
2 Hybrid	Freq	126	175	76	**377**
	Mean	-2.01	0.43	0.28	
	St. Dev.	5.11	0.81	1.08	
3 Intermediated	Freq	39	63	159	**261**
	Mean	-3.65	-0.03	0.4	
	St. Dev.	10.89	1.43	2.89	
Total Frequencies		**247**	**281**	**244**	

Table 5-8 provides the descriptive statistics and the correlation factor of model variables. The correlation matrix showed that the product portfolio variables were slightly correlated with each other. This is expected given the nature of these categorical variables. The Herfindahl-Hirschman index is highly correlated to the product portfolio structure.

Table 5-8: Correlation and Descriptive Statistics

Pearson Correlation Coefficients, N = 772													
Prob > |r| under H0: Rho=0													
	Mean	**Std Dev**	**ROA**	**Gmar**	**Prod Port1**	**Prod Port2**	**Prod Port3**	**Dis_Level**	**Fit**	**HHI**	**Lnat**	**RDI**	**MktS**
ROA	-0.26371	1.7256	1										
Gmar	-0.30892	3.7206	**0.1559*** **	1									
Prod_Port1	0.31995	0.4668	-0.0339	**-0.2407*** **	1								
Prod_Port2	0.36399	0.4815	0.0239	**0.1239*** **	**-0.5189*** **	1							
Prod_Port3	0.31606	0.4652	0.0093	**0.1133*** **	**-0.4663*** **	**-0.5143*** **	1						
Dis_Level	0.42515	0.2847	**0.0712** **	0.0303	**0.3554*** **	**0.1119** **	**-0.4723*** **	1					
Fit	0.42515	0.2847	**0.178*** **	**0.1851*** **	**-0.2847*** **	**0.1274*** **	**0.1538*** **	0.02944	1				
HHI	0.11466	0.0540	-0.0177	**-0.1937*** **	**0.5910*** **	**-0.1058*** **	**-0.4834*** **	**0.4870*** **	**-0.2855*** **	1			
Lnat	5.36085	2.6545	**0.1496*** **	**0.1657*** **	**-0.3142*** **	**0.2029*** **	**0.1052*** **	**-0.1498*** **	**0.3971*** **	**-0.2908*** **	1		
RDI	1.83345	6.7169	**-0.1176*** **	**-0.3747*** **	**0.0786** **	**0.0230*** **	**-0.1027*** **	0.01	**-0.1794*** **	**0.1662*** **	**-0.1268*** **	1	
MktS	0.00993	0.0334	**0.0611***	**0.0843** **	**-0.1460*** **	**0.2325*** **	**-0.0941*** **	**0.0765** **	**0.2393*** **	0.0067	**0.5566*** **	**-0.0738** **	1

5.6.2 Initial Analysis

The preliminary analysis consisted of comparing the different dependent variable means among the different fit levels. First, the fit level as defined in the variable operationalization part represents the spectrum where the firm's distribution strategy is aligned with its product portfolio structure. The misfit is identified as a combination of a distribution strategy that is not aligned with the firm's product portfolio. Wagner et al. (2012) have identified positive and negative misfits: a positive misfit. Firms with a negative misfit are defined as firms that design responsive supply chains while the products are functional. Firms with positive misfits are firms with an efficient supply chain for innovative products. The current study draws on the work of Wagner et al. (2012) and define the positive misfit as using a direct sales strategy for traditional drugs. In other words, this study used supply chain capabilities that exceeded the actual product needs. Firms with negative misfits are identified as the ones using traditional distribution channels for biologic products. Table 5-9 summarizes the descriptive statistics for the gross margin and return on assets across the three different levels of fit and misfit.

Table 5-9: Fit and Misfit Descriptive Statistics

Group Statistics					
		N	**Mean**	**Std. Deviation**	**Std. Error Mean**
GM	**Fit**	416	32.79%	198.21%	9.72%
	Misfit	356	-105.30%	494.39%	26.20%
	Positive Misfit	128	18.00%	105.61%	9.33%
	Positive Misfit	228	-174.52%	602.17%	39.88%
ROA	**Fit**	416	2.02%	201.42%	9.88%
	Misfit	356	-59.54%	123.25%	6.53%
	Positive Misfit	128	-51.96%	130.68%	11.55%
	Negative Misfit	228	-63.80%	118.96%	7.88%

A t-test analysis was performed to compare the different fit and misfit combinations. The results are shown in tables 5-10, 5-11, and 5-12.

Table 5-10: Fit vs. Misfit t-test

		t-test for Equality of Means				
		t	**df**	**Sig. (2-tailed)**	**Mean Difference**	**Std. Error Difference**
GM	Equal variances assumed	5.227	770	.000	138.09%	26.42%
	Equal variances not assumed	4.941	452.061	.000	138.09%	27.95%
ROA	Equal variances assumed	5.018	770	.000	61.56%	12.27%
	Equal variances not assumed	5.199	700.774	.000	61.56%	11.84%

\

The t-test results for fit versus misfit show a statically significant difference. In general, the return on assets t-statistics difference was significant for all three combinations (t= 5.199, 3.522, and 5.210). On the other hand, though, gross margin analysis of fit versus positive misfit did not show a statistical significant difference (t=1.097). The remaining two analyses for gross margin show significant t-test statistics.

Table 5-11: Fit vs. Positive Misfit t-test

		t-test for Equality of Means				
		t	**df**	**Sig. (2-tailed)**	**Mean Difference**	**Std. Error Difference**
GM	Equal variances assumed	.809	542	.419	14.79%	18.28%
	Equal variances not assumed	1.097	405.663	.273	14.79%	13.47%
ROA	Equal variances assumed	2.852	542	.005	53.98%	18.93%
	Equal variances not assumed	3.552	327.047	.000	53.98%	15.20%

Table 5-12: Fit vs. Negative Misfit t-test

		t-test for Equality of Means				
		t	**df**	**Sig. (2-tailed)**	**Mean Difference**	**Std. Error Difference**
GM	Equal variances assumed	6.419	642	.000	207.31%	32.30%
	Equal variances not assumed	5.051	254.268	.000	207.31%	41.05%
ROA	Equal variances assumed	4.520	642	.000	65.81%	14.56%
	Equal variances not assumed	5.210	638.513	.000	65.81%	12.63%

5.6.3 Results

To test for the various hypotheses, an ordinary linear regression was developed. Six models were estimated for return on assets and gross margin. Model A is the controlled model with only the model's control variables (market share, research and development intensity, natural log of total assets, and Herfindahl-Hirschman Index). Model B contains the control model, adding one of the independent variables (disintermediation level). The third model (model C) is similar to the second model with product portfolio, instead of the disintermediation level as the independent variable. Model D has all the independent variables (disintermediation and product portfolio). The fifth model contains the control variables and the fit variable. Finally, a full model represents all the model variables.

The OLS model uses the adjusted R^2 and the F value as part of model validation. The comparison between the adjusted R^2 for model A and models B and C, respectively, provides insights regarding the extent of information provided by the control variables. Model D illustrates the impact of both dependent variables on the financial performance. Comparing model E to the

control model shows the impact of the fit variable. Finally, the full model illustrates the extent of the information explained by all the variables.

Disintermediation Level: The first set of hypotheses relates the disintermediation level to the firm's financial performance. The disintermediation level positively impacts the return on assets. The full model provided support to the positive relationship between disintermediation level and ROA (β=0.5006, $p<0.1$). The results were confirmed through the linear model (with only disintermediation level and control). The nested model's adjusted R^2 increased from 3.03% to 3.70%. This supports hypothesis H1a and, therefore, it can be concluded that supply chain disintermediation positively impacts return on assets. The results for the gross margin regression model showed support for hypothesis H1b. The disintermediation level increase improves the firm's gross margin (β=1.9949, $p<0.01$). Thus, a direct sales model will improve the firm's gross margin. The nested model confirms the results, as the adjusted R^2 increased by 1.23%.

Product Portfolio: the conceptualized model proposed a relationship between the product portfolio structure (biologics and non-biologics) and the firm's financial performance. The results, however, did not provide any support for the relationship between the product portfolio structure and the return on assets. In fact, there was no evidence of a relationship existing between the return on assets and product portfolio. Therefore, hypothesis H2a is not supported. Second, the product portfolio structure did have an impact on the firms' gross margin. The results show that hybrid and traditional drug product portfolios have higher gross margins when compared to biologic medication. Traditional medicine's gross margin is also higher than biologics (β_{hybrid}=1.6141, $p<0.01$ and $\beta_{Traditional}$=1.7360, $p<0.01$). Biologic medications are characterized by a higher cost of goods sold, which harms the gross margin. The results were validated using a nested model with

controls and product portfolio. The adjusted R^2 increased from 16.13% to 17.36%. This provides support for hypothesis H2b.

Product Portfolio and Supply Chain Fit: the final set of hypotheses suggests that the product portfolio and supply chain fit have a positive impact on the firm's financial performance. The results show a positive impact of supply chain disintermediation and product portfolio fit on ROA (β=0.437, $p<0.01$). These findings support hypothesis 3a. On the other hand, the relationship between fit and gross margin was not significant. In fact, the results have shown that alignment between product portfolio and supply chain disintermediation does not impact the firm's gross margin. The discussion section will discuss some of the reasons behind this relationship.

Model Fit: The overall model fit results for the return on assets models show a relatively low return on assets' adjusted R^2 (4.61%). The low adjusted R^2 for ROA model is a common result in research in the supply chain management field, as some previous researchers reported low adjusted R^2 for ROA models (Kim and Henderson, 2015). The gross margin OLS model has an adjusted R^2 of 20.65%. The detailed results are shown in tables 5-13 and 5-14.

Table 5-13: Return on Assets Regression Analysis (Unstandardized Coefficients)

Return on Assets (N=772)												
		Model A: Control Model		**Model B: Linear Model (Dis. Level)**		**Model C: Linear Model (Prod. Portfolio)**		**Model D: Linear Model (Dis. Level and Prod Portfolio)**		**Model E: Linear Model (Fit)**		**Model F: Linear Model (Full)**	
		Estimate	**St Error**	**Estimate**	**St Error**	**Estimate**	**St Error**	**Estimate**	**St Error**	**Estimate**	**St Error**	**Estimate**	**St Error**
Intercept		**-0.9933*** **	0.24307	**-1.1080*** **	0.24648	**-1.0377*** **	0.3151	**-1.2736*** **	0.3262	**-1.2142*** **	0.24866	**-1.3441*** **	0.3252
Dis_Level				**0.6233** **	0.24757			**0.6909*** **	0.2604			**0.5006* **	0.2661
Prod Port 1													
Prod Port 2						0.04581	0.1736	0.05482	0.1730			0.0047	0.1728
Prod Port 3						0.03629	0.1989	0.17204	0.2046			0.0806	0.2056
Fit										**0.4968*** **	0.13643	**0.4370*** **	0.1408
HHI		1.64986	1.2240	0.09552	1.3671	1.8364	1.5268	0.67174	1.5829	2.4929	1.23615	1.4741	1.5951
Lnat		**0.1146*** **	0.0297	**0.1203*** **	0.0297	**0.1138*** **	0.0299	**0.1195*** **	0.0299	**0.0874*** **	0.03041	**0.0949*** **	0.0307
RDI		**-0.0275*** **	0.0093	**-0.0257*** **	0.0093	**-0.0277*** **	0.0093	**-0.0254*** **	0.0093	**-0.0236** **	0.00927	**-0.0224** **	0.0093
MktS		-2.3409	2.2598	-2.9558	2.2652	-2.4173	2.2938	-2.9233	2.2927	-2.8671	2.24663	-3.1916	2.2815
R-Square		3.53%		4.32%		3.54%		4.42%		5.17%		5.61%	
Adjusted-R		3.03%		3.70%		2.78%		3.54%		4.55%		4.62%	
F		7.01***		6.92***		4.68***		5.05***		8.35***		5.67***	

*** Significant at the .01
** Significant at the .05
* Significant at the .1

Table 5-14: Gross Margin Regression Results (Unstandardized Coefficients)

Gross Margin (N=772)												
		Model A: Control Model		**Model B: Linear Model (Dis. Level)**		**Model C: Linear Model (Prod. Portfolio)**		**Model D: Linear Model (Dis. Level and Prod Portfolio)**		**Model E: Linear Model (Fit)**		**Model F: Linear Model (Full)**	
		Estimate	**St Error**	**Estimate**	**St Error**	**Estimate**	**St Error**	**Estimate**	**St Error**	**Estimate**	**St Error**	**Estimate**	**St Error**
Intercept		0.3070	0.4874	-0.0137	0.4923	-1.3230	0.6229	**-2.0284*** **	0.6410	0.0762	0.5018	**-2.0548*** **	0.6428
Dis_Level				**1.7417*** **	0.4945			**2.066*** **	0.5117			**1.9949*** **	0.5260
Prod Port 1													
Prod Port 2						**1.6058*** **	0.3432	**1.6328*** **	0.3399			**1.6141*** **	0.3415
Prod Port 3						**1.3643*** **	0.3932	**1.7702*** **	0.4021			**1.736*** **	0.4065
Fit										**0.5191* **	0.2753	0.1634	0.2783
HHI		**-7.7763*** **	2.4543	**-12.1197*** **	2.7306	-0.8639	3.0183	-4.34644	3.1105	**-6.8956*** **	2.4944	-4.0464	3.1535
Lnat		**0.1137* **	0.0596	0.1297	0.0593	0.0867	0.0591	0.10359	0.0587	0.0854	0.0614	0.0944	0.0607
RDI		**-0.1909*** **	0.0186	-0.1856	0.0185	**-0.1953*** **	0.0184	**-0.1884*** **	0.0183	**-0.1868*** **	0.0187	**-0.1873*** **	0.0184
MktS		1.6190	4.5315	-0.0994	4.5245	-0.9216	4.5343	-2.43483	4.5053	1.0692	4.5333	-2.5352	4.5104
R-Square		16.56%		17.89%		18.92%		20.61%		16.95%		20.65%	
Adjusted-R		16.13%		17.36%		18.28%		19.89%		16.41%		19.82%	
F		38.07***		33.39***		29.75***		28.34		31.26***		24.82***	

*** Significant at the .01
** Significant at the .05
* Significant at the .1

5.6.4 Robustness Check

The robustness check section aims at providing evidence that the results obtained are not sensitive to arbitrary decisions and are not biased by outliers.

5.6.4.1 Sensitivity Analysis

This part addresses how sensitive the data is to the coding decision rule. Product portfolio is a coded variable from the firm's 10k and product descriptions. On the other hand, the disintermediation level is a continuous variable. To create the fit measure, one of the variables needed to be transformed from continuous to code (or vice versa). The product portfolio data did not provide enough insight about the sales level of each product line. Therefore, it was challenging to provide a percentage of sales for biologics and non-biologics firms. The study, instead, translates the disintermediation level into coded measures. The study uses a 20%-80% cutoff for the different disintermediation strategy levels. The 20-80% cutoff means that if the disintermediation level is less than 20%, the distribution strategy is considered intermediated. In case the disintermediation level is greater than 80%, the disintermediation strategy is coded as disintermediated. If the disintermediation level is between 20% and 80%, the disintermediation strategy is considered hybrid.

To avoid any problems resulting from an arbitrary choice, a sensitivity analysis is developed with 5 different cutoff levels (10%-90%, 15%-85%, 20%-80%, 25%-75%, and 30%-70%). The results from the sensitivity analysis shows that both return on assets and gross margin results were not sensitive to the cutoff point. All the parameter signs and significance have been maintained. The detailed results are presented in appendix E.

5.6.4.2 Trimming and Winsorizing

Scholars have suggested using specific techniques such as winsorising and trimming to address the impact of outliers within the data set (Dixon, 1960). Winsorizing will replace the extreme values with a cutoff observation, and trimming will delete the extreme variables. However, there is no general consensus about which is a more appropriate technique to use to deal with outliers (Ghosh and Vogt, 2012). A trimmed and winsorized analysis was performed for ROA and GM at 5% and 1% (Table 5-15 and 5-16).

Table 5-15: ROA Trimmed and Winsorized Analysis

	5% Trimming (N=734)		**1% Trimming (N=764)**		**5% Winsorsing (N=772)**		**1% Winsorsing (N=772)**	
Variable	**Estimate**	**St. Error**	**Estimate**	**St. Error**	**Estimate**	**St. Error**	**Estimate**	**St. Error**
Intercept	**-0.8941*** **	0.0679	**-1.3699*** **	0.1346	**-1.1707*** **	0.0890	**-1.6913*** **	0.1677
Dis_Level	0.0844	0.0553	**0.2158** **	0.1100	**0.1543** **	0.0728	**0.2336***	0.1372
Prod_Port2	**0.1582*** **	0.0356	0.1165	0.0711	**0.1463*** **	0.0473	0.1368	0.0891
Prod_Port3	**0.2417*** **	0.0423	**0.2432*** **	0.0846	**0.2357*** **	0.0563	**0.1904** **	0.1060
Fit	**0.149*** **	0.0292	**0.1907*** **	0.0583	**0.1735*** **	0.0385	**0.1739** **	0.0726
HHI	0.3981	0.3268	0.9209	0.6566	0.7579	0.4365	1.7315	0.8226
Lnat	**0.0771*** **	0.0066	**0.1378*** **	0.0130	**0.111*** **	0.0084	**0.1795*** **	0.0158
RDI	**-0.0093*** **	0.0019	**-0.0213*** **	0.0038	**-0.0125*** **	0.0026	**-0.0204*** **	0.0048
MktS	**-1.6162*** **	0.4655	**-3.9327*** **	0.9410	**-2.9456*** **	0.6243	**-5.5907*** **	1.1765
R-Square	38.29%		26.41%		35.10%		22.85%	
Adj R-Sq	37.61%		25.63%		34.42%		22.04%	
F Value	56.22***		33.87***		51.58***		28.24***	

*** Significant at the .01
** Significant at the .05
* Significant at the .1

Table 5-16: Gross Margin Trimmed and Winsorized Analysis

	5% Trimming (N=734)		1% Trimming (N=764)		5% Winsorsing (N=772)		1% Winsorsing (N=772)	
Variable	**Estimate**	**St. Error**	**Estimate**	**St. Error**	**Estimate**	**St. Error**	**Estimate**	**St. Error**
Intercept	-0.0858	0.2241	**-0.9288*** **	0.4562	**-0.5878*** **	0.2897	**-1.5658*** **	0.5378
Dis_Level	0.2325	0.1858	**1.0154*** **	0.3735	**0.7573*** **	0.2371	**1.5183*** **	0.4400
Prod_Port2	**0.4394*** **	0.1198	**1.0936*** **	0.2423	**0.7765*** **	0.1539	**1.3956*** **	0.2857
Prod_Port3	**0.5778*** **	0.1422	**1.2239*** **	0.2880	**0.9292*** **	0.1832	**1.4808*** **	0.3400
Fit	**0.3171*** **	0.0968	**0.4322** **	0.1969	**0.347*** **	0.1254	0.2807	0.2328
HHI	**-3.6675*** **	1.0925	**-5.3454** **	2.2268	**-4.6366*** **	1.4213	-4.5179	2.6380
Lnat	0.0049	0.0212	**0.0121*** **	0.0431	0.0172	0.0274	0.0567	0.0508
RDI	**-0.0172** **	0.0069	-0.07921	0.0139	**-0.0535*** **	0.0083	**-0.1319*** **	0.0154
MktS	**2.9543***	1.5566	2.0728	3.1854	2.18476	2.0329	-0.2575	3.7732
R-Square	15.97%		15.53%		21.98%		18.94%	
Adj R-Sq	15.04%		14.64%		21.16%		18.09%	
F Value	17.22***		17.36***		26.87***		22.28***	

*** Significant at the .01
** Significant at the .05
* Significant at the .1

The results from the trimmed and winsorized analysis showed an improvement in the model parameters. The elimination of the outliers have provided better results. Moreover, the results are stable and did not change based on the trimming and winsorizing levels. Finally, some of the relationships that were not significant in prior models are now significant. In fact, the fit variable now has a positive impact on the firm's gross margin, which provides support for hypothesis 3b. This was mainly caused by outliers with extraordinary results. A detailed analysis for different disintermediation cutoff results are shown in appendix F.

5.6.4.3 Robust Regression

The main purpose of robust regression is to detect outliers and provide robust results in the presence of outliers. Robust regression limits the impact of outliers by providing different weights

for all observations. To address this problem, several methods have been developed. The method most commonly used today in statistical applications of outlier detection is the Huber M estimation (Huber, 1973). The model analysis can be performed by using four main estimates: M estimation, LTS estimation, S estimation, and MM estimation. The MM estimation combines high breakdown value estimations and provides higher statistical efficiency (Yohai, 1987). The results from the robust regression analysis are presented in tables 5-17 and 5-18.

Table 5-17: ROA Robust Regression

Parameter	DF	Estimate	Standard Error
Intercept	1	**-0.5523*** **	0.0505
Dis_Level	1	**0.1035** **	0.0402
Prod_Port2	1	**0.0785*** **	0.0261
Prod_Port3	1	**0.1731*** **	0.0308
Fit	1	**0.1514*** **	0.0213
HHI	1	0.1480	0.2385
Lnat	1	**0.0411*** **	0.0048
RDI	1	**-0.0297*** **	0.0035
MktS	1	**-0.6144** **	0.3332

Table 5-18: Gross Margin Robust Regression

Parameter	DF	Estimate	Standard Error
Intercept	1	**0.2831*** **	0.0695
Dis_Level	1	**0.1433** **	0.0578
Prod_Port2	1	0.0145	0.0371
Prod_Port3	1	**0.2261*** **	0.0453
Fit	1	**0.1048*** **	0.0290
HHI	1	**-0.8279** **	0.3353
Lnat	1	**0.0243*** **	0.0061
RDI	1	**-0.0057*** **	0.0020
MktS	1	**0.7823** **	0.4370

*** Significant at the .01
** Significant at the .05
* Significant at the .1

The robustness check for the various regression models provides a strong support for the results obtained. The robust regression provides evidence that outliers are harming the model parameters. None of the previously supported hypotheses is driven by outliers' value.

5.6.5 Results Summary

In light of the analysis results and robustness check section, a summary of the results is provided. The results show a strong support of the impact of disintermediation level on financial performance. Product portfolio structure has an impact on gross margin. No evidence was found in the relationship between product portfolio and return on assets. Finally, the results show that the alignment between the product paradigm and supply chain distribution strategy impacts return on assets. A partial support of the fit impact on gross margin is provided. Table 5-19 illustrates the results summary.

Table 5-19: Results Summary

Relationship	**Hypothesis**	**Comment**
Disintermediation Level and Return on Assets	H1a	Supported
Disintermediation Level and Gross Margin	H1b	Supported
Product Portfolio and Return on Assets	H2a	Not Supported
Product Portfolio and Gross Margin	H2b	Supported
Fit and Return on Assets	H3a	Supported
Fit and Gross Margin	H3b	Partially Supported (Trimmed, winsorized, and robust regression)

5.6.6 Post Hoc Analysis

The post hoc analysis aims at providing some insights from the model results and identifying patterns that were not specified in the conceptual development part.

5.6.6.1 Diminishing Return Analysis

The first post hoc analysis assessed the possibility of diminishing return for hypotheses 1 and 2. In other words, this part assessed the impact of an increase of disintermediation level on the firm's financial performance. To assess the diminishing return, a natural log transformation was performed for the disintermediation level.

$$DV_{it} = \beta_0 + \beta_1 Ln(Dis\_Level) + \beta_2 Prod\_Prot_{it} + \beta_3 Fit_{it} + \beta_4 MKS_{it} + \beta_5 HHI_{it} + \beta_6 Ln(Total\_Assets) + \beta_7 RDI_{it} + \varepsilon_{it}$$

The results from the analysis have shown that as the disintermediation level increases, both ROA and gross margin experience a diminishing return. The results are shown in table 5-20.

Table 5-20: Diminishing Return Analysis

		ROA		Gross Margin	
Variable	**DF**	**Estimate**	**Standard Error**	**Estimate**	**Standard Error**
Intercept	1	**-0.9120*** **	0.3452	-0.2336	0.6806
Ln_Dis	1	**0.1791** **	0.0905	**0.7775*** **	0.1784
Prod_Port2	1	-0.0186	0.1726	**1.5177*** **	0.3404
Prod_Port3	1	0.0764	0.2043	**1.7554*** **	0.4027
Fit_80	1	**0.459*** **	0.1384	0.2369	0.2728
HHI	1	1.4835	1.5862	-4.3293	3.1275
Lnat	1	**0.0911*** **	0.0305	0.0808	0.0602
RDI	1	**-0.0222** **	0.0093	**-0.1861*** **	0.0184
MktS	1	-3.0774	2.2771	-2.1496	4.4896

5.6.6.2 Quadratic Return Analysis

The results from the diminishing return analysis suggest that as the disintermediation level increases, the return on assets and gross margin will improve with a diminishing return. The following analysis tests for a quadratic relationship between disintermediation level and financial performance. The disintermediation level variable is mean centered and then squared to avoid a multicollinearity problem.

$$DV_{it} = \beta_0 + \beta_1 Dis\_Level + \beta_2 (Dis\_Level)^2 + \beta_3 Prod\_Prot_{it} + \beta_4 Fit_{it} + \beta_5 MKS_{it} + \beta_6 HHI_{it} + \beta_7 Ln(Total\_Assets) + \beta_8 HHI_{it} + \beta_9 RDI_{it} + \varepsilon_{it}$$

The results from the quadratic analysis did not provide support for the quadratic relationships. The detailed results are shown in table 5-21.

Table 5-21: Quadratic Model

	ROA		**Gross Margin**	
Variable	**Parameter Estimates**	**Standard Error**	**Parameter Estimates**	**Standard Error**
Intercept	**-1.3356*** **	0.3438	**-1.3170** **	0.6807
Dis_Level	0.2808	0.3028	**1.8763*** **	0.5994
Dis_Level^2	**1.6870***	1.1122	0.9100	2.2020
Prod_Port2	0.0618	0.1767	**1.6448*** **	0.3497
Prod_Port3	0.0816	0.2054	**1.7365*** **	0.4067
Fit_80	**0.3955*** **	0.1433	0.1410	0.2837
HHI	1.6401	1.5975	-3.9568	3.1626
Lnat	**0.1044*** **	0.0313	**0.0996***	0.0620
RDI	**-0.0225** **	0.0093	**-0.1874*** **	0.0184
MktS	-3.2892	2.2805	-2.5878	4.5147

5.7 Conclusion and Managerial Implication

5.7.1 Discussion

The current essay investigated the relationship between product portfolio structure and supply chain distribution strategies on financial performance. The study also investigated the fit between product portfolio and the supply chain disintermediation effect on return on assets and gross margin. Additionally, the study addressed the fit between product paradigm and supply chain distribution channels strategy and its impact of firms' financial performance.

First, the results suggest that supply chain disintermediation improves the firm's return on assets and gross margin. Selling directly to end customers (drug stores, hospitals, or, in extreme cases, patients) provides pharmaceutical firms with higher financial performance. The reduction of the middle man role within the supply chain provides pharmaceutical firms with a better understanding of the market needs and requirements, reducing the investment on unnecessary assets and improving the firm's return. The results also show that as firms adopt a more direct sales distribution model, their financial performance will improve, nonetheless with diminishing return. The findings suggest that after a certain disintermediation level, the marginal benefit will be reduced. The results, however, did not provide any evidence of a quadratic relationship.

Second, the product portfolio structure does not have an impact on the firm's return on assets. The findings did not support the relationship between the product portfolio's biological level and the pharmaceutical firm's return on assets. The results are mainly driven by the discrepancy of the firm's return on assets. In fact, many of the pharmaceutical firms, despite the success of its products, are experiencing losses because of the lack of economy of scales and the infancy stage of the market, both of which hamper a firm's return on assets. On the other hand, traditional firms have a higher gross margin. In fact, traditional and hybrid drug manufacturers

experience lower cost of goods sold. Traditional drug manufacturers encounter generic product preparation, which is gaining more popularity and market share. Generic products are less expensive to produce and, therefore, have a higher gross margin. Biologic medicine is more sophisticated to produce and is highly inimitable, causing a high cost of goods sold and, therefore, lower gross margin.

Third, the findings show that the supply chain distribution channels and product portfolio alignment provides a better fit for pharmaceutical firms. Using the adequate distribution channels for the type of product allows pharmaceutical firms to allow for the necessary resources based on product characteristics. The research on fit within operations and supply chain perspectives has emphasized the importance of alignment in achieving higher performance. The current study provides a novel conceptualization of product paradigm and supply chain distribution strategy fit. The results show strong evidence of the crucial role of fit on achieving higher return on assets. Using the adequate distribution channel, depending on the product, allows pharmaceutical firms to better utilize their assets and increase their profit. On the other hand, the results from the regression analysis did not provide evidence of impact on gross margin. The results are driven by extreme observations. The data shows that within the 5 observations with the lowest gross margin, 3 observations had a fit between the product portfolio and the supply chain disintermediation. The robustness section addressed this issue. The results from the trimmed, winsorized, and the robustness regression showed that fit positively impacts the firm's gross margin.

Finally, the study conceptualized the positive and negative misfit and tested for its impact on the firm's financial performance. A positive misfit reflects the use of supply chain capability that exceeds the product portfolio's need (using direct sales strategy for traditional medication portfolio). The negative misfit represents the use of low traditional distribution strategy for drugs

that require more direct distribution channels. The results from the positive vs. negative misfit analysis showed that there is a statistical significant mean difference for the gross margin. In fact, firms with a positive misfit have experienced a larger gross margin average. The results are mainly generated from the fact that firms with the positive misfit are composed of traditional firms that already experienced larger gross margin. Despite the unnecessary spending on more direct distribution channels, the economy of scale impact provides a lower cost of goods sold and the gross margin does not suffer tremendously. On the other hand, the return on assets is not sensitive to the type of misfit. The regression analysis against the misfit type did not provide any statistical significant impact on financial performance. The results are similar to the findings of Wagner et al (2012).

5.7.2 Managerial Implications

The current study provides managerial and practical insights. First, the study illustrates the important role of supply chain disintermediation in achieving higher financial performance. The reduction of the middle man role has a positive impact on the pharmaceutical firm's gross margin and return on assets. Practitioners from the pharmaceutical industry are engaging in more disintermediated distribution channels and are attempting to reduce of intermediaries' role. The direct sales model is also gaining more attention in over the counter medication as well as the more innovative drugs such as biologics. The pharmaceutical supply chain is under the pressure of the traditional distribution channels. Thus, the findings provide managers with financial incentives to engage in more disintermediated distribution models.

Second, managers are interested not only in discovering the impact of a strategy on financial performance, but also in comparing the effect of various factors. The standardized coefficient shown in table 5-21 provides a comparison of the size effect among the various model

parameters. Companies that have their supply chain strategy aligned with their product portfolio will experience the most positive effect on the return on assets. The alignment allows the pharmaceutical firm to better utilize its resources, which then impacts its asset utilization. The gross margin on the other end is influenced by the product portfolio structure more than the distribution strategy. Supply chain managers in pharmaceutical firms can use these results and, based on the firm's goal, develop the best strategy.

Table 5-22: Standardized Coefficients Regression Analysis

	ROA (N=772)				**Gross Margin (N=772)**			
	Linear Model (Dis. Level and Prod Portfolio)		**Linear Model (Full)**		**Linear Model (Dis. Level and Prod Portfolio)**		**Linear Model (Full)**	
	Estimate	**St Error**	**Estimate**	**St Error**	**Estimate**	**St Error**	**Estimate**	**St Error**
Intercept	**0**	0.3262	**0**	0.3252	**0**		**0.0000**	0.6428
Dis_Level	**0.114*** **	0.2604	**0.0826** **	0.2661	**0.1581*** **	0.5117	**0.1526** **	0.5260
Prod Port 1								
Prod Port 2	0.0153	0.1730	0.0013	0.1728	**0.2113*** **	0.3399	**0.2089*** **	0.3415
Prod Port 3	0.04638	0.2046	0.0217	0.2056	**0.2214*** **	0.4021	**0.2171*** **	0.4065
Fit			**0.12634** **	0.1408			0.0219	0.2783
HHI	0.02103	1.5829	0.0461	1.5951	-0.0631	3.1105	-0.0587	3.1535
Lnat	0.1838***	0.0299	**0.146*** **	0.0307	0.0739	0.0587	0.0674	0.0607
RDI	**-0.0987*** **	0.0093	**-0.0873*** **	0.0093	**-0.3402*** **	0.0183	**-0.3382*** **	0.0184
MktS	-0.0565	2.2927	-0.0617	2.2815	-0.0218	4.5053	-0.0227	4.5104

Third, the study's findings show that the fit between product portfolio characteristics and supply chain disintermediation levels positively impacts the firm's return on assets. Pharmaceutical firms need to understand the product characteristics of their product portfolio and the level of personalization. Then, firms have to match the product portfolio characteristics with the most adequate distribution channel strategy. The product characteristics assessment provides managers with a better understanding of the assets investment requirements. With no clear

conclusion for the most beneficial distribution strategy, the current study sheds light on some of the ambiguity as far as the disintermediation strategy goes.

Finally, the study's findings show the positive impact of aligning the supply chain distribution and product portfolio. Assume a company XYZ is specializing in biologic products and is using traditional distribution channels. By changing the distribution strategy and selecting more direct methods, XYZ will experience an average increase of 65% on the return on assets. Aligning a positively misfit configuration provides a 53% increase in the return on assets. The financial analysis comparison provides managers with financial incentives for the impact of fit.

5.7.3 Limitations and Future Research

In the process of conducting the current study, several limitations were encountered. First, the data available for the supply chain network spans from 2010 through 2013. The short span of the data available was an obstacle in conducting a longitudinal study. In addition to that, some of the firms' data were not available during the four years of observations. This was mainly due to new firms entering to the stock market or other firms disappearing as a result of mergers and acquisitions. A longitudinal study would have provided more insight for the firms and years of difference. Second, the data available for the disintermediation level variable was derived from the Bloomberg database. Bloomberg provides a network of the quantified buyers' and suppliers' relationships. The remaining relationship dollars amount is estimated from the firm's customers and suppliers list. This approximation was used to finalize the level of the relationships. Third, the product portfolio approximation was estimated from the firms' annual reports. The product portfolio was coded into three levels. When coding the variables, the amount of information explained is reduced. Finally, the data obtained did not provide the distribution channels per product class. In fact, for a firm with a hybrid product portfolio and hybrid distribution channel strategy, the study

couldn't separate the products being shipped directly versus the products distributed through the wholesales. Despite the apparent fit existing between the product portfolio and supply chain strategy, the pharmaceutical firm could be distributing a biologic product via intermediated channels and traditional medication via a direct sales model.

The limitations discussed provide additional areas of research direction. First, the concept of supply chain disintermediation is gaining interest in other industries, such as automobile, besides pharmaceuticals. A more exhaustive study that contains several industries constitutes a prominent area of additional investigation. In fact, with the multiple distribution channel opportunities and the variety of products and service bundles that businesses offer, firms are working hard to identify the appropriate distribution strategy. Second, the supply chain disintermediation becomes more complicated when firms have global sales. In fact, answering the question of the best distribution channel becomes less trivial in a global context. Third, research on fit in the context of supply chain is gaining more attention. The current study can represent a start of new supply chain and product paradigm fit. The personalization level product paradigm can be assessed in a manufacturing context. The fit between the product paradigm and manufacturing strategy and capabilities represents an interesting area of study. Finally, the study of the supply chain disintermediation can have more conceptual and methodological richness. Supply chain disintermediation can be assessed from a network perspective. The supply chain network represents a complex adaptive system. Complex adaptive systems focus on the "interplay between a system and its environment and the co-evolution of both the system and the environment" (Choi et al., 2001). In other words, supply chain disintermediation impacts the organization network and its whole evolution.

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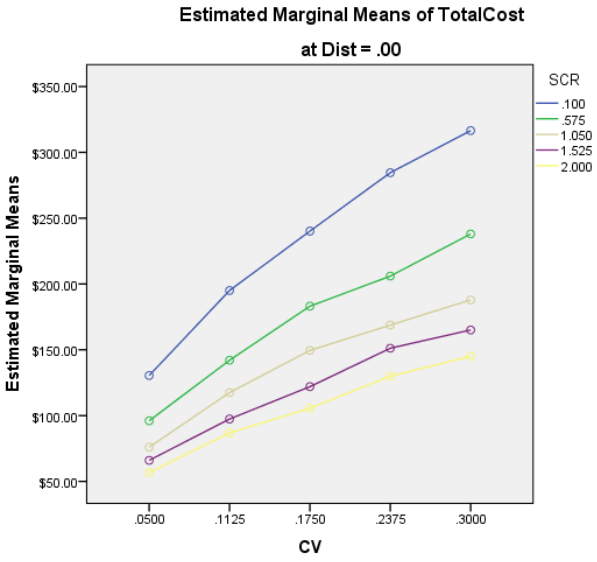
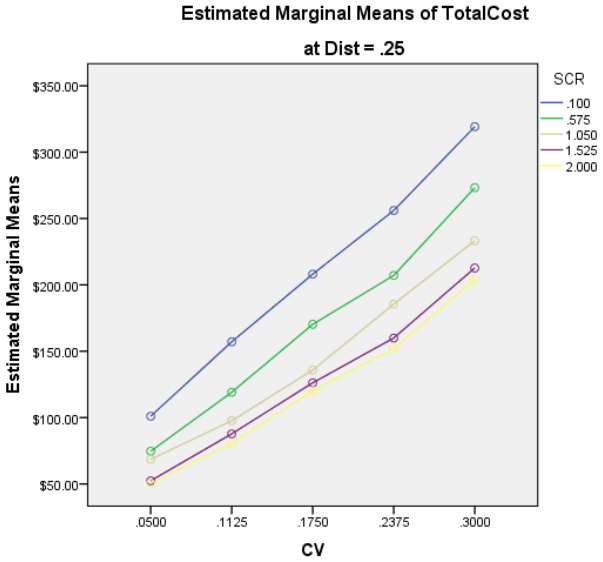
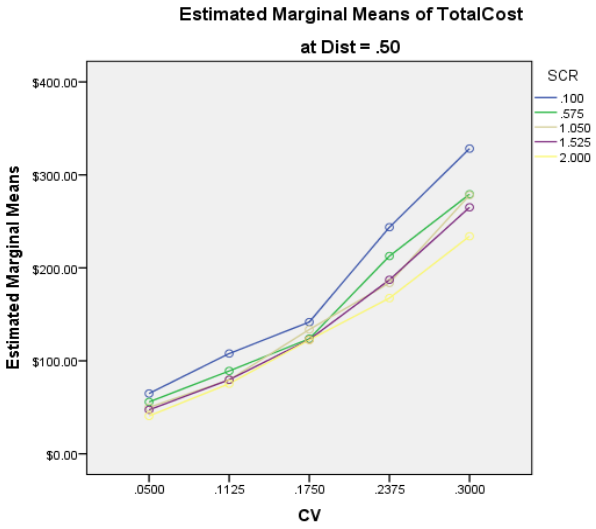
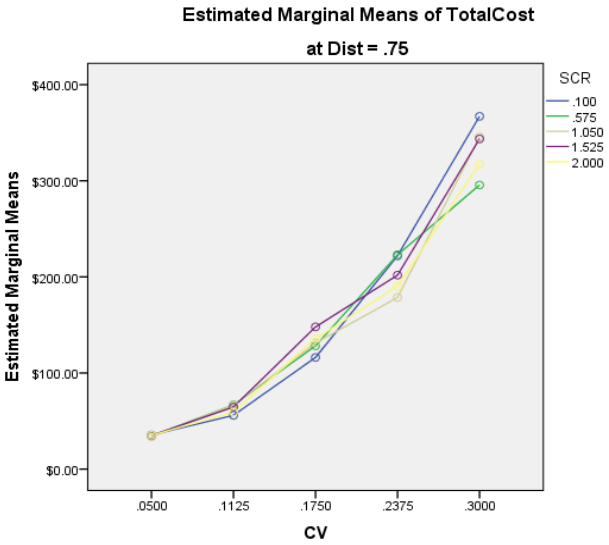
Appendix A: Three way Factor Analysis Plots

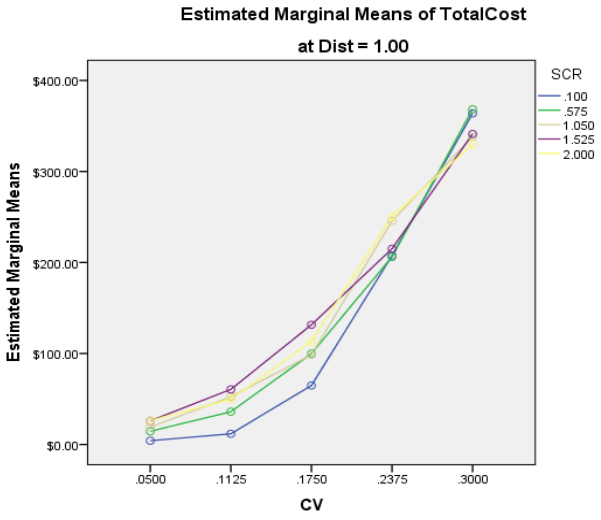
This appendix provides the different graphs from the three factors Anova analysis for a moderate service Level. The three factors interaction was significant, suggesting that there is a change in the lines patterns across the five graphs.











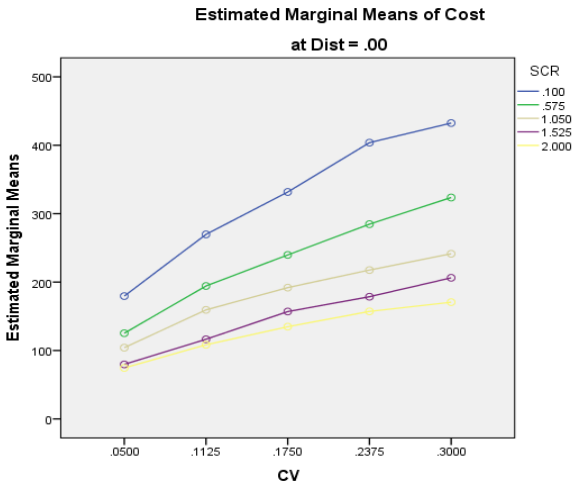
Appendix B: Refined Anova Analysis

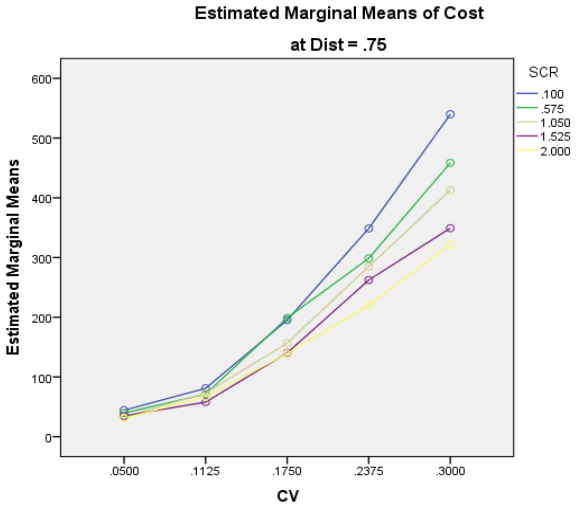
The current appendix contains a refined analysis at an indifference zone combination. The Anova analysis showed an area where the graphs seemed to interestct at one single position. The appendix offers a more detailed investigation for the intersection point. As presented in the analysis section, the market mediation costs for the three lines are close, but not equal. The table below supports the findings.

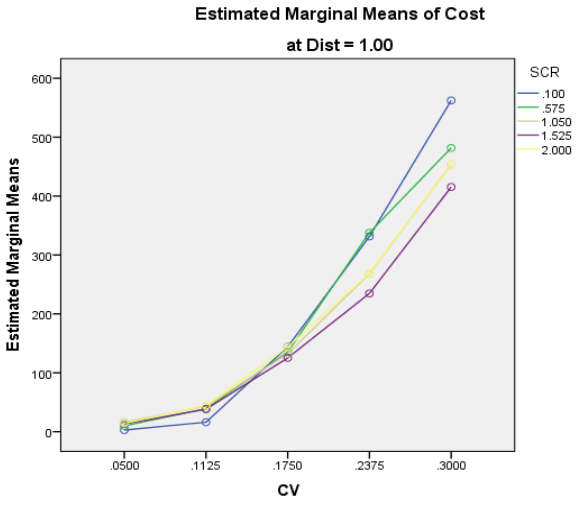
CV	Dist	Mean	Std. Error
0.175	0	159.989	3.403
	0.25	146.685	3.403
	0.5	132.927	3.403
	0.75	119.735	3.403
	1	103.688	3.403
0.191	0	191.158	3.403
	0.25	177.723	3.403
	0.5	163.939	3.403
	0.75	154.477	3.403
	1	138.476	3.403
0.206	0	198.546	3.403
	0.25	190.397	3.403
	0.5	184.951	3.403
	0.75	182.76	3.403
	1	172.393	3.403
0.222	0	205.543	3.403
	0.25	204.02	3.403
	0.5	206.276	3.403
	0.75	207.304	3.403
	1	209.344	3.403
0.2375	0	190.3	3.403
	0.25	192.658	3.403
	0.5	200.452	3.403
	0.75	208.64	3.403
	1	213.976	3.403

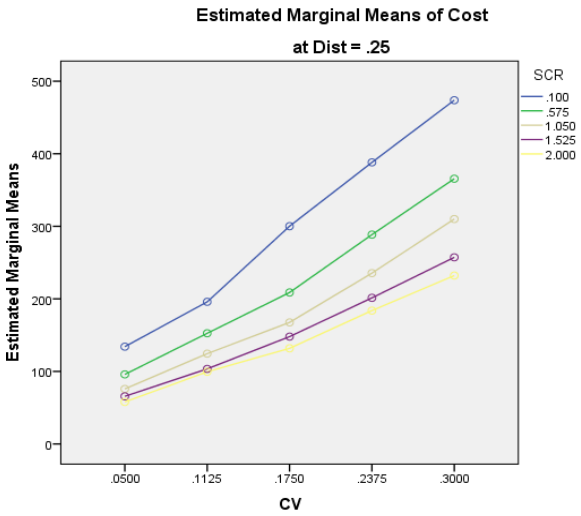
Appendix C: High Service Level Factor Analysis Plots

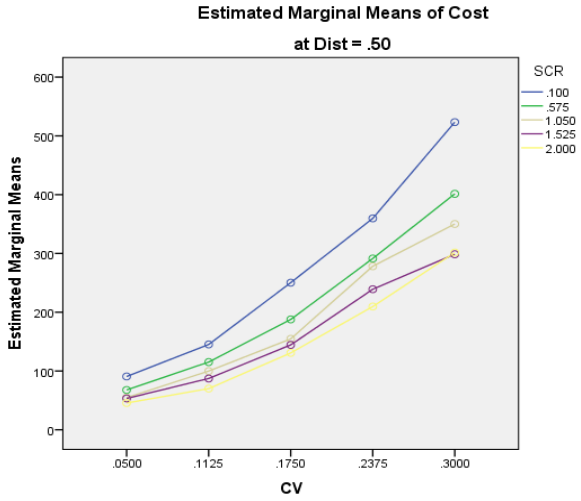
This appendix presents the change of patterns in the Anova Analysis Plots.











Appendix D: Chow Test of Poolability

The tables below shows the results from the restricted regression analysis for the year 2010, 2011, 2012, and 2013.

Analysis of Variance (2010) Dependent Variable= ROA					
Source	**DF**	**Sum of Squares**	**Mean Square**	**F Value**	**Pr > F**
Model	8	5459.08	682.385	3.41	0.0012
Error	175	35036	200.2075		
Corrected Total	183	40495			

Analysis of Variance (2011) Dependent Variable= ROA					
Source	**DF**	**Sum of Squares**	**Mean Square**	**F Value**	**Pr > F**
Model	8	9306.236	1163.279	3.64	0.0005
Error	205	65479	319.4119		
Corrected Total	213	74786			

Analysis of Variance (2012) Dependent Variable= ROA					
Source	**DF**	**Sum of Squares**	**Mean Square**	**F Value**	**Pr > F**
Model	8	7323.903	915.4879	4.76	<.0001
Error	200	38460	192.2992		
Corrected Total	208	45784			

Analysis of Variance (2013) Dependent Variable= ROA					
Source	**DF**	**Sum of Squares**	**Mean Square**	**F Value**	**Pr > F**
Model	8	6.39667	0.79958	6.33	<.0001
Error	156	19.70013	0.12628		
Corrected Total	164	26.09679			

$$SSE_u = 19.7 + 38{,}460 + 65{,}479 + 35{,}036 = 138{,}995$$

The table below shows the results for the pooled regression. The SSEr is determined based on the pooled model.

Analysis of Variance					
Source	**DF**	**Sum of Squares**	**Mean Square**	**F Value**	**Pr > F**
Model	8	17589	2198.58	11.67	<.0001
Error	763	**143771**	188.429		
Corrected Total	771	161360			

F statistics is computed using equation 5-6.

$$F = \frac{(SSE_r - SSE_u)/q}{SSE_u/df_u} = \frac{(143{,}771 - 138{,}995)/1{,}290}{138{,}995/840} = \frac{3.7026}{165.4699} = 0.022$$

The p_value for F(1290, 840)=1.

Appendix E: Disintermediation Sensitivity Analysis

Table 0-1: ROA Sensitivity Analysis

	30%-70%		25%-75%		20%-80%		15%-85%		10%-90%	
Variable	**Estimate**	**St. Error**	**Estimate**	**St. Error**	**Estimate**	**St. Error**	**Estimate**	**St. Error**	**Estimate**	**St. Error**
Intercept	**-1.3902*** **	0.3296	**-1.3715*** **	0.3275	**-1.3441*** **	0.3252	**-1.3613*** **	0.3264	**-1.3805*** **	0.3259
Dis_Level	**0.5129***	0.2718	**0.4929***	0.2714	**0.5006***	0.2661	**0.5494** **	0.2643	**0.5861** **	0.2608
Prod_Port2	0.095	0.1735	0.05563	0.1724	0.0047	0.1728	-0.1403	0.1863	-0.4028	0.2226
Prod_Port3	0.0738	0.2089	0.05197	0.2096	0.0806	0.2056	0.1419	0.2041	0.1751	0.2034
Fit	**0.3168** **	0.1426	**0.3512** **	0.1410	**0.437*** **	0.1408	**0.3996*** **	0.1456	**0.6157*** **	0.1904
HHI	1.38	1.6107	1.3588	1.6015	1.4741	1.5951	1.2274	1.5891	1.2237	1.5824
Lnat	**0.1082*** **	0.0302	**0.1069*** **	0.0302	**0.0945*** **	0.0307	**0.1138*** **	0.0298	**0.1157*** **	0.0297
RDI	**-0.023*** **	0.0094	**-0.0234** **	0.0093	**-0.0224** **	0.0093	**-0.0242** **	0.0093	**-0.0244*** **	0.0093
MktS	-2.56581	2.2925	-2.9944	2.2851	-3.1916	2.2815	-3.2071	2.2853	-3.29608	2.2815
R-Square	5.03%		5.19%		5.61%		5.35%		5.71%	
Adj R-Sq	4.04%		4.2%		4.62%		4.36%		4.72%	
F Value	5.05***		5.22***		5.67***		5.39***		5.78***	

Table 0-2: Gross Margin Sensitivity Analysis

	30%-70%		25%-75%		20%-80%		15%-85%		10%-90%	
Variable	**Estimate**	**St. Error**	**Estimate**	**St. Error**	**Estimate**	**St. Error**	**Estimate**	**St. Error**	**Estimate**	**St. Error**
Intercept	**-2.1485*** **	0.6491	**-2.118*** **	0.6455	**-2.0548*** **	0.6428	**-2.0628*** **	0.6444	**-2.0287*** **	0.6447
Dis_Level	**1.8826*** **	0.5353	**1.8847*** **	0.5350	**1.9949*** **	0.5260	**2.0104*** **	0.5219	**2.0658*** **	0.5160
Prod_Port2	**1.6742*** **	0.3417	**1.6335*** **	0.3398	**1.6141*** **	0.3415	**1.5561*** **	0.3679	**1.6317*** **	0.4405
Prod_Port3	**1.6689*** **	0.4114	**1.6602*** **	0.4131	**1.736*** **	0.4065	**1.7583*** **	0.4029	**1.7702*** **	0.4024
Fit	0.3265	0.2809	0.32149	0.2780	0.1634	0.2783	0.1570	0.2874	0.00149	0.3767
HHI	-3.6165	3.1725	-3.7175	3.1570	-4.04642	3.1535	-4.1281	3.1375	-4.3451	3.1308
Lnat	0.0920	0.0595	0.0921	0.0595	0.0944	0.0607	**0.1014***	0.0588	**0.1036***	0.0587
RDI	**-0.186*** **	0.0184	**-0.1866*** **	0.0184	**-0.1873*** **	0.0184	**-0.1879*** **	0.0183	**-0.1884*** **	0.0183
MktS	-2.0664	4.5154	-2.4999	4.5046	-2.5352	4.5104	-2.5463	4.5120	-2.43574	4.5140
R-Square	20.75%		20.75%		20.65%		20.64%		20.61%	
Adj R-Sq	19.92%		19.92%		19.82%		19.81%		19.78%	
F Value	24.98***		24.97***		24.82***		24.81***		24.76***	

Appendix F: Winsorizing and Trimming Analysis

Table 0-1: ROA 5% Winsorized Results

	30%-70%		25%-75%		20%-80%		15%-85%		10%-90%	
Variable	**Estimate**	**St. Error**	**Estimate**	**St. Error**	**Estimate**	**St. Error**	**Estimate**	**St. Error**	**Estimate**	**St. Error**
Intercept	-1.181***	0.0907	-1.1793***	0.0899	-1.1707***	0.0890	-1.1701***	0.0898	-1.1591***	0.0902
Dis_Level	0.1716**	0.0748	0.156***	0.0745	0.1543**	0.0728	0.1857***	0.0727	0.2138***	0.0722
Prod_Port2	0.1793***	0.0477	0.1664***	0.0473	0.1463***	0.0473	0.1053***	0.0513	0.0964	0.0616
Prod_Port3	0.2398***	0.0575	0.2272***	0.0575	0.2357***	0.0563	0.2626**	0.0562	0.2725***	0.0563
Fit	0.1036***	0.0392	0.131***	0.0387	0.1735***	0.0385	0.1246***	0.0401	0.0939*	0.0527
HHI	0.67107	0.4432	0.6958	0.4398	0.7579	0.4365	0.6128	0.4372	0.5236	0.4381
Lnat	0.1171***	0.0083	0.1161***	0.0083	0.111***	0.0084	0.119***	0.0082	0.1202***	0.0082
RDI	-0.0129***	0.0026	-0.0123***	0.0026	-0.0125***	0.0026	-0.0133***	0.0026	-0.0136***	0.0026
MktS	-2.7222***	0.6308	-2.8657	0.6275	-2.9456***	0.6243	-2.9276***	0.6288	-2.896***	0.6316
R-Square	33.98%		34.36%		35.10%		34.21%		33.65%	
Adj R-Sq	33.28%		33.67%		34.42%		33.52%		32.95%	
F Value	49.08***		49.92***		51.58***		49.59***		48.37***	

Table 0-2: ROA 1% Winsorized Results

	30%-70%		25%-75%		20%-80%		15%-85%		10%-90%	
Variable	**Estimate**	**St. Error**	**Estimate**	**St. Error**	**Estimate**	**St. Error**	**Estimate**	**St. Error**	**Estimate**	**St. Error**
Intercept	-1.7128***	0.1697	-1.7086***	0.1686	-1.6913***	0.1677	-1.6984***	0.1682	-1.6878***	0.1685
Dis_Level	0.2338*	0.1400	0.2177	0.1397	0.2336*	0.1372	0.2527*	0.1362	0.2853**	0.1349
Prod_Port2	0.1739**	0.0893	0.1572*	0.0887	0.1368	0.0891	0.0787	0.0960	0.0520	0.1152
Prod_Port3	0.185*	0.1075	0.1712	0.1079	0.1904**	0.1060	0.2147**	0.1052	0.2274**	0.1052
Fit	0.1345*	0.0734	0.1625*	0.0726	0.1739**	0.0726	0.1599**	0.0750	0.1410*	0.0985
HHI	1.71301	0.8294	1.7302	0.8244	1.7315	0.8226	1.6347	0.8190	1.5388*	0.8184
Lnat	0.1845***	0.0156	0.1834***	0.0155	0.1795***	0.0158	0.187***	0.0154	0.1884***	0.0154
RDI	-0.0205***	0.0048	-0.0206***	0.0048	-0.0204***	0.0048	-0.0210***	0.0048	-0.0213***	0.0048
MktS	-5.3322***	1.1804	-5.5168***	1.1763	-5.5907***	1.1765	-5.5975***	1.1778	-5.5693***	1.1800
R-Square	22.61%		22.77%		22.85%		22.73%		22.48%	
Adj R-Sq	21.80%		21.96%		22.04%		21.92%		21.66%	
F Value	27.86***		28.13***		28.24***		28.05		27.65***	

Table 0-3: Gross Margin 5% Winsorized Results

	30%-70%		25%-75%		20%-80%		15%-85%		10%-90%	
Variable	**Estimate**	**St. Error**	**Estimate**	**St. Error**	**Estimate**	**St. Error**	**Estimate**	**St. Error**	**Estimate**	**St. Error**
Intercept	-0.6653***	0.2927	-0.6291**	0.2911	-0.5878***	0.2897	-0.5944**	0.2910	-0.579**	0.2915
Dis_Level	0.7045***	0.2413	0.7116***	0.2413	0.7573***	0.2371	0.8075***	0.2357	0.8622***	0.2333
Prod_Port2	0.8623***	0.1540	0.8171***	0.1532	0.7765***	0.1539	0.6772***	0.1661	0.6147***	0.1991
Prod_Port3	0.8893***	0.1855	0.8825***	0.1863	0.9292***	0.1832	0.9804***	0.1819	1.0032***	0.1819
Fit	0.3628***	0.1266	0.349***	0.1254	0.347***	0.1254	0.2849**	0.1298	0.2713	0.1703
HHI	-4.4622***	1.4303	-4.5908***	1.4237	-4.6366***	1.4213	-4.8774***	1.4166	-5.0304***	1.4154
Lnat	0.0238	0.0268	0.0242	0.0268	0.0172	0.0274	0.0327	0.0266	0.035	0.0266
RDI	-0.0531***	0.0083	-0.0539***	0.0083	-0.0535***	0.0083	-0.055***	0.0083	-0.0554***	0.0083
MktS	2.8072	2.0357	2.3271	2.0314	2.1848	2.0329	2.1954	2.0372	2.2335	2.0408
R-Square	22.04%		21.99%		21.98%		21.69%		21.46%	
Adj R-Sq	21.22%		21.17%		21.16%		20.87%		20.64%	
F Value	26.96***		26.89***		26.87***		26.42***		26.06***	

Table 0-4: Gross Margin 1% Winsorized Results

	30%-70%		25%-75%		20%-80%		15%-85%		10%-90%	
Variable	**Estimate**	**St. Error**	**Estimate**	**St. Error**	**Estimate**	**St. Error**	**Estimate**	**St. Error**	**Estimate**	**St. Error**
Intercept	-1.6749***	0.5428	-1.6316***	0.5398	-1.5658***	0.5378	-1.5653***	0.5393	-1.5266***	0.5397
Dis_Level	1.4049***	0.4476	1.4161***	0.4474	1.5183***	0.4400	1.5684***	0.4368	1.6347***	0.4320
Prod_Port2	1.481***	0.2857	1.4287***	0.2842	1.3956***	0.2857	1.3282***	0.3079	1.4022***	0.3688
Prod_Port3	1.4095***	0.3440	1.4035***	0.3455	1.4808***	0.3400	1.5242***	0.3372	1.5397***	0.3369
Fit	0.4193*	0.2348	0.398*	0.2325	0.2807	0.2328	0.2038	0.2405	0.0343	0.3153
HHI	-4.0956	2.6527	-4.2545	2.6401	-4.5179	2.6380	-4.7497*	2.6258	-5.0024*	2.6209
Lnat	0.0576	0.0497	0.0582	0.0498	0.0567	0.0508	0.0696	0.0492	0.0722	0.0492
RDI	-0.1307***	0.0154	-0.1316***	0.0154	-0.1319***	0.0154	-0.1332***	0.0153	-0.1338***	0.0153
MktS	0.38802	3.7755	-0.1658	3.7671	-0.2575	3.7732	-0.2299	3.7762	-0.106	3.7789
R-Square	19.12%		19.09%		18.94%		18.86%		18.78%	
Adj R-Sq	18.27%		18.24%		18.09%		18.01%		17.93%	
F Value	22.55***		22.51***		22.28***		22.17***		22.06***	

Table 0-5: ROA 5% Trimmed Results

	30%-70%		25%-75%		20%-80%		15%-85%		10%-90%	
Variable	**Estimate**	**St. Error**	**Estimate**	**St. Error**	**Estimate**	**St. Error**	**Estimate**	**St. Error**	**Estimate**	**St. Error**
Intercept	-0.9031***	0.0693	-0.8996***	0.0689	-0.8941***	0.0679	-0.8893***	0.0690	-0.8773***	0.0692
Dis_Level	0.0989*	0.0571	0.0928	0.0569	0.0844	0.0553	0.1218**	0.0556	0.1455***	0.0550
Prod_Port2	0.1867**	0.0360	0.17604***	0.0357	0.1582***	0.0356	0.1366***	0.0389	0.1495***	0.0467
Prod_Port3	0.2441**	0.0434	0.2381***	0.0434	0.2417***	0.0423	0.2652***	0.0425	0.2722***	0.0426
Fit	0.0887**	0.0298	0.0994***	0.0294	0.149***	0.0292	0.0795***	0.0305	0.0355	0.0402
HHI	0.3184	0.3331	0.3187	0.3309	0.3981	0.3268	0.2286	0.3293	0.1415	0.3295
Lnat	0.0825***	0.0065	0.0822	0.0065	0.0771***	0.0066	0.0847***	0.0065	0.0855***	0.0065
RDI	-0.0097***	0.0020	-0.0098***	0.0020	-0.0093***	0.0019	-0.0102***	0.0020	-0.0104***	0.0020
MktS	-1.432***	0.4720	-1.5585***	0.4698	-1.6162***	0.4655	-1.5944***	0.4718	-1.5585***	0.4737
R-Square	36.84%		37.06%		38.29%		36.66%		36.14%	
Adj R-Sq	36.15%		36.37%		37.61%		35.96%		35.43%	
F Value	52.87***		53.37***		56.22***		52.46***		51.29***	

Table 0-6: ROA 1% Trimmed Results

	30%-70%		25%-75%		20%-80%		15%-85%		10%-90%	
Variable	**Estimate**	**St. Error**	**Estimate**	**St. Error**	**Estimate**	**St. Error**	**Estimate**	**St. Error**	**Estimate**	**St. Error**
Intercept	-1.3802***	0.1368	-1.3810***	0.1358	-1.3699***	0.1346	-1.3699***	0.1346	-1.3665***	0.1356
Dis_Level	0.2439**	0.1127	0.2225**	0.1124	0.2158**	0.1100	0.2158***	0.1100	0.276***	0.1084
Prod_Port2	0.1512**	0.0715	0.1391**	0.0710	0.1165	0.0711	0.1165	0.0711	0.0366	0.0926
Prod_Port3	0.2526**	0.0862	0.2367***	0.0864	0.2432***	0.0846	0.2433***	0.0846	0.2836***	0.0841
Fit	0.0965	0.0590	0.1339***	0.0583	0.1907***	0.0583	0.1907***	0.0583	0.1376*	0.0796
HHI	0.7977	0.6651	0.8423	0.6605	0.9209	0.6566	0.9209	0.6566	0.7014	0.6553
Lnat	0.1459***	0.0128	0.1444***	0.0128	0.1378***	0.0130	0.1378***	0.0130	0.1481***	0.0126
RDI	-0.0218***	0.0038	-0.0218***	0.0038	-0.0213***	0.0038	-0.0213***	0.0038	-0.0223***	0.0038
MktS	-3.7383***	0.9483	-3.8691***	0.9441	-3.9327***	0.9410	-3.9327***	0.9410	-3.9164***	0.9461
R-Square	25.63%		25.89%		26.41%		26.31%		25.66%	
Adj R-Sq	24.84%		25.10%		25.63%		25.53%		24.87%	
F Value	32.53***		32.96***		33.87***		33.70***		32.58***	

Table 0-7: Gross Margin 5% Trimmed Results

	30%-70%		25%-75%		20%-80%		15%-85%		10%-90%	
Variable	**Estimate**	**St. Error**	**Estimate**	**St. Error**	**Estimate**	**St. Error**	**Estimate**	**St. Error**	**Estimate**	**St. Error**
Intercept	-0.165	0.2262	-0.1306	0.2250	-0.0858	0.2241	-0.1103	0.2248	-0.1048	0.2252
Dis_Level	0.1853	0.1883	0.1891	0.1883	0.2325	0.1858	0.2566	0.1845	0.3069*	0.1825
Prod_Port2	0.5187***	0.1199	0.4752***	0.1192	0.4394***	0.1198	0.325***	0.1284	0.1993***	0.1539
Prod_Port3	0.535***	0.1439	0.5271***	0.1445	0.5778***	0.1422	0.619***	0.1412	0.6447***	0.1413
Fit	0.3431***	0.0975	0.3343***	0.0966	0.3171***	0.0968	0.319***	0.1006	0.3762***	0.1325
HHI	-3.4828***	1.0983	-3.599***	1.0932	-3.6675***	1.0925	-3.767***	1.0891	-3.8837***	1.0878
Lnat	0.0109	0.0207	0.0110	0.0207	0.0049	0.0212	0.0181	0.0205	0.0205	0.0205
RDI	-0.0167***	0.0069	-0.0175**	0.0069	-0.0172**	0.0069	-0.0183***	0.0069	-0.0188***	0.0069
MktS	3.5261**	1.5587	3.0709**	1.5546	2.9543*	1.5566	2.8936*	1.5580	2.8923*	1.5605
R-Square	16.16%		16.11%		15.97%		15.89%		15.67%	
Adj R-Sq	15.23%		15.19%		15.04%		14.97%		14.74%	
F Value	17.47***		17.41***		17.22***		17.13***		16.83***	

Table 0-8: Gross Margin 1% Trimmed Results

	30%-70%		25%-75%		20%-80%		15%-85%		10%-90%	
Variable	**Estimate**	**St. Error**	**Estimate**	**St. Error**	**Estimate**	**St. Error**	**Estimate**	**St. Error**	**Estimate**	**St. Error**
Intercept	-1.0356***	0.4605	-0.9861**	0.4582	-0.9288***	0.4562	-0.9401**	0.4582	-0.9155***	0.4588
Dis_Level	0.9395**	0.3796	0.9522**	0.3796	1.0154***	0.3735	1.0901***	0.3706	1.1601***	0.3668
Prod_Port2	1.2025***	0.2423	1.1429***	0.2412	1.0936***	0.2423	0.9828***	0.2609	0.9351***	0.3126
Prod_Port3	1.165***	0.2915	1.1583***	0.2929	1.2239***	0.2880	1.2904***	0.2858	1.3167***	0.2858
Fit	0.4771**	0.1984	0.4527**	0.1965	0.4322**	0.1969	0.3328	0.2034	0.2821	0.2673
HHI	-5.0823**	2.2393	-5.2632**	2.2293	-5.3454**	2.2268	-5.658**	2.2198	-5.8700***	2.2169
Lnat	0.0197	0.0421	0.0204	0.0421	0.0121***	0.0431	0.0323	0.0417	0.0353	0.0417
RDI	-0.0783***	0.0139	-0.0795***	0.0139	-0.07921	0.0139	-0.0811***	0.0138	-0.0818***	0.0138
MktS	2.8661	3.1904	2.2356	3.1828	2.0728	3.1854	2.0668	3.1914	2.1319	3.1954
R-Square	15.64%		15.59%		15.53%		15.30%		15.12%	
Adj R-Sq	14.75%		14.69%		14.64%		14.40%		14.22%	
F Value	17.50***		17.43***		17.36***		17.04***		16.81***	