A Framework for Managing End-of-life Pharmaceutical Products

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ABSTRACT

A product is considered in its end-of-life (EOL) when it completes its service life time. Completion of service life time is either caused by deterioration or obsolescence. Deterioration implies that the product is no longer usable due to disintegration or degeneration. Obsolescence, on the other hand, refers to those products that are rendered invalid due to systemic, functional, and style mismatch or due to notification of expiration set by the manufacturer. Therefore, obsolete products are likely to preserve their initial conditions. Pharmaceutical products, specifically prescription drugs, constitute one product category that completes its service life time before it deteriorates. The mismatch between the utilization period and the obsolescence date leads to accumulation of stored (hibernating) or discarded EOL pharmaceutical products. Furthermore, following their expiration date, some of these pharmaceutical products also become toxic and hence hazardous to human health and the environment. The economically, socially, and environmentally sustainable option is to take back and reuse, recycle, and/or properly dispose of these products. Reverse logistics systems focus on such problems. With these motivations, this study proposes a reverse logistics framework that embodies environmental, economical and

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physical concerns for EOL pharmaceutical products. The Information Technology (IT) infrastructure required for the proposed system along with a comprehensive overview of the existing take-back regulations in the U.S. are also provided.

**Keywords:** End-of-life, information technology, life cycle, pharmaceuticals industry, reverse logistics, take-back programs.
1. Introduction

A product is considered in its end-of-life (EOL) when it completes its service life time. Completion of service life time is either caused by deterioration or obsolescence. Deterioration implies that the product is no longer usable due to disintegration or degeneration [1]. Obsolescence, on the other hand, refers to those products that are rendered invalid due to systemic, functional, and style mismatch or due to notification of expiration set by the manufacturer. Therefore, obsolete products are likely to preserve their initial conditions. Pharmaceutical products, specifically prescription drugs, constitute one product category that completes its service life time before it deteriorates. Research indicates that many patients discontinue the prescribed treatment and switch over to other medications [2, 3]. The mismatch between the utilization period and the obsolescence date leads to accumulation of stored (hibernating) or discarded EOL pharmaceutical products. The Healthcare Distribution Management Association (HDMA) estimates a three to four percent return rate for pharmaceutical products for redistribution, recycle and disposal [4]. These products that are unused and/or expired constitute a significant financial market since the majority of expired drugs in their unopened original container would be expected to remain stable for an average of 57 months after their expiration [3]. Following their expiration date, some of these pharmaceutical products - such as antibiotics - also become toxic and hence hazardous to human health and the environment [5], if not disposed of properly. The economically, socially, and environmentally sustainable option is to take back and reuse, recycle, and/or properly dispose of these EOL products. Reverse logistics systems focus on this problem and involve planning, management and controlling the flow of waste with appropriate EOL processing option, viz.,
reuse, recycle and/or proper disposal [6]. A well established reverse logistics system that holds apparent and consistent information and product flow of prescription drugs would also identify and prevent counterfeit medications. With these motivations, this study proposes a reverse logistics framework that embodies environmental, economical and physical concerns for pharmaceutical products. The Information Technology (IT) infrastructure required for the proposed system along with a comprehensive overview of the existing take-back regulations in the U.S. are also provided.

2. Background Research and Literature Review

The literature offers a broad variety of studies investigating forward logistics of pharmaceutical products. Forward logistics focus on the traditional flow, from manufacturers to distributors to consumers through the retailers. Even though the issue is now of significant importance to pharmaceutical companies, health organizations and governments [7], research on green reverse logistics operations of EOL pharmaceutical products is limited.

One of the few studies that provide data on returned pharmaceuticals is proposed by Sartori [4]. Martin [8] and Teunter [9] estimated the pharmaceutical return management cost to be $2.5 billion dollars and report an approximate $5 billion dollar cost for returned products due to expiration, damage, recall or improper delivery. Hunter et al. [10] reported approximately three to six percent return rate for pharmaceutical products. Cross [11] and Sartori [4] emphasized the social and financial significance of returned prescription drugs. Sartori, investigated various alternatives to transport expired medications for recycling or complete proper disposal, and reported that counterfeit drugs are approximately ten percent of the global pharmaceutical market [4]. The issue of waste transportation is also investigated by Jennings and
Scholar [12]. Lee and Chan [13] proposed an algorithm to determine the customer’s locations in order to reduce the total cost of reverse logistics transportation.

The complexity of reverse logistics systems and the importance of information technology (IT) in company performance are well documented. The proper utilization of IT leads to performance efficiency in the company by eliminating poor information flow and manual mistakes [14-20]. In terms of particular IT solutions, Lee and Chan [13] presented RFID as a solution to identify the category of the collected product in collection point. Vadde and Ilgin [21-23] also studied the economic benefits of sensor embedded products for EOL processing operations. In order to reduce the complexity of the reverse logistics systems and manage the network effectively, outsourcing is also proposed as one of the viable options [24, 25].

3. National Review

This section provides an overview of the current Food and Drug Administration (FDA) drug take-back rules and regulations in the United States. Our research indicates that all U.S. states have developed rules and regulations for drug recycling except the states of North Carolina, South Carolina and Oregon.

Even though not all medicines become toxic immediately after their expiration dates [26], there are still some drugs, such as medications to treat cancer and HIV, that become highly poisonous after the notified expiration date. In order to control the sale of expired drugs the FDA has devised various programs such as the “Shelf Life Extension Program”, which tests the stability of the drugs after their expiration [3].

In 2009, the National Conference of State Legislature (NCSL) has identified the state legislations to create prescription drug recycling, repository or redistribution program for EOL medications. According to the legislation, the EOL medications should be distributed to needy
individuals who cannot afford to purchase the expensive medicines [27]. NCSL also reports that 36 states have laws for drug recycling. Out of these 36 states, six of them, viz., Colorado, Florida, Kentucky, Minnesota, Nebraska and Wisconsin specifically focus on accepting and redistributing cancer medications [27].

Frisman [28] reports that the state of Washington has funded a product stewardship program in which all the drug sellers in the states will be involved and responsible to pay for collecting, transporting and disposing unwanted drugs, supposed to be implemented by January, 2012. The main purpose of drug take-back programs is to allow the safe, legal, and environment friendly disposal of extra drugs which helps to reduce health and environmental impacts of consumer products [29]. The economic viability of such programs is also reported. For instance, Fryer [30] reported that the redistribution of unopened prescription medicines in Pennsylvania is estimated to save the state approximately $1 million annually. Furthermore, Pomerantz [3] emphasizes the role of the FDA in monitoring and eliminating the redistribution of recycled medicines that are impure, misbranded, expired, or counterfeit. However, despite the advantages, laws and programs for redistribution of EOL drugs, pharmacies are reluctant to participate due to the unknown liability to the participants [31]. Figure 1 depicts the state of FDA laws regulating drug recycling in the U.S.A.

4. Methodology

In this section, a reverse logistics system for pharmaceutical products is proposed. The study portrays a composite system for End-of-life processing operations of pharmaceutical products. The system is modeled as a reverse supply chain that includes institutional targets, reverse logistics operations and the information technology (IT) infrastructure required for the EOL operations. The decision input includes uncontrollable and controllable factors. The model
embodies various physical, environmental and financial constraints while targeting multiple objectives.

![Map of the United States showing FDA laws for drug recycling]

**Figure 1** FDA laws in the United States of America for drug recycling processes

The proposed system consists of two main processes: 1) The collection process which includes a ‘Drug Take Back’ program, and 2) The inspection process.

Figure 2 depicts the forward supply chain and proposed reverse supply chain product and information flow, decision variables for the reverse logistics operations, and the EOL processing options for the pharmaceutical products.
Figure 2 Product and information flow for the forward and proposed reverse logistics system (Adopted from: [32])
4.1 Forward supply chain of pharmaceutical products

The forward supply chain starts with the end user’s need and the information flow through distributors, warehouses and manufacturers in order to meet the demand for pharmaceutical products.

4.2 Decision Input for the proposed reverse logistics system

The uncertainty in take-back systems increases the risk in ensuring the sustainability of the overall system. Utilization of accurate data that is shared among the related parties in the reverse logistics supply chain is effective in reducing this complexity. The proposed decision input module aims at reducing the vagueness in the overall reverse supply chain. Long term strategic decisions ensuring economic and environmental sustainability of the take-back operations are made at this level. The module utilizes two main data categories: (1) uncontrollable, and (2) controllable factors. Physical, financial and environmental targets of the company and system restrictions are also included in this module. Uncontrollable factors include the future demand for returned products and the rules and regulations which are imposed by the FDA and other governmental institutions.

Future demand for pharmaceuticals can be forecasted using historical data reported by various organizations such as the Healthcare Distribution Management Association (HDMA) [4]. Furthermore, various statistics on the form of EOL medications, i.e., liquid, gel, pills, or powder, etc.; would reduce the system complexity while allowing more accurate estimates for the profitability of the operations. Collecting data on the end user behavior and recording the reasons of returns; e.g., medication cutoff and deterioration, would aid in determining the reusability rates of prescription drugs. Determining the appropriate EOL operations such as redistribution,
recycling or complete disposition would lead to economic and environmental sustainability in the overall system.

Controllable factors include institutional goals for financial, environmental and performance related variables.

Overall, the proposed system focuses on reducing the lead time as a result of both, poor information flow and the high numbers of actors involved in the forward and reverse logistics operations.

Here, financial targets concentrate on the resale and recycling profits obtained from the reverse logistics operations, while environmental targets focus on reducing the environmental impact of these operations. Performance related targets aim at increasing the customer satisfaction while providing ease in take-back operations.

There are various constraints involved in the reverse logistics process of medications such as physical, financial, and environmental constraints. Physical constraints include capacity restrictions of the overall system including storage, manufacturing, handling, and recycling, in addition to the cooling facility allocations for perishable items. Financial constraints include the cost of reverse logistics of EOL medications such as transportation, storage, and inspection. Environmental constraints restrict the amount of disposal and impose a minimum level for recycling.

The decision phase covers all controllable and uncontrollable factors which are considered as significant input to implement the reverse logistics of EOL pharmaceutical products.
4.3 Product and information flow in the reverse logistics system

The proposed system is mainly partitioned into two processes: 1) Collection / End user notification and (2) Inspection.

Collection / End user notification: The FDA has initiated ‘Drug Take Back’ programs for EOL medications in almost all of the states in United States. Thus, the EOL medications from retailers, customers, and health organizations are accepted at various centers [29]. Once received, these medications are forwarded to next stage, namely the inspection centers. This transfer includes handling operations such as accepting, sorting, packing and the transportation of EOL drugs.

Inspection Process: Expiration dates for pharmaceutical products are set by manufacturers. The date indicates the end of the manufacturer’s responsibility. To determine the expiration date, a stability test is conducted to ensure that the identity, strength, quality and purity of the drug is in compliance with the FDA regulations during its useful life [33].

In the proposed system returned EOL medications are primarily sorted according to their expiration dates. Valid medications are sent to stability tests to ensure the validity of the drugs and are then redistributed. The expired drugs are further tested for their toxicity. Toxic drugs are disposed of properly where as non-toxic drugs are sent to redistribution and/or recycling facilities. Storage is considered for the drugs that have no market value at the given time period and/or for those that will not ensure financial gain.
4.4 IT infrastructure for the EOL pharmaceutical products

The proposed system aims at increasing the data quality and reliability throughout the supply chain. The system also allows the data to be shared among each party in the supply chain through the entire product life cycle.

Figure 3 illustrates the required IT infrastructure for the reverse logistics operations. At the inspection center, the barcode of EOL medications will be scanned and related stored information will be displayed, which will help to identify the drug and its contents. The database will update the status of the drug as EOL. The main input is provided by the barcode on the packaging in prescription medications and other pharmaceutical products. The database is visible to manufacturers, distributors, retailers, and customers. The data provide ease in decisions such as inventory management, warehouse management, and transportation.

After the EOL medications are returned to the collection facility, the information on the medication is read from the barcode and entered to the database. For prescription drugs, the data include the prescription number, the name of the medication, quantity, description of the drug such as color, shape, texture, etc., filling date, patient, prescriber, manufacturer information, and expiration date.

Following the system entry the information is made available to the other parties in the system. The medications are then differentiated based on the toxicity characteristics; i.e., toxic and nontoxic. Generally, the drugs which are used for HIV Aids treatment, Chemotherapy treatment for cancer, etc., become toxic after a period of their expiration date [3].

12
Figure 3 Data Flow Diagram of the Proposed Inspection Process

The drugs will be classified based on the expiration date and toxicity, and future actions take place as described below:

1) Unexpired drugs: Perform stability tests to determine the remaining life of the drug. Accordingly, shelf life of drug is extended and sent back to redistribution centers or warehouses
for further resale. The system database will update the expiration date and store the results of stability test of the drug and mark it as ‘Redistribute’.

2) Expired and Nontoxic drugs: Perform stability tests to analyze reusability of the drug. If it is reusable; meaning, if the drug is still in compliance with the FDA standards, then it is considered as a ‘still functioning’ product (Kongar & Gupta, 2009), and send back to redistribution centers or warehouses for resale. The system database will update the expiration date and store the result of stability test of the drug marking it as ‘Redistribute’.

If the drug is not reusable, further chemical tests will be performed to analyze its recyclability; meaning, regaining the chemical or substance value added to that particular drug (Kongar & Gupta, 2009). If it is recyclable, it will be sent to manufacturers for recycling processes.

If the tests result shows drugs are completely expired, then it will be sent for proper disposal and the system database will mark it as ‘Dispose’.

Regardless of the end destination, the packaging materials of pharmaceutical products: metal, plastic, paper, and glass, are also some of the items which can be regained via recycling operations. The system database will mark these packages as ‘Recycle’.

3) Expired and toxic drugs: Even though most drugs are still usable after their expiration date, there are few exceptions that become toxic following their expiration date. For instance, liquids that contain sugar or other flavoring additives become unstable faster than the remaining drugs. Antibiotic suspensions prepared from powder also become unstable and should be disposed properly. Hence, drugs which fall under this category will be sent for proper disposal processes in order to avoid natural hazards. The system database will be updated and will mark these drugs as ‘Dispose’.
4) Damaged drugs: The proposed database also considers the damaged medications. Damaged medications include broken tablets/pills or drugs with damaged wrappers/packets that would prohibit barcode scanning operations. In these cases where the system is not able to utilize barcode scanning, chemical tests will be performed to identify the contents of the drug. Then, the results of these tests including contents will be matched against the information stored in that particular drug database at the initial stage of the supply chain. Once the drug is identified, the stability tests will be performed to decide whether the drug is reusable, recyclable or subject to disposal. The system database will be updated accordingly.

It is also possible that the results of chemical test will not match the information stored in the database and the system will not be able to identify the drug. In these instances, these drugs will be sent for proper disposal to minimize the potential hazard to human health.

Once the return of EOL medication is submitted, the system will make available the information to all entities in entire supply chain. The overall goal of the information technology infrastructure is to remove inefficiencies such as delays, manual errors, and poor information and product flow from the product return process and to achieve pre-determined targets.

4.5 Challenges and Advantages of the proposed system

Cost: The proposed system includes a large variety of cost measures such as transportation, inventory, inspection, and EOL processing at every step. Furthermore, the proposed IT infrastructure introduces additional cost measures such as equipment, training, and planning to ensure system reliability and efficiency. However, effective use of information technology, government incentives and subsidizing would decrease the overall cost and even help create a financially viable system.
Pricing: When the drugs return to the retailer or manufacturer, a refund must be made based on the original price [3]. Since the price of the medication tends to fluctuate, it is quite difficult to estimate the correct pricing of the EOL drugs. Wholesale reductions, blanketing, and shelf life [34] are also factors that make pricing difficult for the credit system. The proposed IT system aims at creating an automated credit system that eliminates over-credit or under-credit of returns. Governments can also offer insurance and incentives to the customer to encourage buying recycled medications, which would help increase the demand for those medications [3].

Redistribution: The EOL medications that are not expired will be resold again if profitable. Furthermore, if the drugs are in good condition and their shelf life is also long, then those medications can be sold at higher rate than the original one [35]. The recyclers can use the difference between the acquisition cost and sale price to fund the expenses, including operation cost and profit. In addition, donation of these returned and refurbished EOL medications would add value to the public, as well as decrease the environmental damage by preventing unnecessary consumption, incineration or land filling.

Effective Process Management lower operation cost: Effective use of technology incorporates effective management processes to reduce cycle time and cost throughout the entire reverse logistics system. For example, based on history data in the system, forecast will predict the approximate quantity of returned medications at collection centers, which will lead to optimize transportation and inventory cost. The system provides a high level of visibility from one end to the other in the forward and reverse supply chain, which will result in reducing administrative cost.
5. Conclusions and future research

Three to four percents of drugs or pharmaceutical products are returned, corresponding to a significant amount in pharmaceutical manufacturing. Hence, it is important to implement a system for reverse logistics of these EOL pharmaceutical products. Redistributed, recycled or properly disposed products would help the pharmaceutical industry by regaining the chemical or substance value added to them with considerable benefits to human health and society.

The paper demonstrated an IT infrastructure that would ensure data accuracy to trace EOL pharmaceutical products and to improve the overall performance of the reverse logistics system. The uncertainty in the overall system is one of the main concerns in ensuring the financial stability of the reverse logistics operations. However, this study aimed at summarizing the current rules and regulations, highlighting the gaps in the literature, and proposed a reverse logistics system and the required IT infrastructure. The proposed system considered various controllable and uncontrollable constraints, goals and targets to put the idea of reverse logistics into practice.

Future research will include collecting data to analyze the total sale of pharmaceutical products, the number of products returned, the type of products or medication used for particular diseases, and existing ways to dispose of EOL medications in the U.S.

6. Acknowledgements and In Memoriam

This paper is dedicated to the memory of Katherine (Kay) Larobina Macari. This work has been inspired by her courage and strength of character. The authors would like to acknowledge the contribution of Dr. Jani Macari Pallis, who posed the initial problem.
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