Valorization of End-of-Use Medicines in the Pharmaceutical Industry - A Circular Economy Perspective

Vera Ribeiro Alves
Department of Engineering and Management, Instituto Superior Técnico
vera.ribeiro.alves@tecnico.ulisboa.pt

Abstract

Almost everybody requires medication at some point in their lives. The Pharmaceutical Industry is fundamental to human life and well-being and plays a crucial role a medicines' provider. Moreover, the market has experienced significant growth in recent years leading, inevitably, to a considerable growth of waste. Therefore, the sustainability of this industry has received growing attention from policymakers, organizations, and consumers. However, several barriers affect the adoption and development of sustainable supply chain initiatives contributing to waste growth throughout the process. Accordingly, this dissertation aims at creating solutions, tailored to the Portuguese reality, in order to implement the circular economy concepts in end-of-use medicines. To achieve this, it is necessary to comprehend the circular economy, its practices in the pharmaceutical industry and understanding the wastes along the supply chain. Therefore, a characterization of the pharmaceutical industry and a comprehensive literature review on circular economy and sustainability within this industry are going to be performed. Also, a case study in a Portuguese company will be explored as well as a survey made to the Portuguese population in order to propose accurate and feasible solutions. The results proved that there is a long path to be done, nevertheless with some strategic changes, it is possible to leverage the current initiatives and defining new ones. The strict legislation under which the pharmaceutical industry works could be, in fact, lighten and also partially changed without compromising the medicines' quality and minimizing waste, turning this industry more sustainable.

Keywords: Circular Economy; Medicines; Pharmaceutical Industry; Pharmaceutical Supply Chain; Sustainability

1.Introduction

During the last decades, the Circular Economy has been receiving greater attention from the more diverse industries and companies, recognizing sustainability as an important aspect to traditional business (Fogarassy & Finger, 2020). The Pharmaceutical Industry is no exception: consumers, lawmakers, and companies have been paying increasing attention to the industry's sustainability (Milanesi et al., 2020). An aging world population and the significant growth in the global pharmaceutical sector in recent years are raising awareness of the need to pursue sustainable development and a circular economy throughout the supply chain. However, the pharmaceutical sector has some particularities due to its very stringent guidelines and regulations (Faisal, 2015). Afterall, this industry has a direct impact on people's lives, contributing to their well-being in terms of health and quality of life. Therefore, they must follow specific legislation from the manufacturing to the products' end-of-life to guarantee medicines' high quality. This hinders the adoption of sustainable practices while increases the wastage throughout

medicines' life cycle. Moreover, one should not forget that, unlike a usual physical goods, if a medicine is broken, it cannot be “repaired” or, when a consumer no longer needs a medicine, it cannot be easily passed on and reused by other consumers (such as computers), which causes more waste. There is, therefore, an urgent need of reducing the waste present throughout the supply chain. In fact, there are already some contributions of the pharmaceutical sector in a circular economy and relevant examples demonstrate how the most sustainable pharmaceutical companies are addressing this topic and the activities that can be undertaken by the industry to reduce waste and turn the industry more circular. A paradigm shift of applying circular economy principles to achieve sustainable manufacturing is accepted by different manufacturing industries, including the pharmaceutical manufacturing industry, which has started to look into resource loops, such as drug ingredients, solvents, energy consumption (Ang et al., 2021).

Therefore, wastage during medicines' life cycle increases, having social, environmental, and economic impacts. Accordingly, it is necessary to understand how the different entities that integrate the supply chain are responsible for the waste and realize what are the critical issues in order to integrate the circular economy concept. Thus, the goal of this study is to identify the significant causes of waste and problems along the pharmaceutical supply chain and propose different solutions/scenarios and recommendations, taking into consideration the Portuguese reality, to integrate circular economy concepts in this industry, turning the supply chain more sustainable while minimizing waste. The focus will be on the downstream part of the supply chain, i.e., where the final product is already made. Moreover, in order to have a practical and close insight on this topic regarding the Portuguese reality, a case study applied to a Portuguese pharmaceutical company, Bluepharma Genéricos, will be studied to draw conclusions about it.

2. Literature Review

2.1 Circular Economy

The idea of the "circular economy" is not new. Its roots came from a variety of "schools of thought"; therefore, it cannot be traced back to one single date or author (Ellen MacArthur Foundation, 2012). As the concept of circular economy reflects parts of this vast number of theories and is grounded in the study of non-linear systems, there is a significant number of elements that perform an important role in the circular economy concept development. Ellen MacArthur Foundation (2015) incorporated some of these influences on its study and have created three main principles that they believe to be the fundamentals of circular economy definition: 1) Preserve and enhance natural capital by controlling finite stocks and balancing renewable resource flows; 2) Optimize resource yields by circulating products, components, and materials at the highest utility at all times in both technical and biological cycles; 3) Foster system effectiveness by revealing and designing out negative externalities. Moreover, another core content present in circular economy concept is 3Rs: Reduce, reuse and recycle. Later, a new framework, 9R, based on more circular economy strategies was created by Potting et al. (2017), where strategies in terms of increasing power to achieve circularity were emphasized. This approach offers a closed-loop, multiple-product life-cycle system, minimizing the environmental burden of a product in the whole life cycle. The 9R list are: Refuse, Rethink, Reduce, Reuse, Repair, Refurbish, Remanufacture, Repurpose, Recycle, Recover

2.2 Pharmaceutical Sustainable Supply Chain

The pharmaceutical supply chain, in which products are produced, transported, and consumed, is complex since it requires the participation of different stakeholders and has a variety of specific features, such as the high cost, comprehensive research and development and a high level of regulation throughout the supply chain, creating some significant and unique management challenges (Xie & Breen, 2012).

Prior to the manufacturing process, pharmaceutical manufacturers should select the most suitable raw material suppliers that highly comply with environmental and social responsibility (Low et al., 2016). Pharmaceutical manufacturing covers i) Active Pharmaceutical Ingredient preparation; ii) primary product formulation; and iii) secondary pack processing (Fine et al., 2005). Jiménez-Gonzalez et al. (2004) defends that practices such as solvent recovery and recycling are limited owing to the potential risk of cross-contamination and the high level of purity required, which can incur in an increased recovery cost. After the API manufacturing, the focus is on making product packaging recyclable, thus making pharmaceuticals more eco-friendly. The appropriate packaging design of medicine influences the logistic efficiency: poor quality may damage the product throughout the supply chain: transportation, storage, or on the retail shelf (Xie & Breen, 2014). In addition, emissions generated during this process depend on the type of packaging: Raju et al. (2016) performed a study comparing PVC blister packaging and aluminum

blister packaging. It was concluded that the former performs better in most of the impact categories considered.

Regarding the disposal, to facilitate safe disposal, Xie & Breen (2012) emphasized the importance of channels through which expired or unwanted medicines return to manufacturers. These return services (made from logistics providers or wholesalers) have the strategic objective of removing excessive storage of medication at home while reducing the environmental burdens from inappropriate disposal methods. However, their research also shows that customer compliance in returning the medicines is low, which becomes a setback in developing effective healthcare waste management in the pharmaceutical supply chain. Generally, the standard applied disposal approaches include incineration, deep burial, landfill, and sewer (Kwateng et al., 2014; Sreedhar et al., 2018). Regarding waste management, Veleva et al. (2017) analyzed current waste reduction goals and data on different disposal methods of eight biotech and pharmaceutical companies, including GSK, Biogen, Novartis, and Johnson & Johnson. It was concluded that all of them rely predominantly on recycling, energy recovery, and incineration to reduce waste instead of source reduction through changes in manufacturing and supply chain practices. Moreover, regarding the indicators used to measure waste practices, this study demonstrates that, despite the existence of standardized guidelines, reporting of waste data differs significantly, which makes it difficult to effectively compare companies' waste reduction practices and identify opportunities for improvement. Also, according to Milanesi et al. (2020), waste management is one of the concerned areas that remain unexplored and may represent opportunities for future research.

2.3 Integration of Circular Economy in Pharmaceutical Supply Chain

Ang et al. (2021) introduced the PM9R framework to meet the multiple inputs from academic research into a singular matrix to ease circular economy implementation in the pharmaceutical industry. It was concluded that research publications are mainly in the area of alternative chemistry, especially about pharmaceutical manufacturing design, while publications related to existing pharmaceutical manufacturing processes and waste treatment processes are significantly less. Moreover, Silvestri et al. (2021) also highlighted how sustainability and circular economy are strongly related to the concept of green chemistry. Moreover, Viegas et al. (2019) focus their research on reverse flows of end-of-life medicines and have associated circular economy and reverse logistics with Green Supply Chain Management as they keep green principles, such as wastage avoidance, in the supply chain. However, broad research on qualitative aspects of medicines reuse and wastage is scarce (Bekker et al., 2017; Walker et al., 2014).

In the context of end-of-life medicines, reusing becomes increasingly relevant, as significant quantities of medications that are not yet expired are leftover in houses, pharmacies, warehouses, hospitals. Therefore, opportunities for circularity lie mainly in the way patients and health professionals manage and value medicines that can be reused under careful supervision (Viegas et al., 2019). The literature review has revealed some gaps. First, a clear distinction between sustainability and circular economy in the pharmaceutical industry is not available and not made explicit. Second, regarding the few studies integrating the pharmaceutical sector and circular economy, the majority address the upstream part of the supply chain. In fact, the downstream part of the supply chain (use/disposal dimension, where the final product is already made) regarding sustainability remains poorly explored and qualified when compared to the manufacturing dimension.

3. Methodology

The research methodology employed is a multi-methodology approach in order to focus attention and use different methods on the relevant aspects of each phase (Mingers & Brocklesby, 1997). Figure 1 illustrates the generic steps of the methodology. Each step is further explained.

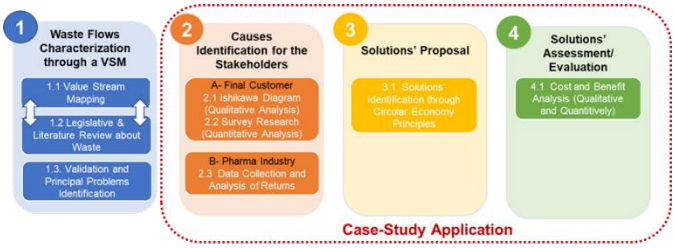

Figure 1: Proposed Research Methodology

Step 1- Waste Flows Characterization through a VSM

The main goal of this phase is to clearly represent the different waste flows throughout the pharmaceutical supply chain. For this, an extended and adapted form of the Value Stream Mapping (VSM) will be depicted, based on the methods created by Rother (1999) while adding environmental and resource wastes from the Environmental Value Stream Mapping- E-VSM- from EPA (2009). To complete this phase, steps 1.1 and 1.2 are essential to construct the VSM and collect information about waste

characterization. Thus, they will be realized simultaneously in order to understand how the map is going to be made as well as how it is going to be filled. As such, two different types of sources are going to be used to collect data: legislation documents and literature review. The literature review is the selection of available documents on the topic, which contain information, data, and evidence from a particular angle (Fink, 2009). Having accomplished the global picture of wastes present along the supply chain, step 1.3 will validate the diagram while also identifying the principal problems in the light of the scope previously determined. For this, expert interviews will be carried where the interviewees are integrated into the study as a representing group and have capacities as experts in a certain field of activity (Meuser & Nagel 2002). According to Flick (2009), an interview guide is developed, and it contains open questions followed by hypothesis-directed and confrontational ones.

Step 2- Causes Identification for the Stakeholders

In the next steps (steps 2, 3, and 4), the focus will be the Portuguese market, and, in some phases, it will be applied a case study methodology to a Portuguese pharmaceutical company, Bluepharma Genéricos. Although step 1 was a qualitative analysis done on a European level, it is important to tapper down to the reality of Portuguese consumers and market, so the universe analyzed be the same in order to propose coherent solutions.

This step aims at understanding the main causes that lead to the principal problems identified in the previous phase. It is crucial to recognize what the root cause of a given problem is, underlining the contributing factors or causes of a system in order to propose and develop sustainable solutions or actions. However, since there are different stakeholders involved (the final consumer and the industry itself), it was decided to employ different methodologies for each one in order to address their needs in a separate form. Therefore, this section is divided into two main subsections, A and B. Steps 2.1 and 2.2 focus on the consumer stakeholder (A).

Firstly, an Ishikawa Diagram is going to be carried to identify potential causes, relations and interdependences between factors, assigning them into different categories (Ishikawa, 1985). The brainstorming is going to be discussed with Portuguese experts in the field of sustainability and pharmaceutical area in order to taper down to the Portuguese reality. Step 2.2 follows, and a survey is going to be carried on in order to analyze the Portuguese consumer behavior and, once again, understand the root causes for the waste present.

As referred by Evans & Mathur (2005), this method allows to gather standardized information from a large sample of participants in a very cost-effective way. Therefore, this survey aims to 1) understand consumer behaviors on unused medicines that they maintain at their homes as well as the main reasons for keeping them 2) assess consumers' actions on disposal medicines and how willing the Portuguese population is to return their no longer needed medicines in pharmacies and 3) understand respondents' environmental and social consciousness and their engagement in activities that are better for the environment and human health.

After analyzing the consumer dimension, step 2.3 focuses on the pharmaceutical industry (stakeholder B) in Portugal and its purpose is to gather information about pharmaceutical waste. As such, Bluepharma Genéricos' data will be analyzed in detail. Hence, the research methodology employed will be a case-study analysis which is an analytical research strategy that investigates a current trend within its real-life context, based on an empirical investigation (Yin, 2003). Therefore, analysing the data from the returns from Bluepharma Genéricos, the final goal is to understand and explore the principal reasons for them to happen while identifying the associated wastage.

Step 3- Solutions' Proposal

The next step is thinking about possible solutions, given the Portuguese context, for some of the addressed problems, taking into account the circular economy principles. Step 3.1 aims at identifying different solutions, in which, there may be (or not) the consideration of different scenarios. According to Nielson & Karlsson (2007), scenarios are used for predicting, exploring, and anticipating the future. Following the research of O'Brien & Meadows (2013) and adapting it to this master thesis context, scenario planning will be proposed. A scenario planning process can be organized into three phases: 1) the preparatory phase: it provides specific issues and factual details about the current situation based on data as well as general theoretical aspects of the situation; 2) the development phase: it involves the development of the scenario narratives themselves; 3) the use phase: where the scenarios are used for their intended purpose. The first phase was accomplished with the previous steps of this study. Therefore, in step 3.1, it is going to be made, simultaneously, the development and part of the use phase. As such, the analysis goes through a step of creating different scenarios to minimize waste (the

development phase) while also analyzing and understanding the implications of the proposed scenarios. A remark should be done about the word “scenarios” in the context of this master thesis. There will be solutions where scenarios may not exist. However, the same reasoning will be applied since scenarios are, in general terms, coherent and plausible stories, described in words and numbers (Swart et al., 2004) that aim at opening the future by creating possible pathways. Therefore, the development phase will represent the description of each solution (or scenario, if it is the case), while the use phase will concern the implications of the solutions, the possible barriers and necessary incentives in order to turn the solutions feasible and concrete. All the solutions will follow the circular economy principles identified in the literature review chapter. Moreover, these solutions will be designed together with pharmaceutical experts in order to ensure their feasibility.

Step 4- Solutions’ Assessment/Evaluation

The final part of the methodology is the assessment of the different proposals created in the previous step. For this, a qualitative analysis of the benefits and trade-offs found will be performed for each of the players involved, in step 4.1. An economic evaluation (quantitative analysis) will also be carried out for the proposals whenever data regarding costs can be found. For that, a cost and benefit economic analysis will be employed. If it not possible to quantify the economic burden, only a qualitatively analysis will be done. According to Boardman et al. (2011), the first four basic steps of a cost-benefit analysis process are: definition of the project; decision on whose cost and benefits are counted for; selection of the measurement and measuring the appropriate costs and benefits (data collection) and estimation of the outcome of cost and benefits. Therefore, throughout this step, different variables and their components will be identified for computing the model alongside with the characterization and data collection process for each variable’s component. The data for the solutions that are feasible to do so will be collected from Bluepharma Genéricos and therefore, the extrapolation for the whole Portuguese market will be performed.

4. Results and Discussion

4.1. Waste Flows Characterization through a VSM

In this section, the VSM is presented, along with relevant data collected about waste characterization. The process of development of the VSM was obtained from the knowledge and information from the literature and legislative review which, although comprehensive, will have its emphasis on the final product itself.

Figure 2 represents the adapted VSM.

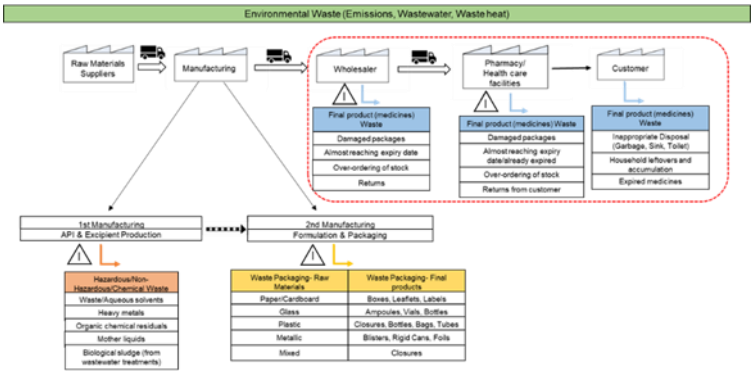

Figure 2: Adapted VSM

The waste and disposal problem starts with the production of the API and finishes with the final disposal of the pharmaceutical product. Therefore, the main entities are manufacturing, distributors, and the final consumer. The study will be focused on the distribution to the end-of-use/life phase, since it was a gap found in the literature review.

Interviews Main Findings

The VSM was validated by 4 experts who work within the pharmaceutical industry and, since the scope is the downstream part, wholesalers and pharmacists were both interviewed, and they give important inputs. All of them mentioned that the VSM presented is very complete and that the main categories of waste were all represented, given the European figure. In addition, it was possible to conclude that the most critical issues are the ones related to the household accumulation, the type of disposal by the end-consumers and some of the industry returns. These include unnecessary waste such as damaged packages (that accidentally may fell off and the damage relies only on the secondary packaging, not compromising the quality of the medicine but, because of the strict legislation, they have to go to waste) and waste concerning expiry date (in Portugal, in practice, any product whose shelf life ends in 6 months can no longer be in the market and cannot be donated). It is, therefore, important to analyze the reasons why consumers accumulate this kind of waste at home, as well as to explore the problem of the returns of the companies, the damaged boxes and expiry date issues.

4.2 Causes Identification for the Stakeholders

4.2.1. Ishikawa Diagram

Taking into account the literature review of the previous step, it is possible to identify a variety of factors throughout the supply chain entities, from

manufacturer to patient, contributing to this problem such as: manufacturers may produce unnecessarily large packages (West et al., 2014); pharmacists are not always allowed to split packages into smaller quantities and thus dispense excessive amounts to the patient that eventually go unused and wasted (Bekker et al., 2018a); the patient may have side effects with the treatment prescribed leading to therapy changes that may result in excess of dispensed medication (Coma et al., 2008; Braund et al., 2007; Ekhedal et al., 2006)

Figure 3 illustrates the Ishikawa Diagram for the main causes of waste concerning the final consumer.

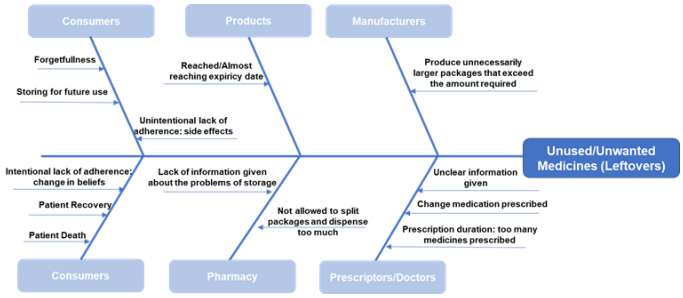

Figure 3: Ishikawa diagram for unused/leftovers medicines

As it is represented, although the waste occurs on the patient level, i.e., the ultimate responsibility is at the patient, causes may rely in other entities. The reasons represented in Figure 3, will serve as the basis to some of the survey's questions, more precisely, in the ones intended to understand why Portuguese people accumulate their medicines at home (both unused/unwanted). Moreover, as pointed out in the literature review, the disposal method is also a main topic that will be addressed in the survey. In that way, the main objective is to identify and assess solutions tailored to solve the critical problems.

4.2.2 Survey Research

The survey responses were gathered online, and a total of 570 responses were achieved. It was possible to conclude that:

People have the tendency to stock accumulate unused and/or expired medications in their homes. In this study, this tendency was confirmed, since 86% of the respondents stated that they had unused/unwanted medications at home and 80% of the respondents have expired medicines. The common reason to possess medicines is storing for future use. However, if they are not used, these medicines will eventually reach their expiry date and end up in the garbage.

It was also found that, among the consumers who have medication leftovers, although the vast majority is aware of the correct way to dispose of unused and/or expired medicines, most proceed incorrectly, putting them in the regular garbage, sink or toilet. This can be justified by laziness and old habits. It is, therefore, important to facilitate this process while give more information and guidance in order to get people more sensitive to this topic and remind them the importance of the medicines' right disposal.

It was also pointed as a common reason for having stockpiled medicines, the number of medicines in each package, that exceed the necessary. There is, therefore, a need for increased cooperation between health systems and the pharmaceutical industry to decrease waste accumulation.

Finally, this study also shows that some practices would make people return more often their pharmaceutical wastage, which could reduce the accumulation of medicines, change their disposal behaviors, and consequently reduce the harmful impacts on the environment and public health. Some of these practices and suggestions will be pointed out on section 5.3.

4.2.3 Analysis of the returned medicines from Bluepharma Genéricos

Analysing the returns sample of Bluepharma Genéricos, it was possible to conclude that the critical problems for the majority of waste that occur is due to legislation obligations. The need to return medicines cannot be completely eliminated since it mainly occurs due to expiry date or having primary packaging indeed damaged which are things that cannot be totally avoided. However, as it was confirmed, several packages are unnecessarily considered waste. Therefore, it should be the possible to reuse these types of packages instead of mandatorily send to be destroyed. Regarding expiry date, the main problem relies with the 6 months stipulated by the current processes of the industry. Regarding damaged boxes, which, although less common than expiry date issues, represent a significant amount of waste when extrapolating for the whole pharmaceutical market.

All this waste represents a burden not only to the pharmaceutical companies but also to the state once the Portuguese National Health Service is in charge of the reimbursement of some medicines and medical devices, i.e., it covers a percentage of the costs of some medicines.

4.3. Solutions' Proposals

Given the identified root causes of the problems and the analysis made throughout this master dissertation, it is now pharmaceutical wastage possible to make some suggestions and propose solutions to reduce the pharmaceutical wastage,

either at consumer or industry level, in a holistic form bearing in mind the Portugal context. When considering the application of circular economy principles to the pharmaceutical supply chain, the best methods for reducing pharmaceutical wastage in the downstream part of the supply chain include reducing, reusing, and recycling the materials and the final product, with the minimization of waste set as a priority. Figure 4 presents a matrix, in which in the center is depicted the general structure three proposed solutions (represented by the black circles) as well as their integration within the pharmaceutical supply chain, which includes the consideration of forward and reverse flows. The forward flow is represented in blue while the reverse flow is represented in dashed arrows, both in green and orange).

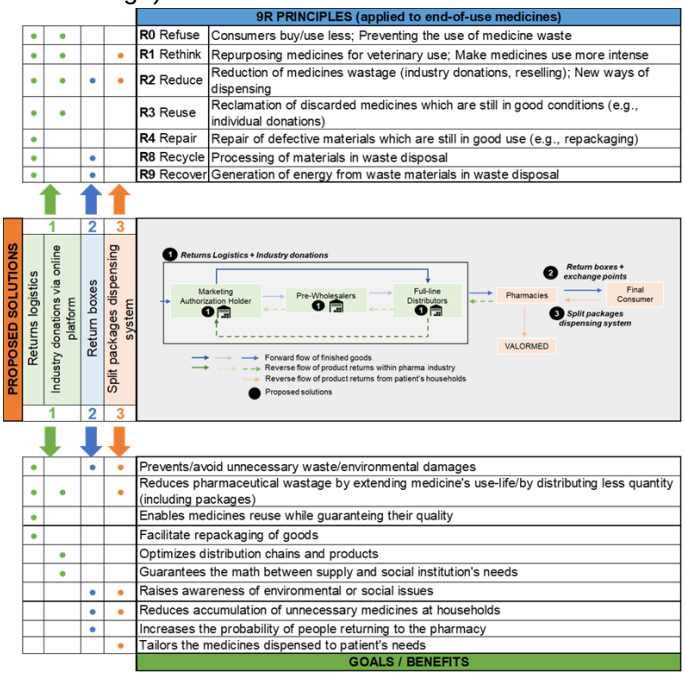

Figure 4: Solutions proposed linked with 9R principles and the according goals/benefits

Solution 1 concerns the returns logistics process, i.e., the creation of space in the facilities/warehouses where the industry "waste" (coming essentially from expiry date issues and damaged materials- as concluded in the previous section) would be processed and managed in order to be redistributed. This solution also includes an online platform where social institutions and the whole pharmaceutical market would be in contact to facilitate the medicines redistribution while matching the real needs of the society and availability on the industry. Therefore, this solution is linked with Refuse (by preventing and avoiding unnecessary waste and environmental changes), Rethink, Reduce (by extending medicines' use-life), Reuse (by donating the medicines), Repair (repackaging of goods), Recycle and Recover. The goal of this proposal is to extend these medicines' use-life while reducing the waste. As such, industry donations are the most feasible option. In fact, donations can improve the access to medicines from people in need while reducing pharmaceutical waste. In fact, the Medicines Bank, which is an initiative that already exists within the pharmaceutical companies) has already developed a similar platform that, according to the experts, is friendly user and fulfills its purpose. However, this sharing platform is exclusively meant for medication that has always remained under the strictly controlled storage conditions legally imposed. As such, the solution proposed leverages it. Moreover, another difference regarding the existing Medicines Bank proposal is to extend the doable products to wholesaler distributors and pre-wholesalers since these entities also have in their facilities their own waste created due to regulations and that cannot be sold for the following supply chain entities (the internal waste).

Solution 2 concerns sustainable cardboard boxes delivered by pharmacies to end-consumers in order to incentivize them to return more often unwanted/expired medicines. This is linked with the following Rs: Reduce, Recycle and Recover and leverages the pharmaceutical wastage in the following ways: prevents/avoid unnecessary waste/environmental damages; raises awareness of environmental or social issues; reduces accumulation of unnecessary medicines at households; increases the probability of people returning to the pharmacy.

As concluded by the survey, the accumulation of unwanted medicines represents a problem for pharmaceutical waste. Moreover, respondents believe that it is desirable to return unused household medicines to a collection point, which indicates that the use of these boxes would be a well-received and beneficial idea. As such, it would be a complement of the take-back program that already exists, promoted by VALORMED to encourage people to make the domestic collection of medicine residues and returning them to a pharmacy. Moreover, this solution also proposes a points-exchange incentive to form a more effective system for collecting unwanted medicines. To incentivize their returns, whenever individuals return their unwanted medicines to the pharmacy, they would obtain points for this delivery.

The accumulation of these points achieved by the packages returned in the pharmacy can be redeemed, by a certain proportion, into cash vouchers that can be used to have discount in some products (over-the-counter medicines). These exchange points also serve to encourage

people to change their old habits. As concluded by the survey, more than 70% of the respondents use just one method of disposal. Therefore, from a changing behavior strategy, if they begin to only dispose of their medicines by going to a pharmacy, chances are higher of not having a combination of other different (incorrectly) means.

Solution 3 is a new way of dispensing in pharmacies where packages could be split on smaller units which would turn the dispensing method tailored to the customers' needs (and according to what doctors prescribed). It is linked with Rethink and Reduce since it prevents the unnecessary waste (it tailors the medicines dispensed to patient's needs) and reduces it once the quantity distributed would be less. Therefore, the accumulation of unnecessary medicines in households will be reduced. By dispensing only the right quantity, unnecessary waste and the accumulation of medicines will be avoided, and it will ensure that patients do not take more medicines than the prescribed. With the splitting, the user is prevented from keeping medicine leftovers at home, reducing the possibility of adverse effects and intoxications, derived from self-medication. In addition, there is less environmental impact resulting from the disposal of medicines. The fractioning procedure would be carried out in pharmacies, under the responsibility of a qualified pharmacist. In order to ensure the safety of the fragmented drugs, the packaging should allow for their subdivision, ensuring the characteristics of the original form of the product until it reaches the final consumer. The subdivision of the drug packaging occurs without breaking of the primary packaging.

The feasibility of this solutions relies on the assumption that Portuguese legislation is adapted in such a way that it allows the dispensing on pharmacies in this splitting packages. This will need regulated documents, rules and clear guidelines to be delivered to pharmacies as well the appropriate and timely training of pharmacists. Moreover, doctors should be aware of this practice to begin to prescribe the quantities in terms of number of pills instead of number of packages.

4.4. Solutions' Analysis/Assessment

Given the proposed solutions, this section aims at assessing the benefits and trade-offs of implementing each solution. Each solution is going to be evaluated separately: a qualitative analysis will be made for each solution however, for the first one, a more in-depth quantitative analysis with Bluepharma Genéricos' data is going to be carried. Based on the results (both benefits and drawbacks, it will be possible to assess whether the stakeholders involved will leverage in implementing these systems.

Solution 1: Reverse logistics + industry donations

Table 1 analyses the overall benefits and disadvantages for the different stakeholders.

Table 1: Qualitative analysis of solution 1

	Pharma market	State	Final consumer
Benefits	• transportation costs to social institutions eliminated • integration of this initiative into the social responsibility strategy • reduce disposal costs • promotion of their products	• spare the reimbursement cost of the medicines that otherwise would have to be bought. • the reduction of waste disposal (incineration/recycling) contributes to the fulfillment of the established environmental goals	• free access to medication • quality life improvement
Drawbacks	• alocattion of human resources to sort and manage the process • disregard of the core activities	• transportation costs • the legislative changes require a task force involving all the stakeholders	

As demonstrated in Table 1, for the companies, the transportation costs to social institutions will be eliminated and transferred for the state however, the "burden" of logistics and the possible need to allocate human resources to sort and manage the process in an accurate way can be seen as a drawback. The state will have gains: by reducing prescriptions, it would save in their reimbursement. The end-consumer: both social institutions and patients will only benefit from this solution since they have access to the medicines that otherwise they could not afford thus contributing to their quality of life. Regarding the quantitative analysis, two different scenarios are considered: the Actual Scenario (AS) and the Proposed Scenario (PS), where the main differences are represented in Table 2.

Table 2: Differences between the AS and the PS.

	Actual Scenario	Proposed Scenario
Online platform	INFARMED	INFARMED
Donor entities	MAH	MAH Pre-wholesalers FLW
Donate medicines with shelf life < 6 months	No	Yes
Donate damaged packages	No	Yes
Transportation costs	MAH	State

INFARMED would continue to be in charge of the online platform management. One of the differences rely on the possibility of not only MAH but also pre-wholesalers and FLWs to donate their medicines since all these entities have internal waste (e.g., damaged packages from operations inside their warehouses). Moreover, the shipment of traded goods would be organized in a safe, GDP compliant manner to guarantee safety and quality at every stage however, the state would cover this cost. As such, this would not be a burden for pharmaceutical companies, and they would have more incentives to embrace this initiative. Moreover, as aforementioned, damaged packages if in compliance with certain criteria and medicines with shelf life of less than 6 months would be possible. Table 3 analysis the cost and benefits, comparing both scenarios.

Table 3: Cost and Benefit Analysis for solution 1

	ACTUAL SCENARIO (AS)			PROPOSED SCENARIO (PS)		
COSTS	**COMPANIES**	**STATE**	**CONSUMER**	**COMPANIES**	**STATE**	**CONSUMER**
Transportation Costs						
Number of deliveries	6 deliveries/month	-	-	-	14 deliveries/month	-
Unit cost	5€/delivery	-	-	-	5€/delivery	-
Total Transportation Costs	360,00 €	-	-	-	900,00 €	-
Disposal Costs						
Unit item disposal cost	0,16€/package	-	-	0,16€/package	-	-
Quantity of items disposable	2283	-	-	0	-	-
Total Disposal Costs	365,28 €	-	-	0,00 €	-	-
Total Costs	725,28 €	-	-	0,00 €	900,00 €	-
Total Costs for Pharma Market	72 528,00 €	-	-	0,00 €	90 000,00 €	-
BENEFITS (Cost Savings)						
Economic Value of Avoided Waste						
Quantity of items donable	-	2283	2283	-	16460	16460
NHS reimbursed	-	8,04 €	-	-	8,04 €	-
User-copayment	-	-	4,43 €	-		4,43 €
Total Value of Avoided Waste	-	18 355,32 €	10 113,69 €	-	132 338,40 €	72 917,80 €
Avoided Cost for the Disposal						
Unit item disposal cost	0,16€/package	-	-	0,16€/package	-	-
Quantity of items for disposal	2283	-	-	16460	-	-
Total Value of Avoided Disposal	365,28 €	-	-	2 633,64 €	-	-
Total Savings	365,28 €	18 355,32 €	10 113,69 €	2 633,64 €	132 338,40 €	72 917,80 €
Total Savings for Pharma Market	36 528,00 €	1 835 532,00 €	1 011 369,00 €	263 364,00 €	13 233 840,00 €	7 291 780,00 €

As such, for the AS, companies have more costs than benefits. However, for the proposed scenario, they will clearly have more benefits than costs since transportation costs would be the State's responsibility and the number of social institutions actively participating on this initiative will have a significant growth. Moreover, the State will have more savings derived from the increased number of packages that will be donated. The final consumer will also increase their savings in 86%. A remark should be done about the extrapolated data. The extrapolated results did not take into consideration both pre-wholesalers and FLW internal waste once it cannot be found. Therefore, the gains from the proposed solution would be increased, for the three main entities represented.

Solution 2: Return boxes + incentive scheme

Table 4 summarizes the overall benefits and disadvantages of this solution for the different actors.

Table 4: Qualitative analysis of solution 2

	Pharmacies	Final consumer
Benefits	• increase in sales caused by people going to the pharmacy and exchanging points • boost customers' loyalty to the participating pharmacies	• contribution to a better environment • discounts on the purchase of goods at the pharmacy
Drawbacks	• allocation (albeit in a small percentage) of customer service time to the accounting of returned packaging and respective points on the card	• the inconvenience of storing medicines at home and having to go to the pharmacy to return them instead of throwing in the trash

With the points exchange incentive scheme, it is expected that the pharmacies in which the points will be swap, will enhance their sales. However, a setback that can be pointed out is related to the increase of the time spent with each customer. From the consumer point of view, although the "inconvenient" of having to go to the pharmacy more regularly in order to return their medicines, there are advantages related to the possibility to benefit from the discounts on goods bought at the pharmacies. Moreover, taking into account the natural attitude of people, this scheme could boost customers' loyalty to the participating pharmacies. A remark should be done regarding the benefit of the end consumer of contributing to a better environment. Concern is increasing about the harm the medicines do to human health and the environment. Protecting the planet is everyone's responsibility and each one of us can play an active role protecting the environment and achieving a better world.

Solution 3: Split package dispensing system

Table 5 depicts the pros and cons regarding the split package dispensing system.

Table 5: Qualitative analysis of solution 3

	Pharmacies	Final consumer	State
Benefits		• contributing to a better environment • avoid having to take unnecessary medicines at home, having to store them, and having to return them so often	• do not have to reimburse so many medicines
Drawbacks	• increase of time handling the medication amount needed by the user • re-evaluation of stock identification inside the	• cost allocated to the bags (if needed)	

As represented in the table, this proposal essentially favors the user, who will not need to keep unneeded medication, and the State, which will see its level of co-payments reduced. For the pharmacies there is no additional value with this proposal. In fact, pharmacists will increase the time spent dispensing the right number of medicines for each customer. Moreover, a reorganization of stocks' identification is going to be need as well as strict guidelines to be followed by pharmacists. The consumer may have, however, an additional charge: the cost of the bag whenever a package needs to be split in order to deliver the right quantity to the patient. On the other hand, regarding the benefits, the non-inconvenience of having to return the medicines to the pharmacy so often can be pointed out as well as the contribution to a better environment.

5. Conclusions and Future Work

This master's dissertation aimed at using circular economy principles in the downstream part of the pharmaceutical supply chain, focusing on the use/disposal part in order to reduce the waste present in this sector. A detailed study of the pharmaceutical was presented, starting on a European level, and then tapering down to the Portuguese reality to propose tailored solutions. The conclusion to be taken from this master's dissertation points out that there are some good practices going on that can still be leveraged and increase their scale so the impact of such practices can be even enlarged, and sustainability improved overall. For that, one crucial stakeholder has a decisive role: the government and its regulations which, most of the times, hinder the sustainable process. Due to the unique nature of medicines and their critical role in global health, their quality must be guaranteed. However, there are some measures that could be lighten and would not compromise it. Therefore, it is also proposed to work on legislation and lightening some regulations (for example, in terms of validity and damaged packages). For future research, it would be interesting to develop a quantitatively analysis to the solution of the split package dispensing system as well as a life cycle analysis for the solutions presented throughout this dissertation. Also, the possibility of having an established link between veterinary and human medicine could be developed, such as procedures or methodologies to use medicines to humans for animals. Lastly, a thorough study of the regulations to analyze the global impacts of the change of specific regulations and common practices among the pharmaceutical world towards a greater sustainability should be made.

6. References

Ang, K. L., Saw, E. T., He, W., Dong, X., & Ramakrishna, S. (2021). Sustainability framework for pharmaceutical manufacturing (PM): A review of research landscape and implementation barriers for circular economy transition. *Journal of Cleaner Production*, *280*, 124264.

Bekker, C. L., Gardarsdottir, H., Egberts, T. C. G., Bouvy, M. L., & van den Bemt, B. J. F. (2017). Redispensing of medicines unused by patients: a qualitative study among stakeholders. *International Journal of Clinical Pharmacy*, *39*(1), 196–204.

Bekker, C., Gardarsdottir, H., Egberts, A., Bouvy, M., & van den Bemt, B. (2018a). Pharmacists' Activities to Reduce Medication Waste: An International Survey. *Pharmacy*, *6*(3), 94.

Boardman, A., Greenberg, D., Vining, A., Weimar, D. (2011). Cost-Benefit Analysis. Concepts and Practise. Pearson Prentice Hall, New Jersey, USA.

Braund, R., Peake, B. M., & Shieffelbien, L. (2009). Disposal practices for unused medications in New Zealand. *Environment International*, *35*(6), 952–955.

Coma, A., Modamio, P., Lastra, C. F., Bouvy, M. L., & Mariño, E. L. (2008). Returned medicines in community pharmacies of Barcelona, Spain. *Pharmacy World and Science*, *30*(3), 272–277.

Ekedahl, A. B. E. (2006). Reasons why medicines are returned to Swedish pharmacies unused. *Pharmacy World and Science*, *28*(6), 352–358.

EPA. (2009). *The Lean and Chemicals Toolkit*. 82.

Evans, J. R., & Mathur, A. (2005). The value of online surveys. *Internet Research*, *15*(2), 195–219.

Faisal, M. (2015). Research Analysis on Barriers to Green Supply Chain Management in Pharmaceutical Industries. *Review of Public Administration and Management*, *03*(01), 1–5.

Fine, C. H., Singh, M. P., & Others. (2005). *The pharmaceutical supply chain: a diagnosis of the state-of-the-art*. 1–158.

Flick Uwe. (2009). An Introduction To Qualitative Fourth Edition. *SAGE Publications*.

Fogarassy, C., & Finger, D. (2020). Theoretical and practical approaches of circular economy for business models and technological solutions. *Resources*, *9*(6), 1–9.

Ellen MacArthur Foundation. (2012). Towards the Circular Economy: Economic and Business Rationale for an Accelerated Transition. Report. Available at: https://www.ellenmacarthurfoundation.org/assets/downloads/publications/Ellen-MacArthur-Foundation-Towards-the-Circular-Economy-vol.1.pdf (Accessed: 10 November 2020)

Ellen MacArthur Foundation. (2015). Towards a Circular Economy: Business Rationale for an Accelerated Transition. Report. Available at: https://www.ellenmacarthurfoundation.org/assets/downloads/TCE_Ellen-MacArthur-Foundation_9-Dec-2015.pdf (Accessed: 10 November 2020)

EPA. (2009). *The Lean and Chemicals Toolkit*. 82.

Ishikawa K. (1985). "What is Total Quality Control?" The Japanese Way, Prentice Hall, New Jersey

Jiménez-Gonzalez, C., Curzons, A. D., Constable, D. J. C., & Cunningham, V. L. (2004). Expanding GSK's Solvent Selection Guide - Application of life cycle assessment to enhance solvent selections. *Clean Technologies and Environmental Policy*, *7*(1), 42–50.

Kwateng, K. O., Debrah, B., Parker, D. V., Owusu, R. N., & Prempeh, H. (2014). Reverse Logistics Practices in Pharmaceutical Manufacturing Industry: Experiences from Ghana. *Global Journal of Business Research*, *8*(5), 17–26.

Low, Y. S., Halim, I., Adhitya, A., Chew, W., & Sharratt, P. (2016). Systematic Framework for Design of Environmentally Sustainable Pharmaceutical Supply Chain Network. *Journal of Pharmaceutical Innovation*, *11*(3), 250–263.

Meuser, M., & Nagel, U. (2002). The Expert Interview and Changes in Knowledge Production. In book: Interviewing Experts (pp.17-42). https://doi.org/10.1057/9780230244276_2

Milanesi, M., Runfola, A., & Guercini, S. (2020). Pharmaceutical industry riding the wave of sustainability: Review and opportunities for future research. *Journal of Cleaner Production*, *261*, 121204.

Mingers, J., & Brocklesby, J. (1997). Multimethodology: Towards a framework for mixing 87 methodologies. Omega, 25(5), 489–509.

Nielson, S.K., Karlsson, K. (2007). Energy Scenarios: A Review of Methods, Uses and Suggestions for Improvement. *International Journal of Global Energy Issues* 27(3):302-322.

O'Brien, F. A., & Meadows, M. (2013). Scenario orientation and use to support strategy development. *Technological Forecasting and Social Change*, *80*(4), 643–656.

Potting, J., Hekkert, M., Worrell, E., & Hanemaaijer, A. (2017). Circular Economy: Measuring innovation in the product chain - Policy report. *PBL Netherlands Environmental Assessment Agency*, *2544*, 42.

Raju, G., Sarkar, P., Singla, E., Singh, H., & Sharma, R. K. (2016). Comparison of environmental sustainability of pharmaceutical packaging. *Perspectives in Science*, *8*, 683–685.

Rother, M. (1999). *Learning to See value stream mapping to add value and eliminate muda*.

Silvestri C, Silvestri L, Forcina A, Di Bona G, Falcone D. (2021). Green Chemistry contribution towards more equitable global sustainability and greater Circular Economy: A systematic literature review, *Journal of Cleaner Production*.

Sreedhar, A., Apte, M., & Mallya, R. (2018). Pharmaceutical Waste Management. *International Journal of Pharmaceutical Sciences Review and Research*, *52*(1), 82–86.

Swart, R. J., Raskin, P., & Robinson, J. (2004). The problem of the future: Sustainability science and scenario analysis. *Global Environmental Change*, *14*(2), 137–146.

Veleva, V., Bodkin, G., & Todorova, S. (2017). The need for better measurement and employee engagement to advance a circular economy: Lessons from Biogen's "zero waste" journey. *Journal of Cleaner Production*, *154*, 517–529.

Viegas, C. V., Bond, A., Vaz, C. R., & Bertolo, R. J. (2019). Reverse flows within the pharmaceutical supply chain: A classificatory review from the perspective of end-of-use and end-of-life medicines. *Journal of Cleaner Production*, *238*.

Walker, P. H., Seuring, P. S., Sarkis, P. J., & Klassen, P. R. (2014). Sustainable operations management: recent trends and future directions. *International Journal of Operations & Production Management*, *34*(5), 1–12.

West, L. M., Diack, L., Cordina, M., & Stewart, D. (2014). A systematic review of the literature on 'medication wastage': an exploration of causative factors and effect of interventions. *International Journal of Clinical Pharmacy*, *36*(5), 873–881.

Xie, Y., & Breen, L. (2012). Greening community pharmaceutical supply chain in UK: A cross boundary approach. *Supply Chain Management*, *17*(1), 40–53.

Yin, R. K. (2003). Case Study Research, Design and Methods (3rd ed). Newbury Park: SagePublications.