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

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Abstract

Hospitals, as the main customers of medications, typically adopt conservative inventory control policies by keeping large quantities of drugs in stock. Given the perishable nature of medications, such strategies lead to the expiration of excess inventory in the absence of patients' demand. Consequently, producers are faced with governmental penalties and environmental reputation forfeit due to the negative impact that disposing expired medications pose to the environment. This article aims to improve the sustainability of a pharmaceutical supply chain using a real case study. An analytical model is proposed to explore the effect of implementing a Vender-Managed Inventory (VMI) system in minimizing the quantity of the expired medications at hospitals. Further, a set of Monte-Carlo simulation tests are conducted to investigate the robustness of the VMI model under demand uncertainty. Experimental results on a real case study under deterministic demand show the efficiency of the VMI model in eliminating the amount of expired medications without compromising customer's satisfaction. The results also demonstrate that the safety stock (SS) level and the capacity assigned to the customer are crucial factors in the overall cost of the pharmaceutical supply chain (PSC). The PSC cost could be reduced by 19% when reducing the SS level by 50%. Moreover, the producer is recommended to increase the capacity assigned to the customer by a factor of 1.5 so as to fully satisfy the customer's demand. Finally, the simulation results confirm the efficiency and robustness of embracing a VMI system under random demand scenarios. More precisely, zero amount of expired medications is obtained in 93% of cases. Thus, adopting this strategy could minimize drug wastage and ultimately improve the reputation of the producer in the market in terms of implementing Lean and sustainable practices.

1 Introduction

As the presence of pharmaceutical sediments in the environment and its negative impact on human health are being revealed in recent years, many countries are being forced to impose new regulations for tackling the pharmaceutical supply chain (PSC) recovery processes (Kumar et al., 2009). Social pressure from customers also plays a major role in determining sustainable corporate strategies and performance measures. However, most PSC recovery actions are still rudimentary and harmful to the environment. Creative approaches are therefore necessary to minimize the introduction of pharmaceutical wastes to the environment and

to improve PSC sustainability.

Medications, like any other perishable products, typically have a fixed shelf life set by a use-by or a sell-by date. They also contain active molecular ingredients that degrade with time even when using modern storing conditions (Laínez et al., 2012). These particularities lead to challenges for inventory control management, by trading off stockouts and on-shelf availability against wastage due to expiry (Nahmias, 1982; Hariga, 2014). In addition, any shortage in medication deliveries has serious consequences on the illness or the death of patients. Therefore, governments and customers (such as hospitals) might adopt a conservative inventory control policy by ordering more products as a hedge against uncertainty (Uthayakumar and Priyan, 2013). 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 (Shen et al., 2011). Given the perishable nature of medications, such a strategy would lead to the expiration of the excess inventory in the absence of patients' demand. A statistical survey in 2003 estimated the cost for expiration of branded medications, in the United States drugstores, by more than 500 million dollars (Karaesmen et al., 2011).

On the other hand, leaving expired medications at customer zones and disposing them improperly generate a significant negative environmental footprint. Also, it might jeopardize people's health if redistributed illegally in undeveloped countries. This has led to strict legislation in Europe and the United States on the take back (collection and safe disposal) of leftover medications available at hospitals and pharmacies by the medication producers. Although pharmaceutical companies are not motivated to invest in the recovery of expired medications due to their low salvage value, failure to respect such regulations would incur high penalties and loss of customer goodwill in the market. Therefore, improving PSC sustainability effectively is essential not only to protect the environment and patients from exposure to expired medications but also to reduce the associated cost (Laínez et al., 2012).

Because of the aforementioned particularity, there has been very little research tackled 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. (2016a,b), 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 address the fact of having available unwanted/expired medications at customer zones that have to be collected. In this article, instead of a reactive practice for collecting unwanted/expired medications, we propose a proactive approach by obstructing the entry of excess medications in to supply chain inventories. This can be achieved by implementing one of the most widely used initiatives for perishables known as the 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 timings for its retailer (customer). The customer provides the producer with access to its real-time inventory level physically or via electronic messaging (Waller et al., 1999). 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 such a policy because of its benefits. Irregular large orders from retailers are costly since producers need to maintain excess items in stock to satisfy the demands of their customers. Therefore, implementing VMI system attenuates fluctuation in customers' demand and, hence, alleviates the bull-whip effect (Disney and Towill, 2003).

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 of this article, we propose a VMI model, from the producer's 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 shortages and inventory levels. The model is validated in a deterministic setting by considering a realistic foretasted demands. Nevertheless, the demand of medications fluctuates in hospitals. Therefore, a set of Monte-Carlo simulation tests are also conducted in order to investigate the robustness of the VMI model in the presence of such fluctuations. According to the knowledge of the authors and the literature provided in section 2, the VMI model would enhance the supply chain performance and could reduce the quantity of expired medications.

The remainder of this paper is structured as follows. A summary of the literature related to VMI and PSC inventory management is given in Section 2. In Section 3, 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 Section 4. Finally, concluding remarks and future recommendations are provided in Section 5.

2 Literature Review

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

2.1 *Inventory management models for perishables*

The initial literature available on perishable inventory management is chronicled by Nahmias (1982). 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 (2001) provided a more recent review on the same topic and items mentioned in (Nahmias, 1982). 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, whereas pharmaceuticals have a varied shelf life from days to years. In addition, the replenishment lead time of blood supply is generally 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 (Chapman et al., 2004; Haijema, 2014; Gunpinar and Centeno, 2015; Civelek et al., 2015). An extensive review of the available literature on inventory and supply chain management of blood products prior to 2012 can be found in (Beliën and Forcé, 2012).

Chapman et al. (2004) 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 (2014) 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 discount price. Gunpinar and Centeno

(2015) 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 the cost for blood replenishment at the hospitals. Latterly, Civelek et al. (2015) 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 performing 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. (2015) 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.

Utilizing the VMI models in perishable supply chains appears as scare in the literature. Alftan et al. (2015) presented an operation model for retail replenishment collaboration for a grocery supply chain. Their model could improve demand responsiveness and availability of products in retail stores. Recenlty, Kaasgari et al. (2017) proposed a VMI strategy with discounts for managing the inventory of a perishable product in a supply chain encompassing a single vendor and multiple retailers. Their results revealed that adopting VMI models could reduce the inventory levels while increasing the replenishment rates of the supply chain.

Research conducted on inventory management with applications on the pharmaceutical value chain is limited. Uthayakumar and Priyan (2013) 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. (2014) studied a public pharmaceutical inventory system with respect to the strategic national stockpile in the United States that requires maintaining 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 herein have inventory management models for perishable items with the goal of cost minimization. However, the objective of reducing the number of expired medications and their effect on the environment have generally overlooked.

2.2 *VMI systems*

Since first being adopted by Wal-Mart in the 1980s, many articles treat VMI superiority over traditional replenishment techniques for supply chains in general (Cachon and Fisher, 2000; Claassen et al., 2008; Marquès et al., 2010; Borade et al., 2015). For more details on the VMI benefits, the reader is referred to (Govindan, 2013). Implementing VMI system leads suppliers to a higher replenishment frequency with smaller replenishment quantities as stated by Dong et al. (2007). 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 (Çetinkaya and Lee, 2000; Zhao and Cheng, 2009).

There is a great dearth of literature that can be found on implementing VMI systems for perishables supply chains. The available research focus is on the grocery industry or blood banks but not on PSC. Ketzenberg and Ferguson (2008) evaluated two structures in a grocery supply chain. The authors tested the value of information sharing under centralized control in a VMI system relative to the case when no information is shared and decision making is decentralized. Stanger (2013) 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 define the responsibility of each entity involved. Recently, Gunpinar and Centeno (2016) developed an integer programming model to assist blood centers in managing their resources more efficiently. By relaxing the inventory constraints and keeping the planning horizon shorter, small instances of the problem were solved optimally using branch and price method. Candan and Yazgan (2016) provided a MIP model for implementing a VMI system so as to maximize the profit of a pharmaceutical supply chain. The results highlighted the importance of considering medication's shelf-life as a crucial constraint in the PSC inventory planning model.

Krichanchai and MacCarthy (2017) identified the factors that affect the adoption of a VMI system in the PSC. The authors developed an inventory control model from the hospitals' perspective, where the medications are supplied by one distributor. The findings ascertain the importance of top management willingness to share information in a successful implementation of the VMI system. They also found that the VMI adoption encompasses the risk

of relinquishing control of critical items to a particular supplier.

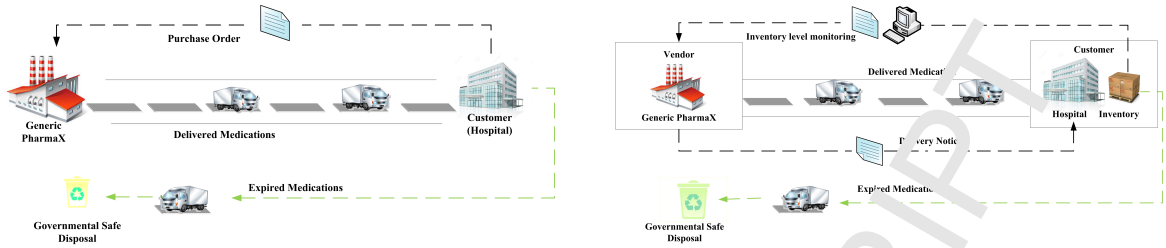
The summarized literature, provided in this section, clearly indicates the opportunity to apply VMI systems to the PSC. Thus, in this work we develop a mathematical model, from the producer perspective, for the implementation of VMI in this supply chain with the goal of reducing the leftovers as well minimizing the total inventory and shortage costs of the supply chain.

3 Problem Statement

In this section, we provide a brief description of the PSC structure at the real case study. Due to the confidentiality agreement with the producer, the real name of the company cannot be revealed. Hence, a false name is used through this article which is *Generic PharmaX*. 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.

3.1 *Generic PharmaX supply chain*

Generic PharmaX is a leading multinational pharmaceuticals producer that was founded in the Middle East in 1978. The company focuses on developing a branded pharmaceutical 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's archival data, in some countries like the United States, large amounts of 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 transportation providers to pick up those medications and send them to government disposal sites. The producer is obligated to pay fees to the government to safely dispose the wastage of medications. Currently, around 18% of the branded medications at customer sites have expired and must be collected, which incurs penalties to the producer. Figure 1a visualizes the current PSC practice in *Generic PharmaX*.



(a) The current PSC (b) VMI supply chain framework

Figure 1: The PSC of *Generic PharmaX* practice

Against the current practice, we believe that cutting off the SKUs level at hospital 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 government fees and penalties could be avoided when an efficient inventory control management is utilized. This can be achieved by implementing a VMI system as explained in the following subsection.

3.2 *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 (De Toni and Zamolo, 2005). 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 a 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 of 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 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 life at the hospital site with every replenishment. Any medication that reaches the end of its shelf life is quarantined and then shipped to government safe disposal sites, while unexpired medications remain at the hospital to be used in a next period. Figure 1b 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 producer supplies medications to several hospitals, hence, the capacity dedicated to each is limited for each type of medication in every period over the planning horizon; (2) the hospital demand is fulfilled with zero transportation lead time, which is quite realistic given the necessity for the freshness of shipped medications; (3) the oldest medications are consumed first, i.e., a FIFO issuing policy is considered in the model to reflect the actual policy adopted the hospital under investigation; (4) the producer ships only fresh medications to the hospital to minimize the chance of expiration; (5) the age and quantity of medications available in the hospital at the beginning of the planning horizon are known; and (6) the SS level of medications needs to be respected by the producer in every period; the latter reflects the current contract terms between the producer and the hospital.

3.3 *Mathematical model for the VMI system in the PSC*

In this subsection, inspired by recent research done by Gunpinar and Centeno (2015) and Gunpinar and Centeno (2016), 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 medication type, $p = 1, 2, ..., P$;

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

t: index of time period (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 ($). Although the distance between the producer and the hospital is constant, some medications require certain conditions while being shipped, such as temperature, light, or humidity. Therefore, the transportation cost varies with respect to each medication type;

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 forecast 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 government 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 defined to guarantee that the FIFO policy when consuming inventory of medications at the customer site (hospital) is respected. It 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 med-

ications type p of age i in period t that are 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 (1) seeks to minimize producer costs which involve shipping cost from the producer site to the hospital site ($\sum_{p\in P}\sum_{i\in I}\sum_{t\in T} TR^p.Q^p_{it}$); 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 ($\sum_{p\in P}\sum_{t\in T}(CD^p+TS^p)E^p_t$); 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 ($\sum_{p\in P}\sum_{t\in T}(\pi^p+O^p)S^p_t$); and the holding cost of medication at the hospital site paid by the producer ($\sum_{p\in P}\sum_{i\in I}\sum_{t\in T} h^p.v^p_{it}$).

$$\begin{aligned} min \quad & \sum_{p\in P}\sum_{i\in I}\sum_{t\in T} TR^p.Q^p_{it} + \sum_{p\in P}\sum_{t\in T}(CD^p+TS^p)E^p_t + \\ & \sum_{p\in P}\sum_{t\in T}(\pi^p+O^p)S^p_t + \sum_{p\in P}\sum_{i\in I}\sum_{t\in T} h^p.v^p_{it} \end{aligned} \tag{1}$$

The objective function is constrained by the capacity of the producer as shown in equation (2). The medications from all ages shipped to the hospital in period t cannot exceed the capacity of the producer in that period.

$$\sum_{i\in I} Q^p_{it} \leq CAP^p_t, \qquad \forall p \in P, \quad \forall t \in T \tag{2}$$

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 (3).

$$Q^p_{it} = 0, \qquad \forall i \neq 1, \quad \forall p \in P, \quad \forall t \in T \tag{3}$$

To make sure that the FIFO policy when consuming inventory of medications at the customer site (hospital) is respected, the binary decision variable F^p_{it} is introduced. The same decision variable, F^p_{it}, is also used to keep a track of the age of medications available in stock as depicted in constraints (6), (10), and (11).

Constraint (4) formulates the FIFO policy and constraint (5) states that no medication of

age zero is used to satisfy the demand.

$$F^p_{it} \geq F^p_{(i-1)t}, \qquad \forall i \in I, \quad \forall p \in P, \quad \forall t \in T \tag{4}$$

$$F^p_{0t} = 0, \quad \forall p \in P, \quad \forall t \in T \tag{5}$$

Constraint (6) indicates that the demand for medication type p in each period t can be either satisfied from the inventory on-hand of medication type p of all ages ($\sum_{i \in I}((v^p_{(i-1)(t-1)} + Q^p_{it})F^p_{it})$) or the demand cannot be fully satisfied due to shortage of that type of medication (i.e.,$S^p_t > 0$). In the case in which the demand can be satisfied, two situations are possible: either no more inventory of that medication type will be left to be carried forward to the next period ($L^p_{it} = 0$) or L^p_{it} will take a positive value.

$$d^p_t = \sum_{i \in I}((v^p_{(i-1)(t-1)} + Q^p_{it})F^p_{it} - L^p_{it}) + S^p_t, \qquad \forall p \in P, \quad \forall t \in T \tag{6}$$

It is evident that in any period, only one of the decision variables L^p_{it} and S^p_t can take positive values. It is also noteworthy that the binary variable F^p_{it} is multiplied by $(v^p_{(i-1)(t-1)} + Q^p_{it})$ (i.e., the inventory of medication of age $(i-1)$ in period $(t-1)$ that will be carried forward to period t plus the replenishment quantity of medication p of age i in period t) to guarantee that if the model decides to use a certain age of medication type p, then the medication of that age can be used to satisfy the demand.

Constraint (7) calculates the amount of shortage of medication type p in period t as the difference between the demand and the inventory on-hand of medication type p of all ages ($\sum_{i \in I}(v^p_{(i-1)(t-1)} + Q^p_{it})$).

$$d^p_t - \sum_{i \in I}(v^p_{(i-1)(t-1)} + Q^p_{it}) \leq S^p_t, \qquad \forall p \in P, \quad \forall t \in T \tag{7}$$

Constraint (7) with constraint (6) capture the number of unsatisfied demands by the producer.

The inventory from different ages available at the beginning of the planning horizon is shown in constraint (8). Moreover, there are no medications of age zero in the inventory at the hospital site, as shown in constraint (9).

$$v^p_{i(0)} = VI^p_{i(1)}, \qquad \forall p \in P, \quad \forall i \in I \tag{8}$$

$$v^p_{(0)t} = 0, \qquad \forall p \in P, \quad \forall t \in T \tag{9}$$

Both constraints (8) and (9) set the initial inventory level for old and new medications, respectively

Constraint (10) assures that the amount of medication type p of age i left in period t does not exceed the number of the available medications of the same age in that period.

$$(F^p_{it} - F^p_{(i-1)t})(v^p_{(i-1)(t-1)} + Q^p_{it}) \geq L^p_{it}, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{10}$$

Constraint (11) expresses the inventory update of medication type p of age i at the end of period t.

$$v^p_{it} = (1 - F^p_{it})(v^p_{(i-1)(t-1)} + Q^p_{it}) + (F^p_{it} - F^p_{(i-1)t})L^p_{it}, \quad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{11}$$

More precisely, this constraint (11) formulates the inventory carry forward condition. The inventory level of medication p of age i in period t is updated according to two possibilities:

1. $F^p_{it} = 1$: In this case, the first term in the right-hand-side (RHS) of constraint (11) equals zero. Then two more cases might happen:

   1.1. $F^p_{(i-1)t} = 1$: This case means that there is no more medication p of age i left in stock in period t which makes sense according to FIFO policy.

   1.2. $F^p_{(i-1)t} = 0$: In this case, we can update stock level according to constraint (10). As indicated in section 3.3, the auxiliary decision variable, L^p_{it}, is defined to measure the quantity of medication p of age i in period t that is left to be used in the next period. According to constraint (10), if $F^p_{it} = 1$ and $F^p_{(i-1)t} = 0$, L^p_{it} is equal to the inventory of medication of age $(i-1)$ in period $(t-1)$ that will be carried forward to period t plus the replenishment quantity of medication p of age i in period t. Otherwise, if $F^p_{(i-1)t} = 1$, there will be nothing left in stock from medication type p of age i. Because of the FIFO constraint (4), $F^p_{it} = 0$ and $F^p_{(i-1)t} = 1$ is not a feasible solution.

2. $F^p_{it} = 0$: In this case, the second term in the right-side of constraint (11) will be equal to zero ($F^p_{(i-1)t} = 1$ due to constraint (4)). In other words, this constraint indicates that the inventory level of medication p of age i in period t equals the inventory of medication of age $(i-1)$ in period $(t-1)$ that will be carried forward to period t plus the replenishment quantity of medication p of age i in period t.

Constraint (12) depicts the SS level for each medication.

$$\sum_{i \in I} v^p_{it} \geq SS^{p^{min}}_t, \quad \forall p \in P, \quad \forall t \in T \tag{12}$$

Constraint (13) captures the number of expired medications in stock that has to be sent to

the governmental safe disposal site.

$$E_t^p = v_{(I)t}^p, \qquad \forall p \in P, \quad \forall t \in T \tag{13}$$

Finally, domain constraints are provided in equations (14)-(16).

$$Q_{it}^p, v_{it}^p, L_{it}^p \geq 0, \qquad \forall p \in P, \quad t \in T, \quad i \in I \tag{14}$$

$$F_{it}^p \in \{0, 1\}, \qquad \forall p \in P, \quad t \in T, \quad i \in I \tag{15}$$

$$E_t^p, S_t^p \geq 0, \qquad \forall p \in P, \quad t \in T \tag{16}$$

3.4 *A solution methodology for the MINLP model corresponding to the VMI system*

In order to transform the MINLP model (1)-(16) 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 remaining set of constraints (Glover, 1975). 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 (1)-(16), consider the product of the binary variable F_{it}^p and the continuous variable Q_{it}^p that appear in constraint (6). A new discrete variable, α_{it}^p, is used to replace $F_{it}^p Q_{it}^p$. Constraints (45)-(48) are also added to the model, as detailed in the *Appendix*.

After replacing all of the nonlinear terms in model (1)-(16) with linearization variables, constraints (6), (10), and (11) are represented by constraints (22), (26), and (27), respectively.

The linearized model is reformulated and provided in (17)-(57).

$$min \quad \sum_{p\in P}\sum_{i\in I}\sum_{t\in T} TR^p.Q^p_{it} + \sum_{p\in P}\sum_{t\in T}(CD^p + TS^p)E^p_t + \sum_{p\in P}\sum_{t\in T}(\pi^p + O^p)S^p_t + \sum_{p\in P}\sum_{i\in I}\sum_{t\in T} h^p.v^p_{it} \tag{17}$$

$$\sum_{i\in I} Q^p_{it} \leq CAP^p_t, \qquad \forall p \in P, \quad \forall t \in T \tag{18}$$

$$Q^p_{it} = 0, \qquad \forall i \neq 1, \quad \forall p \in P, \quad \forall t \in T \tag{19}$$

$$F^p_{it} \geq F^p_{(i-1)t}, \qquad \forall i \in I, \quad \forall p \in P \quad \forall t \in T \tag{20}$$

$$F^p_{0t} = 0, \quad \forall p \in P, \quad \forall t \in T \tag{21}$$

$$d^p_t = \sum_{i\in I}(\gamma^p_{it} + \alpha^p_{it} - L^p_{it}) + S^p_t, \qquad \forall p \in P \quad \forall t \in T \tag{22}$$

$$d^p_t - \sum_{i\in I}(v^p_{(i-1)(t-1)} + Q^p_{it}) \leq S^p, \qquad \forall p \in P, \quad \forall t \in T \tag{23}$$

$$v^p_{(0)t} = 0, \qquad \forall p \in P \quad \forall t \in T \tag{24}$$

$$v^p_{i(0)} = VI^p_{i(0)}, \qquad \forall p \in P, \quad \forall i \in I \tag{25}$$

$$\gamma^p_{it} + \alpha^p_{it} - \mu^p_{(i-1)t} - \beta^p_{it} \geq L^p_{it} \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{26}$$

$$v^p_{it} = v^p_{(i-1)(t-1)} + Q^p_{it} - \gamma^p_{it} - \alpha^p_{it} + \lambda^p_{it} - \delta^p_{it}, \quad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{27}$$

$$\sum_{i\in I} v^p_{it} \geq SS^p_t, \quad \forall p \in P, \quad \forall t \in T \tag{28}$$

$$F^p_t = v^p_{(I)t}, \qquad \forall p \in P, \quad \forall t \in T \tag{29}$$

$$Q^p_{it}, v^p_{it}, L^p_{it} \geq 0, \qquad \forall p \in P, \quad t \in T, \quad i \in I \tag{30}$$

$$\gamma^p_{it} \in \{0, 1\}, \qquad \forall p \in P, \quad t \in T, \quad i \in I \tag{31}$$

$$E^p_t, S^p_t \geq 0, \qquad \forall p \in P, \quad t \in T \tag{32}$$

and constraints (33)-(57) in the $Appendix - A$

4 Results and Implementation Insights

In this section, we present the case data and parameters used to solve the VMI model (17)-(57). Some numerical results, sensitivity analysis, and Monte-Carlo simulation tests are then provided. Finally, managerial insights to help the producer and the hospital in implementing the VMI system are proposed.

4.1 *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 the VMI system is valuable only for high volume items and consistent demand, which usually come from key customers (Cooke, 1998). Therefore, one of the producer's 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 at the age of 1 month. If the medication is kept unused, it would be at the age of 2 months 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 to forecast the hospital demand. Figure 2 depicts the demand profile fluctuating over a year.

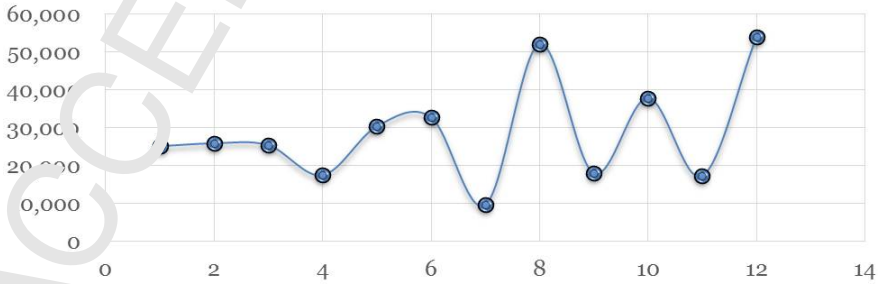


Figure 2: Hospital forecast demand distribution of medications (units)

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's monthly forecast demand for that medication (i.e., deterministic demand). Otherwise, 2.5% of the forecast demand was used. Furthermore, to test the effect of SS level on model (17)-(57), two different SS levels were generated and compared with the basic case. They are dubbed by low-SS and high-SS. Table 1 summarizes the SS levels as a percentage of the hospital demand for both essential and nonessential medications.

Table 1: SS levels as a percentage of the hospital forecast demand, d_t^p

Case	Essential medications	Nonessential medications
Basic case	$d_t^p * 5\%$	$d_t^p * 2.5\%$
Low-SS	$d_t^p * 2.5\%$	$d_t^p * 1.25\%$
High-SS	$d_t^p * 10\%$	$d_t^p * 5\%$

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 (0.5 times the basic case) and High-Capacity (1.5 times the basic case).

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 (17)-(57).

4.2 *Numerical results*

The model described by (17)-(57) was solved separately for each case using the parameters mentioned in subsection 4.1. The average time *CPLEX* taken to solve these cases was 267 seconds. The average optimality gap for all cases was around 0.1%.

Table 2 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 shipping, holding, and shortage costs for the essential medications represent 47%, 64%, and 28%, respectively. The expired medication cost is zero since the expired medication quantity at the hospital site is zero. The total shipping quantities are given in row 8 in the same table.

As expounded in subsection 3.2, currently, 18% of the shipped branded medications to the

Table 2: Solution results for the basic case

Total cost	Essential medications($)	Non-Essential medications($)	Total ($)
Objective function value			722,698
Shipping cost	117,778	133,432	251,210
Holding costs	152,750	84,488	237,238
Shortage costs	65,722	168,523	234,245
Expired medication costs	0	0	0

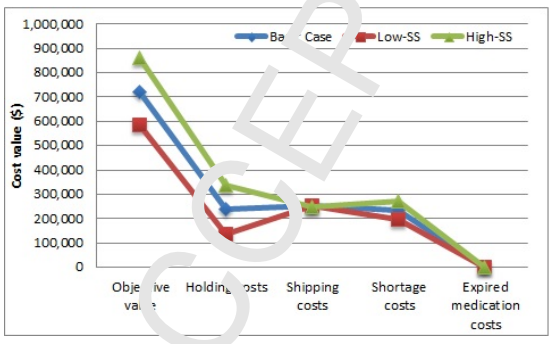
Total medication quantities	Essential medications (unit)	Non-Essential medications (unit)	Total
Shipping quantities	164,118	140,303	304,421
Shortage quantities	1,195	2,800	3,995
Expired medication quantities	0	0	0

hospital are expired at the customer zone. Implementing a VMI model under the assumption of deterministic demand, in contrast, would eliminate the medication expiration as also reported in Table 2.

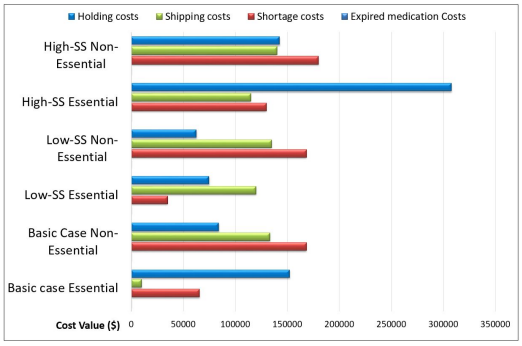
4.2.1 *Sensitivity analysis*

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

Figure 3 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%. The same behavior was noted for the holding and shortage costs. This comes as no surprise, since reducing the SS level reduces the total medication shortage and holding quantities by 16% and 43%, respectively. 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%.



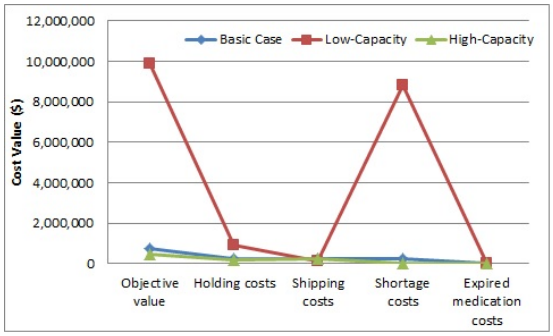
(a) Effect of SS level on the PSC costs



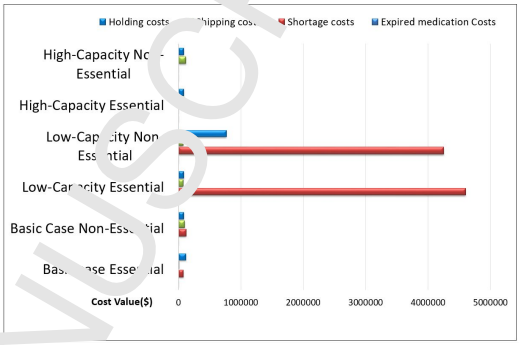
(b) Effect of SS level on the PSC costs per medication type

Figure 3: Effect of SS level on the various costs of the VMI model

The allocated capacity level has a direct influence on the shortage costs as shown in Figure 4. As anticipated, reducing the producer capacity assigned for the hospital to 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. It is noteworthy that the expired medication quantities under the VMI model are zero for all cases.



(a) Effect of allocated capacity levels on the PSC cost



(b) Effect of capcaity level on the PSC costs per medication

Figure 4: Effect of allocated capacity levels on the various costs of the VMI model

4.3 *Monte-Carlo simulation*

The VMI models in the previous subsections (4.1 and 4.2) are solved by considering a deterministic demand that was obtained from the real case study archived data. As expected, the VMI model succeeded in improving the sustainability of the supply chain under investigation. That is, no expired medications are observed in all cases. However, the demand of the hospital is an unknown parameter for which the producer is not certain about in advance. In order to mimic the reality, the effect of the demand uncertainty on the VMI model and on the quantity of expired medication is studied in this subsection.

We conduct a set of Monte-Carlo simulation experiments, Rubinstein and Kroese (2016), in order to quantify the quantity of expired medications under randomly generated demand profiles when the replenishment plan obtained from the deterministic VMI model (17)-(57) is implemented. To this end, we first generate a set of scenarios that mimic the uncertain behavior of demand. The simulation engine receives the replenishment amounts (Q^p_{it}) obtained from the deterministic VMI model along with random demand scenarios as inputs. Afterwards, it calculates the quantity of expired medications. The VMI simulation engine

contains an optimization model similar to the deterministic VMI one where the replenishment quantities (Q_{it}^p) are considered as a parameter (instead of a decision variable). The aforementioned simulation process is depicted in figure 5.

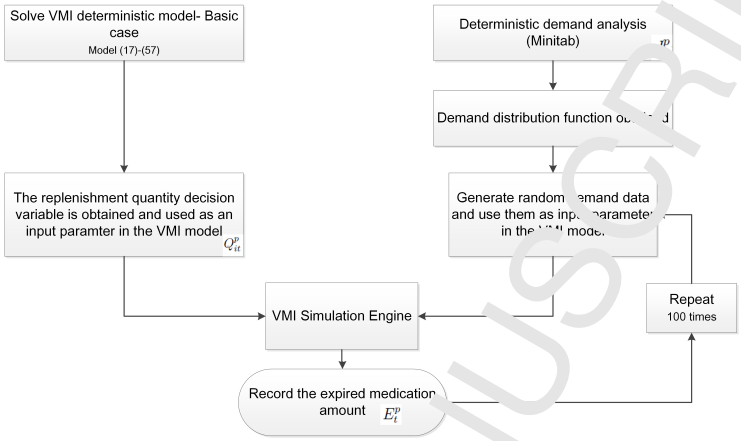


Figure 5: VMI model Monte-Carlo simulation process

It should be noted that the actual demand data collected from the real case was analyzed using a statistical package (Minitab 17) in order to obtain the demand distribution function and its parameters. The analysis revealed that the demand of all medications follow the Gamma distribution function. Table 3 represents the Gamma distribution function scales and shapes for all products.

Table 3: Demand distribution function analysis - Minitab Output

Product	Distribution function	Shape	Scale
Product 1	Gamma	0.68	873.06
Product 2	Gamma	0.39	10302.02
Product 3	Gamma	0.61	3538.98
Product 4	Gamma	0.37	5011.91

The results obtained from the 100 scenarios revealed that in 93% of the time no expired medications were observed. However, in 7 scenarios (7%), a positive amount of expired medications was noticed, especially for low demand scenarios. The quantity of expired medications for the aforementioned scenarios are reported in table 4. The third column in this table corresponds to the ratio of expired amounts over the quantity shipped to the customer (hospital). In fact, when the actual demand is significantly lower than the forecast (deterministic one, medications would remain in stock and get expired before being used.

Table 4: The medication expired (units and %) for some scenarios

Scenario no.	Expired medications (unit)	Expired medications (%)
1	84,726	27.83
2	82,852	27.22
3	82,734	27.18
4	77,792	25.55
5	65,676	21.57
6	56,142	18.44
7	39,216	12.88

4.4 *Managerial insights*

The results obtained from the the previous subsections (4.2 and 4.3) could provide the stakeholders of PSC, i.e., the producer and the hospital, some insights in order to improve the overall cost of the value chain in general and the sustainability image of the producer, in particular.

According to the results of sensitivity analysis on the SS level, this factor has a significant impact on reducing the shortage and holding costs. Therefore, the producer is prompted to review SS levels with the hospital and update them periodically in order to reduce the cost of the PSC.

Moreover, when testing two levels of the capacity assigned to the hospital against the basic case, the results demonstrate its crucial impact on the shortage costs. Therefore, the producer is advised to boost the capacity assigned to the hospital under investigation by a factor of 1.5 so as to avoid a significant amount of outsourcing and penalty cost, while ensuring a high service level. Likewise, by reducing medication shortages, the producer not only saves but he also receives more information on the hospital demand patterns that aid him in a more efficient planning of medication inventories.

Finally, the results of the Monte-Carlo simulation tests clearly indicate the robustness of the VMI model in the presence of the changes in the demand of medications in the hospital. In other words, despite considering the foretasted values of the demand, the replenishment plans proposed by this model result in zero wastage in 93% of scenarios while not affecting the amount of shortage. Hence, at the presence of realistic demand forecasts, the proposed model could be exploited by the producer and the hospital as a reliable strategy to reduce the amount of expired medications while maintaining a high service level.

4.5 *Sustainability implications*

The term sustainability typically consists of three pillars; society, environment, and economy. Our proposed model leads to improvement of all three pillars. The environmental impact of the supply chain is improved by eliminating expired medication; hence avoiding further issues regarding their disposal. It is true that adopting VMI model incurs a cost. Nevertheless, the major part of the cost is associated with the fixed cost of technological implementations. On the contrary, zero expired medications policy would save governmental penalties to the producer due to improper disposal and adverse environmental impacts. In addition, VMI enables the producer to better manage its capacity among all customers, and consequently increase revenue via providing medication to more customers. As a consequence, the fix set-up cost of implementing VMI is expected to be paid off in long-term. Finally, rather than spoiling medications due to inappropriate inventory policies, more patients would be able to receive them. This can be interpreted as the social impact of adopting this policy in pharmaceutical SC.

4.6 *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 (2013), 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 3.

Figure 6 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 according 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

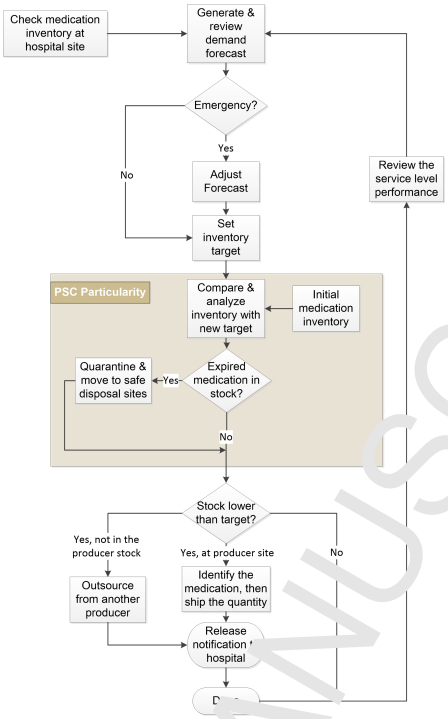


Figure 6: Proposed VMI process between *Generic PharmaX* and the hospital

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 this is the case, the expired medications are quarantined and then stock level is refined. The expired medications are sent to the government 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 treatment efficiency as 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 adjustments through the software updates. Upon the shipment release, the producer notifies 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.

5 Concluding remarks

In this article, we proposed a VMI model for the PSC that seeks the optimal quantity of medications that must be shipped by the producer to the hospital in each period over a planning horizon. The goal of the model is to minimize medication shortage at producer's site and the amount of expired medications at customer's site. Our experimental results on a real pharmaceutical company reveal the importance of adopting VMI system for the PSC entities on greening the supply chain through eliminating the medication wastage. In other words, sharing the medication stock level with the producer not only assists the pharmaceutical company to better manage the medication replenishment and to avoid outsourcing cost, it also guarantees no shortage at the customer site (hospital). Furthermore, it improves the sustainability of the whole value chain through minimizing the amount of expired medications that are featured with low salvage value, negative environmental footprint, and high recovery cost.

A sensitivity analysis was also provided to illustrate the effect of SS level and producer capacity on the inventory control management. From the results, it is recommended that the producer increase its capacity assigned to the hospital demand to avoid high outsourcing

costs. 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 the right amount of medications is kept in stock. Finally, a Monte-Carlo simulation was performed to investigate the demand uncertainty effect on the model. The results affirmed the efficiency of adopting VMI model in reducing the amount of waste medications.

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 its customer.

Although our model is representative of certain pharmaceutical value chains, we recognize that our results are limited due to specific assumptions made in the case study. In particular, 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 the VMI system implementation. For future work, considering more medication types and more than one hospital can be suitable. In this case, an efficient solution algorithm for solving the resulting large-scale MINLP model would be necessary. Also, current VMI model could be extended to incorporate the uncertain demand and a non-zero replenishment lead time. Finally, VMI partnership may be more beneficial for one stakeholder (e.g., the hospital). Therefore, research on methods to manage sharing of possible benefits among PSC stakeholders would also be of practical value.

Acknowledgments

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Appendix-A

Replacing $F^p_{it}.v^p_{(i-1)(t-1)}$ by γ^p_{it} imposes constraints (33), (34), and (36) to the model.

$$\gamma^p_{it} \leq M.F^p_{it}, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{33}$$

$$\gamma^p_{it} \leq v^p_{(i-1)(t-1)}, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{34}$$

$$\gamma^p_{it} \geq M.(F^p_{it} - 1) + v^p_{(i-1)(t-1)}, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{35}$$

$$\gamma^p_{it} \geq 0, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{36}$$

Replacing $F^p_{it}.L^p_{it}$ by λ^p_{it} imposes constraints (37), (38), and (40) to the model.

$$\lambda^p_{it} \leq M.F^p_{it}, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{37}$$

$$\lambda^p_{it} \leq L^p_{it}, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{38}$$

$$\lambda^p_{it} \geq M.(F^p_{it} - 1) + L^p_{it}, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{39}$$

$$\lambda^p_{it} \geq 0, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{40}$$

Replacing $F^p_{(i-1)t}.Q^p_{it}$ by β^p_{it} requires adding constraints (41), (42), and (44) to the model.

$$\beta^p_{it} \leq M.F^p_{(i-1)t}, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{41}$$

$$\beta^p_{it} \leq Q^p_{it}, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{42}$$

$$\beta^p_{it} \geq M.(F^p_{(i-1)t} - 1) + Q^p_{it}, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{43}$$

$$\beta^p_{it} \geq 0, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{44}$$

Replacing $F^p_{it}.Q^p_{it}$ by α^p_{it} requires adding constraints (45), (46), and (48) to the model.

$$\alpha^p_{it} \leq M.F^p_{it}, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{45}$$

$$\alpha^p_{it} \leq Q^p_{it}, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{46}$$

$$\alpha^p_{it} \geq M.(F^p_{it} - 1) + Q^p_{it}, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{47}$$

$$\alpha^p_{it} \geq 0, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{48}$$

Replacing $F^p_{(i-1)t}.L^p_{it}$ by δ^p_{it} requires adding constraints (49), (50), and (52) to the model.

$$\delta^p_{it} \leq M.F^p_{(i-1)t}, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{49}$$

$$\delta^p_{it} \leq L^p_{it}, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{50}$$

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

$$\delta^p_{it} \geq 0, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{52}$$

Replacing $F^p_{(i-1)t}.v^p_{(i-1)(t-1)}$ by $\mu^p_{(i-1)t}$ imposes constraints (53), (54), and (57) to the model.

$$\mu^p_{(i-1)t} \leq M.F^p_{(i-1)t}, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{53}$$

$$\mu^p_{(i-1)t} \leq v^p_{(i-1)(t-1)}, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{54}$$

$$\mu^p_{(i-1)t} \geq M.(F^p_{(i-1)t} - 1) + v^p_{(i-1)(t-1)}, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{55}$$

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

$$\mu^p_{(i-1)t} \geq 0, \qquad \forall p \in P, \quad \forall t \in T, \quad \forall i \in I \tag{57}$$