COORDINATION MECHANISMS FOR SUSTAINABLE SUPPLY CHAIN MANAGEMENT IN PHARMACEUTICAL INDUSTRY

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ABSTRACT

Coordination mechanisms for sustainable supply chain management in pharmaceutical industry

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At the beginning of the twenty-first century, the human environmental problems resulting from industrial manufacturing activities have affected pharmaceutical supply chain management. Governments have imposed legislations and policies on producers to tackle the medications recovery process. Besides, customers social pressure plays a major role in determining corporate sustainable strategies and performance measures. Creative and proactive approaches are therefore necessary to reduce the introduction of pharmaceutical wastes to the environment and to improve the sustainability of the value chain.

In this dissertation, we propose different coordination mechanisms for sustainable pharmaceutical value chains inspired by traditional supply chains coordination mechanisms. For this purpose, a real case study for a generic pharmaceutical company, *Generic PharmaX*, is considered. We first focus on the reverse supply chain activities in order to reduce medication leftovers at customer sites. We develop a negotiation-based mechanism by the aid of a linear mathematical model to reflect the relationship between the supply chain entities. Results show that up to 28% more products could be collected if companies coordinate their operations efficiently. Moreover, the proposed coordination approaches leads to a win-win situation for the reverse supply chain entities, where each effort is rewarded.

Next, we explore the role of providing incentives to customers in order to facilitate leftover returns and improve the sustainability for the pharmaceutical reverse supply chain. Coordination model is therefore presented between the producer and third-party logistics companies, responsible for collecting unwanted medications from customer zones. A technique is also proposed to share the expected saving between the supply chain entities. The experimental results indicate that introducing incentives to customers could decrease the amount of leftovers from 18% up to 6.5%. Furthermore, having a proper coordination with 3PL companies, in addition to customer incentives, could guarantee a full medication recovery.

Finally, we focus on the inventory control management activities of the value chain. The effect of implementing a Vendor-Managed Inventory (VMI) system on minimizing the quantity of expired medications at customer zones is investigated. Results reveal that implementing the VMI system could improve the sustainability of the supply chain. More precisely, the amount of expired medications could reach zero against the current 18% expiration rate of shipped items. Some insights to guide the supply chain entities through the VMI implementation are also provided.

Preface

This thesis has been prepared in "Manuscript-based thesis" format under the co-direction of Dr. Masoumeh Kazemi Zanjani, at the Mechanical and Industrial Department of Concordia University, and Dr. Nadia Lehoux, at the Mechanical Engineering Department of Université Laval. The research has been performed based on a real case study in a generic pharmaceutical company.

The first article entitled: "Coordinating a Green Reverse Supply Chain in Pharmaceutical Sector by Negotiation", co-authored by Dr. Masoumeh Kazemi Zanjani and Dr. Nadia Lehoux, was submitted to "*Computer & Industrial Engineering*" journal. A minor revision with respect to the reviewers comments has been submitted on October 2015.

The second article entitled: "Two-echelon Pharmaceutical Reverse Supply Chain Coordination with Customers Incentives", co-authored by Dr. Masoumeh Kazemi Zanjani and Dr. Nadia Lehoux, is submitted to "*International Journal Production Economics*" on May 2015.

The third article entitled: "Improving Sustainability in a Two-level Pharmaceutical Supply Chain through Vendor-Managed Inventory System", co-authored by Dr. Masoumeh Kazemi Zanjani and Dr. Nadia Lehoux, is submitted to the *Journal of the Operational Research Society* on September 2015.

All the articles presented in this thesis were co-authored and reviewed prior to submission for publication by Dr. Masoumeh Kazemi Zanjani and Dr. Nadia Lehoux. The author of this thesis performed the mathematical models development, coding the algorithms, analysis and validation of the results, as well as writing the first drafts of the articles.

To Mom and Dad,

who always encouraged me to go on every adventure, especially this one

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Above ground, I am deeply indebted to my family; my parents and my siblings for their spiritual and financial support throughout writing this thesis and my life in general. This work was not possible without their presence. To them I tribute a fervent thanks.

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Chapter 1

Introduction

The depletion and overuse of natural resources, and their negative impacts on society and economy, have been pointed out clearly and alarmingly by several comprehensive studies. The current economic crisis, on the other hand, calls for supply chains to be more cost effective in order to survive and stay competitive in the marketplace. Thus, environmental and economic pressures are pushing firms to tackle their social and environmental responsibilities simultaneously. Regarding the new regulations, firms are requested to address environmental issues in their supply chains and manage the mounting cost threats to maintain competitiveness.

Recently, rigorous academic research has been dedicated to the study of the effects of coordination in improving supply chain efficiency. Nonetheless, and despite its evident importance, the role of coordination on the success of greening supply chains has been less investigated in the literature. Further investigations of real-world case studies on the integration of sustainability in supply chain management are required to find some better practices for coordination mechanisms.

Motivated by a real case study in a generic pharmaceutical company, the focus of this thesis is on proposing appropriate coordination mechanisms for sustainable supply chain management. In this chapter, a description for the supply chain of the

case study is presented. A preliminary analysis of its environmental complications and challenges are also provided. The outline of the thesis is given at the end of this chapter.

1.1 *Generic PharmaX* supply chain

Generic PharmaX, the producer, is a leading pharmaceutical producer that was founded in the Middle East 39 years ago. The company focuses on developing a branded pharmaceuticals business across the Middle East, North Africa, Europe, and in the United States. The activities of the Generic PharmaX Company start from the sales and marketing unit, which works to get contracts and find markets for their products. Based on sales amount, the demand is planned through communication with the finance department to check the available cash. The forecasting department will improve the plan of demand and issue purchasing orders to buy raw materials and equipment. Furthermore, purchasing activities in the company have specific perspectives and criteria. More precisely, the priority of performing a customer order depends on the importance of that customer, the shelf life of raw materials, warehouse capacity, holding cost, etc. Also, the suppliers are either from the national market (for packaging materials, some basic chemicals and raw materials) or from international markets (for active raw materials). The company manufactures two main forms of drugs: liquid form and solid form. Legislations and regulation should be obeyed, especially with toxic materials. Through quality assurance activity, the drugs are tested before going to the packaging unit and later to warehouses. Based on purchasing orders received from customers (i.e., pharmacies and hospitals), the producer ships medications with respect to the regulations in the destination countries.

Any shortage in medications delivery has a high cost in terms of preventable illness and death [1]. Therefore, customers tend to order more products from *Generic*

PharmaX in order to be hedged against an unexpected demand. On the other hand, medications have a fixed shelf life set by a used-by or a sell-by date. They contain some ingredients that degrade with time even when using modern keeping conditions [2]. The expiration of the excess inventory in the absence of patients demand raises more challenges on the pharmaceutical inventory control management, by trading off stock outs and on-shelf availability against wastage due to expiry [3, 4].

The regulations imposed by governments on the producer oblige the company to take care and collect any unused or expired medication at customer zones. Knowing that the medications salvage value is very low, *Generic PharmaX* is not motivated to invest in the recovery process. Instead, the producer contracts with one or more third-party logistic (3PL) companies to collect these items at customer zones by offering non-negotiable collecting fees. Thereafter, 3PL companies collect the medications and ship them to one of the governmental safe disposal sites. Consequently, the producer pays disposal fees to the government for those shipped items. Currently, around 20%-40% of medications at customer sites are remain uncollected by 3PL companies, which incurs penalties to the producer. Figure 1 visualizes the process followed in *Generic PharmaX* supply chain to take care of unused medications. Moreover, leaving expired

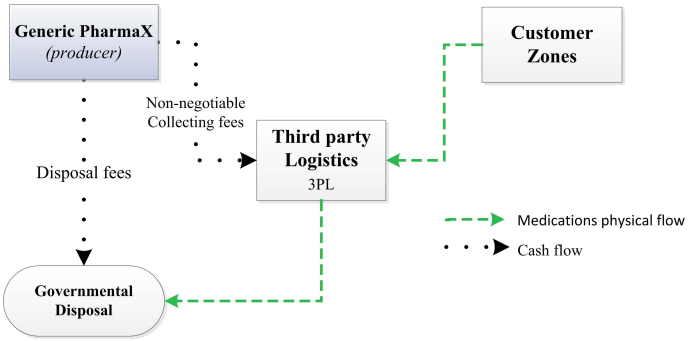

Figure 1: The current *Generic PharmaX* supply chain of collecting unused medications

medications at customer zones and disposing them improperly lead to penalties that must be paid to governments. It might also turn into a jeopardy to people's health if

being redistributed illegally in developing countries. This puts producers' reputation in the market in peril due to the negative environmental footprint of their products. Therefore, improving the PSC sustainability effectively is essential not only to protect the environment and patients from exposing to expired medications but also to reduce the associated cost [2].

1.2 Outline of the thesis

The layout of the manuscript-based thesis consists of five chapters, which includes three original contributions (presented as three articles), as follows. In chapter 1, a description of the pharmaceutical supply chain activities and environmental challenges is provided.

In chapter 2, we investigate the pharmaceutical reverse supply chain (RSC) of *Generic PharmaX*. Since the RSC is usually not owned by a single company, a decentralized negotiation process is thus presented in order to coordinate the collection of unwanted medications at customer zones. A Lagrangian relaxation method is used to mimic the negotiation process. In addition, a bonus sharing technique is also proposed in order to reward each entity's investment in the coordination process.

Chapter 3 explores the role of providing incentives to customers in order to facilitate leftover returns and improve the sustainability of the RSC. The chapter also investigates the effect of having a proper coordination method between the producer and 3PL companies, responsible for collecting unwanted medications from customer zones. Finally, a technique is proposed to share the RSC's saving among the producer and the 3PL companies.

Chapter 4 seeks improving the sustainability the PSC for *Generic PharmaX*. An analytical model is proposed to explore the effect of implementing a Vendor-Managed

Inventory (VMI) system on minimizing the quantity of expired medications at customer zones. Furthermore, some insights for VMI implementation are provided.

A summary of the major contributions of the thesis is provided in chapter 5, along with a discussion of possible research perspectives.

Chapter 2

Coordinating a Green Reverse Supply Chain in Pharmaceutical Sector by Negotiation

This chapter is dedicated to the article entitles "*Coordinating a Green Reverse Supply Chain in Pharmaceutical Sector by Negotiation*". A minor revision of the article has been submitted to the *Computers & Industrial Engineering* journal on October 2015. The titles, figures, and mathematical formulations have been revised to keep the coherence through the thesis.

2.1 Abstract

This paper investigates the pharmaceutical reverse supply chain. For this industry, the reverse supply chain is usually not owned by a single company. A decentralized negotiation process is thus presented in order to coordinate the collection of unwanted medications at customer zones. Using a Lagrangian relaxation method, the model is solved for a real generic pharmaceutical company. Coordination efforts are required from the supply chain entities, facing environmental regulations, to collect and recycle unwanted medications. Therefore, a bonus sharing technique is also proposed based on each entity's investment in the coordination process. Some numerical results are presented and discussed for two case studies. It shows that up to 28% more products could be collected if companies coordinate their operations efficiently. Besides, future insights on the same network are highlighted.

2.2 Introduction

Alterations in the state of the environment, which result from industrial manufacturing activities, caused a quantum leap for the supply chain management (SCM) and business practices. Customer pressure and environmental legislations also raise the complexity for performance measurement of reverse supply chains (RSC). Up till now, most of RSC actions are market-driven; i.e. companies take the initiative to reduce costs by reusing the waste of unsold parts. However, in Europe some actions are legislation-driven to fulfill the obligatory regulations of collecting specific amounts of end-of-life products (return stream) in order to avoid penalties forced by governments [5].

A good example is the pharmaceutical industry. In fact, this industrial field has developed at a very fast rate in the last decades. It is a rapidly growing market due

to the increased rate of modern century diseases and the raised number of old-age nations. Likewise, the presence of pharmaceutical products as trace pollutants for environment has been firmly established. Knowing the potential severity of using expired or improper drugs, the recovery process of unsold or unwanted medications is essential [6]. A wide range of proactive actions is therefore necessary to reduce or minimize the introduction of pharmaceutical wastes to the environment. Pharmaceutical RSC is considered as one of the complicated supply chains because of the restricted percentages of chemicals in medications and the regulated conditions for distribution and storage. Furthermore, the zero-salvage value of returned medications hinders the development of RSC [7]. In other words, it differs from other RSC, such as electronics industry RSC, where the salvage value of the returned products is significant.

This study focuses on tactical planning in the pharmaceutical RSC. In general, tactical level decisions include many actions, such as collection of waste materials, recycling, long-term RSC chain coordination contract drafting, recovery channels of reverse logistics, and recovery efforts designing [8, 9]. Since pharmaceutical RSC activities fall outside core functions of a company, the majority of the activities are usually handled through third-party logistics (3PL) providers [10]. Using 3PLs enables companies to focus more on their own core processes and reduce the associated costs. Moreover, 3PL providers usually update their information technology and techniques, which are more flexible than in-source logistics. Despite the aforementioned advantages, some companies might lose control inherent in outsourcing particular functions, due to the limited collaboration between the supply chain entities [11]. For example, in our case, due to the lack of collaboration, a part of unsold/expired medications remains at customer zones.

In reality, supply chains are not typically owned by one company. They consist of facilities that are managed by different companies, like producers, retailers, 3PLs,

etc. Hence decision-making system in such supply chains is bound to fail unless a coherent approach of coordination is utilized. Coordination in networks are either a centralized process that has a unique decision maker who possesses all information on the entire network, or a decentralized process that has multiple decision makers [12]. Product recovery problem is complex; i.e. many factors and constraints of information sharing are required for accurate modeling. For example, information are needed about collection volume, frequencies, locations, and cost associated with collection and disposal [13]. In the pharmaceutical industry, paucity of information may be observed as a result of the lack of trust between entities, hence, prohibiting the coordination of the RSC [14]. This paper assumes a decentralized decision-making process and proposes a negotiation approach as a coordination mechanism in the RSC described herein.

We propose a coordination model for a real pharmaceutical RSC from the retailer point of view, who represents the producer company, *Generic PharmaX*. In the past, the producer policy did not include collecting the unsold items from outside the country because she believed that medications have a null salvage value. As a result, the company, through her retailer, used to send new items instead and ask the retailer to either burn or bury the unwanted drugs. This type of disposal harms the environment and the groundwater. As a result, the environmental reputation of the company was affected.

Under the new business context, the producer pays the retailer for collecting the unwanted or unused medications at customer zones (i.e. hospitals and pharmacies). The retailer is thus responsible for negotiation with 3PLs over quantities that must be collected, i.e. the retailer controls the reverse supply chain communication. The retailer next pays fees, i.e. *current collecting fees* to 3PLs, for collecting the discarded

medications at customer zones, as well as sorting and delivering to sinks of the network. The sinks are governmental safe disposal and recycling facilities. Currently, the coordination between the retailer and 3PL companies is insufficient. In other words, about 20% to 40% of the unwanted medications remain uncollected.

Because the company used to pay penalties to governments for uncollected medications at customer zones, we suggest her to share that amount with RSC entities instead and green her reputation. In other words, to minimize the fees and penalties that she pays to governments, we suggest the producer to offer the retailer an extra fixed amount, i.e. a *bonus*, on top of the regular collecting fees. The bonus is paid if, and only if, all unwanted products at customer zones are collected. We believe that this extra income for RSC entities will motivate those who are eager to collaborate and participate in greening the network. Therefore, the retailer's objective is to ensure that all unwanted products are collected. As a result, the retailer has to pay adequate collecting fees for 3PL companies to collect more products. Moreover, the retailer needs to share the predictable bonus with the 3PLs to guarantee a complete collection of products at customer zones. The reason is that the 3PLs objective is to maximize the individual profit from collecting products and from recycling some of returned products.

This paper, as a first research on the pharmaceutical RSC coordination, contributes to the available literature by modeling this RSC in order to meet environmental legislations and reduce the amount of wastes. It is a challenging RSC because the recovered products have almost no economical values to recyclers or to producers. Using data from a real case study, a single period tactical planning model is developed. The producer has to fulfill the regulations and improve her green image among competitors and customers. The RSC model considered herein consists of one retailer, four third-party logistics, and four recycling companies. A coordination

approach based on a negotiation mechanism is applied to handle the communication within the network. With the aid of Lagrangian relaxation, four sub-problems are solved for small-case and large-case problems. In addition, an appropriate method to share the network gain from an improved coordination is suggested, which shares the savings based on each entity's effort. Moreover, the effect of the proposed coordination method on the performance of the RSC is analyzed.

The reminder of this paper is organized as follows. A literature review regarding RSC and coordination mechanisms is first proposed. A brief description of the case study context and the pharmaceutical RSC tactical planning model are next given in section 2.4. Also, section 2.4 covers the proposed negotiation methodology to solve the model and the suggested profit sharing technique. Some numerical results and discussions for the real case study are given in section 2.5. Finally, some concluding remarks are provided in section 2.6.

2.3 Literature Review

There is a growing stream of literature on product recovery and RSC. However, the available literature on the pharmaceutical RSC is still limited and the existence research is scant. Detailed reviews on RSC models can be found in [15, 16]. Blackburn et al. [17] highlighted the growing interest in RSC in today's business. As the large body of literature on RSC planning shows, mixed integer programming (MIP) models are the common models for the quantitative planning of many case studies [18, 19]. However, most of the discussed models are for single facility problems. Very recently, Brandenburg et al. [20] presented a holistic review of the available literature prior to 2014 on quantitative models for SCM including RSC. Lambert et al. [21] proposed a conceptual framework for RSC including generic process decisions, economic aspects, and performance measures with respect to the tactical level decisions. Sbihi and

Eglese [13] focused on combinatorial optimization problems in a network with waste management and reverse logistics. Hoshino et al. [22] constructed a linear goal programming model to maximize the total profit and recycling rate for recycle-oriented manufacturing systems. Likewise, Karakayalı et al. [23] investigated the pricing and recovery planning problem in a single-period setting. By using a target rebate-punish contract, Yan and Sun [24] modeled a multi-echelon RSC for a scrap recycling. Their results on a steel RSC, involving a manufacturer and multi- 3PLs companies, revealed that the target rebate-punish may coordinate the RSC under certain conditions.

Regarding the literature on pharmaceutical RSC, few works can be found. Shih and Lin [25] presented a multiple criteria optimization approach to minimize the cost for collection system planning for medical waste. Recently, Kumar et al. [10] proposed a framework to state each party's responsibility in the pharmaceutical RSCs. They suggested the usage of consistent information systems and carriers to streamline the supply chain. The absence of collaboration in their model with 3PLs draws into question the ability of the model in tracking the products. In addition, the study ignored the criterion of sharing any possible benefits of using this technology as well as sharing the implementation cost among the entities. Lately, Xie and Breen [7] designed a green pharmaceutical supply chain model to reduce preventable pharmaceutical waste and to dispose inevitable waste. The study revealed that the RSC is not really utilized in the pharmaceutical industry since returned medications cannot be reused or resold. Hence, with the new environmental regulations, supplier collaboration and customer cooperation were addressed to boost the RSC. However, the cost of recycling or collecting returned/unwanted medications was not considered.

Collaboration in supply chains can be defined as a long-term relationship among entities through sharing resources and knowledge. Camarinha-Motas [26] presented a holistic overview on the key concepts, classifications, and some applications related

to collaboration. The relevant literature on coordination and collaboration in RSC is very recent because of the complexity in these chains. Examples on the intricacies are anti-trust problems, lost of control, and the inherent uncertainty, such as local policies, quality of returned products, etc [27]. To reduce uncertainty, efforts are needed to increase the coordination in the RSC by changing the relationship between cost-value-profit equations [28]. One of the coordination mechanisms that we focus on, herein, is negotiation process. However, most of the available literature, concerning this coordination mechanism, is on the forward supply chain.

Jung et al. [29] proposed a negotiation process for a distributor and a manufacturer to find a feasible plan for supply quantities from the manufacturer to the distributor with a minimum amount of information revelation to partners. They stated that complete information sharing is essential to solve centralized planning model. Dudek ans Stadtler [30, 31] suggested using some incentives to boost the negotiation process. Li [32] examined the incentives in a two-level supply chain (one manufacturer and many retailers). His study expressed that the direct and leakage effects of information sharing discourage retailers from collaboration. Hence, Cachon [33] suggested the use of contracts based on five types of incentives to facilitate the coordination of partners' activities in the forward supply chain. One of the incentives can be the price charged by the supplier to the customer, which is known as wholesale-price. The second is the use of buyback policy of returning all unsold items. When the retailers have a portion of the revenue as an incentive, they will go for long-term collaboration, as they will be part of the profit cycle. Another incentive is to give some flexibility to the supplier of the demand over the minimum quantity to provide. Finally, reducing the cost by increasing the quantity will encourage the buyer to have more. Recently, Lehoux et al. [34] studied a two-echelon supply chain in the pulp and paper industry. They explained that using different coordination mechanisms provided higher gains

for network entities. Moreover, Kusukawa and Arizono [35] suggested a profit sharing mechanism for a forward supply chain. Bellantuono and Pontrandolfo [36] proposed four contract-based models to share the salvage and recovery values of a closed-loop supply chain.

In reality, as mentioned earlier, the information access between RSC entities is very limited. Therefore, Walther et al. [37] developed a decentralized negotiation model to enable allocating product recovery tasks for recycling companies. Lagrangian relaxation optimization method was used to solve the model. The method was applied to an electronic case study in Europe. It can be said that, up till recently, Walther et al. [37] research is the only mathematical model available in the literature for coordination in RSC. The recovery activities in the electronic industry have a value-added to the supply chain income. However, in the pharmaceutical industry, the salvage value of the medication recovery is almost negligible. Hence, coordination approach in the latter is more challenging. Furthermore, the profit sharing among the network entities was not studied in [37]. Since the negotiation requires an invested effort from RSC entities, this should be rewarded by sharing the benefits among the entities. In our contribution, we present a negotiation process as well as a technique to share the savings based on invested efforts for each entity.

2.4 The Model

2.4.1 RSC Single Period Tactical Planning Problem in the Case Study

As estated earlier, the producer of medications, Generic PharmaX, is facing governmental legislations to green her supply chain activities. Moreover, she used to pay penalties to governments for uncollected medications at customer zones. Therefore, in

order to help the producer improving her RSC, we propose her a coordination model to guarantee the collection of all available amounts of medications at customer zones. However, because the medication recovery process involves a certain logistics cost but a small salvage value, the coordination model in such supply chains is bound to fail unless a motivation technique is utilized to encourage RSC entities to collaborate. This mechanism is shown in figure (2). The figure depicts the RSC entities of the proposed coordination model and illustrates the interaction among them.

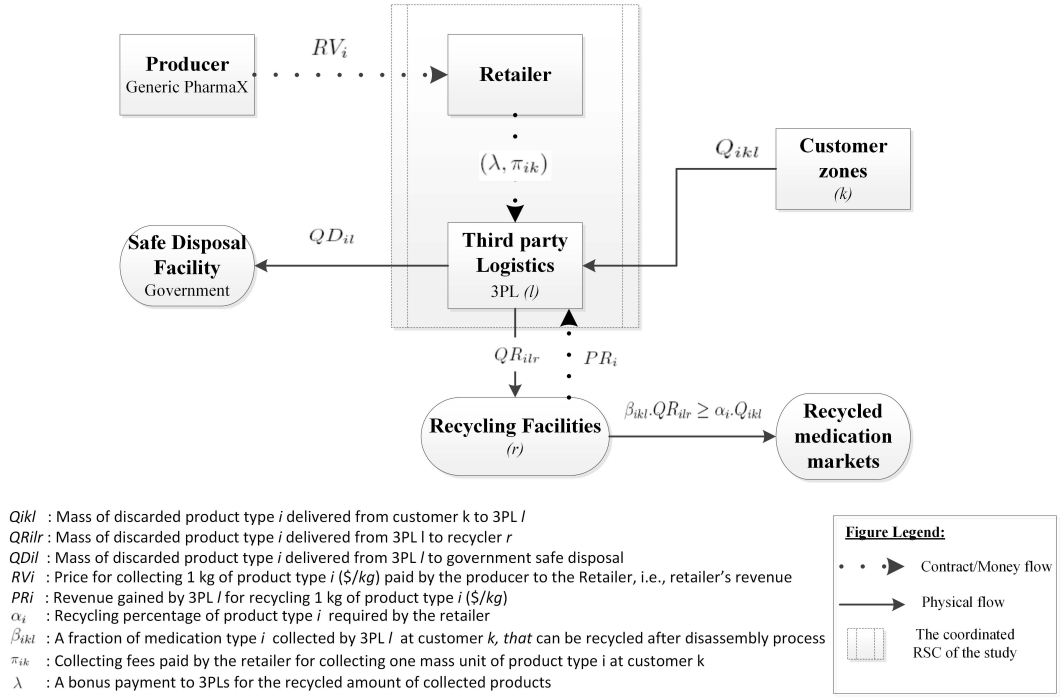

Figure 2: The Pharmaceutical RSC based on the Proposed Coordination Model

Since the RSC activities fall outside core functions of the producer, the majority of those activities are outsourced. The producer pays a retailer for collecting medications at customer zones. More precisely, she pays the retailer a price of RV_i for collecting 1 kg of product type i. The retailer, as a representative of the producer in the RSC, controls the RSC activities. However, the retailer is not qualified to handle the returns by himself. Hence, he contracts with one or more third-party logistics (3PL) companies to pick up and recycle the leftover medications at customer zones. With

the goal of greening the RSC, the retailer, as the representative of the producer in the RSC, sets a target for recycling certain percentages (α_i) of the total medication collected by 3PL companies at customer zones. 3PL companies reach the target through sending the collected mass to recyclers, which are assumed to be under their control. Furthermore, in order to avoid penalties due to the uncollected medications at customer zones, the retailer needs to make sure all leftovers are collected by 3PL companies. Hence, the retailer proposes a contract to 3PL companies. The contract has two parameters; the first parameter stands for collecting fees for one unit of product type i at customer zone k (calculated collecting fees π_{ik}). On the other hand, the recycling process is infrequent in the pharmaceutical industry because it has almost no economical values to 3PL companies. Therefore, in order to motivate the 3PL companies to recycle some medications, the second parameter is offered by the retailer for each unit recycled from the collected medications (bonus payment λ). In the light of the contract offers, the role of 3PL companies is to pick up the available medications at customer zones (Q_{ikl}). Furthermore, 3PL companies have to deliver the medications, after sorting and separating them, to the RSC sinks; encompassing government safe disposal and different recycling facilities.

As aforementioned, the retailer requests a certain percentage from each product to be recycled (α_i). Therefore, the 3PL companies have to meet the recycling mass required by the retailer ($\alpha_i.Q_{ikl}$). Then, 3PL companies send the mass (QR_{ilr}) to recycling facilities as shown in figure (2). In the recycling facilities, the medications are disassembled to packaging, containers, etc. The recyclable fraction of a medication type i at recycling facilities is represented as β_{ikl}. The recyclable amounts of the delivered medications at recycling facilities should at least reach the target imposed by the retailer ($\beta_{ikl}.QR_{ilr} \geq \alpha_i.Q_{ikl}$). By the same token, the recycled masses at recycling facilities are fractions of the collected amounts at customer zones ($\beta_{ikl}.QR_{ilr}$). The

recycling facilities sell the recycled mass in recycled medication markets, at a price of PR_i. For example, an ethanol of 98% purity can be extracted from medications and sold to paints factories, where it can be used as a solvent in paints. At last, hazardous and non-recyclable medications have to be sent to the governmental safe disposal facilities to be disposed in a secure area (QD_{il}). Based on this context, a mathematical model for the case study can be formulated as shown in the following sections.

Centralized Model

Currently, the retailer contracts with many 3PLs to collect the unwanted products based on fixed non-negotiable prices (current collecting fees) as follows. The retailer has the information about the available amounts at each customer zone, i.e. she has the power over other entities. She informs 3PLs with contract parameters (current collecting fees and recycling targets) for collecting medications. Then, each 3PL company sends the retailer the amount that they are willing to collect. Each 3PL company's objective is to maximize her profit of collecting with respect to her own collecting cost, transportation cost, and collection and recycling capacities. In contrary, the retailer's goal is to fulfill the recovery targets.

A comprehensive solution for the whole RSC could be obtained if the retailer has all the required information for each 3PL company. She could manage and assign each 3PL company an amount to collect in order to ensure a complete collection for the medications. Following is the model in case of full information availability to the retailer, corresponding to RSC depicted in figure (2).

Indices and Sets

i index of products, $i \in I$

k index of customers (hospitals and pharmacies), $k \in K$

l index of 3PL, $l \in L$

r index of recyclers, $r \in R$

Parameters

RV_i Price for collecting 1 kg of product type i ($\$/kg$) paid by the producer to the retailer, i.e., retailer's revenue

PR_i Revenue for recycling 1 kg of product type i ($\$/kg$)

P_i Fees paid to government to dispose 1 kg of product type i ($\$/kg$)

RC_{ir} Recycling cost of product i at recycler r

DC_{il} Cost for collecting and sorting product type i at 3PL l

TC_{ikl} Transportation costs of 1 kg of product type i from customer k to 3PL l

TCR_{ilr} Transportation costs of 1 kg of product type i from 3PL l to recycler r

TD_{il} Transportation costs of 1 kg of product type i from 3PL l to governmental safe disposal

α_i Recycling percentage of product type i

M_{ik} Mass of product type i that has to be collected at customer k

CAP_l Capacity available at 3PL l ($)

$CAPR_r$ Capacity available at recycler r ($)

β_{ikl} a fraction of medication type i collected by 3PL l at customer k that can be recycled after disassembly process

Decision Variables

Q_{ikl} Mass of discarded product type i delivered from customer k to 3PL l

QR_{ilr} Mass of discarded product type i delivered from 3PL l to recycler r

QD_{il} Mass of discarded product type i delivered from 3PL l to government safe disposal sink

rec_{rl} Total mass approved to be sent to recycling facility r by 3PL l

RSC centralized model

The objective function (1) maximizes the total profit of the RSC.

$$\textbf{Maximize } \mathbf{Z} = \mathbf{Rev}_{Collecting} + \mathbf{Rev}_{Recycling} - \mathbf{Ct}_{Collecting} - \mathbf{Ct}_{Recycling} - \mathbf{Ct}_{Disposal} \quad (1)$$

where, $\mathbf{Rev}_{Collecting}$ is the retailer's revenue from collecting medications, paid by the producer $(\sum_{l\in L}\sum_{k\in K}\sum_{i\in I} RV_i.Q_{ikl})$. $\mathbf{Rev}_{Recycling}$ stands for 3PL companies revenue from recycling medications $(\sum_{l\in L}\sum_{r\in R}\sum_{i\in I} PR_i.QR_{ilr})$. $\mathbf{Ct}_{Collecting}$ reflects the cost of collection/sorting and transportation of medication from all customers incurred by all 3PLs $(\sum_{l\in L}\sum_{k\in K}\sum_{i\in I}(DC_{il}+TC_{ikl})Q_{ikl})$. $\mathbf{Ct}_{Recycling}$ represents medication recycling process and transportation costs $(\sum_{l\in L}\sum_{r\in R}\sum_{i\in I}(RC_{ir}+TCR_{ilr})QR_{ilr})$. Medication safe disposal fees and transportation costs are considered in $\mathbf{Ct}_{Disposal}$ as $\sum_{l\in L}\sum_{i\in I}(P_i+TD_{il})QD_{il}$.

The model is constrained by conservation of flow through network channels and capacity constraints for recycling facilities and for each 3PL company site. In addition, the masses that have to be sent to each recycling facility are considered, based on the percentage of recycling of that product type. In other words, each product has a possibility to recycle part of it, for example packages, etc. The recycled masses have to meet the recycling target of each product. Moreover, all of unsold products at each customer site have to be collected and moved to 3PL facilities, as provided in equations (2)-(8).

subject to:

$$\sum_{k\in K} Q_{ikl} = \sum_{r\in R} QR_{ilr} + QD_{il} \qquad \forall i \in I, \forall l \in L \quad (2)$$

$$\sum_{l\in L}\sum_{i\in I} TCR_{ilr}.QR_{ilr} \leq CAPR_r \qquad \forall r \in R \tag{3}$$

$$\sum_{k\in K}\sum_{i\in I} DC_{il}.Q_{ikl} \leq CAP_l \qquad \forall l \in L \tag{4}$$

$$\sum_{l\in L}\sum_{k\in K}\sum_{i\in I} \alpha_i.Q_{ikl} \leq \sum_{l\in L}\sum_{r\in R} rec_{rl} \tag{5}$$

$$\sum_{r\in R} rec_{rl} = \sum_{r\in R}\sum_{k\in K}\sum_{i\in I} \beta_{ikl}.QR_{ilr} \quad \forall l \in L \tag{6}$$

$$M_{ik} = \sum_{l\in L} Q_{ikl} \qquad \forall i \in I, \forall k \in K \tag{7}$$

$$Q_{ikl}, QR_{ilr}, QD_{il}, rec_{rl} \geq 0$$
$$i \in I, k \in K, r \in R, l \in L \tag{8}$$

The first constraint (2) ensures the conservation of mass flow on the 3PLs node; masses collected from customer k equal to masses sent to recycling plus masses sent to governmental sink. Constraints (3) explains the capacity of the recyclers in dollars as a unit of medication type i delivered from 3PL l to recyclers r multiply by transportation costs of 1 kg of product type i from 3PL l to recyclers r. Constraint (4) is a capacity constraint in dollars for 3PL company and it is calculated by multiplying the cost of 1 kg collected from product type i with the collected masses of that medication type i. Constraint (5) calculates the masses that have to be sent to each recycling

facility by multiplying the collected masses of product type i with the percentage of recycling of that product type. Constraint (6) guarantees that the recycled masses at least reach the target of recycling of product type i. Constraint (7) confirms that all of unsold product type i at customer k are collected and moved to 3PL facilities. The last constraints are non-negativity constraints.

However, the 3PLs might not accept the prices and quantities offered by the retailer or would not agree to share their information. It therefore becomes necessary to model the tactical planning problem in a decentralized manner and to use a mechanism in order to coordinate it efficiently.

Coordination Model Based on Negotiation Approach

Solving the centralized model, as mentioned earlier, needs private information sharing between RSC entities. As some examples we can mention the capacity available at 3PLs (CAP_l), transportation cost from 3PLs to recyclers (TCR_{ilr}), transportation cost from 3PLs to safe disposal (TD_{il}), and so on. In fact, RSC entities are not currently willing to share this knowledge with others. Moreover, some constraints are common constraints for all 3PLs, such as collecting all of unwanted medications (constraint (7)). Therefore, a decentralized approach is needed to reflect business reality.

Inspired by [37], a negotiation-based coordination approach is suggested to optimize the value of collected quantities and the collecting fees. The retailer leads the negotiation process and offers calculated collecting and recycling fees to 3PLs. The offers and reactions are exchanged until both parties agreed upon certain values of the parameters, as summarized in figure (3).

Looking at the structure of the centralized model, it can been seen that constraints (5) and (7) are related to the retailer, who tries to ensure the collection and recycling

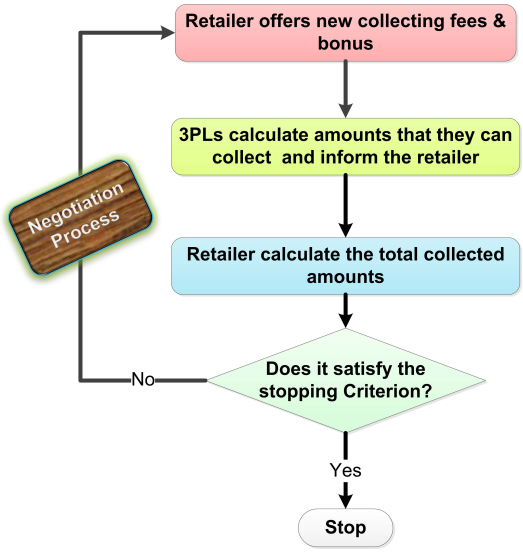

Figure 3: Negotiation Procedure in the Pharmaceutical RSC

of medications. However, those constraints are dependent constraints based on private information of 3PLs. In other words, by deleting constraints (5) and (7) from the centralized model, a sub-model for each 3PL company can be obtained. Even so, those deleted constraints have to be satisfied in order to solve the model. Therefore, the retailer proposes contract offers to 3PLs and checks the collected amounts. Two parameters are considered as contract parameters: π_{ik} and λ. π_{ik} is calculated collecting fees paid by the retailer for collecting one mass unit of product type i at customer k. Besides, in order to green the supply chain, λ is a given bonus payment to 3PLs for the recycled amount of collected products. If not all of the medications are collected, the retailer will revise the contract offers (figure (3)).

This negotiation process can be mathematically represented by the aid of Lagrangian relaxation method. Details of Lagrangian relaxation method can be found in [38, 39]. More precisely, the retailer relaxes the common constraints (constraints (5) and (7)) and adds them to the objective function of the model as shown in equation (9). Also, the violation of the constraints is penalized in the objective function by Lagrangian multipliers (the contract parameters). The extra notations used in the

negotiation process are shown below.

Coordination model notations

$Z^{LR}(\lambda, \pi_{ik})$ is the objective function of the RSC Lagrangian relaxation model;

$Z^{LR}(\lambda, \pi_{ik})^*$ is the optimal objective function value of the RSC Lagrangian relaxation model;

$Z_l(\lambda, \pi_{ik})$ is the objective function for each 3PL model l;

$Z_l^*(\lambda, \pi_{ik})$ is the optimal objective function value for each 3PL model;

$\sum_{l \in L} Z_l^*(\lambda, \pi_{ik})$ is the summation of optimal objective function values for all 3PL companies.

Lagrangian Relaxation function of the RSC model

$$Z^{LR}(\lambda, \pi_{ik})^* = Maximize\ Z^{LR}(\lambda, \pi_{ik})$$

$$\begin{aligned}
&= \sum_{l \in L} \sum_{k \in K} \sum_{i \in I} RV_i.Q_{ikl} + \sum_{l \in L} \sum_{r \in R} \sum_{i \in I} PR_i.QR_{ilr} - \sum_{l \in L} \sum_{i \in I} TD_{il}.QD_{il} \\
&- \sum_{l \in L} \sum_{k \in K} \sum_{i \in I} TC_{ikl}.Q_{ikl} - \sum_{l \in L} \sum_{r \in R} \sum_{i \in I} TCR_{ilr}.QR_{ilr} - \sum_{l \in L} \sum_{r \in R} \sum_{i \in I} RC_{ir}.QR_{ilr} \\
&- \sum_{l \in L} \sum_{i \in I} P_i.QD_{il} - \sum_{l \in L} \sum_{k \in K} \sum_{i \in I} DC_{il}.Q_{ikl} - \lambda(\sum_{l \in L} \sum_{r \in R} rec_{rl} - \sum_{l \in L} \sum_{k \in K} \sum_{i \in I} \alpha_i.Q_{ikl}) \\
&- \sum_{i \in I} \sum_{k \in K} \pi_{ik}.(M_{ik} - \sum_{l \in L} Q_{ikl}) \qquad (9)
\end{aligned}$$

After some rearrangements for equation (9), we can rewrite the same equation (equation (9)) for the RSC model as shown in equation (10). More mathematical details

are provided in the *Appendices*.

$$Z^{LR}(\lambda, \pi_{ik})^* = Maximize \ \sum_{l \in L} Z_l^*(\lambda, \pi_{ik}) - \sum_{i \in I} \sum_{k \in K} \pi_{ik}.M_{ik} \tag{10}$$

From equation (10), a separate model is extracted for each 3PL company with a profit maximization objective function as shown in equation (11) and with respect to constraints (12)-(16). The 3PL model generates an optimal local plan for each 3PL company l with respect to the contract offered by the retailer.

3PL model

$$Z_l^*(\lambda, \pi_{ik}) = Maximize \ Z_l(\lambda, \pi_{ik}) = \sum_{k \in K} \sum_{i \in I} ((RV_i + \pi_{ik} + \lambda.\alpha_i) - TC_{ikl} - DC_{il})Q_{ikl}$$
$$+ \sum_{r \in R} \sum_{i \in I} (PR_i - RC_{ir} - TCR_{ilr})QR_{ilr} - \sum_{i \in I} (TD_{il} + P_i)QD_{il} - \lambda \sum_{r \in R} rec_r \tag{11}$$

subject to:

$$\sum_{k \in K} Q_{ikl} = \sum_{r \in R} QR_{ilr} + QD_{il} \qquad \forall i \in I \tag{12}$$

$$\sum_{i \in I} TCR_{ilr}.QR_{ilr} \leq CAPR_r \qquad \forall r \in R \tag{13}$$

$$\sum_{k \in K} \sum_{i \in I} DC_{il}.Q_{ikl} \leq CAP_l \tag{14}$$

$$\sum_{r\in R} rec_r = \sum_{r\in R}\sum_{k\in K}\sum_{i\in I} \beta_{ikl}.QR_{ilr} \qquad \forall r \in R \tag{15}$$

$$Q_{ikl}, QR_{ilr}, QD_{il}, rec_r \geq 0$$
$$i \in I, k \in K, r \in R, l \in L \tag{16}$$

Solving the Lagrangian relaxation model starts with proposing values for λ and π_{ik} by the retailer. Each 3PL company solves the model to find the optimal plans and presents the values to the retailer. Afterwards, the retailer checks the common constraints based on 3PLs' values. If the common constraints are not satisfied, the retailer reviews the values again and iterates over them with 3PLs. As mentioned before, no information is shared between entities. Consequently, a sub-gradient procedure of Lagrangian dual function is used to get a global optimal of this model.
For the Lagrangian relaxation model, $Z^{LR}(\lambda, \pi_{ik})$, let π_{ik}^t be the value of π_{ik} at iteration t and $\sum_{l\in L} Q_{ikl}^t$ be the optimal value of $\sum_{l\in L} Q_{ikl}$ at the same iteration.

$$g_{\pi_{ik}}^t = \sum_{l\in L} Q_{ikl}^t - M_{ik} \tag{17}$$

Equation (17) is the sub-gradient function of the corresponding relaxed constraint (constraint (7)) at π_{ik}^t, i.e. $g_{\pi_{ik}}^t$ represents the violation of the relaxed constraint in iteration t. As long as the relaxed constraint is unsatisfied, the new Lagrangian multiplier (π_{ik}) is calculated as follows:

$$\pi_{ik}^{t+1} = \pi_{ik}^t + \mu_t.g_{\pi_{ik}}^t \tag{18}$$

where μ_t is a positive scalar step size at iteration t and is calculated as $\mu_t = b/t||g||$, b is a scalar quantity and $||g||$ is the Euclidean norm of the sub-gradient. By the same

token, let λ^t be the value of the bonus payment (λ) at iteration t, hence

$$g_\lambda^t = \sum_{l \in L} \sum_{k \in K} \sum_{i \in I} \alpha_i . Q_{ikl}^t - \sum_{r \in R} rec_{rl}^t \tag{19}$$

represents the violation of the corresponding relaxed constraint (constraint (5)) at iteration t. As long as the relaxed constraint is unsatisfied, the Lagrangian multiplier is updated as follows:

$$\lambda^{t+1} = max(0, \lambda^t + \mu_t . g_\lambda^t) \tag{20}$$

The process is repeated for a number of iterations until both relaxed constraints are satisfied.

The solution of the sub-model is not necessarily an optimal solution for the centralized network model. Therefore, the solution space of the model needs to be restricted to generate a global feasible solution. We add a new constraint to the sub-model (11)-(16) in order to ensure that the maximum value of the collected product has to be less than or equal to the maximum available medication for each 3PL company. The value of Q_{ikl}^{max} is a fraction of the available masses (equation (21)):

$$Q_{ikl} \leq Q_{ikl}^{max} \quad \forall i, k, l \tag{21}$$

The aforementioned procedure runs until the targeted amounts in constraints (5) and (7) are collected. Based on the assigned values to each 3PL company, the retailer calculates her cost, which is the money paid to each 3PL company and the money paid to the government (for safe disposal and penalty for uncollected masses at customer zones). Also, the 3PLs calculate their cost along with their revenue.

2.4.2 Sharing the Bonus Between RSC Entities

As mentioned earlier, the retailer is willing to share her bonus, received from the producer, with RSC entities based on their coordination efforts. Motivated by a recent work of [35], the following is a suggested procedure for sharing the bonus between the retailer and 3PLs.

1. Find the difference between the collected amount in the proposed negotiation-based approach with the current collected amounts (based on Generic PharmaX historical data) ($\Delta E = Q_{ikl}^{negotiation-based} - Q_{ikl}^{historical}$).

2. If $\Delta E > 0$, calculate the cost of collecting this difference based on the negotiation-based model for each 3PL company.

3. Calculate the investment rates (N) of the 3PL company in both cases (the case of negotiation-based approach and the current collected amount) as:

$$N_{3PL} = \frac{\text{The cost of collecting } \Delta E}{\text{Total cost of collecting } Q_{ikl}^{negotiation-based}}$$

and for the retailer calculate the ratio as the money paid to 3PLs divided by the money received from the producer:

$$N_{Retailer} = \frac{\pi_{ik}.Q_{ikl} + \lambda.rec}{RV_i.Q_{ikl}}$$

Then, normalize the investment ratios (N^{nor}) as follows:

$$N_{3PL}^{nor} = \frac{N_{3PL}}{N_{3PL} + N_{retailer}} \quad and \quad N_{Retailer}^{nor} = \frac{N_{Retailer}}{N_{3PL} + N_{retailer}}$$

4. Calculate the share of the retailer and 3PL from the bonus (S) as:

$$S_{3PL} = Bonus.N_{3PL}^{nor} \quad and \quad S_{Retailer} = Bonus.N_{Retailer}^{nor}$$

2.5 Numerical Results and Discussions

Through the communication with the head of Generic PharmaX supply chain department, the required data were obtained from the producer. The data were next refined based on the top markets and medication groups of the company. The four 3PLs were also selected among the largest collectors, where the top four and twenty medications selling amounts were selected for the small and large cases, respectively. The model was solved for small and large cases using Lagrangian relaxation. Results are given for 4 third-party logistics and 4 recyclers. Each 3PL company has different values for transportation and recycling costs, capacities, location, etc. Table 1 shows the capacity for each 3PL company.

Table 1: Third-Party Logistics Capacities ($)

	Large case	Small case
3PL 1	4,700.00	75.00
3PL 2	3,000.00	100.00
3PL 3	4,560.00	78.00
3PL 4	2,850.00	150.00

The next sections describe the results from the negotiation-based model and the real amounts of the collected medications which have led to some managerial insights. Each entity effort is also rewarded by sharing the bonus of the network. Finally, a validation of the results is presented for the shared amounts between RSC entities and corresponding costs.

2.5.1 Negotiation Model Results

As we mentioned earlier, the main concern in this research is how to coordinate independent RSC players towards a common goal for the network. Negotiation was therefore used as a way to encourage 3PLs to recover as much products as possible while taking into account both retailer and 3PLs constraints. The model was solved by relaxing the two common constraints (Equations (5) and (7)) and penalizing them

in the objective function. Using *Cplex*, the model was run for many iterations and evaluated for different values of b. The used values for b were 5, 10, and 30. When all the available amounts (M_{ik}) were collected, we stop running the model. With respect to the step size, small step sizes resulted in smaller optimality gap, i.e. more stable results. The values of calculated collecting fees, π_{ik}, were varied as shown in the second column of Table 2. The current collecting fees are given in the third column in the same table. The last row in the table corresponds to the price of each mass of unwanted medications that is approved to be recycled. The last four columns in the table represent the Q_{ikl} that has been collected by each 3PL company. Similar table for large scale problem (i.e., twenty products are recovered) is given in the *Appendices*.

Table 2: Small Case: Collecting fees , recycling bonus ($/kg), and amounts assigned for each 3PL

	Calculated collecting fees	Current collecting fees	3PL 1	3PL 2	3PL 3	3PL 4
π_{11}	0	0.5	3.75	3.75	3.75	3.75
π_{12}	0.224	0.5	9	9	9	9
π_{13}	0.388	0.5	7.5	7.5	7.5	7.5
π_{14}	0.015	0.5	1.25	1.25	1.25	1.25
π_{21}	0.495	0.45	8.75	8.75	8.75	8.75
π_{22}	0.793	0.45	11.36	11.36	11.375	11.375
π_{23}	0.012	0.45	6.38	6.38	6.38	6.375
π_{24}	0.089	0.45	2.5	2.5	2.5	2.5
π_{31}	0.583	3.55	0	4	2.75	4.25
π_{32}	2.718	3.55	4.60	13.75	13.75	22.90
π_{33}	4.340	3.55	21	21	21	21
π_{34}	3.061	3.55	13.75	21.25	0	20
λ	0.306	-	-	-	-	-

It can be seen, in table 2, that some of the calculated collecting fees are lower than the current collecting fees and some are higher. For example in the small case, for product type 3 at customer zone 3, π_{33}, the current collecting fees is lower than calculated collecting fees in the coordinated model. Since 3PL 2 and 3PL 4 fully utilize their capacities, the assignable amount to 3PL 1 or 3PL 3 cannot be taken by them. Hence, the retailer has to increase the calculated collecting fees up to a

certain limit where 3PL 1 and 3PL 3 can collect all jobs allocated to them. On the other hand, 3PL 2 and 3PL 4 gain more from the higher calculated collecting fees. The reason is that 3PL 2 and 3PL 4 could collect the allocated quantities with lower contractual collecting fees, as shown in Table 3.

The profit of each RSC entity is given in the first four rows of Table 3. 3PL 4 has the largest profit for the small case, where for the large case, 3PL 1 has the largest profit. Also, the transfer payment from the retailer to each 3PL is given in rows from 6-9. The total transfer payments are given in row 10. It is calculated by multiplying the calculated collecting fees (π_{ik}) and recycling bonus (λ) with the collected and recycled amounts.

Table 3: Profits and Transfer Payments Paid to 3PLs

	Small case	Large case
Profit of 3PL 1(in $1000)	1,796.9	146,179.0
Profit of 3PL 2 (in $1000)	1,705.9	106,507.2
Profit of 3PL 3 (in $1000)	1,478.9	122,533.3
Profit of 3PL 4(in $1000)	1,884.8	111,871.9
Total profits of 3PL companies (in $1000)	6,866.2	487,091.3
Transfer payments from the retailer to 3PL 1 (in $1000)	2,074.2	7,578.6
Transfer payments from the retailer to 3PL 2 (in $1000)	2,065.3	2,625.6
Transfer payments from the retailer to 3PL 3 (in $1000)	1,690.2	4,481.0
Transfer payments from the retailer to 3PL 4 (in $1000)	2,205.1	3,229.8
Total transfer payments	8,034.8	17,915.1
Capacity utilization of 3PL 1 (%)	88	100
Capacity utilization of 3PL 2 (%)	100	78
Capacity utilization of 3PL 3 (%)	86	100
Capacity utilization of 3PL 4 (%)	100	90

The retailer has to pay an extra $312.675 thousands to ensure that all products for the small case are collected. This is calculated as the difference between the current collecting fees minus the calculated collecting fees in the coordination model. By the same token, we calculated the value for this large scale as $1,807.34 thousands.

2.5.2 Results Validation and Bonus Sharing

To understand the effect of different collecting fees on the collected amounts, the model was solved using the current collecting fees as Lagrangian multipliers in the sub-model (11)-(16). The results show that the current collecting fees leads to lower collected amounts than the collected amount in the coordinated model. In particular, up to 28% more products are collected for small case and up to 18% in case of large scale problem when the RSC is coordinated, as it can be observed in Table 4. In the small case, based on the governmental penalties for not collecting unwanted medications, the uncollected amounts with the current collecting fees would cost Generic PharmaX around $2 millions. In the large scale problem, the penalties could be around $93 millions.

Table 4: Total Amounts Collected (kg) with Different Collecting Fees

		Coordinated model	Current situation
Small Case	Total collected amounts	407	294.64
	Total uncollected amounts	0	112.36
Large case	Total collected amounts	24,060	19,768.48
	Total uncollected amounts	0	4,291.51

In table 5, we compare the profit of each entity for the small and the large case regarding the actual collecting fees and the collecting fees in the coordinated model. For 3PL 2, 3PL 3, and 3PL 4, it can be seen that their profits in the coordinated model are less than their profits in the current model for the small case. As a result, they have to gain some extra bonus in order to be encouraged to collaborate with the retailer and to be compensated for profit lost. However, for the large scale, all of the 3PLs have increased their profits. We therefore investigated the impact of different values of bonus paid by Generic PharmaX to the retailer on the RSC using the procedure mentioned earlier.

Tables 6 and 7 provide the part of the bonus obtained by each 3PL company and

Table 5: Profit Comparison (in $1,000)

	Coordinated model	Current status	The difference
		Small case	
3PL 1	1,796.89	1,522.54	271.35
3PL 2	1,705.92	1,966.67	-260.75
3PL 3	1,478.9	1,674.12	-195.22
3PL 4	1,884.84	2,176.85	-292.01
Retailer*	-763.087	-450.675	-312.41
		Large case	
3PL 1	146,179	112,011.32	34,167.68
3PL 2	106,507.2	91,973.51	14,533.69
3PL 3	122,533.3	116,231.73	6,301.572
3PL 4	111,871.9	90,980.38	20,891.52
Retailer*	-19,768.5	-17,915.13	-1,853.37

* Since the fees, paid by the producer to the retailer, are constant, they are neglected from the calculations for the retailer.

by the retailer from different amounts paid by the producer (Generic PharmaX) for collecting the whole amount of unwanted medications at customer zones. The first row of the aforementioned tables provides different amounts of bonus while the rest of the rows provide the bonus shared based on the procedure proposed in subsection 2.4.2.

Table 6: Small Case: Bonus Sharing Between RSC Entities (in $1,000)

	N	N_{3PL}^{nor}	$500	$1,500	$2,000	$2,100	$2,200	$2,250	$2,300
3PL 1	0.23	0.12	60	180	240	252	264	270	276
3PL 2	0.87	0.45	225	675	900	945	990	1,012.5	1,035
3PL 3	0.19	0.11	55	165	220	231	242	247.5	253
3PL 4	0.36	0.18	90	270	360	378	396	405	414
Retailer	0.28	0.14	70	210	280	308	308	315	322

As we can see in table 6, a bonus of $500 thousands would only be profitable for 3PL 1 since it is the only entity that has a positive profit. However, it is not the case for the rest of RSC entities. Expressly, by looking at table 5, we can see that 3PL 2 will loose about $260 thousands via a negotiation protocol. By considering a bonus of only $500 thousands, the part obtained by 3PL 2 would be of $225 thousands, which is less than the loss by about $35 thousands. For the $1,500 thousands bonus scenario, this would be beneficial for 3PL 1 and 3PL 2 but not for the rest of RSC

entities. The third scenario of $2,000 thousands is valuable for all 3PLs but not for the retailer. The sixth scenario is satisfactory for all RSC entities. Henceforth, the offered bonus by Generic PharmaX has to be greater than or equal to $2,250 thousands to ensure that every RSC entity gains some bonus and that the loss due to accepting the coordinated collecting fees is compensated.

Table 7: Large Case: Bonus Sharing Between RSC Entities (in $1,000)

	N	N_{3PL}^{nor}	$50,000	$60,000	$65,000	$70,000	$75,000	$80,000
3PL 1	0.284	0.205	10,227.854	12,273.425	13,296.210	14,318.995	15,341.781	16,364.566
3PL 2	0.179	0.128	6,422.977	7,707.573	8,349.870	8,992.168	9,634.466	10,276.763
3PL 3	0.115	0.0830	4,147.280	4,976.736	5,391.464	5,806.192	6,220.912	6,635.648
3PL 4	0.412	0.296	14,816.722	17,780.067	19,261.739	20,743.411	22,225.083	23,706.755
Retailer	0.400	0.288	14,385.167	17,262.201	18,700.717	20,139.234	21,577.751	23,016.267

For the large case (table 7), it can be seen that any amount of the bonus would be beneficial for the 3PLs. However, the retailer's effort would be rewarded in the case the producer pays at least $65,000 thousands as a bonus. In this case, the producer would not only avoid paying penalties, but also could save around $30,952 thousands of the money that she used to pay to government. From the results, we can see that if partners agree on better coordinating their activities, more products could be collected. The latter would lead to a green supply chain for the producer while the investment of other supply chain entities would be rewarded.

2.6 Conclusion

The pharmaceutical industry has developed at a very fast rate in the last decades, facing a rapidly growing market. However, environmental and governmental changes pressurize the companies to step ahead and change their practices. The recovery process and reverse supply chains of unsold or unwanted medications become an essential asset for this industry. A wide range of proactive actions could be implemented in the supply chain for reducing or minimizing the amount of pharmaceutical wastes left in

the environment.

The pharmaceutical supply chain is a complex decision-making system at the tactical level. In general, it includes many actions, such as placement of waste materials recycling, long-term RSC chain coordination contract drafting, recovery channels of reverse logistics, and recovery efforts designing [8, 9]. Since pharmaceutical RSC activities fall outside core functions of a company, the majority of the activities are handled through third-party logistics providers (3PL) [10]. Hence, the reverse supply chain is not usual to be managed by one company. To optimize the network efficiency, effective coordination mechanism is necessary.

This paper has addressed the coordination method in a RSC of a real pharmaceutical case study. Inspired by Walther et al. [37], we developed a negotiation-based mechanism by the aid of a linear mathematical model that reflects the relationship between the retailer (producer representative) and several 3rd party logistics companies. The model was decentralized and a sub-model for each 3PL company was extracted. In order to solve the sub-models, the Lagrangian relaxation method was used. Numerical results for a small and a large case study were obtained and discussed. Finally, a bonus was shared between the RSC entities based on their contribution to the supply chain. Results show that coordination could ensure the complete collection of all unsold medications at customer zones. As a result, the producer would not pay penalties and she will be in a good reputation in the market. At the same time, the proposed coordination approaches leads to a win-win situation for the reverse supply chain entities, where each effort is rewarded. It is worth mentioning that implementing this way of coordination is not straight forward. RSC coordination is still a new reality for many of the network entities who are change reluctant.

Further research is necessary to involve customers (3rd echelon) of the network in the coordination model and introduce some incentives for their coordination efforts.

Considering a multi-period tactical planning model could also be investigated. Finally, a thorough examination of how this new planning approach could be implemented would be relevant.

2.7 Appendices

2.7.1 RSC Lagrangian Relaxation mathematical details

Lagrangian Relaxation function of the RSC model is provided in equation (9) as follows;

$$Z^{LR}(\lambda, \pi_{ik})^* = Maximize\ Z^{LR}(\lambda, \pi_{ik})$$

$$\begin{aligned}
&= \sum_{l\in L}\sum_{k\in K}\sum_{i\in I} RV_i.Q_{ikl} + \sum_{l\in L}\sum_{r\in R}\sum_{i\in I} PR_i.QR_{ilr} - \sum_{l\in L}\sum_{i\in I} TD_{il}.QD_{il} \\
&- \sum_{l\in L}\sum_{k\in K}\sum_{i\in I} TC_{ikl}.Q_{ikl} - \sum_{l\in L}\sum_{r\in R}\sum_{i\in I} TCR_{ilr}.QR_{ilr} - \sum_{l\in L}\sum_{r\in R}\sum_{i\in I} RC_{ir}.QR_{ilr} \\
&- \sum_{l\in L}\sum_{i\in I} P_i.QD_{il} - \sum_{l\in L}\sum_{k\in K}\sum_{i\in I} DC_{il}.Q_{ikl} - \lambda(\sum_{l\in L}\sum_{r\in R} rec_{rl} - \sum_{l\in L}\sum_{k\in K}\sum_{i\in I} \alpha_i.Q_{ikl}) \\
&- \sum_{i\in I}\sum_{k\in K} \pi_{ik}.(M_{ik} - \sum_{l\in L} Q_{ikl})
\end{aligned}$$

After aggregating the terms with similar indices in equation (9), we can rewrite the same equation (equation (9)) for the RSC model as shown in equation (22).

$$\begin{aligned}
Z^{LR}(\lambda, \pi_{ik})^* &= \sum_{l\in L}\sum_{k\in K}\sum_{i\in I}(RV_i - TC_{ikl} - DC_{il} + \lambda.\alpha_i + \pi_{ik})Q_{ikl} \\
&+ \sum_{l\in L}\sum_{r\in R}\sum_{i\in I}(PR_i - TCR_{ilr} - RC_{ir})QR_{ilr} - \sum_{l\in L}\sum_{i\in I}(TD_{il} + P_i)QD_{il} \\
&- \lambda\sum_{l\in L}\sum_{r\in R} rec_{rl} - \sum_{i\in I}\sum_{k\in K} \pi_{ik}.M_{ik}
\end{aligned} \tag{22}$$

It can be noticed that in equation (22) all the terms, except the last one, are related to 3PL companies. Therefore, the equation can be reformulated as shown in equation (23).

$$Z^{LR}(\lambda, \pi_{ik})^* = \sum_{l \in L}(\sum_{k \in K}\sum_{i \in I}(RV_i - TC_{ikl} - DC_{il} + \lambda.\alpha_i + \pi_{ik})Q_{ikl}$$
$$+ \sum_{r \in R}\sum_{i \in I}(PR_i - TCR_{ilr} - RC_{ir})QR_{ilr} - \sum_{i \in I}(TD_{il} + P_i)QD_{il}$$
$$- \lambda \sum_{r \in R} rec_{rl}) - \sum_{i \in I}\sum_{k \in K} \pi_{ik}.M_{ik} \tag{23}$$

The compact form of equation (23) is provided in equation (10) as follows.

$$Z^{LR}(\lambda, \pi_{ik})^* = Maximize \ \sum_{l \in L} Z_l^*(\lambda, \pi_{ik}) - \sum_{i \in I}\sum_{k \in K} \pi_{ik}.M_{ik}$$

2.7.2 Table of large case Collecting fees, recycling bonus ($/kg), and amounts assigned for each 3PL

Table 8: Large Case: Collecting Fees ($/kg) for 1 kg of a Product

Product	Customer	Calculated Collecting Fees	Current Collecting Fees	3PL 1	3PL 2	3PL 3	3PL 4
1	1	0.66	0.45	540.00	540.00	540.00	540.00
1	2	1.05	0.45	1,080.00	1,080.00	1,080.00	1,080.00
1	3	0.55	0.45	810.00	810.00	810.00	810.00
1	4	0.55	0.45	270.00	270.00	270.00	270.00
2	1	0.07	0.03	86.25	86.25	86.25	86.25
2	2	0.00	0.03	86.25	86.25	86.25	86.25
2	3	0.00	0.03	517.50	517.50	517.50	517.50
2	4	0.02	0.03	172.50	172.50	172.50	172.50
3	1	0.48	0.75	192.00	0.00	192.00	0.00
3	2	1.11	0.75	498.97	0.00	397.03	0.00
3	3	0.32	0.75	192.00	0.00	64.00	0.00
3	4	1.26	0.75	502.43	0.00	502.43	19.14
4	1	0.00	0.02	93.75	93.75	93.75	93.75

Table 8: Large Case: Collecting Fees ($/kg) for 1 kg of a Product

Product	Customer	Calculated Collecting Fees	Current Collecting Fees	3PL 1	3PL 2	3PL 3	3PL 4
4	2	0.00	0.02	93.75	93.75	93.75	93.75
4	3	0.00	0.02	112.50	112.50	112.50	112.50
4	4	0.00	0.02	75.00	75.00	75.00	75.00
5	1	0.32	0.45	70.25	70.25	70.25	70.25
5	2	0.49	0.45	158.06	0.00	158.06	105.38
5	3	0.63	0.45	181.79	57.92	181.79	140.50
5	4	0.17	0.45	52.69	0.00	52.69	35.13
6	1	0.45	0.35	138.30	0.00	138.30	92.20
6	2	0.11	0.35	34.58	0.00	34.58	23.05
6	3	0.40	0.35	94.08	0.00	147.94	80.68
6	4	0.17	0.35	79.36	0.00	0.00	34.58
7	1	0.18	0.15	59.40	0.00	59.40	39.60
7	2	0.28	0.15	89.10	0.00	89.10	59.40
7	3	0.23	0.15	74.25	0.00	74.25	49.50
7	4	0.23	0.15	74.25	0.00	74.25	49.50
8	1	0.03	0.03	12.60	12.60	12.60	12.60

Table 8: Large Case: Collecting Fees ($/kg) for 1 kg of a Product

Product	Customer	Calculated Collecting Fees	Current Collecting Fees	3PL 1	3PL 2	3PL 3	3PL 4
8	2	0.03	0.30	12.60	12.60	12.60	12.60
8	3	0.06	0.30	25.20	25.20	25.20	25.20
8	4	0.18	0.30	75.60	75.60	75.60	75.60
9	1	0.08	0.20	16.88	16.88	16.88	16.88
9	2	0.21	0.20	45.00	45.00	45.00	45.00
9	3	0.13	0.20	28.13	28.13	28.13	28.13
9	4	0.11	0.20	22.50	22.50	22.50	22.50
10	1	0.02	0.03	22.68	22.68	22.68	22.68
10	2	0.02	0.03	19.32	19.32	19.32	19.32
10	3	0.02	0.03	21.84	21.84	21.84	21.84
10	4	0.02	0.03	20.16	20.16	20.16	20.16
11	1	0.01	0.01	7.35	7.35	7.35	7.35
11	2	0.02	0.01	18.38	18.38	18.38	18.38
11	3	0.03	0.01	29.40	29.40	29.40	29.40
11	4	0.02	0.01	18.38	18.38	18.38	18.38
12	1	0.00	0.01	12.75	12.75	12.75	12.75

Table 8: Large Case: Collecting Fees ($/kg) for 1 kg of a Product

Product	Customer	Calculated Collecting Fees	Current Collecting Fees	3PL 1	3PL 2	3PL 3	3PL 4
12	2	0.00	0.01	25.50	25.50	25.50	25.50
12	3	0.00	0.01	6.38	6.38	6.38	6.38
12	4	0.00	0.01	19.13	19.13	19.13	19.13
13	1	0.00	0.02	5.90	5.90	5.90	5.90
13	2	0.00	0.02	8.85	8.85	8.85	8.85
13	3	0.00	0.02	23.60	23.60	23.60	23.60
13	4	0.00	0.02	20.65	20.65	20.65	20.65
14	1	0.11	0.05	22.50	22.50	22.50	22.50
14	2	0.03	0.05	5.63	5.63	5.63	5.63
14	3	0.02	0.05	3.75	3.75	3.75	3.75
14	4	0.03	0.05	5.63	5.63	5.63	5.63
15	1	0.03	0.03	6.60	6.60	6.60	6.60
15	2	0.05	0.03	9.90	9.90	9.90	9.90
15	3	0.04	0.03	8.25	8.25	8.25	8.25
15	4	0.04	0.03	8.25	8.25	8.25	8.25
16	1	0.03	0.01	19.50	0.00	19.50	13.00

Table 8: Large Case: Collecting Fees ($/kg) for 1 kg of a Product

Product	Customer	Calculated Collecting Fees	Current Collecting Fees	3PL 1	3PL 2	3PL 3	3PL 4
16	2	0.02	0.01	15.17	0.00	15.17	15.17
16	3	0.01	0.01	6.50	0.00	6.50	6.50
16	4	0.01	0.01	4.33	0.00	4.33	4.33
17	1	0.00	0.02	1.05	1.05	1.05	1.05
17	2	0.00	0.02	2.10	2.10	2.10	2.10
17	3	0.00	0.02	3.15	3.15	3.15	3.15
17	4	0.00	0.02	4.20	4.20	4.20	4.20
18	1	0.00	0.15	2.00	2.00	2.00	2.00
18	2	0.00	0.15	3.00	3.00	3.00	3.00
18	3	0.00	0.15	2.50	2.50	2.50	2.50
18	4	0.00	0.15	2.00	2.00	2.00	2.00
19	1	0.00	0.01	2.50	2.50	2.50	2.50
19	2	0.00	0.01	0.50	0.50	0.50	0.50
19	3	0.00	0.01	3.75	3.75	3.75	3.75
19	4	0.00	0.01	1.25	1.25	1.25	1.25
20	1	0.00	0.01	1.20	1.20	1.20	1.20

Table 8: Large Case: Collecting Fees ($/kg) for 1 kg of a Product

Product	Customer	Calculated Collecting Fees	Current Collecting Fees	3PL 1	3PL 2	3PL 3	3PL 4
20	2	0.00	0.01	2.80	2.80	2.80	2.80
20	3	0.00	0.01	0.80	0.80	0.80	0.80
20	4	0.00	0.01	3.20	3.20	3.20	3.20

Chapter 3

Two-echelon Pharmaceutical Reverse Supply Chain Coordination with Customers Incentives

This chapter is dedicated to the article entitles "*Two-echelon Pharmaceutical Reverse Supply Chain Coordination with Customers Incentives*". It has been submitted to the *International Journal of Production Economics* on May 2015. The titles, figures, and mathematical formulations have been revised to keep the coherence through the thesis.

3.1 Abstract

In the pharmaceutical industry, leftover medications that have not been properly disposed not only damage the environment but also might turn into a peril to people's health if being redistributed illegally in undeveloped countries. In contrary, if they are returned to the pharmaceutical producer before their expiry dates, they can be sold at subsidized prices or donated in such countries. In this research, we explore the role of providing incentives to customers in order to facilitate leftover returns and improve the sustainability for a real pharmaceutical reverse supply chain (RSC). Moreover, this research investigates the effect of having a proper coordination method between a producer of medications and third-party logistics (3PL) companies, responsible for collecting unwanted medications from customer zones. Finally, a technique is also proposed to share the RSC's saving among the producer and the 3PL companies. The experimental results on a real case study indicate that introducing incentives to customers could decrease the amount of uncollected medications from 18% up to 6.5%. Furthermore, having a proper coordination with 3PL companies could guarantee a full medication recovery.

3.2 Introduction

The pharmaceutical industry has witnessed significant changes in recent years. New regulations have been imposed by governments for tackling the recovery of unwanted/ expired medications at different customer zones [10]. Hospitals and pharmacies, as the main consumers of medications, are faced with uncertain and fluctuating demand. Since the shortage of certain medications might lead to severe consequences for patients, customers might adopt a conservative inventory control policy through keeping large quantities of drugs in stock. Given the perishable nature of medications, such

a strategy would lead to the expiration of excess inventory in the absence of patients demand. In contrary, if unwanted medications are returned to the producer prior to the end of their shelf-lives, they can be either sold in subsidiary markets or donated in developing and undeveloped countries. This humanitarian aid could improve the quality of health care in such communities. Accordingly, improving the reverse supply chain (RSC) is one way to gain and maintain strategic advantages in this industry.

Medications recovery process is complex in the sense that information about available amounts of leftovers, the willingness of customers to return medications, and the cost associated with the collection and disposal processes are not always known by the producer [13]. The paucity of such information could be indeed the result of the lack of trust and coordination between producers, customers, and 3PL companies. Moreover, the direct and leakage effects of information sharing discourage companies from collaboration [32]. Hence an efficient decision-making process in such RSCs is bound to fail unless a coherent coordination mechanism is utilized [14].

While many studies have investigated the impact of coordination on forward supply chain networks [40, 41], the literature is scant on the benefits of coordination in RSC networks. The available literature is limited to the profitable RSCs, such as the electronics recovery networks [37, 42]. This is due to the possibility of reusing the precious metals in such networks. On the other hand, knowing the complexity of the pharmaceutical RSC, little attention has been addressed for the coordination of this specific value chain. The negligible salvage value of the expired medications has also encumbered the investment in this RSC.

In this research, we investigate the use of coordination methods to ensure full medication recovery while sharing the savings fairly between members of a pharmaceutical RSC. The current structure of this pharmaceutical RSC involves the producer, the

3PL companies, and the RSC customers. We can observe that hospitals and pharmacies, as the RSC customers, keep medications to expire at their sites; then, they inform the producer about the quantity of the expired medications. Because it is a non profitable activity, the producer is not motivated to collect the expired medications by herself. Instead, she contracts with one or more 3PL companies to collect the expired items at customer zones by offering non-negotiable collecting fees. Thereafter, 3PL companies collect the medications and ship them to one of the governmental safe disposal sites. Consequently, the producer pays disposal fees to the government for those shipped items.

It is worth mentioning that depending on the collecting fees offered by the producer, 3PL companies might only collect a percentage of the available leftovers according to their own profit margins. If we look at the archival data of the pharmaceutical producer under investigation, we can notice that the collecting fees that are paid currently to 3PL companies are insufficient. In other words, about 20% to 40% of the available unwanted medications remain uncollected. Leaving expired medications at customer zones and disposing them improperly (e.g., thrown away in water resources), lead to penalties that must be paid by the producer to the government. Furthermore, this puts company's reputation in the market in peril due to the negative environmental footprint of her products. Therefore, new strategies have to be implemented to ensure the RSC effectiveness and to reduce the negative environmental impacts.

Against the current reactive approach in collecting unwanted medications, in this article, we propose a proactive approach. It involves offering incentives to customers to encourage them to return those medications that have high stock levels and less demand before their expiry date. By involving customers in the recovery process, medications could be collected in a sufficient time to expiry date. Hence, they could be donated or sold in subsidiary markets. The idea is to have more efficient and

sustainable RSC by involving customers in the recovery process [43]. In other words, these alternative reduces the risk of medical traces in groundwater by decreasing the quantity of medications that are landfilled while ensuring humanitarian aid. Besides, producers can earn revenue by selling the unexpired medications in subsidiary markets and benefit from tax deductions after donating them to developing countries.

To achieve this, we propose two coordination schemes between the pharmaceutical producer, the 3PL companies, and the customers. They have been modeled by the aid of nonlinear mathematical programming to reflect the decision-making process of the pharmaceutical RSC under study. While the first model is mainly focused on producer-customer coordination, the second one incorporates a negotiation mechanism to the first model in order to motivate 3PL companies to collect the total amount of leftover medications at customer zones. Finally, in order to reward the 3PL coordination efforts, we propose a procedure for sharing the expected savings in the enhanced RSC. To the best of our knowledge, this study is the first contribution to the literature that develops a coordination mechanism among all entities of RSC (i.e., customer, producer, and 3PL companies) in the pharmaceutical industry.

Our experimental results on a real case study reveal the importance of ensuring customers' coordination in increasing the return volume up to 6.5% while creating extra revenue/tax deduction for the producer. Furthermore, by implementing the proposed negotiation mechanism with 3PL companies, all leftovers can be collected at customer zones, hence no more penalties will be paid to the government. The cost of such coordination for the company would incorporate the incentive paid to customers, increased collection fees, as well as a portion of the savings that would have to be paid to 3PL companies. In return, adopting sustainable practices, such as the safe disposal of expired medications and regulated redistribution of unexpired ones to developing countries, is expected to improve the company's image in the

market. Furthermore, the proposed producer-customer coordination has financial benefits for the producer as opposed to the current practice where the disposal of expired medications has no cash return.

This paper is structured as follows. A brief summary of the literature related to RSC coordination is given in section 3.3. In section 3.4, the description of the case study context and two different coordination models are proposed. Numerical results for each model are presented in 3.5. Finally, concluding remarks and future recommendations are provided in section 3.6.

3.3 Literature Review

With the imposed environmental regulations, a stream of research has been focused on involving the recovery process in supply chain practices [17]. For example, detailed reviews on RSC models can be found in [15, 16]. Knowing that supply chains inherently involve multiple independent decision-makers, profitable solutions for every member are complicated and seldom to be obtained unless a proper coordination mechanism is utilized. A coordination mechanism can be used to conquer the anti-trust problems, loss of control, the uncertainty about local policies, the variability of a returned product quality, etc [27].

Camarinha-Motas et al. [26] reviewed the key concepts, classifications, and some applications related to supply chain coordination. Kanda et al. [40] presented a holistic review of the available literature prior to 2008 on the supply chain coordination. According to the authors, coordination mechanisms for supply chains can be achieved through (1) supply chain contracts, (2) information technology, (3) information sharing, or (4) joint decision making. Many papers in the available literature on coordination mechanisms deal with forward supply chains and focus on coordinative contracts, such as revenue-sharing [8, 12, 44], buyback contracts [45], and quantity

discounts [33]. In particular, if we look at the revenue-sharing techniques investigated, Cachon and Lariviere [44] studied the effect of revenue-sharing on the supply chain performance. They highlighted the limitations of revenue-sharing contract, such as the administrative burden it imposes on supply chain entities. Cao et al. [46] implemented a revenue-sharing contract to coordinate a decentralized supply chain for one manufacturer and multiple retailers. Giannoccaro and Pontrandolfo [12] proposed another revenue-sharing contract to coordinate a three-stage model. By tuning the contract parameters, they could achieve supply chain's efficiency and improve the profits of all the entities. Recently, Du et al. [47] studied a two-echelon supply chain coordinated by a credit payment and a wholesale price discount offer. Their results lead to the determination of the retail price and the quantity to order by a buyer, as well as the wholesale discount for the supplier.

A part of the literature also considers negotiation as a coordination method. For example, Dudek and Stadtler [30, 31] proposed negotiation models for two independent supply chain partners. Their results stated that using coordinative mechanisms could improve the overall performance of a forward supply chain. Jung et al. [29] proposed a negotiation process for a distributor and a manufacturer. The coordination was directed by the distributor. They aimed at finding a feasible plan for supply quantities from the manufacturer to the distributor with a minimum amount of information revelation to partners.

As aforementioned, the coordination in RSC is troublesome due to the uncertain quality of the returns, the associated costs, the volume of returns, etc [15]. Therefore, the relevant literature on coordination in RSC is very recent and limited to few of the coordination mechanisms already implemented for the forward supply chains, such as revenue-sharing contracts.

Due to the profitability of recovery practices in electronics industry, the majority

of articles on RSC coordination are focused on this industry. Very recently, Govindan and Popiuc [42] investigated two and three-echelon RSCs for the personal computer industry. They coordinated the network through the implementation of revenue-sharing contracts. Moreover, the authors suggested discounts to the RSC customers to return obsolete units. Their results stated that RSC performance and total profit could be improved through revenue-sharing and customer incentives contracts. Kulshreshthaa and Sarangib [48] investigated the effect of offering deposit-refund scheme to promote the return and reuse of product packages. The refund is deducted from a deposit that is added to the price of the product and is known at the time of purchase. More precisely, the company chooses a price for a product and offers a refund for the same product at the time of purchasing. Walther et al. [37] developed a decentralized negotiation model to enable allocating product recovery tasks to recycling companies in the electronic industry. Their negotiation model enables the generation of contracts between the RSC entities which consist of masses to collect and recycle, as well as transfer prices to pay.

In contrary, due to the particularities of the pharmaceutical RSC, such as the null salvage value of medication recovery and the associated costs, the available literature on this RSC is mainly limited to theoretical frameworks for such supply chains. For example, Kumar et al. [10] proposed a framework to state each party's responsibility in the pharmaceutical RSC. Xie and Breen [7] designed a green pharmaceutical supply chain model to reduce preventable pharmaceutical waste. The study revealed that the RSC practices are hard to implement in the pharmaceutical industry since returned medications cannot be reused or resold.

Lately, Weraikat et al. [49] proposed a negotiation mechanism in order to coordinate the recovery process between a producer and 3PL companies in the pharmaceutical RSC. They also proposed a mechanism for sharing the savings of such

coordination among RSC entities. However, their approach is based on the current situation of the industry where all leftover medications are remained at customer zones to expire. Therefore, in this article, we propose involving customers in the coordination process of the RSC and encouraging them to participate in the process. By including customers in the recovery process, the producer could collect more of the unexpired medications, then donate or sell them in subsidiary markets.

3.4 Pharmaceutical RSC coordination models

In this section, we first provide a brief description of the current RSC structure in the pharmaceutical company under discussion, *Generic PharmaX*; then we provide the producer-customer and producer-customer-3PL coordination models developed for better coordinating the RSC and ensuring full medication recovery.

As aforementioned, hospitals and pharmacies keep the medications to expire at their sites, then they inform the producer about the quantities available. Since the collecting process is not one of the core functions for *Generic PharmaX*, she contracts with 3PL companies to pick up the leftover medications at customer zones. In turn, 3PL companies send the medications to the governmental disposal sites. Consequently, the producer needs to pay fees to the government for the disposed medications. Moreover, she is obligated to pay penalties for uncollected medications at customer zones. Figure 4 visualizes the current RSC practices in *Generic PharmaX*.

3.4.1 Producer-customer coordination scheme

According to *Generic PharmaX*, there are always some amounts of medication at customer zones that are at risk of being expired due to low demand. If such medications are collected at a sufficient time before the expiry date, they can be resold in

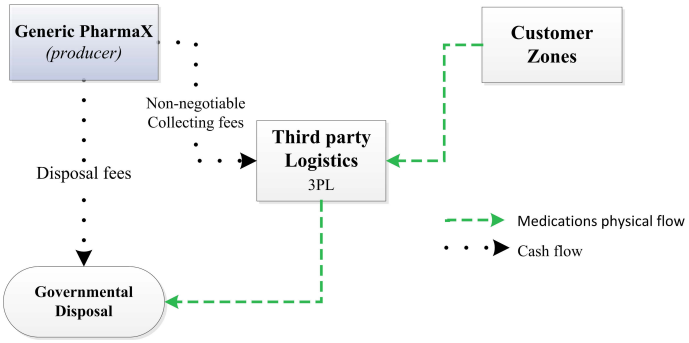

Figure 4: The current RSC of *Generic PharmaX*

subsidiary markets or be donated. In the latter case, the producer can benefit from tax deductions while the former option creates revenue for the company.

In the first coordination model, we suggest to pay incentives to customers in order to encourage them to collaborate and to return unwanted medications that have not yet reached their expiry dates. The suggested incentives are offered with respect to shelf-life of the collected medications. The following categories are considered for classifying the unwanted medications:

1. **Category A** represents the medications that have a shelf-life of two years or more. The producer can resell these medications in a subsidiary market at a selling price less than the price of a new medication;
2. **Category B** represents the medications that have less than two years and more than a year shelf-life. The producer can donate these medications to developing countries and hence, benefit from tax deductions;
3. **Category C** represents medications with the expiry date of less than or equal to one year from the collecting date. In this case, the medication is safely disposed at one of the governmental sites.

Knowing that there are always chances to use the unexpired medications, it is a recondite judgment for customers to think about these medications as unwanted products.

Hence, customers might be averse to give back the medications that are from categories A and B. Therefore, to reflect the reality, we introduce customer willingnesses to return medications from these two categories. We define customer willingness as the ratio of the incentive that the producer offers to customers over an incentive threshold (denoted as d^{max}) that is imposed by the customer. If the producer could provide that threshold, the customers would return the total available amounts of that category, i.e., the customer willingness to return would be 1. It is noteworthy that many factors affect the value of the customer incentive threshold such as the criticality of that medication, its price, and the demand. Nonetheless, the producer cannot pay incentives to customers greater than products prices in subsidiary markets for medications in category A or the amounts of tax deduction for returning medications in category B. Hence, customer willingness will always take a value less than or equal to 1. On the other hand, sorting and keeping track of the unexpired medications involve extra cost for the customers. Therefore, they request a minimum value for the incentives offered in order to collaborate and return part of such medications. This lower bound is denoted as d^{min} for both categories.

The proposed producer-customer coordination model is shown in figure 5. The figure illustrates that the producer offers incentives to customers for medications in categories A and B. Furthermore, the producer contracts with the 3PL companies to collect the medications, where collecting fees are non-negotiable. The 3PL companies collect and sort the medications with respect to expiry-dates. Medications from category C are sent directly to governmental disposal sites, where the rest of the medications are sent to the producer. The producer sells medications of category A in subsidiary markets and donates the medications from category B to some developing countries.

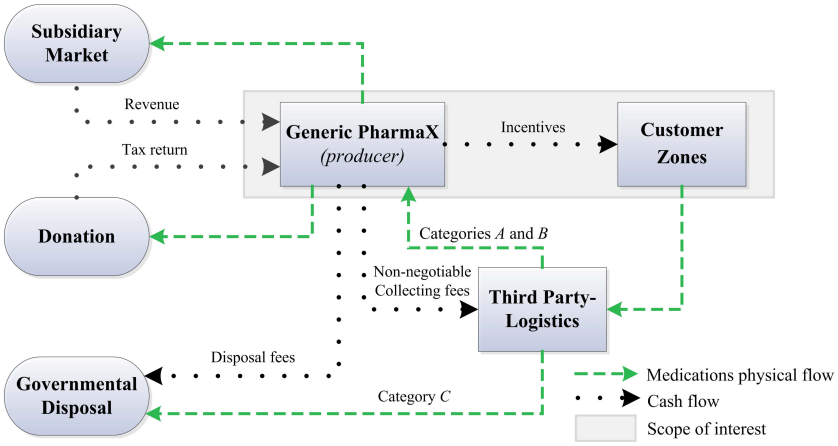

Figure 5: A producer-customer coordination RSC

Producer-customer coordination model

In what follows, we provide the nonlinear mathematical programming model proposed in this article, in order to formulate the producer-customer coordination scheme in the pharmaceutical RSC under discussion.

Notations

Index sets:

i: index of medications, $i \in I$;

k: index of customers, $k \in K$;

j: index of 3PL companies, $j \in J$;

The producers' parameters:

P_i: the selling price of a medication type i at a subsidiary market ($);

TX_i: the monetary deductive value from the producer's tax if she donates a unit of medication type i ($);

CD_i: the obligatory disposal fees by governments for each unit of medication type i sent to governmental disposal sinks ($);

M_i: the transportation cost of shipping a unit of medication type i to a subsidiary market ($);

α: the available percentage of medications in category A;

β: the available percentage of medications in category B;

γ: the available percentage of medications in category C;

ϕ_i: the penalties enforced by governments for each unit of uncollected medication type i ($);

A_{ik}: total mass of medication type i that is potentially available to be collected at customer zone k;

The customers' parameters:

dm_i^{max}: the threshold of incentive that a customer requests in order to return all of the medication type i in category A ($);

dd_i^{max}: the threshold of incentive that a customer requests in order to return all of the medication type i in category B ($);

dm_i^{min}: the minimum incentive a customer requests in order to collaborate and return a medication type i in category A ($);

dd_i^{min}: the minimum incentive customers requests in order to collaborate and return a medication type i in category B ($);

The 3PL companies' parameters

S_{ij}: collecting and sorting costs incurred by 3PL company j for each unit of medication type i ($);

TS_{ij}: unit transportation cost of medication type i from 3PL company j to safe disposal sites ($);

TC_{ij}: unit transportation cost of medication type i from 3PL company j to the producer ($);

D_j: collecting and sorting capacity of 3PL company j ($)

Decision variables:

dm_i: the incentive the producer offers to customers for returned medication type i in

category A ($);

dd_i: the incentive the producer offers to customers for returned medication type i in category B ($);

Qm_{ikj}: the collected amount of medications type i from category A by 3PL company j at customer zone k;

Qd_{ikj}: the collected amount of medications type i from category B by 3PL company j at customer zone k;

Qs_{ikj}: the collected amount of medications type i from category C by 3PL company j at customer zone k;

$QE_{M_{ik}}$: the uncollected amount of medications type i from category A at customer zones k;

$QE_{D_{ik}}$: the uncollected amount of medications type i from category B at customer zones k;

$QE_{S_{ik}}$: the uncollected amount of medications type i from category C at customer zones k;

ω_{m_i}: customers' willingness to return medications of type i from category A expressed as ratio of the incentive value offered by the producer to the customer incentive thresholds ($\omega_{m_i} = dm_i/dm_i^{max}$, where $0 \leq \omega_{m_i} \leq 1$);

ω_{d_i}: customers' willingness to return medications of type i from category B expressed as ratio of the incentive value offered by the producer to the customer incentive thresholds ($\omega_{d_i} = dd_i/dd_i^{max}$, where $0 \leq \omega_{d_i} \leq 1$).

The nonlinear mathematical model that represents the producer-customer coordination scheme is provided in equations (24)-(35) as follows.

The objective function is shown in equation (24). It represents the profit of the RSC determined as the revenues minus the costs and denoted as Z_{RSC}. The revenue involves the revenue of selling the returned medications at subsidiary markets and

the monetary tax deduction after donating collected medications. The costs include the disposal fees paid to the government, the transportation cost to the subsidiary market, the incentives paid to customers, the penalties paid to the government for the uncollected amounts of categories B and C, the collecting and sorting costs, transportation costs to the governmental disposal, and transportation costs to the producer.

$$
\begin{aligned}
Maximize\ Z_{RSC} = & \sum_{i\in I}\sum_{j\in J}\sum_{k\in K} P_i.Qm_{ikj} + \sum_{i\in I}\sum_{j\in J}\sum_{k\in K} TX_i.Qd_{ikj} \\
& - \sum_{i\in I}\sum_{j\in J}\sum_{k\in K} CD_i.Qs_{ikj} - \sum_{i\in I}\sum_{j\in J}\sum_{k\in K} M_i.(Qm_{ikj} + Qd_{ikj}) - \sum_{i\in I}\sum_{j\in J}\sum_{k\in K} dm_i.Qm_{ikj} \\
& - \sum_{i\in I}\sum_{j\in J}\sum_{k\in K} dd_i.Qd_{ikj} - \sum_{i\in I}\sum_{k\in K} \phi_i * (QE_{D_{ik}} + QE_{S_{ik}}) - \sum_{i\in I}\sum_{j\in J}\sum_{k\in K} S_{ij}.(Qm_{ikj} \\
& + Qs_{ikj} + Qd_{ikj}) - \sum_{i\in I}\sum_{j\in J}\sum_{k\in K} TS_{ij}.Qs_{ikj} - \sum_{i\in I}\sum_{j\in J}\sum_{k\in K} TC_{ij}.(Qm_{ikj} + Qd_{ikj})
\end{aligned}
\tag{24}
$$

The objective function is constrained by the amounts of medications that are potentially available at customer zones to be collected. The available amounts at customer zones incorporate medications from all categories (equation 25).

$$
A_{ik} = \sum_{j\in J}(Qm_{ikj} + Qd_{ikj} + Qs_{ikj}) + QE_{M_{ik}} + QE_{D_{ik}} + QE_{S_{ik}}, \quad \forall i \in I, \forall k \in K \tag{25}
$$

As mentioned earlier, the quantities of collected medications from category A are affected by the willingness of customers to collaborate and by the available amounts from that category (constraint 26). Moreover, medications from the same category

are either collected or uncollected as depicted in constraint (27).

$$\sum_{j \in J} Qm_{ikj} \leq \omega_{m_i}.\alpha.A_{ik}, \quad \forall i \in I, \quad \forall k \in K \tag{26}$$

$$\alpha.A_{ik} = \sum_{j \in J} Qm_{ikj} + QE_{M_{ik}}, \quad \forall i \in I, \quad \forall k \in K \tag{27}$$

By the same token, the collected medications from category B are affected by the willingness of customers to collaborate and by the available amounts from that category (constraint 28). Constraint (29) reflects the fact that the available amounts from category B can be collected or uncollected.

$$\sum_{j \in J} Qd_{ikj} \leq \omega_{d_i}.\beta.A_{ik}, \quad \forall i \in I, \quad \forall k \in K \tag{28}$$

$$\beta.A_{ik} = \sum_{j \in J} Qd_{ikj} + QE_{D_{ik}}, \quad \forall i \in I, \quad \forall k \in K \tag{29}$$

For category C medications, constraint (30) expresses the fact that the collected amounts from this category cannot exceed the available medications from the same category. Constraint (31) reflects possible options for the available amounts from category C, i.e., to be collected or uncollected.

$$\sum_{j \in J} Qs_{ikj} \leq \gamma.A_{ik}, \qquad \forall i \in I, \quad \forall k \in K \tag{30}$$

$$\gamma.A_{ik} = \sum_{j \in J} QS_{ikj} + QE_{S_{ik}}, \qquad \forall i \in I, \quad \forall k \in K \tag{31}$$

The customer incentive thresholds for the medications from categories A and B are given in constraints (32) and (33).

$$dm_i^{min} \leq dm_i \leq dm_i^{max}, \quad \forall i \in I \tag{32}$$

$$dd_i^{min} \leq dd_i \leq dd_i^{max}, \quad \forall i \in I \tag{33}$$

Constraint (34) indicates that the collected medications from all categories by each 3PL company cannot exceed its capacity.

$$\sum_{i \in I} \sum_{k \in K} S_{ij}.(Qm_{ikj} + Qs_{ikj} + Qd_{ikj}) \leq D_j, \quad \forall j \in J \tag{34}$$

Finally, domain constraints are provided in (35).

$$dm_i, dd_i, Qm_{ikj}, Qd_{ikj}, Qs_{ikj}, QE_{M_{ik}}, QE_{D_{ik}}, QE_{S_{ik}} \geq 0, \quad \forall j \in J \tag{35}$$

3.4.2 Producer-customer-3PL coordination scheme

In the producer-customer coordination scheme, provided in 3.4.1, offering incentives to customers might be enough to motivate them to inform the producer regarding the amounts of available unwanted/unexpired medications. However, it does not necessarily guarantee the complete collection of such leftovers by 3PL companies due to the non-negotiable collecting fees offered by the producer. In order to solve this issue, a negotiation mechanism between the producer and 3PL companies is proposed.

Figure 6 visualizes the producer-customer-3PL coordination scheme. In order to motivate the 3PL companies to collect all of the available leftover medications at customer zones, we propose that the producer negotiates with the 3PL companies over

contracts' parameters, i.e., collecting fees offered by the producer and the quantities that must be collected by 3PL companies. Once the producer and 3PL companies reach to a contract all agree on, the 3PL companies pick up the medications from the three different categories.

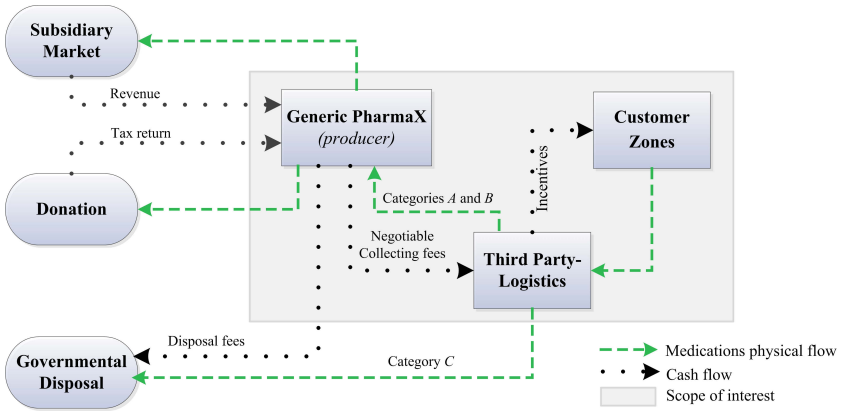

Figure 6: Producer-customer-3PL coordination RSC

This negotiation mechanism is summarized in figure 7. The producer leads the negotiation process and offers collecting fees to 3PL companies. We assume that the producer delegates the responsibility of offering incentives to customers to 3PLs. In other words, part of the collecting fees that are offered by the producer must be paid to customers as incentive in order to return medications from categories A and B. This assumption is essential in order to represent the proposed negotiation mechanism as a mathematical model. After receiving contract parameters, each 3PL company determines the incentive that must be offered to customers as well as the quantities that can be collected from all categories with respect to its capacity and profit margins. Afterwards, the producer will be informed regarding 3PLs decisions. It is evident that if the incentives offered to customers are not attractive enough, only part of medications from categories A and B might be returned to 3PLs. In turn, the producer checks the total amount collected from all 3PL companies. If not all of the available medications are collected, the producer will revise the contract parameters.

As summarized in figure 7, the offers and reactions are exchanged until both parties agreed upon customer incentives as well as collecting fees such that all available medications are collected by 3PL companies. In what follows, this negotiation process is mathematically represented by the aid of Lagrangian relaxation method.

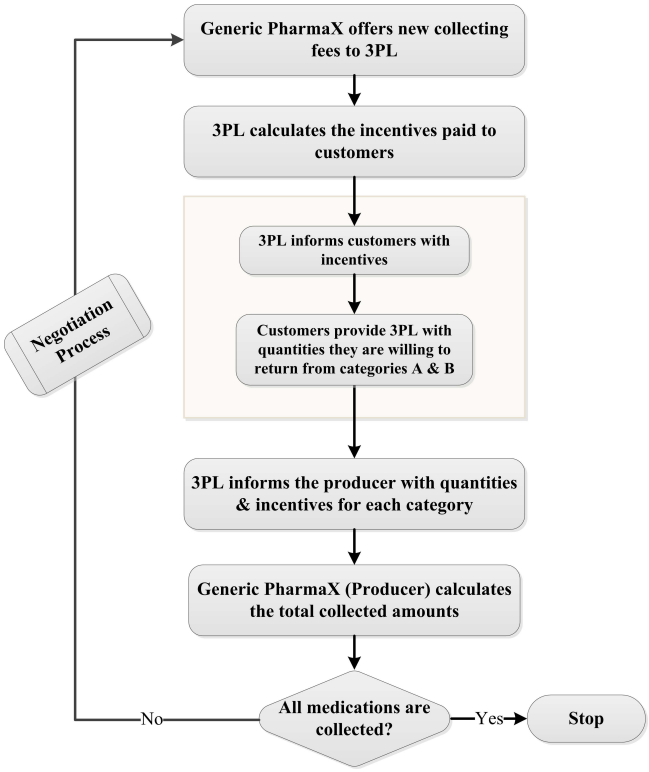

Figure 7: The negotiation approach in the RSC

Producer-customer-3PL coordination model

In order to mathematically represent the above mentioned negotiation process, the RSC coordination model (24)-(35) must be decomposed into "producer" and "3PLs" sub-models. Inspired by [49], this decomposition can be implemented by the aid of Lagrangian relaxation method [38, 39]. More specifically, by relaxing constraints (25) to (31) that link the producer decisions to 3PL ones from the model (24)-(35) and by penalizing their violation in the objective function with the aid of Lagrangian multipliers, we obtain a RSC model that only involves 3PLs information and decisions.

On the other hand, the producer will only need to verify the satisfaction of relaxed constraints (25)-(31) that correspond to the collection of all available medications at customer zones. In the case of violation of such constraints, penalties would be calculated and new collecting fees would be offered to 3PL companies accordingly. In what follows, we provide mathematical models corresponding to the producer-customer-3PL coordination scheme. In this negotiation model, the following notations are used in addition to those provided in section 3.4.1.

Producer-customer-3PL coordination model extra notations

π_{ik}^{m}: Lagrangian penalties corresponding to the uncollected mass unit of medication type i in category A at customer zones k ($);

π_{ik}^{d}: Lagrangian penalties corresponding to the uncollected mass unit of medication type i in category B at customer zones k ($);

π_{ik}^{s}: Lagrangian penalties corresponding to the uncollected mass unit of medication type i in category B at customer zones k ($);

ϵ_{ik}: collecting fees paid by the producer to 3PL companies to collect the medication type i in category A at customer zones k ($);

ζ_{ik}: collecting fees paid by the producer to 3PL companies to collect the medication type i in category B at customer zones k ($);

η_{ik}: collecting fees paid by the producer to 3PL companies to collect the medication type i in category C at customer zones k ($);

Z_C^{LR}: the objective function of the RSC Lagrangian relaxation model;

Z_{3PL}: the objective function of a 3PL company Lagrangian relaxation model.

As mentioned earlier, in order to extract the "3PLs" sub-models from model (24)-(35), we relax constraints (25) to (31) and penalize their violation in the objective

function with the Lagrangian multipliers (π^m_{ik}, π^d_{ik}, π^s_{ik}). Consequently, the RSC coordination model can be formulated as (36) subject to constraints (32) to (34).

$$
\begin{aligned}
Maximize\ Z^{LR}_C &= \sum_{i\in I}\sum_{j\in J}\sum_{k\in K}(P_i - M_i - dm_i - \pi^m_{ik} - S_{ij} - TC_{ij}).Qm_{ikj} \\
&+ \sum_{i\in I}\sum_{j\in J}\sum_{k\in K}(TX_i - M_i - dd_i + \phi_i - \pi^d_{ik} - S_{ij} - TC_{ij}).Qd_{ikj} \\
&+ \sum_{i\in I}\sum_{j\in J}\sum_{k\in K}(-CD_i + \phi_i - \pi^s_{ik} - S_{ij} - TS_{ij}).Qs_{ikj} + \sum_{i\in I}\sum_{k\in K}\pi^m_{ik}.\omega_{m_i}.\alpha A_{ik} \\
&- \sum_{i\in I}\sum_{k\in K}(\phi_i - \omega_{d_i}.\pi^d_{ik}).\beta A_{ik} - \sum_{i\in I}\sum_{k\in K}(\phi_i - \pi^c_{ik}).\gamma A_{ik} \qquad (36)
\end{aligned}
$$

After reformulating the objective function (equation (36)) and the replacement of (1) $P_i - M_i - \pi^m_{ik} = \epsilon_{ik}$, (2) $TX_i - M_i + \phi_i - \pi^d_{ik} = \zeta_{ik}$, and (3) $-CD_i - \phi_i - \pi^s_{ik} = \eta_{ik}$, we obtain model (37) with respect to constraints (32) to (34), which correspond to 3PL companies decision model.

$$
\begin{aligned}
Maximize\ Z^{LR}_C &= \sum_{i\in I}\sum_{j\in J}\sum_{k\in K}(\epsilon_{ik} - dm_i - S_{ij} - TC_{ij}).Qm_{ikj} + \sum_{i\in I}\sum_{j\in J}\sum_{k\in K}(\zeta_{ik} - dd_i \\
&- S_{ij} - TC_{ij}).Qd_{ikj} + \sum_{i\in I}\sum_{j\in J}\sum_{k\in K}(\eta_{ik} - S_{ij} - TS_{ij}).Qs_{ikj} + \sum_{i\in I}\sum_{k\in K}\pi^m_{ik}.\omega_{m_i}.\alpha A_{ik} \\
&- \sum_{i\in I}\sum_{k\in K}(\phi_i - \omega_{d_i}.\pi^d_{ik}).\beta A_{ik} - \sum_{i\in I}\sum_{k\in K}(\phi_i - \pi^c_{ik}).\gamma A_{ik} \qquad (37)
\end{aligned}
$$

Next, a separate model is extracted from (37) for each 3PL company, as shown in (38)-(42).

$$
\begin{aligned}
Maximize\ Z_{3PL} &= \sum_{i\in I}\sum_{k\in K}(\epsilon_{ik} - dm_i - S_{ij} - TC_{ij}).Qm_{ikj} + \sum_{i\in I}\sum_{k\in K}(\zeta_{ik} - dd_i - \\
&S_{ij} - TC_{ij}).Qd_{ikj} + \sum_{i\in I}\sum_{k\in K}(\eta_{ik} - S_{ij} - TS_{ij}).Qs_{ikj} \qquad (38)
\end{aligned}
$$

Subject to:

$$\sum_{i\in I}\sum_{k\in K} S_{ij}.(Qm_{ikj} + Qs_{ikj} + Qd_{ikj}) \leq D_j \tag{39}$$

$$dm_i^{min} \leq dm_i \leq dm_i^{max} \qquad \forall i \in I \tag{40}$$

$$dd_i^{min} \leq dd_i \leq dd_i^{max} \qquad \forall i \in I \tag{41}$$

$$Qm_{ikj}, Qd_{ikj}, Qs_{ikj}, dm_i, dd_i \geq 0 \tag{42}$$

The negotiation process starts with initializing contract parameters by the producer, i.e., the values of the Lagrangian multipliers (π_{ik}^m, π_{ik}^d, π_{ik}^s), as well as the values of the collecting fees (ϵ_{ik}, ζ_{ik}, η_{ik}). In addition to that, the producer informs the 3PL companies with these values. Each 3PL company solves model (38)-(42) and obtains the customers incentives for categories A and B. Next, the amounts of medications that can be collected and the incentives values that are offered to customers are presented to the producer. Afterwards, the producer checks constraints (25)-(31) to make sure that all available medications have been collected. If some leftovers are still uncollected, the producer revises those parameters and informs 3PL companies, as visualized in figure 7. This process is repeated until all medications are collected or constraints, i.e., (25)-(31) are satisfied.

As we are using a Lagrangian relaxation approach, a sub-gradient procedure is utilized in order to update contract parameters (Lagrangian multipliers). For example, in the RSC coordination model (Z_C^{LR}), let $\pi_{ik}^{m^t}$ be the value of π_{ik}^m at iteration t

and $\sum_{j\in J} Qm^t_{ikj}$ be the optimal value of $\sum_{j\in J} Qm_{ikj}$ at the same iteration. Then

$$g^t_{\pi^m_{ik}} = \sum_{j\in J} Qm^t_{ikj} - \omega_{m_i}.\alpha.A_{ik} \qquad \forall i \in I, \quad \forall k \in K \tag{43}$$

equation (43) represents the sub-gradient function of the corresponding relaxed constraint (constraint (26)) at $\pi^{m^t}_{ik}$. In other words, $g^t_{\pi^m_{ik}}$ is the violation of the relaxed constraint in iteration t. As long as the relaxed constraint is unsatisfied, the new Lagrangian multiplier (π^m_{ik}) is calculated as follows:

$$\pi^{m^{t+1}}_{ik} = max(0, \pi^{m^t}_{ik} + \mu_t.g^t_{\pi^m_{ik}}) \tag{44}$$

where μ_t is a positive scalar step size at iteration t and is calculated as $\mu_t = b/t||g||$, b is a scalar quantity and $||g||$ is the Euclidean norm of the sub-gradient function.

Finally, we add constraints (45)-(47) to each 3PL company model (38)-(42) in order to ensure that the maximum collected medication from each category is less than or equal to that maximum limit for each category.

$$Qm_{ikj} \leq Qm^{max}_{ikj} \quad \forall i, k, j \tag{45}$$

$$Qd_{ikj} \leq Qd^{max}_{ikj} \quad \forall i, k, j \tag{46}$$

$$Qs_{ikj} \leq Qs^{max}_{ikj} \quad \forall i, k, j \tag{47}$$

3.4.3 RSC coordination efforts reward methodology

In order to encourage the 3PL companies to invest in the negotiation process while supporting the coordination effort, the producer is willing to share the monetary savings from penalties used to be paid to government for uncollected medications at customer zones. Inspired by two recent articles [35, 49], sharing the savings is proposed based on the investment of RSC entities (i.e., the producer and 3PL companies) in the coordination model as follows.

1. Calculate the investment value (R) of the RSC entities in the negotiation model. This can be calculated as the difference between the profit value of each RSC entity in the producer-customer-3PL coordination model and the current situation.

2. Then, normalize the investment value (R) as follows:

$$R_{3PL}^{nor} = \frac{R_{3PL}}{R_{3PL} + R_{Producer}} \quad and \quad R_{Producer}^{nor} = \frac{R_{Producer}}{R_{3PL} + R_{Producer}}$$

3. Calculate the share of each RSC entity from the savings (S) as:

$$S_{3PL} = Saving.R_{3PL}^{nor} \quad and \quad S_{Producer} = Saving.R_{Producer}^{nor},$$

   where *Saving* represents penalties the producer could save if all the expired medications at customer zones are collected.

3.5 Numerical results and discussion

In the following, we extend the current RSC practices of *Generic PharmaX* to fit the models proposed in section 3.4. First, we describe the producer-customer coordination

model results. Second, the results for the producer-customer-3PL coordination models are presented. Afterwards, we compare the results of both models. Finally, the reward of coordination efforts is provided.

Parameters corresponding to the two proposed models such as different costs and fees were obtained through communication with the head of $GenericPharmaX$ supply chain department. After refining the data, four 3PL companies and four customers were selected among the largest collectors and customers. Twenty types of medications among the most important products were also selected from the producer records.

3.5.1 Producer-customer coordination model results

In this section, we provide the results of implementing the producer-customer coordination model on the case study described above. Also, we investigate the impact of the percentage of available medications from each category and the customer incentive thresholds on the performance of RSC by the aid of design of experiments (DOE) [50].

For this purpose, three factors were considered in the experimentation, i.e., (1) the percentage of available medications from each category at customer zones, (2) the customer incentive threshold for category A, and (3) the customer incentive threshold for category B. Moreover, the most important key performance indicators (response variables) for the producer incorporate the objective function value of model (48)-(62) (RSC profit), the amount of uncollected medications from category C, and the customer willingness values for categories A and B.

Factor level combinations in the designed experiments are depicted in figure 8. According to the producer, the most likely ratio for the available medications from each category at customer zones is (10:20:70), i.e., 10% of the available amounts

at customer zones are from category A, 20% are from category B, and 70% are from category C. The customer incentive thresholds are considered as 50%, 70%, 100% of the medication prices in secondary markets and tax deduction amounts for medications in categories A and B, respectively. The smallest incentive value required by the customers to inform the producer about the available medications in categories A and B (d^{min}) is considered as 20% of medication prices in subsidiary markets and tax deduction amounts. Afterwards, model (24)-(35) was solved (by $Cplex$) for 27

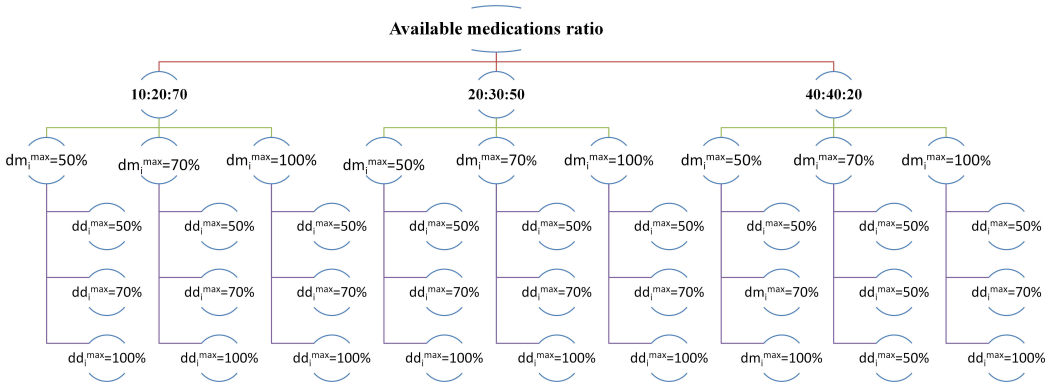

Figure 8: Factor level combinations for producer-customer coordination model

iterations and the results are provided in table 9.

Minitab 16 was used to analyze the relationships between percentages of available medication as well as the customer incentive thresholds and the RSC profit. The results reveal that the percentage of available medications from each category and the customer incentive threshold for category A have significant impact on the objective function value (profit). Also, the results display that the customer incentive threshold for category B has no significant impact on the profit (i.e., medications donated to developing countries). The reason can be due to small tax deduction amounts that the government is willing to offer to the producer for donating medications. Nevertheless, such humanitarian aids would improve the producer's image in the market. Same

Table 9: Some of the producer-customer coordination model results

d^{max}	**Category A= 50%**			Category A = **50%**			Category A =**50%**		
d^{max}	Category B = 50%			Category B = 70%			Category B = 100%		
AMR^*	**10:20:70**	**20:30:50**	**40:40:20**	**10:20:70**	**20:30:50**	**40:40:20**	**10:20:70**	**20:30:50**	**40:40:20**
Objective value ($)	**49,928.49**	**123,181.77**	**257,670.21**	**44,553.46**	**115,119.21**	**246,920.14**	**38,955.08**	**106,721.64**	**235,723.39**
QE_M (kg)	80.14	143.78	287.55	80.14	143.778	287.55	80.14	143.78	287.55
QE_D (kg)	0.00	0.00	0.00	164.26	246.39	328.51	1,242.83	1,864.24	2,485.66
QE_S (kg)	1,647.75	0.00	0.00	1,647.75	0.00	0.00	1,647.75	0.00	0.00
ω_m	0.97	0.97	0.97	0.97	0.97	0.97	0.97	0.97	0.97
ω_d	1.00	1.00	1.00	0.98	0.98	0.98	0.84	0.84	0.84
d^{max}	**Category A = 70%**			**Category A = 70%**			**Category A= 70%**		
d^{max}	Category B = 50%			Category B = 70%			Category B = 100%		
AMR^*	**10:20:70**	**20:30:50**	**40:40:20**	**10:20:70**	**20:30:50**	**40:40:20**	**10:20:70**	**20:30:50**	**40:40:20**
Objective value ($)	**32,309.30**	**87,653.25**	**186,613.18**	**26,934.26**	**79,590.69**	**175,863.11**	**21,335.89**	**71,193.13**	**164,666.36**
QE_M (kg)	744.67	1,477.56	2,955.11	744.67	1,477.56	2,955.11	744.67	1,477.56	2,955.11
QE_D (kg)	0.00	0.00	0.00	164.26	246.39	328.51	1,242.83	1,864.24	2,485.66
QE_S (kg)	1,577.52	0.00	0.00	1,577.52	0.00	0.00	1,577.52	0.00	0.00
ω_m	0.70	0.70	0.70	0.69	0.69	0.70	0.69	0.70	0.70
ω_d	1.00	1.00	1.00	0.97	0.97	0.97	0.84	0.84	0.84
d^{max}	**Category A = 100%**			**Category A = 100%**			**Category A = 100%**		
d^{max}	Category B = 50%			Category B = 70%			Category B = 100%		
AMR^*	**10:20:70**	**20:30:50**	**40:40:20**	**10:20:70**	**20:30:50**	**40:40:20**	**10:20:70**	**20:30:50**	**40:40:20**
Objective value ($)	**19,094.73**	**61,006.87**	**133,320.41**	**13,719.69**	**52,944.31**	**122,570.33**	**8,121.32**	**44,546.74**	**111,373.58**
QE_M (kg)	1,242.98	2,477.89	4,955.78	1,242.98	2,477.89	4,955.78	1,242.98	2,477.89	4,955.78
QE_D (kg)	0.00	0.00	0.00	164.26	246.39	328.51	1,242.83	1,864.24	2,485.66
QE_S (kg)	1,524.77	0.00	0.00	1,524.77	0.00	0.00	1,524.77	0.00	0.00
ω_m	0.49	0.49	0.49	0.49	0.49	0.49	0.49	0.49	0.49
ω_d	1.00	1.00	1.00	0.97	0.97	0.97	0.84	0.84	0.84

AMR^*: Available Medication Ratio

results were obtained from the main effect plot, as shown in figure 9. Moreover, from the interaction analysis between factors, we conclude that for a low level medication ratio of category A (i.e., 10%), there is a slight negative effect of the customer incentive threshold on the profit.

We first discuss the impact of medication ratio and customer incentive thresholds on the RSC profit. As it can be observed in table 9, the profit, as the first response in the analysis, increases when the percentage of available medications from category C decreases (i.e., medications safely disposed at government sites). For example, considering the case of 50% for customer incentive thresholds, when 20% of available medications are from category C, the objective function value is higher than the case where the percentage is 50% or 70% for the same category. This is mainly due to negligible salvage value of returned medications in category C. In contrary, since returned medications in category A can be sold at subsidiary markets, higher percentages of category A increases the RSC profit. On the other hand, our results reveal that the

customer incentive threshold of medications in category A has a negative impact on profit. The reason is that higher incentive thresholds indicates customer reluctance in returning medications. Hence, the producer needs to increase the incentives offered to customers in order to increase their willingness to return such medications. The latter has a negative impact on the profitability of the RSC.

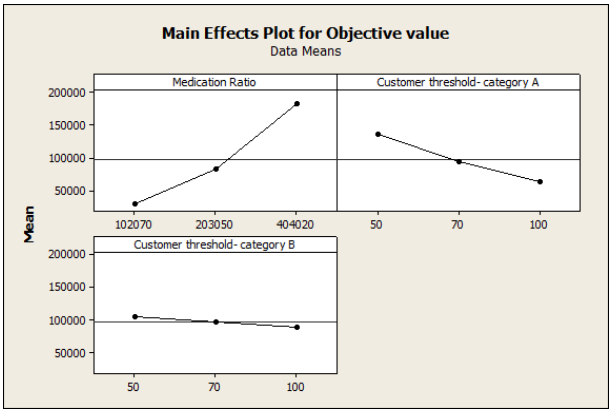

Figure 9: The main effects plot for the objective function- *Minitab*

Next, we look at the impact of the aforementioned factors on the amount of the uncollected medication from category C, $QE_{S_{ik}}$. Considering the most realistic case for percentage of available medications (i.e., 10:20:70), it can be said that regardless the customer incentive threshold, the available medications from category C are not completely collected, i.e., $QE_s \neq 0$. In other words, introducing customer incentives is not enough to ensure a full recovery when the majority of the available medications are from category C, as also highlighted in table 9. In contrary, the offered incentives have been adequate for the recovery of all medications for the other percentages of available medications (i.e., 20:30:50 and 40:40:20). However, knowing that the current average total uncollected amounts is equal to $4,292$ units, it can be said that introducing customer incentives could reduce that amount by up to $1,524.77$ units, i.e., 11.5% reduction. Hence it can be concluded that the percentage of available medications from each category has a negative significant impact on the uncollected medications from category C. However, the customer incentive threshold for category A has a

slight significant impact on the uncollected medications from category C. This comes at no surprise, since the recovery process is less profitable in the presence of higher amounts of medications in category C no matter the value of customer willingness to return medications in category A is. Moreover, the results state that the customer incentive threshold for category B is insignificant, as shown in figure 10.

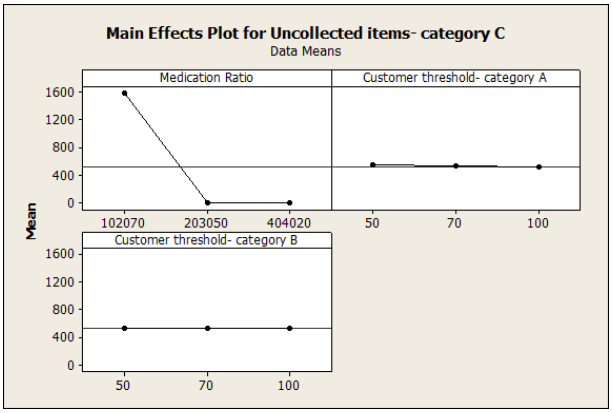

Figure 10: The main effects plot for the uncollected medication in category C- *Minitab*

Finally, we analyze the impact of medication ratio and incentive thresholds on customer willingness on returning those medications. As it can be observed in table 9, increasing the customer incentive thresholds has a negative impact on the willingness values and on the uncollected medications from different categories. This means that the producer is not willing to offer incentives more than certain limits to make the RSC more profitable. Recall that the customer willingness is $\omega = d/d^{max}$, where d is the incentives offered by the producer and d^{max} is the customer threshold. For example, consider the case of 50% customer incentives, the average willingness of category A is about 0.97 and 1.00 for category B. In other words, the producer is willing to pay this threshold (which is equal to 50% of medication prices in subsidiary markets). On the other hand, raising the customer incentive thresholds of category A to 100% results in willingness values of 0.49 for the same category. This is because the producer is not willing to pay more than 50% of the medications prices as incentives. Furthermore, the uncollected amounts from categories A and B are higher when the

willingness values decreases, as illustrated in table 9.

3.5.2 Producer-customer-3PL coordination model results

As demonstrated in section 3.5.1, introducing incentives to customers per se is not enough to ensure complete collection of medications at customer zones. This is more obvious when the majority of those medications are from category C, as shown in table 9. The producer has to motivate the 3PL companies to go and pick up the medications at customer zones. Because the current collecting fees are imposed by the producer, the 3PL companies could be willing to collect more medications if the collecting fees would rather reflect their effort.

Therefore, the negotiation model proposed in section 3.4.2 is implemented to optimize the collecting fees as well as the amounts of collected medications by 3PL companies. In this section, we consider the most realistic ratio of available medications (i. e. $10 : 20 : 70$) for the producer-customer-3PL coordination model. Figure 11 demonstrates factor level combinations used to validate the producer-customer-3PL coordination model.

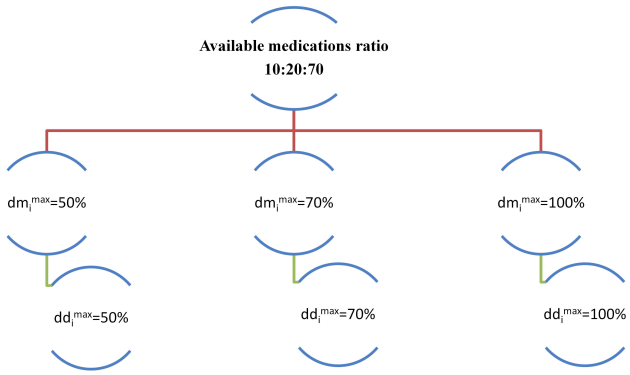

Figure 11: Factor level combinations for for producer-customer-3PL coordination model

We first investigate the impact of customer incentive threshold on the 3PLs' profit. As it can be observed in table 10, higher customer incentive thresholds decreases the 3PL companies profits. The reason is that in the case of high incentive threshold, it is not profitable for 3PL companies to offer incentives close to that threshold. Hence, the amount of returned medications in category A would decrease due to lower customer willingness (table 10). Also, the third 3PL company could gain the best profit in all

Table 10: Some of the producer-customer-3PL coordination model results

d^{max} d^{max}	**Category A= 50%** Category B = 50%	**Category A = 70%** Category B = 70%	**Category A =100%** Category B = 100%
3PL 1 Objective value ($)	**46,367**	**44,173**	**42,568**
3PL 2 Objective value ($)	**52,505**	**54,282**	**50,426**
3PL 3 Objective value ($)	**68,807**	**68,366**	**63,414**
3PL 4 Objective value ($)	**58,689**	**60,076**	**58,387**
QE_M (kg)	0	0	0
QE_D (kg)	0	0	0
QE_S (kg)	0	0	0
ω_m	0.20	0.20	0.20
ω_d	0.40	0.40	0.20

cases. The reason can be due to high collecting capacity as well as low transportation cost of this company.

Finally, we analyze the impact of incentive threshold on customer willingness. As depicted in table 10, although in this coordination scheme, customer willingness to return medications in categories A and B is reduced comparing to the former coordination model (section 3.5.1), our results indicate that all available medications that the customer is willing to returns are collected by 3PL companies. Hence, in this case the producer would avoid paying penalties to government for uncollected leftover medications at customer zones.

3.5.3 Comparison between producer-customer and producer-customer-3PL models

According to the case data, *Generic PharmaX* currently fails to collect 18% of leftover medications at customer zones. Hence, she incurs legislative penalties. As our results indicate, by introducing customer incentives, the uncollected medications could be reduced up to 6.5%. Moreover, implementing the negotiation approach between the producer and 3PL companies, in addition to the customer incentives, lessens the percentage of the uncollected amounts to zero.

Table 11 summarizes the results for the percentage of uncollected medications as well as the RSC profit at the percentage of 10:20:70 over all categories and the worst case regarding customer willingness to return medications in categories A and B (i.e., 100%). The results for the other customer incentive thresholds are provided in the *Appendix*. As stated earlier, proposing customer incentives reduces the penalties paid for the uncollected medications. Yet, the incentives could not assure a complete leftover medication recovery. With the aid of the negotiation process proposed in section 3.4.2, not only the penalty could be eliminated, but also the overall RSC profit (equation 36) could be increased.

Table 11: The averages of the uncollected medications and penalties for each model

Coordination Model	Customer incentives	Producer-3PL negotiation	Average percentage of uncollected medications	RSC objective function ($1000)	Penalties ($1000)
Current situation	×	×	18%	-	93,000
Producer-customer *	✓	×	6.5%	8,121.32	9,991
Producer-customer-3PL *	✓	✓	0%	102,431.02	0

* The given values are for the case of 10:20:70 at 100% customer incentive thresholds for categories A and B

To implement the negotiation process, collaboration efforts are required from 3PL companies. Therefore, in the following section we present a technique to reward their efforts with respect to their investment in the customer-producer-3PL coordination scheme.

3.5.4 Sharing RSC coordination savings

The producer-customer-3PL coordination model for the customer incentive threshold of 100% enhances the profit of each 3PL company, as shown in table 12. The results for the other customer incentive thresholds are visualized in figure 12 and figure 13. At the same time, the producer could avoid huge penalties paid to governments by collecting all leftover medications at customer zones. Nevertheless, the 3PL companies have to invest time and efforts in the negotiation process. Therefore, the *Generic PharmaX* is willing to share a part of the expected savings with the 3PL companies.

Table 12: Profit improvement with producer-customer-3PL coordination model (in $1,000)

	Producer-customer-3PL coordination*	Current situation	The difference
3PL 1	42,568.21	39,842.57	2,725.57
3PL 2	50,426.21	47,200.82	3,225.39
3PL 3	63,414.32	58,590.18	4,824.14
3PL 4	58,387.44	52,379.16	6,008.28
Producer	-9,967.10	-17,915.13	7,948.03

* The given values are for the case of 10:20:70 at 100% customer incentive thresholds for categories A and B

Using the technique proposed in section 3.4.3, figures 12 and 13 visualize the expected share of the savings between the producer and 3PL companies considering different customer incentive thresholds of categories A and B. For example, the corresponding results to 50%-50% represent the RSC entities saving shares for the case of 50% customer incentive thresholds for categories A and B, respectively. It can be seen that the expected share of the savings for each 3PL company varies with respect to its capacity to collect the available medications at customer zones. The highest saving shares for 3PL companies are obtained at 70% customer incentive thresholds for categories A and B.

On the other hand, the best expected share for the producer is when the customer incentive thresholds are set at 50% for both categories A and B. In this case, the collecting fees paid by the producer to 3PL companies are higher than the customer

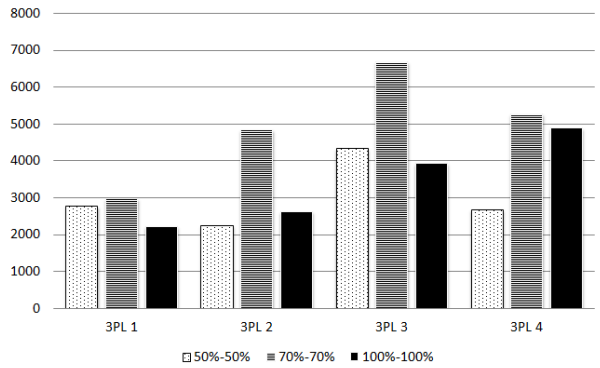

Figure 12: Saving shares for 3PL companies at different customer incentive thresholds ($1,000)

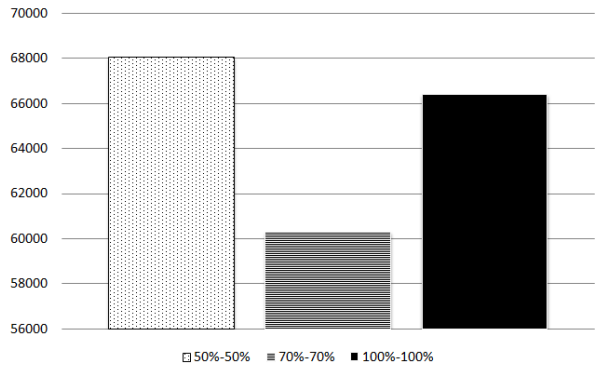

Figure 13: Saving shares for the producer at different customer incentive thresholds ($1,000)

incentives paid by 3PL companies to customers for returning medications in category A.

To conclude, in one hand, 3PL companies would gain the maximum saving shares when the customer incentive thresholds are set at 70% for both categories A and B. In other words, 3PL companies need to negotiate with the customers for those thresholds to obtain higher saving shares. On the other hand, the producer would gain more saving shares when the customer incentive thresholds are set at 50%. However, any threshold value could improve the producer sustainable image, in the sense that she would not have to pay penalties to the government for uncollected medications at customer zones.

3.6 Conclusion

Governments' regulation on the pharmaceutical industry and customers attention to sustainable practices all play a crucial role in changing the RSC practices in this industry. Hence, pharmaceutical companies have to be proactive in addressing the growing needs for improving their RSC performance.

This article proposed analytical models to support its objectives related to improving RSC performance in this industry. First, an analytical model based on customer incentives was proposed to encourage the RSC customers to return unexpired medications. Second, another model was proposed to motivate 3PL companies and customers to collaborate in the recovery process. Finally, the proposed models were implemented for the real pharmaceutical company, *Generic PharmaX*.

The results demonstrated the improvement of the collected amounts of medications by introducing incentives to customers. Furthermore, by implementing the negotiation model between the producer and 3PL companies, in addition to customers incentives, all the available medications are collected. Knowing that the negotiation process requires the commitment of RSC entities, such as cost and time investment, a technique for sharing the savings was also provided to reward the investment of the RSC entities.

This study is the first to direct attention for involving customers in the recovery process of the pharmaceutical products. With providing incentives, customers are motivated to return medications prior to their expiry dates. Hence, the producer can resell or donate the returned medications in subsidiary markets and gain monetary profits. In addition to the financial benefits, the producer would be step ahead of her competitors in implementing sustainable RSC practices. In particular, selling the medications instead of disposing them reduces the environmental harmful incineration process.

Future research would investigate the role of implementing a vendor-managed inventory system at customer zones (i.e., hospitals and pharmacies) on reducing the amount of effort required for collection and disposition of leftover medications. The idea is to reduce the amount of medications that reach their expiry dates. Cost/benefit implication of this coordination mechanism in addition to efforts required by supply chain entities in pharmaceutical industry would be worth being investigated.

3.7 Acknowledgment

The authors would like to thank the Fonds de Recherche du Québec - Nature et Technologies (FRQNT) for the financial support in this research project.

3.8 Appendix

Table 13: The averages of the uncollected medications and penalties for each model-customer incentive threshold = 50% for categories A and B

Coordination Model	Customer incentives	Producer-3PL negotiation	Average percentage of uncollected medications	RSC objective function ($1000)	Penalties ($1000)
Current situation	×	×	18%	-	93,000
Producer-customer	✓	×	6.8%	49,928.49	5,861.8
Producer-customer-3PL	✓	✓	0%	117,383.80	0

Table 14: The averages of the uncollected medications and penalties for each model-customer incentive threshold = 70% for categories A and B

Coordination Model	Customer incentives	Producer-3PL negotiation	Average percentage of uncollected medications	RSC objective function ($1000)	Penalties ($1000)
Current situation	×	×	18%	-	93,000
Producer-customer	✓	×	6.6%	26,934.26	5,602.59
Producer-customer-3PL	✓	✓	0%	111,438.16	0

Chapter 4

Improving Sustainability in a Two-level Pharmaceutical Supply Chain through Vendor-Managed Inventory System

This chapter is dedicated to the article entitles "*Improving Sustainability in a Two-level Pharmaceutical Supply Chain through Vendor-Managed Inventory System*". It has been submitted to the *Journal of the Operational Research Society* on September 2015. The titles, figures, and mathematical formulations have been revised to keep the coherence through the thesis.

4.1 Abstract

In the pharmaceutical industry, wide range of regulations have been imposed on producers in the last decade to green their supply chains and to minimize the impact of their medications unused or burnt in the environment. On the other hand, hospitals, as the main consumers of medications, adopt a conservative inventory control policy through keeping large quantities of drugs in stock. Given the perishable nature of medications, such a strategy would lead to the expiration of excess inventory in the absence of patients demand. Consequently, producers are faced with governmental penalties and environmental reputation forfeit for their leftovers at customer sites. This article aims at improving the sustainability of a pharmaceutical supply chain in a real case study. An analytical model is proposed to explore the effect of implementing a Vendor-Managed Inventory (VMI) system on minimizing the quantity of expired medications at customer zones. Results reveal that the amount of expired medications could reach zero against the current 18% expiration rate of shipped items. Some insights for VMI implementation are also provided.

4.2 Introduction

As the presence of pharmaceutical sediments in the environment and its negative impact on humans' health are being revealed in recent years, many countries imposed new regulations for tackling the pharmaceutical supply chain (PSC) recovery processes [10]. Customers social pressure also plays a major role in determining corporate sustainable strategies and performance measures. However, most of recovery actions of PSC are still rudimentary and harmful to environment. Creative approaches are therefore necessary to reduce or minimize the introduction of pharmaceutical wastes to the environment and to improve the PSC sustainability.

Medications, as any other perishable product, typically have a fixed shelf life set by a used-by or a sell-by date. They also contain active molecular ingredients that degrade with time even when using modern keeping conditions [2]. These particularities lead to challenges on inventory control management, by trading off stock outs and on-shelf availability against wastage due to expiry [3, 4]. Any shortage in medications delivery has furthermore a high cost in terms of preventable illness and death. Therefore, governments and customers (such as hospitals) might adopt a conservative inventory control policy by ordering more products to be hedged against uncertainty [1]. For example, the federal government of the United States requires large quantities of stock keeping units (SKUs) of medications as part of its strategic national stockpile to protect its population in case of a health emergency [51]. Given the perishable nature of medications, such a strategy would lead to the expiration of the excess inventory in the absence of patients demand. In a 2003 survey, statistics estimated that the cost for expiration of branded medications in the United States drug stores was over 500 million dollars [52].

Since the medications salvage value is very low, pharmaceutical companies are not motivated to invest in the recovery process for such products. On the other hand, leaving expired medications at customer zones and disposing them improperly lead to penalties that must be paid to governments. It might also turn into a jeopardy to people's health if being redistributed illegally in undeveloped countries. This puts producers' reputation in the market in peril due to the negative environmental footprint of their products. Therefore, improving the PSC sustainability effectively is essential not only to protect the environment and patients from exposing to expired medications but also to reduce the associated cost [2].

Because of the aforementioned particularity, little attention has been addressed to tackle the leftovers of this specific value chain. Most of the practices followed

are to keep the unwanted/expired medications in confined zones or to incinerate them under the safeguard of governments. Such practices are more harmful to the environment. Therefore, in recent works by Weraikat et al. [49, 53], different ways are presented to either facilitate the recovery of expired medications or to reduce their amount at customer zones through proposing different cooperative methods in PSC. Nevertheless, the proposed approaches are post-solutions to the expired medications problem in the PSC. In other words, they tackle the fact of typically having available unwanted/expired medications at customer zones that have to be collected because of a large SKUs strategy implementation.

Against the current reactive practices in collecting unwanted/expired medications, we propose, in this article, a proactive approach by obstructing the entrance of excess medications to the supply chain inventories at first place. This can be achieved by implementing one of the most widely used initiatives for perishables dubbed as Vendor-Managed Inventory (VMI) system. Implementing the VMI system requires both information sharing and coordination between vendors and customers. The vendor (usually the producer) is responsible for making decisions concerning replenishment quantities and timing for its retailer (customer). The customer provides the producer with access to its real-time inventory level physically or via electronic messaging [54]. More precisely, the customer relinquishes control of replenishment decisions and transfers financial responsibility to the producer. It is worth mentioning that producers are usually engaged in a such policy because of its benefits. Irregular large demand orders from retailers are very expensive since producers need to maintain excess items in stock to satisfy their customers' demand. Therefore, implementing VMI system attenuates the fluctuation in the customer's demand and, hence, alleviates the bullwhip effect [55].

Along with the aforementioned advantages, our goal in implementing a VMI system is to reduce the large quantities of expired medication at customer zones through a more realistic inventory replenishment policy. As the main contribution in this article, we propose a VMI model, from the producer perspective, between him and one of his customers (a hospital). The model is a nonlinear mixed-integer program (MINLP) that seeks the optimal quantity of medications that must be shipped to the hospital in each period over a planning horizon with the goal of minimizing the quantity of expired medications as well as shortage and inventory levels. Our experimental results on a real case study reveal the importance of adopting a VMI system in decreasing the amount of expired medications at the customer zone from 18% to no expired medications of the shipped items. That is expected to improve the company's sustainable image in the market.

The remainder of this paper is structured as follows. A brief summary of the literature related to VMI and PSC inventory management is given in section 4.3. In section 4.4, the description of the PSC under investigation and the VMI model is provided. Numerical results and discussion of the model, in addition to managerial insights of implementing the VMI system, are presented in 4.5. Finally, concluding remarks and future recommendations are provided in section 4.6.

4.3 Literature Review

In this section, a concise review of the literature on the inventory management of perishables is given. A brief summary about the relevant research on implementing a VMI system, in general, and for PSC, in particular, is also provided.

4.3.1 Inventory management models for perishables

The first initial literature available on the perishable inventory management is chronicled by Nahmias [3]. The author gave a holistic review on perishable supply chains and touched briefly on applications of these models in blood bank inventory management. Goyal and Giri [56] provided a more recent review on the same topic and items mentioned in [3]. Despite the similarities between the inventory management of blood and pharmaceuticals, there are substantial differences between them. For example, the shelf life of blood is technically 4-5 days, where pharmaceuticals have varied shelf life from days to years. In addition to that, the replenishment lead time of blood supply is shorter than pharmaceuticals. Furthermore, not every successful technique for blood supply chain would be suitable for the PSC according to storage and lead time otherness. Several studies have focused on the inventory management of blood supply chains as [4, 57–59]. An extensive review of the available literature on inventory and supply chain management of blood products prior to 2012 can be found in [60].

Chapman et al. [57] applied just-in-time (JIT) inventory management techniques for a blood supply chain. Due to the consequences of an inventory shortage, the authors concluded that the JIT technique is not suitable for such perishable supply chains. Haijema [4] addressed the importance of an optimal disposal policy in combination with optimal ordering policies for blood supply chain. It was suggested that the average costs of this supply chain could be reduced by selling old products at a discounted price. Gunpinar and Centeno [58] proposed an integer programming model to minimize the total cost of blood inventory system from a hospital perspective over a planning horizon. The proposed inventory management approach could reduce the wastage rates and cost in the hospital. Latterly, Civelek et al. [59] proposed an inventory replenishment heuristic model to minimize the expected total cost over an

infinite time horizon for blood platelet supply chain. The authors suggested to perform the inventory replenishment with fixed quantities. A First-In-First-Out (FIFO) policy was also imposed by limiting some substitutions when making allocation decisions according to a safety stock level. Önal et al. [61] considered an economic lot-sizing problem for perishable products, where items have deterministic expiration periods that depend on their procurement periods. Their model for a FIFO allocation mechanism stated that the order of inventory consumption has a significant impact on the cost of the optimal plan of the supply chain.

Few research has been conducted on inventory management in the pharmaceutical value chain. Uthayakumar and Priyan [1] developed a two-echelon PSC inventory model to minimize the total cost of a supply chain that involves a pharmaceutical company and a hospital. Lee et al. [62] studied a public pharmaceutical inventory system with respect to the strategic national stockpile in the United States that requires to maintain a high minimum inventory volume at all times. The authors presented an optimal issuing policy for a deterministic demand to maximize the profit of the system they investigated.

It is worth mentioning that all of the contributions reviewed above has developed inventory management models for perishable items with the goal of cost minimization. In contrary, reducing the amount of expired items and their effect on the environment have been capturing less attention.

4.3.2 VMI systems

Since the first adoption by Wal-Mart in 1980s, many articles treat VMI superiority over traditional replenishment techniques for supply chains in general [63–66]. For more details on VMI benefits, the reader is referred to [67]. Implementing VMI system leads suppliers to a higher replenishment frequency with smaller replenishment

quantities as stated by Dong and Dresner in [68]. Consequently, VMI system implementation leads to utmost inventory cost saving without negatively impacting the overall performance of the supply chain or the customer service level [69, 70].

Very dearth literature can be found on implementing VMI systems for perishables supply chains. The available research focus is on grocery industry or blood banks but not on PSC. Ketzenberg and Ferguson [71] evaluated two structures in a grocery supply chain. The authors tested the value of information sharing or centralized control in a VMI system relative to the case when no information is shared and decision making is decentralized. Recently, Stanger [72] developed a seven-step framework for the assessment of a VMI system implementation in a blood bank in Germany. The author applied the proposed framework on 13 cases to conclude that hospitals hesitate to enter a VMI relationship due to the fear of losing control over critical resources or sharing information. However, this obstacle could be avoided by having explicit VMI implementation steps, that clearly defines the responsibility of each entities involved.

The literature review summarized above clearly indicates the lack of application of VMI systems in PSC. This article aims at developing an analytic model for the implementation of VMI in this supply chain with the goal of reducing the leftovers as well minimizing the total inventory and shortage costs of the supply chain.

4.4 Problem statement

In this section, we first provide a brief description of the current PSC structure in the company under discussion. Then, we extend the current value chain and construct a multi-period, capacitated, finite-horizon VMI model for a two-echelon PSC, i.e., a producer (*Generic PharmaX*) and a customer (hospital). A mathematical model for the proposed VMI system is then presented.

4.4.1 *Generic PharmaX* supply chain

Generic PharmaX is a leading multinational pharmaceutical producer that was founded in the Middle East 39 years ago. The company focuses on developing a branded pharmaceuticals business across the Middle East, North Africa, Europe, and in the United States. Based on purchasing orders received from hospitals, the producer ships his medications with respect to the regulations in the destination countries. According to the producer archival data, in some countries like the United States, large amounts of the shipped medications expire in hospitals' stock. Upon their expiry, the hospitals inform the producer about the quantities of the expired medications. *Generic PharmaX*, then, contracts with transportation providers to pick up those medications and send them to governmental disposal sites. The producer is obligated to pay fees to the government to safely dispose the wastage of medications. Currently, around 18% of branded medications at customer sites are expired and must be collected, which incurs penalties to the producer. Figure 14 visualizes the current PSC practice in *Generic PharmaX*.

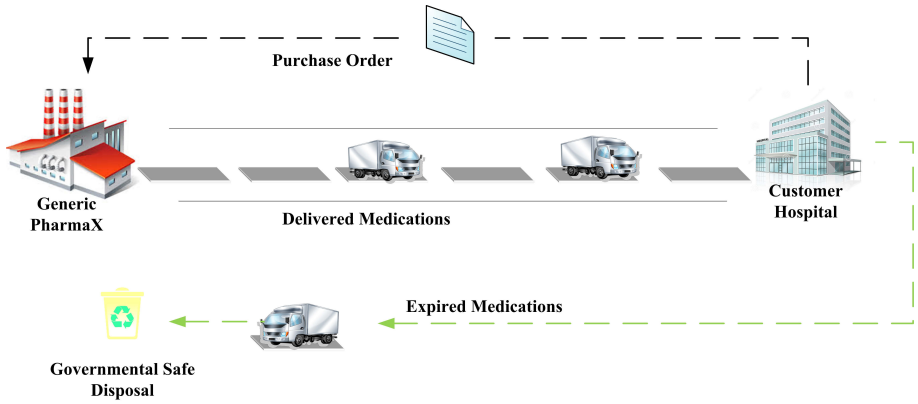

Figure 14: The current PSC of *Generic PharmaX* practice

Against the current practice, we believe that cutting off the SKUs level at hospitals sites, without sacrificing their customer demand satisfaction rate, is helpful in improving the PSC sustainability. More precisely, reducing the inventory level

can lessen the quantity of expired medications and their negative environmental impact. In addition, the governmental fees and penalties could be avoided when an efficient inventory control management would be utilized. This can be achieved by implementing a VMI system as explained in the following subsection.

4.4.2 *Generic PharmaX* VMI supply chain

The implementation of the VMI system requires private information sharing and a certain level of trust between supply chain entities [73]. For this reason, only one key hospital is elected to implement the VMI system with *Generic PharmaX*. Besides its long-term relationship with the producer, it is chosen due to its high demand rate of medications. Moreover, the hospital has high level of technology and infrastructure that would facilitate the future implementation of a technological system supporting VMI.

Considering the case where the producer and the hospital have agreed to implement the VMI system, *Generic PharmaX* is responsible for managing the hospital inventory and creating its monthly replenishment orders. In addition, the producer communicates with the hospital to decide on a minimum amount from each medication that has to be available in the hospital stock at all times, dubbed as safety stock (SS) level. Some medications are essential because they can be life-saving, such as respiratory and cardiovascular medicines. They have to be available in the hospital stock at all times in adequate amounts. Therefore, the SS level of essential medications is higher than nonessential medications as explained in the next section. Having an access to the on-hand level inventory is also required in order to enable the producer to provide on-site inventory planning.

Medications move from the producer, through a transportation provider, to the

hospital site to satisfy its demand in each period of the planning horizon. The producer issues a notification of delivery to the hospital upon the shipment release in stock. Given the perishable nature of medications, the producer checks their shelf

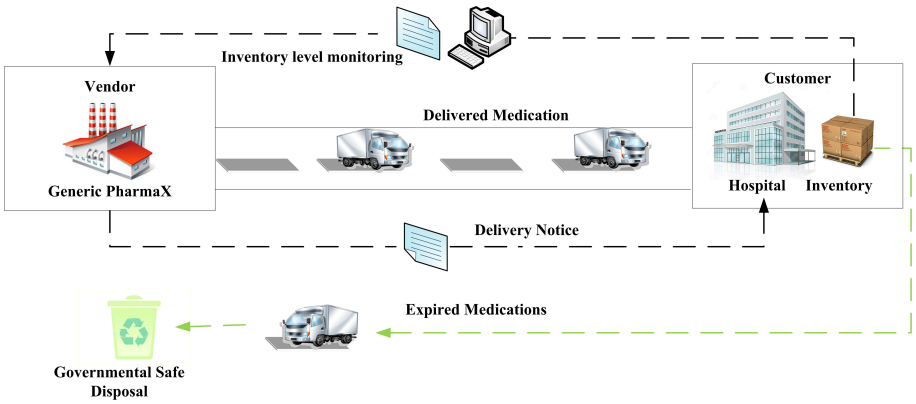

Figure 15: VMI supply chain Framework

life at the hospital site with every replenishment. Any medication that reaches to the end of its shelf life is quarantined and then shipped to governmental safe disposal sites, while unexpired medications remain at the hospital to be used in a next period. Figure 15 depicts the PSC of *Generic PharmaX* under a VMI system.

Because of the criticality of medications, the demand of the hospital has to be fulfilled by the producer over the planning horizon. *Generic PharmaX* managing the inventory through the VMI system, he is obliged to pay monetary penalties to the hospital for any shortage in the supply. The producer could also be coerced to outsource that shortage with same or equivalent medications from another pharmaceutical company to satisfy the hospital demand. Besides, the following assumptions are considered when formulating the VMI model; (1) the capacity of the producer is limited for each type of medication in every period, (2) the hospital demand is fulfilled with no time, i.e., lead time is zero, (3) the oldest medications are consumed first, i.e., a FIFO issuing policy is considered, (4) the producer ships only fresh medications to the hospital, (5) ages and quantities of medications in the hospital stock at the

beginning of the planning horizon are known, and (6) a SS level of medications has to be fulfilled by the producer in every period.

4.4.3 Mathematical model for the VMI system in the PSC

In this subsection, we propose a mixed-integer nonlinear programming (MINLP) model for implementing the VMI system in the PSC described previously. The notations listed below are used in the model. Additional notations are provided when required.

Notations

Index sets:

p: index of medications, $p = 1, 2, ..., P$;

i: index of medication ages (in months), $i = 1, 2, ..., I$;

t: index of time periods (in months), $t = 1, 2, ..., T$;

Parameters:

O^p: unit cost of outsourced medication type p that the producer could not satisfy ($);

CD^p: fees obligated by governments for each unit of medication type p disposed at their sites ($);

TR^p: unit transportation cost of medication type p shipped to the hospital ($);

TS^p: unit transportation cost of expired medication type p sent to government disposal site ($);

π^p: penalty the producer pays to the hospital for each unit of shortage in the supply of medication type p ($);

h^p: unit holding cost of medication type p at the hospital site ($);

CAP_t^p: producer capacity of medication type p in period t;

d_t^p: hospital demand of medication type p in period t;

$SS_t^{p^{min}}$: minimum SS level at the hospital for medication type p in period t;

VI_{i1}^p: the inventory level of product type p of age i at the beginning of the planning horizon;

M: the upper bound on the inventory level of medications at the hospital site;

Decision variables:

Q_{it}^p: replenishment quantity of medication type p of age i shipped to the hospital in period t;

E_t^p: quantity of expired medication type p sent to governmental disposal site in period t;

S_t^p: shortage quantity of medication type p that is needed to be outsourced in period t;

v_{it}^p: inventory level of medication type p of age i of period t;

F_{it}^p: binary variable that is equal to 1 when medication type p of age i is used to satisfy the demand in period t, 0 otherwise;

L_{it}^p: auxiliary variable associated with the medication age. It captures the number of medications type p of age i in period t that left to be used for the next period if not all medications from this age are used to satisfy the demand in the current period.

It should be noted that the VMI model has been formulated from the producer's perspective. The objective function as shown in equation (48) seeks to minimize the producer costs which involve shipping cost from the producer site to the hospital site; expired medication costs which incorporate the safe disposal fees for expired medication at government sites and the transportation cost from the hospital to the safe disposal sites; the shortage costs that consist of the penalty paid by the producer to the hospital for unsatisfied demand and the cost of satisfying that demand from another pharmaceutical producer; and the holding cost of medication at the hospital

site.

$$min \quad \sum_{p\in P}\sum_{i\in I}\sum_{t\in T} TR^p.Q^p_{it} + \sum_{p\in P}\sum_{t\in T}(CD^p + TS^p)E^p_t + \sum_{p\in P}\sum_{t\in T}(\pi^p + O^p)S^p_t + \sum_{p\in P}\sum_{i\in I}\sum_{t\in T} h^p.v^p_{it} \tag{48}$$

The objective function is constrained by the capacity of the producer as shown in equation (49). The medications from all ages shipped to the hospital in period t cannot exceed the capacity of the producer in that period.

$$\sum_{i\in I} Q^p_{it} \leq CAP^p_t, \qquad \forall p \in P, \quad \forall t \in T \tag{49}$$

Also, medication shipped to the hospital should always be fresh, i.e., only medications of age 1 are shipped to the hospital, as shown in constraint (50).

$$Q^p_{it} = 0, \qquad \forall i \neq 1, \quad \forall p \in P, \quad \forall t \in T \tag{50}$$

The FIFO policy is depicted in constraint (51). Constraint (52) states that no medication of age zero is used to satisfy the demand.

$$F^p_{it} \geq F^p_{(i-1)t}, \qquad \forall i \in I, \quad \forall p \in P, \quad \forall t \in T \tag{51}$$

$$F^p_{0t} = 0, \quad \forall p \in P, \quad \forall t \in T \tag{52}$$

Constraint (53) requires demand to be fully satisfied, otherwise a shortage occurs. In fact, L^p_{it} captures the number of medications type p of age i left in stock for the next period when at least one item from that age is absorbed from inventory in period t.

Otherwise, it would be equal to zero and S_t^p would take a positive value.

$$d_t^p = \sum_{i \in I}((v_{(i-1)(t-1)}^p + Q_{it}^p)F_{it}^p - L_{it}^p) + S_t^p, \qquad \forall p \in P, \quad \forall t \in T \tag{53}$$

Constraint (54) with constraint (53) capture the number of unsatisfied demand by the producer.

$$d_t^p - \sum_{i \in I}(v_{(i-1)(t-1)}^p + Q_{it}^p) \leq S_t^p, \qquad \forall p \in P, \quad \forall t \in T \tag{54}$$

The inventory from different ages available at the beginning of the planning horizon is shown in constraint (55). Moreover, there are no medications of age zero in the inventory at the hospital site, as shown in constraint (56).

$$v_{i(0)}^p = VI_{i(0)}^p, \qquad \forall p \in P, \quad \forall i \in I \tag{55}$$

$$v_{(0)t}^p = 0, \qquad \forall p \in P, \quad \forall t \in T \tag{56}$$

Constraint (57) assures that the amount of medication type p of age i left in period t do not exceed the number of the available medication of the same age in that period.

$$(F_{it}^p - F_{(i-1)t}^p)(v_{(i-1)(t-1)}^p + Q_{it}^p) \geq L_{it}^p, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{57}$$

Constraint (58) expresses the inventory update of medication type p of age i at the end of period t. It simply indicates that medication type p of age i has been used to satisfy the demand, in which case if medication of a younger age has also been used to satisfy the demand, no more medications of age i will be left in stock. Otherwise,

the leftover inventory of age i would be equal to L_{it} calculated in constraint (53).

$$v_{it}^{p} = (1 - F_{it}^{p})(v_{(i-1)(t-1)}^{p} + Q_{it}^{p}) + (F_{it}^{p} - F_{(i-1)t}^{p})L_{it}^{p}, \quad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{58}$$

Constraint (59) depicts the SS level for each medication.

$$\sum_{i \in I} v_{it}^{p} \geq SS_{t}^{p^{min}}, \quad \forall p \in P, \quad \forall t \in T \tag{59}$$

Constraint (60) captures the number of expired medications in stock that has to be sent to the governmental safe disposal site.

$$E_{t}^{p} = v_{(I)t}^{p}, \qquad \forall p \in P, \quad \forall t \in T \tag{60}$$

Finally, domain constraints are provided in equations (61)-(63).

$$Q_{it}^{p}, v_{it}^{p}, L_{it}^{p} \geq 0, \qquad \forall p \in P, \quad t \in T, \quad i \in I \tag{61}$$

$$F_{it}^{p} \in \{0, 1\}, \qquad \forall p \in P, \quad t \in T, \quad i \in I \tag{62}$$

$$E_{t}^{p}, S_{t}^{p} \geq 0, \qquad \forall p \in P, \quad t \in T \tag{63}$$

4.4.4 A solution methodology for the MINLP model corresponding to the VMI system

In order to transform the MINLP model (48)-(63) into a linear one, the following approach has been employed. In this method, the product of two variables (one

binary and one continuous) are replaced by one new variable, on which a number of constraints is appended to the rest set of constraints [74]. Let x_1 be a binary variable and x_2 be a continuous variable with a known upper bound u. To linearize the product of the two variables, a new variable, y, is introduced to replace the product of x_1 and x_2, i.e., $y = x_1 x_2$. In addition to that, the following constraints are imposed to force y to take a value equal to $x_1 x_2$:

$$y \leq u x_1$$

$$y \geq x_2 - u(1 - x_1)$$

$$y \leq x_2$$

$$y \geq 0$$

By the same token, in model (48)-(63), consider the product of the binary variable F_{it}^p and the continuous variable Q_{it}^p that appear in constraint (53). A new discrete variable, α_{it}^p, is used to replace $F_{it}^p.Q_{it}^p$. Constraints (92)-(95) are also added to the model, as detailed in the *Appendices*.

After replacing all of the nonlinear terms in model (48)-(63) with linearized variables, constraints (53), (57), and (58) are represented by constraints (69), (73), and (74), respectively. The linearized model is reformulated and provided in (64)-(104).

$$min \quad \sum_{p\in P}\sum_{i\in I}\sum_{t\in T} TR^p.Q_{it}^p + \sum_{p\in P}\sum_{t\in T}(CD^p + TS^p)E_t^p + \sum_{p\in P}\sum_{t\in T}(\pi^p + O^p)S_t^p + \sum_{p\in P}\sum_{i\in I}\sum_{t\in T} h^p.v_{it}^p \tag{64}$$

$$\sum_{i\in I} Q_{it}^p \leq CAP_t^p, \qquad \forall p \in P, \quad \forall t \in T \tag{65}$$

$$Q_{it}^{p} = 0, \qquad \forall i \neq 1, \quad \forall p \in P, \quad \forall t \in T \tag{66}$$

$$F_{it}^{p} \geq F_{(i-1)t}^{p}, \qquad \forall i \in I, \quad \forall p \in P, \quad \forall t \in T \tag{67}$$

$$F_{0t}^{p} = 0, \quad \forall p \in P, \quad \forall t \in T \tag{68}$$

$$d_{t}^{p} = \sum_{i \in I} (\gamma_{it}^{p} + \alpha_{it}^{p} - L_{it}^{p}) + S_{t}^{p}, \qquad \forall p \in P, \quad \forall t \in T \tag{69}$$

$$d_{t}^{p} - \sum_{i \in I} (v_{(i-1)(t-1)}^{p} + Q_{it}^{p}) \leq S_{t}^{p}, \qquad \forall p \in P, \quad \forall t \in T \tag{70}$$

$$v_{(0)t}^{p} = 0, \qquad \forall p \in P, \quad \forall t \in T \tag{71}$$

$$v_{i(0)}^{p} = VI_{i(0)}^{p}, \qquad \forall p \in P, \quad \forall i \in I \tag{72}$$

$$\gamma_{it}^{p} + \alpha_{it}^{p} - \mu_{(i-1)t}^{p} - \beta_{it}^{p} \geq L_{it}^{p}, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{73}$$

$$v_{it}^{p} = v_{(i-1)(t-1)}^{p} + Q_{it}^{p} - \gamma_{it}^{p} - \alpha_{it}^{p} + \lambda_{it}^{p} - \delta_{it}^{p}, \quad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{74}$$

$$\sum_{i \in I} v_{it}^{p} \geq SS_{t}^{p^{min}}, \quad \forall p \in P, \quad \forall t \in T \tag{75}$$

$$E_t^p = v_{(I)t}^p, \qquad \forall p \in P, \quad \forall t \in T \tag{76}$$

$$Q_{it}^p, v_{it}^p, L_{it}^p \geq 0, \qquad \forall p \in P, \quad t \in T, \quad i \in I \tag{77}$$

$$F_{it}^p \in \{0, 1\}, \qquad \forall p \in P, \quad t \in T, \quad i \in I \tag{78}$$

$$E_t^p, S_t^p \geq 0, \qquad \forall p \in P, \quad t \in T \tag{79}$$

and constraints (80)-(104) in the *Appendices*

4.5 Results and implementation insights

In this section, we present the case data and parameters used to solve the VMI model (64)-(104). Some numerical results and sensitivity analysis are then provided. Finally, managerial insights to help the producer and the hospital in implementing the VMI system are proposed.

4.5.1 Case data and parameters

The parameters of the model were obtained through communication with the head of the supply chain department in *Generic PharmaX* and then refined as follows. It is well known that VMI system is valuable only for high volume items and consistent demand, which usually come from key customers [75]. Therefore, one of the producer key hospitals was selected to implement the VMI model. The producers' sales of

medications for the last three years were reviewed. Only the top 4 types of sold medications were selected. 2 out 4 medications were characterized as essential due to their disease prevalence and life-saving effectiveness; one from the respiratory medications group and one from the cardiovascular medications group. The lifetime of medicines usually varies from 24 to 36 months, therefore 24 months were considered for the medications age. Medication shipped to the hospital is always fresh of 1 month age. If the medication is kept unused, it would be of 2 month age in the next period. In addition, 36 months is considered as the planning horizon. The upper bound on the hospital inventory of medications, M, as well as the capacity of the producer were considered based on archival data. Furthermore, purchasing orders from the hospital on a monthly basis were revised and used in computing the hospital demand.

The criticality of medications was considered in calculating the SS level as follows. For essential medications, the level was set as 5% of the hospital monthly demand for that medication (i.e., deterministic demand). Otherwise, 2.5% of the demand was used. Furthermore, to test the effect of SS level on model (64)-(104), two different SS levels were generated and compared with the basic case. They are dubbed by low-SS and high-SS. Table 15 summarizes the SS levels as a percentage of the hospital demand for both essential and nonessential medications.

Table 15: SS levels as a percentage of the hospital demand (%)

Case	Essential medications	Nonessential medications
Basic case	5	2.5
Low-SS	2.5	1.25
High-SS	10	5

The capacity of the producer assigned for the hospital has a direct impact on medication quantities shipped to the hospital. Therefore, two levels of allocated capacity were issued and compared with the basic case to test the effect on the model; namely Low-Capacity and High-Capacity as provided in table 16.

Table 16: Allocated capacity levels of the producer compared to basic case capacity

Case	Percentage of capacity
Basic case	100%
Low-Capacity	50%
High-Capacity	150%

To analyze the effect of freshness assumption on the expired medication quantities, another case named as Freshness was considered (table 17).

Table 17: Scenarios for the Freshness of the shipped medications

Case	Only fresh medications are shipped to the hospital
Basic case	✓
Freshness	×

IBM ILOG CPLEX 12.3 was used on DELL VOSTRO 3450 with 2.30GHz CPU and 4GB of RAM to solve the VMI supply chain model (64)-(104).

4.5.2 Numerical results

The model described by (64)-(104) was solved separately for each case using the parameters mentioned in subsection 4.5.1. The average time *CPLEX* took to solve these cases (except the Freshness case) is 267 seconds. The model solved for the freshness case was model (64)-(104) without constraint (66), i.e., constraint guaranties that medications are always fresh. The Freshness case has therefore higher solution time than the other cases, which is 3807.95 seconds. The average optimality gap for all cases is 0.1%.

Table 18 summarizes the results for the basic case. The objective function value, as the total cost of the PSC, is given in the second row. It can be concluded that shipping, holding, and shortage costs represent 34%, 33%, and 32% of the total cost, respectively. The expired medication cost is zero since the expired medication quantity at the hospital site is zero. More details for the basic case are provided in the *Appendices*.

Table 18: Solution results for the basic case

Total cost	($)
Objective function value	722,698
Shipping cost	251,210
Holding costs	237,238
Shortage costs	234,245
Expired medication costs	0

Total medication quantities	(unit)
Shipping quantities	304,421
Shortage quantities	3,995
Expired medication quantities	0

As expounded in subsection 4.4.2, the percentage of expired branded medications is currently 18% of the shipped items to the hospital. Implementing a VMI system, in contrary, eliminates the medication expiration, as provided in table 18.

Sensitivity analysis

In this subsection, we aim at analyzing the impact of various SS levels, producer capacities, and medication freshness condition on PSC costs following a VMI strategy.

Figure 16 depicts the comparison between the basic case and two SS levels. As the SS level is decreased to the Low-SS, the total PSC cost decreases by 19%. Same behavior was noted for the holding and shortage costs. This comes at no surprise, since reducing the SS level reduces the total medication shortage and holding quantities by 16% and 43%, respectively, as provided in table 19. By the same token, increasing the SS level to the High-SS increases the total PSC cost by 20%, the medication holding quantities by 30%, and the shortage quantities by 15%. Given the significant impact of this constraint, the producer is instigated to review SS levels with the hospital and update them periodically.

The allocated capacity level has a direct influence on the shortage costs as shown in figure 17. As anticipated, reducing the producer capacity assigned for the hospital to

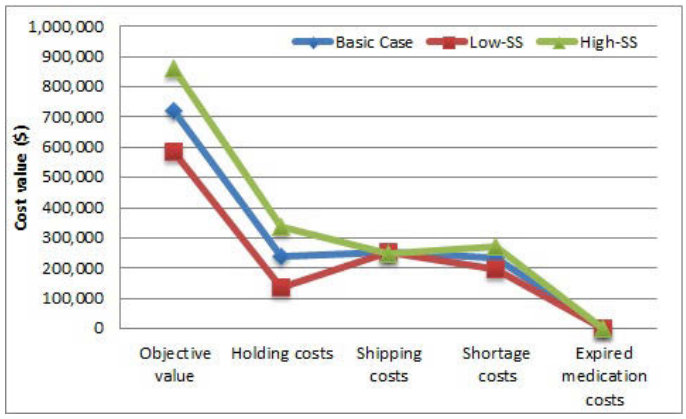

Figure 16: Effect of SS level on the various costs in the VMI model

Table 19: Effect of SS level on the total medication quantities (Unit)

	Basic case	Low-SS	High-SS
Holding quantities	11,236	6,392	16,056
Shortage quantities	3,995	3,354	4,665

the Low-Capacity increases the objective value by 92% since the outsourcing process is very expensive, besides the penalties provoked. On the other hand, increasing the producer capacity to High-Capacity could fully satisfy the hospital demand and ship more medications as summarized in table 20. Therefore, the producer is advised to boost his capacity assigned for this customer by 1.5 times the basic case capacity to avoid expensive outsourcing and penalty cost, while ensuring greater service level. Besides, with the reduced medication shortages, the producer not only saves but he also receives more information on the hospital demand patterns that aids him in better planning on his own inventories. It is note worthy that the expired medication quantities under VMI model is zero for all cases.

Table 20: Effect of allocated capacity levels on the total medication quantities (Unit)

	Basic case	Low-Capacity	High-Capacity
Shipped quantities	304,421	153,294	308,447
Shortage quantities	3,995	136,362	0
Expired quantities	0	0	0

Regarding the freshness assumption in shipping medication to the hospital, model

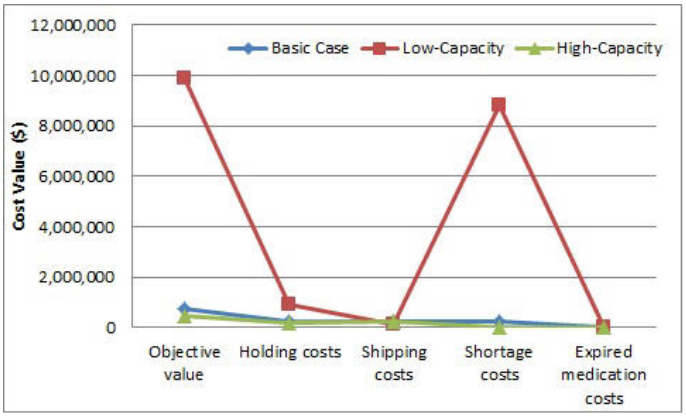

Figure 17: Effect of allocated capacity levels on the various costs in the VMI model

(64)-(104) was solved after eliminating constraint (66) (i.e., allowing the producer to ship less fresh medications). The results indicate that shipping aged medications has low impact on the objective function and other costs (figure 18). However, it increases the expired medication quantities by 545 unit (which is 0.18% of the shipped medications) as shown in table 21. To improve his PSC sustainability, the producer is therefore recommend to only ship fresh medications to the hospital.

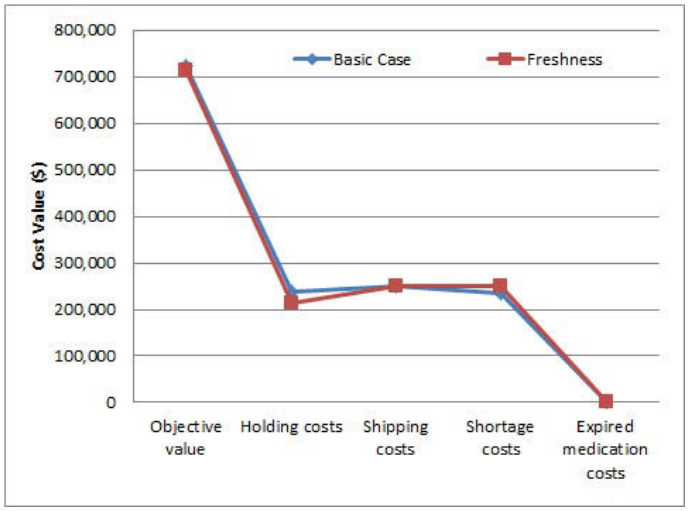

Figure 18: Effect of medications age shipped on the PSC costs

Table 21: Effect of medications age shipped on the PSC medication quantities (unit)

	Basic case	Freshness
Quantity of shipped medications	304,421	304,711
Quantity of expired medication	0	545

To conclude, implementing a VMI system could reduce the expired medication percentage from 18% of shipped medications in the current status (extracted from the producer archival data) to 0% for most of the cases. Allowing aged medications being delivered would, on the other hand, lead to a certain expired medication level to collect (i.e., 0.18% from the shipped medications). Therefore, it could certainly be profitable for the producer to implement the VMI system with his key customer while shipping fresh medications. The level of the capacity allocated to this hospital should be reviewed to avoid high outsourcing and penalty costs and poor service level.

4.5.3 Insights into VMI implementation

Despite the well-known benefits, implementing a VMI system is not a straightforward process. Sharing of data and information throughout the whole supply chain is a key element of an efficient implementation. As pointed out by Stanger [72], hospitals may be afraid of losing control over their inventories. A solid base of trust between PSC entities is therefore required. In this section we propose some steps and practical procedures that would help the producer and the hospital to implement the VMI model mentioned in section 4.4.

Figure 19 depicts the process of the inventory management by the producer at the hospital, i.e., the VMI system. The implementation starts by a profound communication between the producer and the hospital. The producer has to agree with the hospital on the SS levels to manage for essential and nonessential medications. These levels would change and be revised periodically with respect to the hospital's demand and the emergency. The producer needs to know the actual level of inventory. This can be accomplished via sending a sales representative to take a physical count of medications on hand, sending inventory status via EDI or e-mails, or even using compatible VMI software platforms at both PSC entities sites. The main feature of

a VMI software is to enable the producer to get up-to-date inventory information as often as desirable over the entire planning horizon. The expenses of the VMI software can be covered by the savings expected in the safe disposal fees and penalties that the producer used to pay to government for expired medications.

The producer checks whether any medication in stock is expired. If it is the case, the expired medications are quarantined and then stock level is refined. The expired medications are sent to the governmental safe disposal sites using a transportation provider. Based on the SS levels assigned for each item, *Generic PharmaX* calculates the next replenishment quantity and issues replenishment plans. Once replenishment plans are in place, the producer generates them into order plans. The orders must be reviewed and approved by the producer, and perhaps the hospital, depending on their preference. A summary report is issued based on parameters including lead-time (if any), minimum safety stock, days of supply, initial inventory level, amount on-order or in-transit, etc.

In out-of-stock situations, *Generic PharmaX* communicates with another pharmaceutical company to fulfill the demand of the hospital with equivalent medications. Equivalent medications may not always have the same treating efficiency like the original ones. Besides, the price of the outsourced medications is usually more expensive than the insourced. Therefore, a shortage penalty is paid by the producer to the hospital for any shortage in the demand. The producer is also obliged to pay the outsourcing expenses. It is noteworthy that shipping more frequently is the most obvious leverage provided by VMI system, which will permit the producer to address out-of-stock situations faster. The producer managers can then make adjustments to the order and review the impact of these adjustments. Also, the hospital can revise these adjustment through the software updates. Upon the shipment release, the producer notifies the hospital.

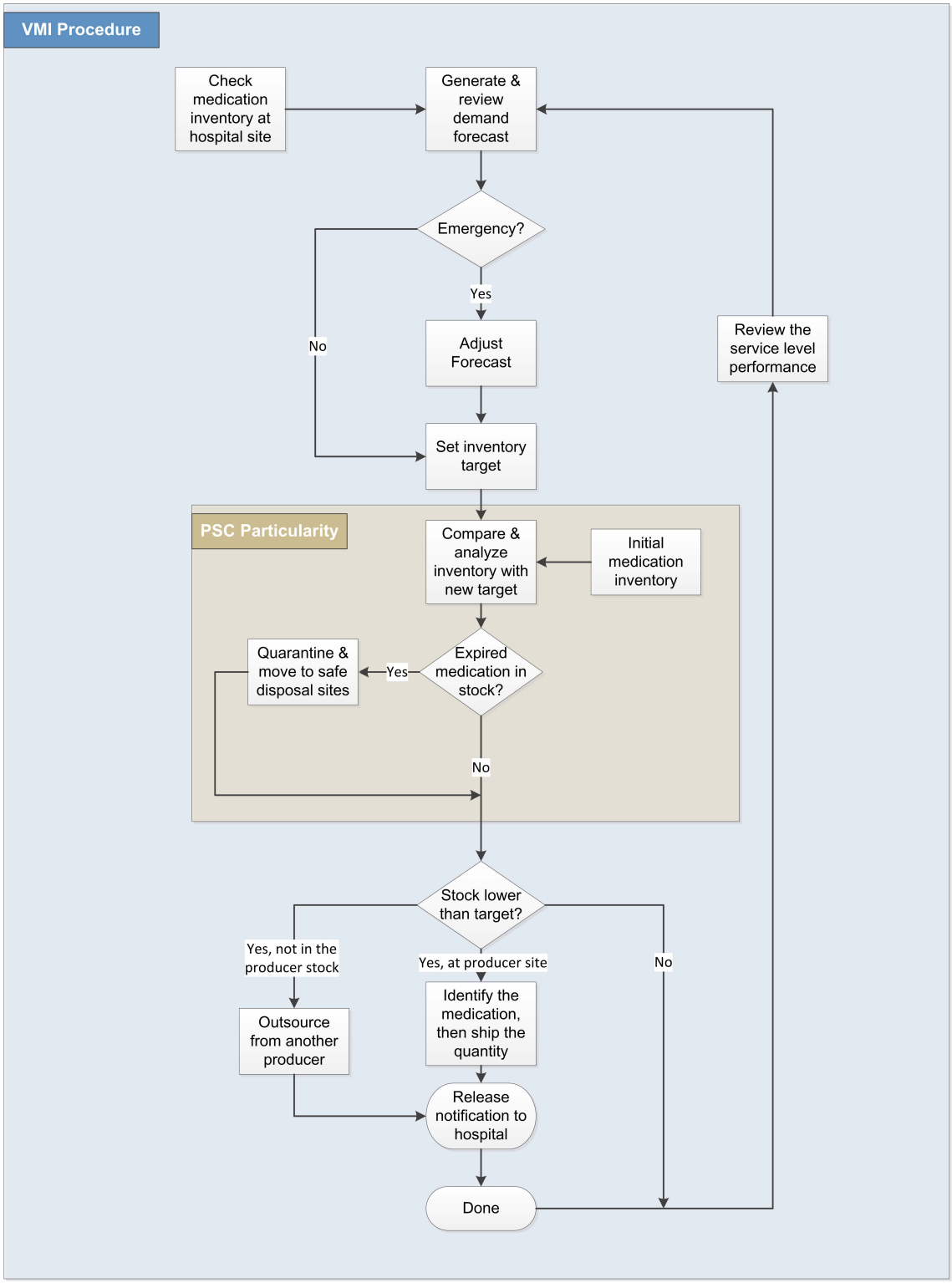

Figure 19: Proposed VMI process between *Generic PharmaX* and the hospital

On a periodic basis, performance indicators reflecting the actual results, such as expired medications percentages, inventory turns, stock-outs, and days of supply, will demonstrate whether the producer's control is sufficiently profitable for both PSC entities. As a final remark, benefits gained from VMI system go beyond a simple switchover. In other words, in a longer period when both *Generic PharmaX* and the hospital adjust their efforts to take advantage of this lower cost of inventory level system, the final satisfaction level will likely increase.

4.6 Conclusions and implications

Nowadays, improving the sustainability of PSC is a pressing need for pharmaceutical companies. Governments impose strict legislations on producers to minimize the introduction of their pharmaceutical waste into the environment. Typically, hospitals follow a conservative inventory control policy, through large SKUs, since shortages of essential medications have high costs in terms of preventable illness and death. Given their perishable nature, significant percentages of branded medications expired in stock. Consequently, producers need to pick up these medication. Otherwise, they are faced with governmental penalties and environmental reputation forfeit. Therefore, an efficient inventory management is required to reduce the SKUs level of medications without scarifying the customer demand or affecting human beings' lives.

In this article, we proposed a VMI model for the PSC, from the producer perspective, that seeks the optimal quantity of medications that must be shipped to the hospital in each period over a planning horizon. The goal of the model is to minimize medication shortage and the amount of expired medications. Our experimental results on a real pharmaceutical company reveal the importance of adopting VMI system for the PSC entities. Furthermore, the expired medication could be eliminated against the current status, in which the quantity of expired medication is about 18%

of shipped items.

A sensitivity analysis has also been provided to illustrate the effect of SS level, producer capacity, and medication freshness on the inventory control management. From the results, we conclude that implementing a VMI system could help the producer to improve the PSC sustainability and to avoid the expired medications at the hospital site. On the other hand, the producer is recommend to increase his capacity assigned to the hospital demand to fully satisfy the demand. In addition, the SS level has significant impact on the PSC total cost. Therefore, we advise the producer to review SS levels with the hospital more often to make sure that right amount of medications is kept in stock. Finally, the producer should only ship fresh medications to avoid expired medication leftovers, which would improve his sustainability image.

The VMI system implementation, however, is not a straightforward process. A key element in VMI system, that facilitates the implementation, concerns the sharing of data and information. It is usually refused by the PSC entities due to fears of losing control over their processes. For this purpose, we proposed some steps and practical procedures that would help in the implementation of the VMI model between the producer and one of his customer.

Although our model is representative of certain pharmaceutical value chains, we recognize our results are limited due to the case study and the assumptions made. In particular, demand is assumed to be known with certainty. In addition to that, the costs are assumed to be unchangeable after implementing VMI system. In other words, costs used to solve the model are the current cost before VMI system implementation. Although these limitations affect the amount of costs savings to be realized from VMI system, we anticipate that the direction of the results should remain unchanged when these limitations are modified.

For future work, considering more medication types and more than a hospital

can be suitable. In this case, efficient solution algorithms for solving the resulting large-scale MINLP model are necessary. Also, a replenishment lead time and its effect on the shipped medications quantities could be examined. VMI partnership may be more beneficial for one entity over other entities. Therefore, research on methods to manage benefits sharing among PSC entities would also be of practical value.

4.7 Acknowledgment

The authors would like to thank the Fonds de Recherche du Québec - Nature et Technologies (FRQNT) for the financial support in this research project.

4.8 Appendices

4.8.1 Mathematical linearized equations for the MINLP model

Replacing $F^p_{it}.v^p_{(i-1)(t-1)}$ by γ^p_{it} imposes constraints (80), (81), and (83) to the model.

$$\gamma^p_{it} \leq M.F^p_{it}, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{80}$$

$$\gamma^p_{it} \leq v^p_{(i-1)(t-1)}, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{81}$$

$$\gamma^p_{it} \geq M.(F^p_{it} - 1) + v^p_{(i-1)(t-1)}, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{82}$$

$$\gamma^p_{it} \geq 0, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{83}$$

Replacing $F^p_{it}.L^p_{it}$ by λ^p_{it} imposes constraints (84), (85), and (87) to the model.

$$\lambda^p_{it} \leq M.F^p_{it}, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{84}$$

$$\lambda^p_{it} \leq L^p_{it}, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{85}$$

$$\lambda^p_{it} \geq M.(F^p_{it} - 1) + L^p_{it}, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{86}$$

$$\lambda^p_{it} \geq 0, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{87}$$

Replacing $F^p_{(i-1)t}.Q^p_{it}$ by β^p_{it} requires adding constraints (88), (89), and (91) to the model.

$$\beta^p_{it} \leq M.F^p_{(i-1)t}, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{88}$$

$$\beta^p_{it} \leq Q^p_{it}, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{89}$$

$$\beta^p_{it} \geq M.(F^p_{(i-1)t} - 1) + Q^p_{it}, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{90}$$

$$\beta^p_{it} \geq 0, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{91}$$

Replacing $F^p_{it}.Q^p_{it}$ by α^p_{it} requires adding constraints (92), (93), and (95) to the model.

$$\alpha^p_{it} \leq M.F^p_{it}, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{92}$$

$$\alpha_{it}^{p} \leq Q_{it}^{p}, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{93}$$

$$\alpha_{it}^{p} \geq M.(F_{it}^{p} - 1) + Q_{it}^{p}, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{94}$$

$$\alpha_{it}^{p} \geq 0, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{95}$$

Replacing $F_{(i-1)t}^{p}.L_{it}^{p}$ by δ_{it}^{p} requires adding constraints (96), (97), and (99) to the model.

$$\delta_{it}^{p} \leq M.F_{(i-1)t}^{p}, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{96}$$

$$\delta_{it}^{p} \leq L_{it}^{p}, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{97}$$

$$\delta_{it}^{p} \geq M.(F_{(i-1)t}^{p} - 1) + L_{it}^{p}, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{98}$$

$$\delta_{it}^{p} \geq 0, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{99}$$

Replacing $F_{(i-1)t}^{p}.v_{(i-1)(t-1)}^{p}$ by $\mu_{(i-1)t}^{p}$ imposes constraints (100), (101), and (104) to the model.

$$\mu_{(i-1)t}^{p} \leq M.F_{(i-1)t}^{p}, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{100}$$

$$\mu_{(i-1)t}^{p} \leq v_{(i-1)(t-1)}^{p}, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{101}$$

$$\mu_{(i-1)t}^{p} \geq M.(F_{(i-1)t}^{p} - 1) + v_{(i-1)(t-1)}^{p}, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{102}$$

$$\mu^{p}_{(0)t} \quad = 0, \qquad \forall p \in P, \quad \forall t \in T \tag{103}$$

$$\mu^{p}_{(i-1)t} \quad \geq 0, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{104}$$

4.8.2 Basic Case results

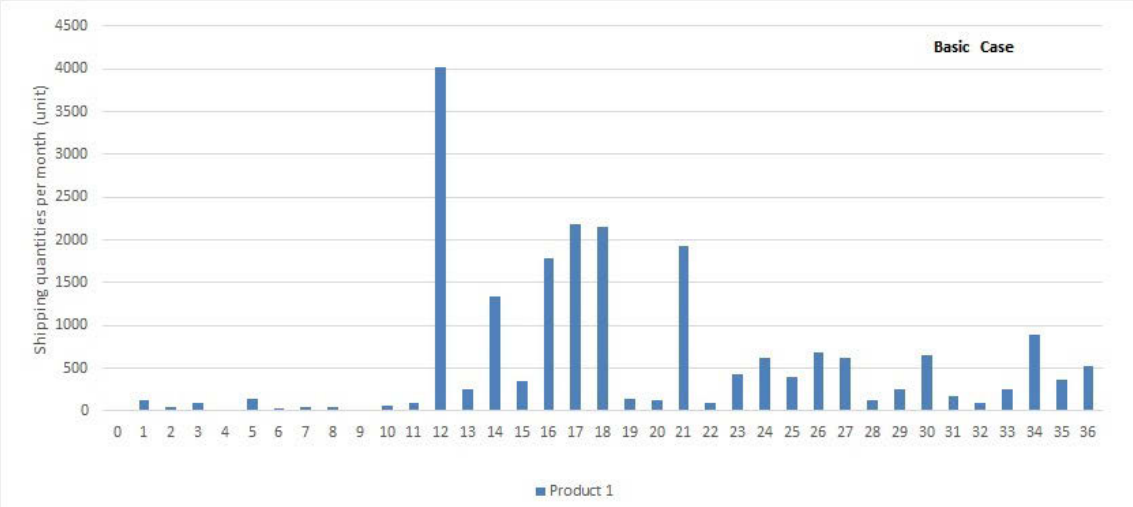

Figure 20: Product 1 shipping quantities over planning horizon (unit)

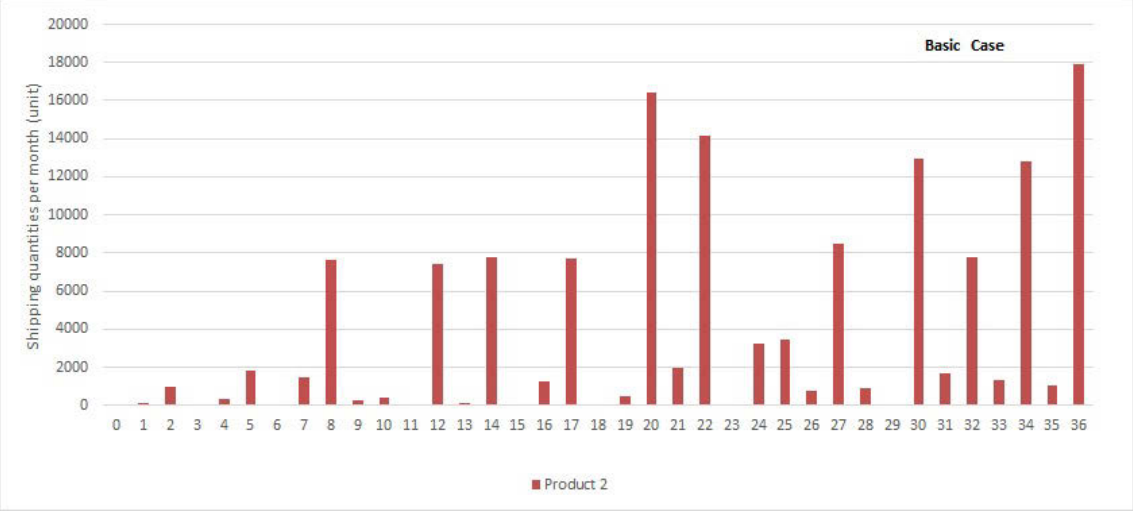

Figure 21: Product 2 shipping quantities over planning horizon (unit)

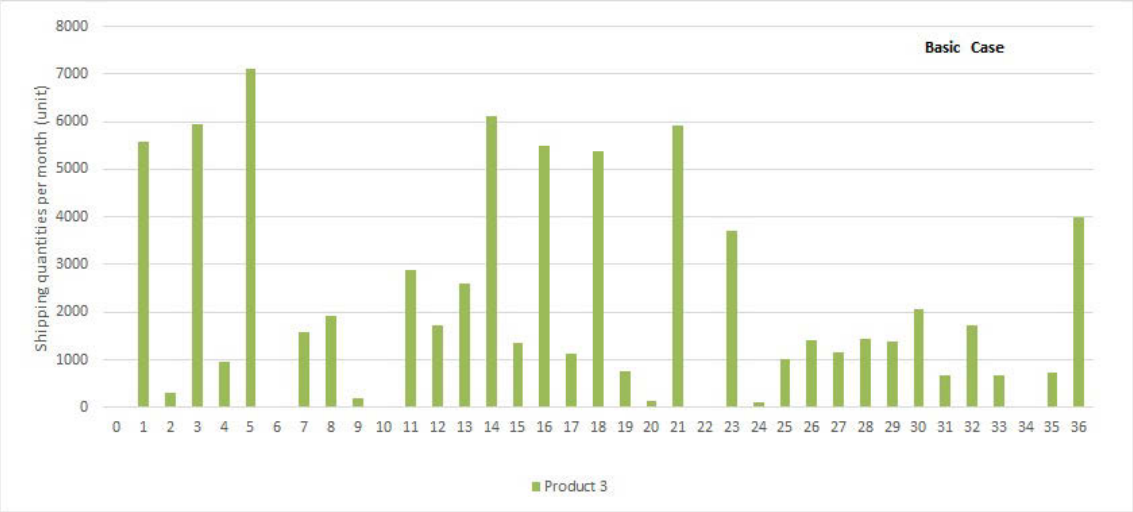

Figure 22: Product 3 shipping quantities over planning horizon (unit)

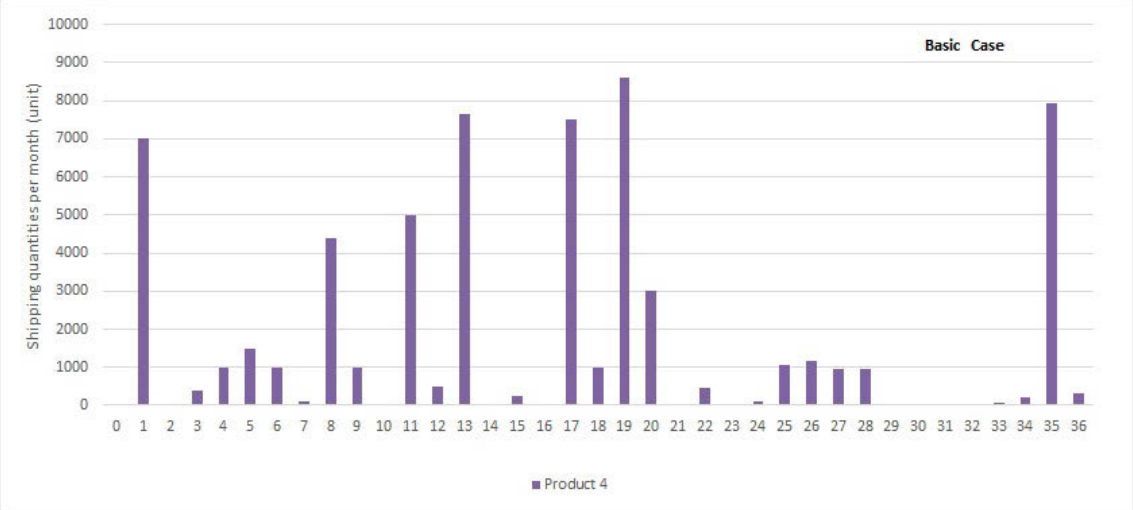

Figure 23: Product 4 shipping quantities over planning horizon (unit)

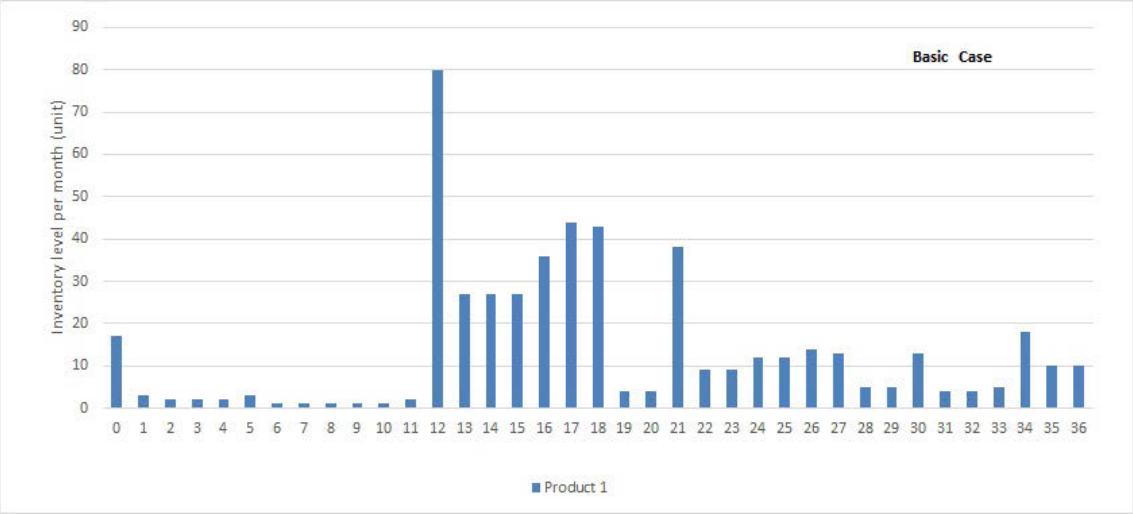

Figure 24: Product 1 inventory level over planning horizon (unit)

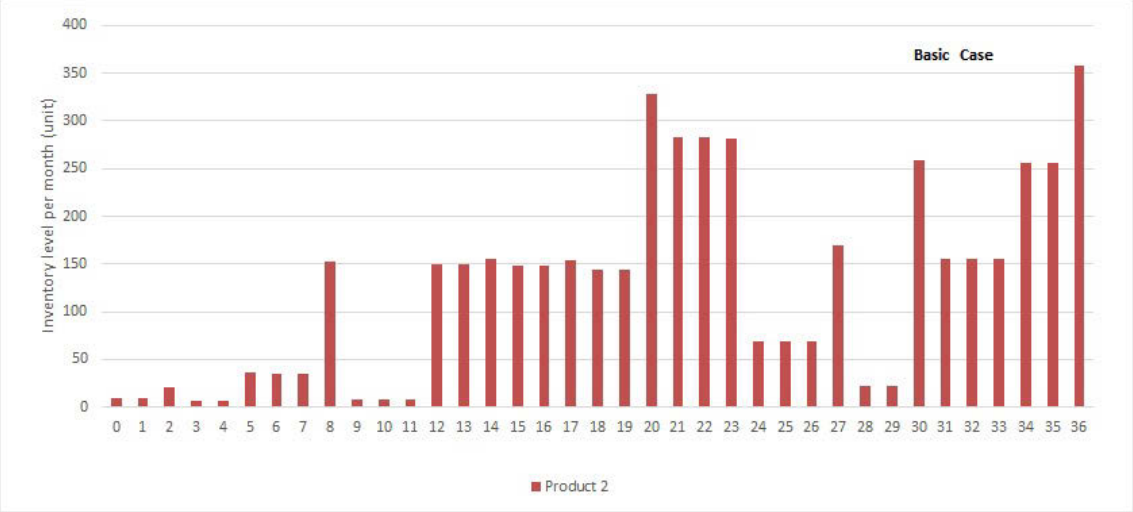

Figure 25: Product 2 inventory level over planning horizon (unit)

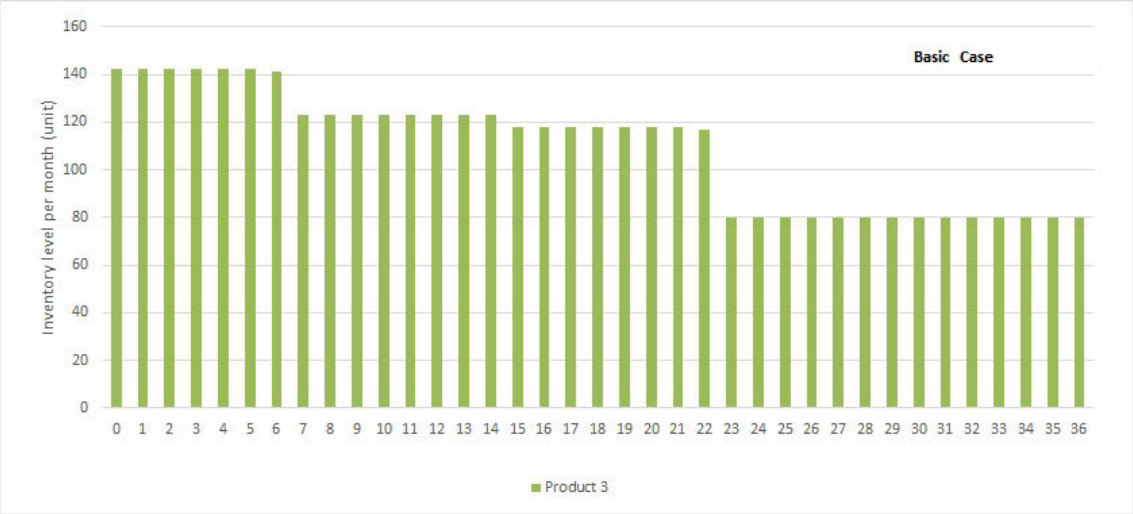

Figure 26: Product 3 inventory level over planning horizon (unit)

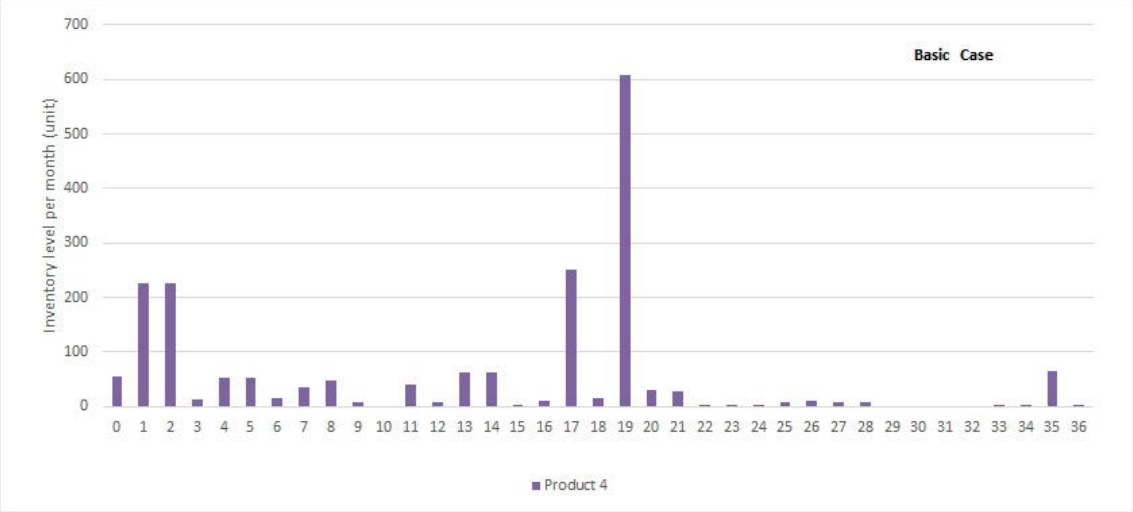

Figure 27: Product 4 inventory level over planning horizon (unit)

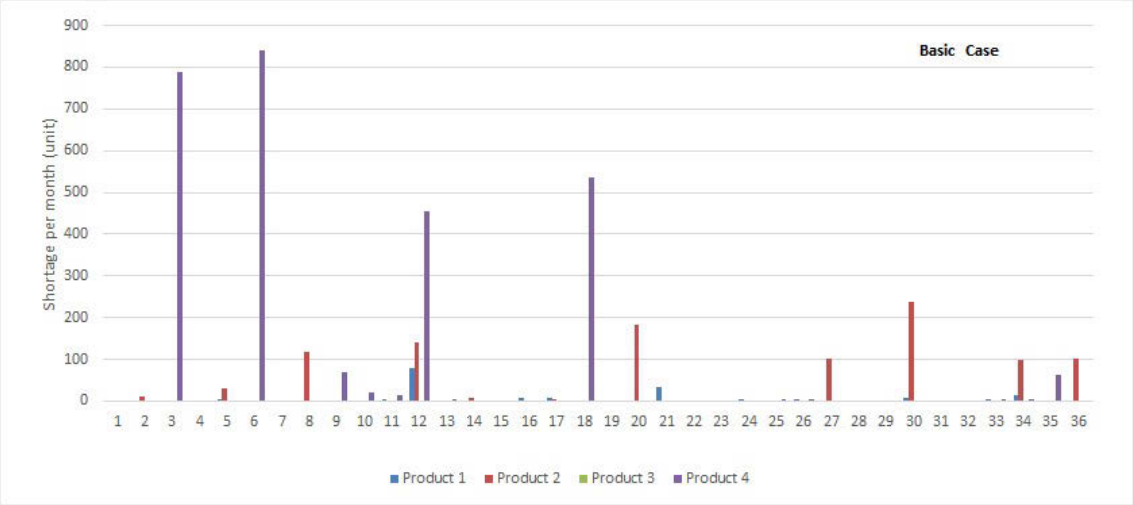

Figure 28: Shortage quantities for products over planning horizon (unit)

Chapter 5

General Discussion and Conclusion

This thesis investigated some coordination mechanisms for a sustainable pharmaceutical supply chain (PSC) management. A summary of the current supply chain for a real case study was first provided. Then, we touched briefly on the environmental provocations that pharmaceutical producers are nowadays faced with. Inspired by traditional supply chain activities, we believe that implementing coordination mechanisms between supply chain entities could improve the sustainability of the PSC.

In the first article, a decentralized negotiation process was presented in order to coordinate the collection of unwanted medications at customer zones. Using a Lagrangian relaxation method, the model is solved for a real generic pharmaceutical company. Since coordination efforts are required from the supply chain entities to collect and recycle unwanted medications, a bonus sharing technique is proposed based on each entity's investment in the coordination process. Results show that up to 28% more products could be collected if companies coordinate their operations efficiently. Hence, the producer would not pay penalties to the government and thus improve its reputation in the market. At the same time, the proposed method for sharing the savings leads to a win-win situation for the RSC entities, where each effort is rewarded.

Alternative channels dealing with medication leftovers were investigated in the second article. Two analytical models were therefore provided and implemented to improve the pharmaceutical RSC performance of *Generic PharmaX*. The first analytical model focused on customer involvement by paying incentives to encourage them to return unexpired medications. The second model was proposed to motivate 3PL companies and customers to collaborate in the recovery process. The results manifested the importance of introducing incentives to customers in improving the collected amounts of medications. Furthermore, utilizing a proper negotiation mechanisms between the producer and 3PL companies, in addition to customers incentives, could ensure a complete collection of unwanted medications. To motivate the RSC entities in the coordination mechanism, a technique for sharing the savings was also provided to reward the investment of the RSC entities.

In the third article, we focused on improving the sustainability of the PSC through implementing a VMI system. An analytical model, from the producer perspective, is therefore proposed to explore the effect of VMI on minimizing the quantity of expired medications at customer zones. Results reveal that the amount of expired medications could reach zero against the current 18% expiration rate of shipped items. The producer was recommend to increase his capacity assigned to his customer to fully satisfy the demand. In addition, we advised the producer to review safety stock levels with the hospital more often to make sure that the right amount of medications is kept in stock. The results demonstrated that *Generic PharmaX* should only ship fresh medications to avoid expired medication leftovers, which would improve his sustainability image. Finally, in order to facilitate the VMI implementation, we proposed some steps and practical procedures that would help in the implementation of the VMI model proposed between the producer and one of his customers.

5.1 Future insights

This dissertation, as a first research on the pharmaceutical supply chain coordination, contributes to the available literature by modeling this value chain in order to meet environmental legislations and reduce the amount of wastes. However, it can be improved by further suggestions as follows.

As explained earlier, the salvage value of medication recovery is almost negligible in the pharmaceutical industry. Therefore, illustrating the impact of collaboration in different networks could be examined. In other words, comparing the profit of two networks: non-profitable, such as pharmaceutical value chain, with profitable one, such as electronic or forest supply chain under various coordination mechanisms would be worth investigated.

In the first article, the model was proposed for a single-period tactical planning model. Considering a multi-period model could also be investigated. In addition, presenting some administrative insights for implementing the negotiation model could be of practical value.

The analytical models presented in the second article focused only on coordination approaches to encourage the RSC entities to return unexpired medications prior to the expiration date. Therefore, cost/benefit implication of these coordination mechanisms in addition to efforts required by supply chain entities in pharmaceutical industry would be worth being investigated.

The third article dealt with one key customer and few number of medications. Considering more medication types and more than a hospital can be suitable. Efficient solution algorithms for solving the resulting large-scale mixed-integer programming model would be therefore necessary. Future research could also focus on the replenishment lead time and its effect on the shipped medications quantities. Finally, research on methods to manage sharing of the benefits from implementing a VMI system among PSC entities could be examined.

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