Reverse logistics for the end-of-life and end-of-use products in the pharmaceutical industry: a systematic literature review

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Abstract

Purpose – The aim of this paper is to develop a systematic literature review (SLR) aiming to identify reverse logistics (RL) concepts and practices applied to the end-of-life (EOL) and end-of-use (EOU) of pharmaceuticals and to identify and synthesize, through bibliometric indicators, research opportunities on RL, considering the analysis of publications in the periodical *Supply Chain Management: An International Journal* (*SCMij*).

Design/methodology/approach – The SLR followed two steps, namely, search for articles on the subject and content analysis of selected material and bibliometric analysis of publications using VOSviewer®.

Findings – The SLR allowed the compilation of evidences regarding pharmaceutical RL in the groups: environmental risk, the RL evolution and regulatory and stakeholder's educational perspective. Despite the timid specific literature on pharmaceutical RL, it was also possible to point out research gaps and opportunities. Pharmaceutical RL seems to be influenced by studies from traditional RL including mathematical modeling, managerial strategies and technologies but prescind of a systemic solution. Besides reducing environmental impact, the motivation to implement pharmaceutical RL resides in its potential for revenue. Considering integrated logistics as a trend and an emerging issue, RL for the pharmaceutical industry needs to be addressed more thorough and broadly.

Research limitations/implications – The limited number of papers returned in this SLR of pharmaceutical RL impaired the bibliometric analysis of them, leading to the inclusion of papers on general RL.

Originality/value – This study provides an overview of the evolution of RL in the pharmaceutical industry, it also clarifies concepts and EOL/EOU practices, particularly directed to the pharmaceutical industry RL.

Keywords Systematic literature review, Reverse logistics, Pharmaceuticals

Paper type Literature review

1. Introduction

Increasingly competitive pressures, environmental, governmental laws and economic factors impose on the industry the obligation and responsibility of returning the product to the manufacturer in a sustainable way (Sharma *et al.*, 2011; Bravo and Carvalho, 2013; Agrawal *et al.*, 2015, Govindan *et al.*, 2015). Reverse logistics (RL) meets the demand of reducing the negative impacts on the environment, as the manufacturer has the responsibility for the reverse flow and collection of products that have already completed their life cycle, providing them with a correct destination (Ravi and Shankar, 2005; Sharma *et al.*, 2011; Agrawal *et al.*, 2015).

As observed in the studies of González-Torre and Adenso-Díaz (2006) and Govindan *et al.* (2015), any type of product, when released in nature, triggers some sort of negative impact and, consequently, generates a complex problem for the environment, governments and society in general. Such impact has been largely reported for pharmaceuticals over the past 20 years, regarding product end-of-life (EOL) or end-of-use (EOU) (Daughton and Ternes, 1999; Ritchie *et al.*, 2000; Amaro and Barbosa-Póvoa, 2008; Xie and Breen, 2014; Kongar *et al.*, 2015).

The term EOL indicates that a product has completed its lifetime service and has reached the end of its useful life (Kongar *et al.*, 2015, p.51). Prescription drugs are one pharmaceutical category that is likely to complete its lifetime service prior to deterioration. The gap between the shelf life

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and the actual obsolescence date leads to storage, reuse or disposal of pharmaceutical products. This fact, coupled with the significant hazard potential of these products, requires a well-established RL system capable of handling EOL operations such as taking back or disposal (Gualtero, 2005). Reuse or recycling, on its turn, are operations related to the EOU concept, which means those situations where the user has an opportunity to return a product at a certain life stage of it. It not only refers to leased products and returnable containers (like bottles) but also refers to returns of unused products to second-hand markets (De Brito, 2008, p. 55).

Studies on RL are typically described in electronics and automotive industries' literature and denote a broad spectrum of themes and problems addressed in the past decades, attesting the complexity of the subject. In the case of electronics, there are initiatives in many countries. Guarnieri *et al.* (2015); Prakash *et al.* (2015); Guarnieri *et al.* (2016), for instance, have developed frameworks to support decision-making, using problem structuring methods (PSM) and multiple criteria decision aid (MCDA). The linear programming approach was used to model the integration of formal and informal waste sectors (Li and Tee, 2012); the structuring of RL networks is focused on different studies such as Kilic *et al.* (2015) and Ayvaz *et al.* (2015).

While in segments such as electronics and automotive, RL can be developed in a more efficient, economic and environmentally feasible way if compared to the production of new products (Pokharel and Mutha, 2009), in the case of the pharmaceutical segment, the purpose of RL is more related to avoiding harm to health. Narayana *et al.* (2014b) highlighted that although RL is relevant to pharmaceutical segment, studies related to it are still scarce. When incorrectly discharged, drugs cause numerous problems, such as toxicity and contamination by chemical substances, posing a risk to human life and aquatic organisms (Ternes, 2001; Cleuvers, 2003; Payan *et al.*, 2010; Buchberger, 2011; Narvaez and Jimenez, 2012). Besides the chemical hazard potential, such products comprise a different chain. In other segments, materials used in packaging such as plastic, metal and glass may be collected, fixed and processed into new products that would return to the same or other market. Pharmaceutical products must be collected and incinerated (Persson *et al.*, 2009; Glassmeyer *et al.*, 2009; Tong *et al.*, 2011; Kabir, 2013). Weraikat *et al.* (2016a, 2016b) state that there are several opportunities that could be implemented in pharmaceutical industry to solve the problem of waste.

Despite RL has been discussed in general literature since the end of the 1990s, pharmaceutical products removal has been an important operation in this industry long before. When products not yet consumed present any manufacturing-related issue that may cause any harm on consumers' health, market withdrawal is performed regardless the cost it represents (Rogers and Tibben-Lembke, 1998). Hence, the most frequent destination of returned products is incineration (Daughton and Ruhoy, 2011; Xie and Breen, 2014; Kongar *et al.*, 2015), independently of the cost generated or the stage of the product, EOL or EOU (Daughton and Ruhoy, 2011; Giacchetta and Marchetti, 2013).

That industry has faced the challenge of integrating traditional logistics and the reverse flow, as demonstrated by the studies from Danese *et al.* (2006), Howard and Singh (2009) and Guarnieri *et al.* (2016). Thus, considering the peculiarities and the relevance of RL to the pharmaceutical segment, the research questions guiding this paper are:

RQ1. How is RL evolving in the pharmaceutical industry? What are the practices concerning recycling, reusing, reducing or other alternatives, implemented for the EOL and EOU products by the pharmaceutical industry?

RQ2. What research gaps in RL can be identified from bibliometric maps of the papers published from 1996 to 2015 that would drive studies in the pharmaceutical industry?

The purposes of *RQ1* are to identify how structured, efficient or organized are the RL practices in the pharmaceutical industry and, additionally, to explore if other purposes would drive RL in this segment besides reducing risks of harm.

The purpose of *RQ2* is to contribute with this field of research. Some original publications on RL in the pharmaceutical field focus on technological efforts such as the use of radio frequency identification (RFID) for real-time tracking of its EOL in their reverse cycle (Kongar *et al.*, 2015). Narayana *et al.* (2014a) presented a systemic analysis of the interaction of factors that affect RL processes in the pharmaceutical supply chain (PSC). However, there are other challenges related to the pursuit of efficiency for RL regarding pharmaceutical industry when compared to direct logistics, revealing that the theme lacks broader investigation.

The systematic literature review (SLR) identified three thematic categories: the environmental risk, the formal RL evolution and the regulatory/stakeholders' education perspective. The topic formal RL evolution was further organized in the following segments: pharmaceutical and chemical industries; hospitals; pharmacy; national health systems; and household.

The SLR also identified the periodic *Supply Chain Management: An International Journal – SCMij* as the most prominent, which presented the highest number of publications in this field of research. For this reason, a bibliometric analysis of the articles was performed on this journal to map out the main countries, sources, universities, keywords and focus of the papers published. The bibliometric analysis allowed the identification of research gaps related to RL and the determination of a research agenda, useful for academics and practitioners on the pharmaceutical field.

The academic contribution of this research corroborates the current literature to support advanced studies of RL in the pharmaceutical industry and indicates opportunities for further investigation. Another contribution is to clarify some of the RL concepts and practices already available and their benefits for industrial practitioners and academics, which can motivate further studies in this field.

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2. Literature review

2.1 Reverse logistics

Due to the competitiveness of the industry standard and technological advances, greater attention has been paid to research on supply chains' reverse flow, whether EOL or EOU products. This fact gradually consolidates and reflects the efforts toward corporate, social and political awareness (Khan and Subzwari, 2009; Antai and Mutshinda, 2010; Huang and Su, 2013; Guarnieri *et al.*, 2015; Guarnieri *et al.*, 2016). For Rogers and Tibben-Lembke (1998, p. 2), RL is:

> [. . .] the process of planning, implementing and controlling the efficient, cost-effective flow of raw materials, in-process inventory, finished goods, and related information from the point of consumption to the point of origin for the purpose of recapturing value or of proper disposal.

RL should be considered at the moment a product's life cycle is being conceived, because a late insertion limits the possibility of economic viability. In addition, RL operational activities include collection, packaging, storage, sorting, transaction processing, delivering, integration and/or correct disposal (Meade and Sarkis, 2002).

RL is responsible for the reverse flow of materials and information with the purpose of reusing, reconditioning and recycling useful components that can be placed on the market once again through their transformation into new products (Mishra and Napier, 2014).

Govindan and Soleimani (2017) state that the closed-loop supply chain have two main duties:

1. It is responsible for value added processes to cover customers' demand.
2. It attempts to collect the EOL products from customers and determine the best ways to account for them.

Mafakheri and Nasiri (2013) studied coordinating issues of a reverse supply chain consisting of a manufacturer and a retailer in a revenue-sharing based in collecting EOL products from customers. The management of EOL or EOU products becomes important not only for economic, social and environmental factors; the uncontrolled worldwide consumption trend also increases the amount of waste discharged inadequately (Persson *et al.*, 2009; Glassmeyer *et al.*, 2009; Tong *et al.*, 2011; Huang and Su, 2013; Demirel *et al.*, 2016). The lack of awareness concerning the benefits of RL is the main barrier to its implementation (Sharma *et al.*, 2011).

Abdulrahman *et al.* (2014) grouped the barriers to RL in China into four categories: management; financial; policy; and infrastructure (lack of systems to monitor the returns). Chileshe *et al.* (2015) identified and grouped the barriers to its implementation: organizational operational and social and environmental.

Bouzon *et al.* (2015) studied RL development in Brazil and identified 25 barriers that they classified into seven categories: technology and infrastructure; governance and supply chain process; economic; knowledge; policy; market and competitors; and management. Prakash *et al.* (2015) found the following barriers to the implementation of RL in the Indian electronics industry: strategic barriers; economic barriers; policy barriers; infrastructural barriers; and market-related barriers.

The three most cited barriers by these authors were lack of coordination/collaboration with third-party logistics providers, customer perception about RL and lack of a system to monitor returns.

Thus, strategically speaking, practices that involve the return of EOL products – RL – have received increasingly attention in the recent decades due to numerous factors, such as competition between companies, social marketing, environmental interference and economic aspects (Kabir, 2013). The implementation of these practices can be a risky venture for top management, as it involves financial and operational aspects, which represents a long-term performance of the company. A critical analysis of the barriers to RL and its interaction with the various aspects can be a valuable source of information for decision makers (Ravi and Shankar, 2005; Nikolaou *et al.*, 2013; Mishra and Napier, 2014; Bazan *et al.*, 2016). Granlie *et al.* (2013) realized that it would be more appropriate to treat it as a strategic business unit, no matter the difficulties of dealing with the management of direct and reverse flow.

When considering emerging economies, the risks and challenges are even bigger than in developed countries for considering that the RL is still embryony in most industry sectors in the latter (Abdulrahman *et al.*, 2014; Bouzon *et al.*, 2015).

De Brito *et al.* (2005) analyzed the literature related to case studies on RL and classified them in network structures, relationships, inventory management, planning and control and information and technology (IT) for RL. Regarding the segments, the authors found that 60 per cent of the cases are related to manufacturing, 20 per cent to wholesale and retail trade and about 10 per cent are related to construction. They also found cases related to transport and communication, public administration and defense and other community, social and personal service activities.

2.2 Pharmaceutical products, policies and reverse flow

Pharmaceutical products are a group of chemicals used for diagnosis, treatment or prevention of diseases and/or health conditions. Commonly, key residues from drug products found in soil or water are acidic drugs, such as hydrochloric acid, salicylic acid, diclofenac, ibuprofen, xenobiotics among others (Ternes, 2001; Payan *et al.*, 2010). The presence of these residues is found in effluents from sewage treatment plants, disposed into the water cycle through domestic sources. Drug residues can also be ingested by humans via oral ingestion of treated water (Sebastine and Wakeman, 2003; Buchberger, 2011).

Abbas and Farooquie (2013) examine the relevance of some key issues regarding reverse flow management in Indian pharmaceutical companies from a customer perspective. The researchers measured RL performance using two parameters, namely, "ease of the return process" and "timely settlement of the returned medicines". They found that most of the customers wish to return their unwanted medicines in exchange for a refund or other usable medicine; however, their return rate of medicines was usually very lower in comparison to their average purchasing.

Weraikat *et al.* (2016a) states that a decentralized negotiation process is a reality in pharmaceutical segment to

coordinate the collection of unwanted medications at customer zones. Despite waste management (WM) and pollution prevention are essential to pharmaceutical segment, studies related to RL are scarce (Narayana *et al.*, 2014a).

Given the high competition and challenges faced by the pharmaceutical industry, in the attempt to constantly improve traditional logistics systems and RL, there is a need to develop actions and adopt strategies for the reverse flow of drugs. Often, stringent regulations may affect supply chain performance though not enough to meet the demand of direct logistics or RL. The industries need that supply chain to operate in highly sophisticated circuits to remain competitive and, most of all, with the main focus on measures to ensure that medicines will not be incorrectly disposed in the environment (Sundaramoorthy and Karimi, 2004; Narayana *et al.*, 2014b).

3. Methods

Considering the objectives proposed, the principles of Tranfield *et al.* (2003) and Higgins and Green (2011) guided this application. The review was divided into two steps: SLR and bibliometric mapping, detailed in the sequence.

3.1 Step 1: systematic literature review

The *Preferred Reporting Items for Systematic Protocol Review and Meta-Analysis* (Moher *et al.*, 2009) was used. Seeking to identify gaps in RL and practices applied in the pharmaceutical industry, the keywords were defined using the acronym proposed by Higgins and Green (2011) and Stone (2002): population, intervention, comparison and outcome. It provided the following search strings: (*pharmac* industry OR drug OR drug produc* OR drug industry OR pharmac*) AND (*RL *OR waste manag* OR expired medication OR medicine waste OR drug waste OR medicine collection OR disposal of medicines) AND (concepts OR methods OR practices OR sustainable practices)*. Using a temporal sampling of 20 years (1996-2015), a search for articles in the *Web of Science, Science Direct, Scopus* and *Emerald* databases was performed. These databases cover a representative number of journals from different areas, with significant impact. Initially, a total of 3,084 articles was found (Figure 1).

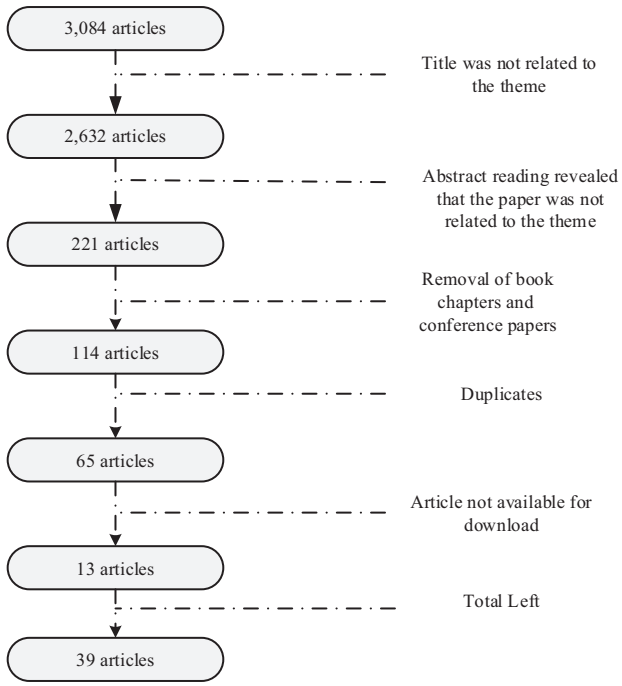
Although the first studies and activities of RL were reported in the 1970s and 1980s, it has received particular interest in business and academia in the past decades, which is reflected in the main journals on production and operations management (Rubio *et al.*, 2008). The authors analyzed the evolution of publications on RL from 1995 to 2005 and found an increasing interest in the period of analysis. Thus, the length of 20 years was delimited because it covers the establishment of the RL concept, as revealed by a previous exploratory search. After applying the filtering procedures, 39 papers were considered adequate to compose bibliographic portfolio for this research. Content analysis following Bardin (1977) and Bauer and Gaskell (2000) was performed.

3.2 Step 2: bibliometric mapping of reverse logistics publications

The objective of this paper is to organize the available knowledge on RL for the EOL of and EOU products in the pharmaceutical industry. To reach this purpose, it was necessary:

- to identify the articles on RL focused on pharmaceutical industry;

Figure 1 Number of papers discarded by the filtering procedures



- to classify and codify characteristics of these articles; and
- to provide a brief summary of each article's methodological procedures and main results.

By doing this, research gaps and opportunities were detected, which can guide future studies on this matter.

Considering that in the field of social sciences the SLR is relatively recent, this kind of study is relevant. In addition, SLRs are important for summarizing research on emerging issues, pointing out the gaps for future studies (Govindan and Soleimani, 2017; Jabbour, 2013).

Bibliometric tools provide scientists a quantitative assess to core journal titles and publications in particular disciplines and was used in this investigation to support the literature review and the analysis of RL gaps. Considering the timid literature on specific pharmaceutical RL, the *SCMij* was selected as the main base for the bibliometric analysis because it is the journal with a larger number on publications directly related to RL. Besides that, for the choice of *SCMij*, it was considered the Classifications of portfolio by the Australian business deans' council (ABDC) (see Appendix). This way, based on the bibliometric data, this paper also provides a map showing the distribution of scientific knowledge on RL all over the world.

All articles published by SCMij during 1996-2015 were searched, and a total of 753 publications (586 articles, 162 reviews, 4 editorials and 1 erratum) was found; thus, 748 papers were selected, considering the overall scope of topics in the SCM interface. They were analyzed considering: the country of the authors who published in the journal, most cited journals, authors' affiliations (universities) and the co-occurrence of keywords.

This step was conducted with the aid of the VOSviewer® software, which draws up bibliometric maps with the characteristics of publications. The software uses the VOS

algorithm (similarities view) to minimize the Euclidean distance between all pairs of items (van Eck and Waltman, 2010).

The literature points out several alternatives of direct logistics. Nevertheless, in the case of RL, despite the initiatives are still scarce in pharmaceutical industry, publications emphasize a broader possibility of profits with the process of recovering the discarded product on the recycling process.

The creation of maps brings the perception of how the publications by country are and the characteristics of the journals concerning publications in the area of direct logistics or RL and the authors' affiliations.

Regarding the keywords identified in the map, it is based on co-occurrence relationships, words are grouped into clusters as represented by the colors of the nodes, they represent a group, node size represents number of occurrence and links represent co-occurrence relationship. We do the analysis of key words to show topics that can be used in new studies approaching the most varied aspects of direct logistics and RL and the horizontal collaboration, as described by Weraikat *et al.* (2016b).

4. Results and discussion

In this section, we present the results of the SLR accomplished in four databases cited previously to identify the publications dedicated to RL in the pharmaceutical industry. Concepts, practices and gaps elicited from the SLR are presented in Subsection 4.1. Subsequently, bibliometric maps developed with publications from 1996 to 2015 are presented.

4.1 Results of the systematic literature review on RL – Step 1

Considering the evolutionary threshold of RL in literature and the fact that product removal is a common practice in the pharmaceutical industry, the purpose of this SLR was to comprehend if and how RL has evolved formally and technically in this segment of the industry. As stated by Govindan and Soleimani (2017), it is important to comprehend the past to develop a vision to the future research.

The distribution of the 39 articles included in the portfolio according to its methodological procedures comprehend empirical studies – *Case Study (CS)(9), Survey (S)(8), TM (Teaching Method)(1)*; theoretical studies –*SLR and Review (R)(16)*; and modeling studies – *Mathematical Model (MM)(5)*. All of them are presented in the sequence.

Using the constructivist and interpretative techniques, the content units of analysis have included the practices, methods performed along the time, the existence of a systemic view on supply chain and RL technologies already tested in the segment. For purposes of analysis, a timeline was created with the main subjects treated in the 39 articles included in the investigation (Figures 2-4), considering the period from 1996 to 2015. The timelines provide an overview of the evolution of RL, covering three main classification topics: the environmental risk, the regulatory/educational perspective and the formal RL evolution. The three timelines are approached in Section 4.1.1 due to the complementarity of the themes. Section 4.1.2 presents the deployment of the specific pharmaceutical RL thematic, clearing the RL practices found in literature.

4.1.1 Environmental risk and regulatory/educational

The environmental risk is a master line in all publications and the main justification for RL. A strong concern about the harm imposed by incorrect disposal of drugs along the value chain (in manufacturers, hospitals, clinics or domestic sites) draws the attention of researchers in all 39 articles and along the entire period of analysis (Figure 2). On the contrary of the other segments, as electronic industry, which has a well-established regulation related to disposal of residues

Figure 2 Timeline of publications – focus the environmental risk of pharmaceuticals

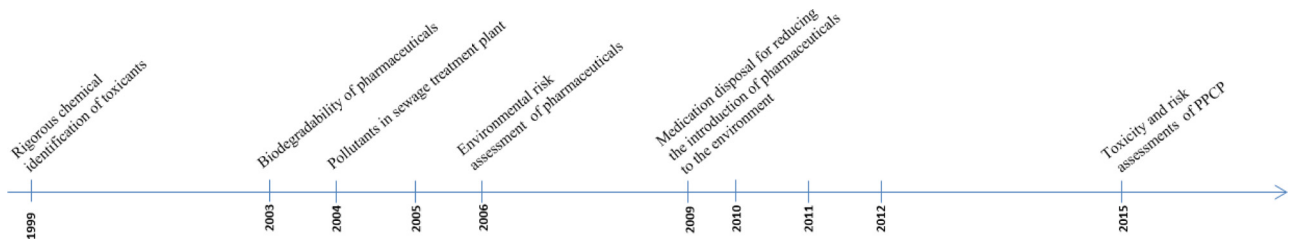


Figure 3 Timeline of publications – focus the RL evolution in pharmaceutical industry

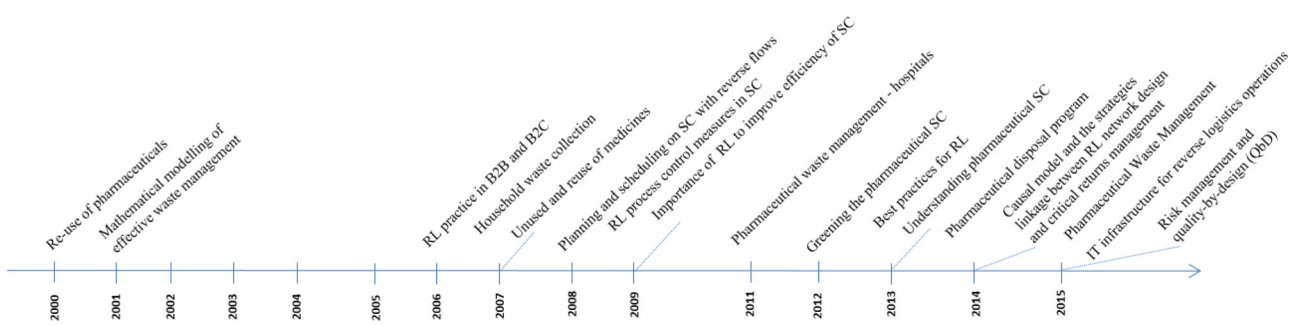
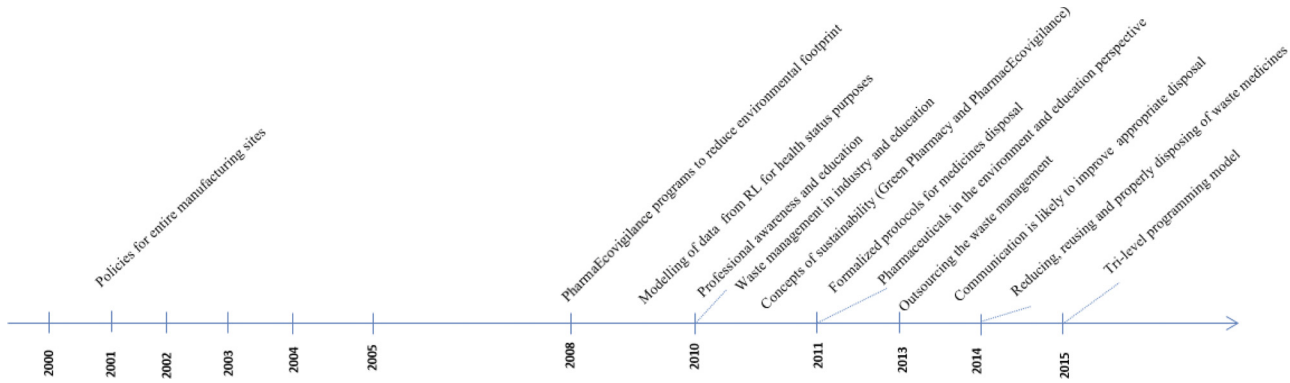


Figure 4 Timeline of publications – focus on regulatory and stakeholder's educational perspective



(except for some developing countries), according Govindan and Soleimani (2017), there are not a clear regulation related to disposal of drugs, what can reveal an opportunity of investigation. Despite Govindan and Soleimani (2017) make a literature review of RL in the *Journal of Cleaner Production*, that is considered as one of the most active journals in the field, the pharmaceutical segment was not found among the industries scrutinized in the journal's publications.

The papers disposed on Figure 2, however, are not properly discussing RL but highlighting the strong unknown impact of the presence of pharmaceutical products and metabolites in environment. There is an evolution observed in these papers regarding some aspects. Some studies defend the rigorous chemical identification of toxicants in water and effluents. These studies name the principal sources of contamination: residues from pharmaceutical industry, residues from hospital activities, human metabolization in urine and feces and the incorrect disposal of pharmaceuticals in the EOL or EOU (Daughton and Ternes, 1999; Sebastine and Wakeman, 2003; O'Brien and Dietrich, 2004; Tong *et al.*, 2011). Some other studies list substances found in environment and their potential toxicity (Zuccato *et al.*, 2006; Narvaez and Jimenez, 2012). Other studies, mention sensitive techniques to detect trace quantities of substances in nature (Cizmas *et al.*, 2015).

While in the past years of the 1990's researchers demand for better IT resources do deal with large databases and more analytical sensitive techniques (Daughton and Ternes, 1999), this is already a reality in Cizmas *et al.* (2015). The latter describe the occurrence, effects and risk assessment of pharmaceuticals and active ingredients in personal care products (PPCP) in aquatic systems, as well as the sustainability of current methods for managing PPCP (Figure 2), denoting the evolution of assessment technology in the period.

Parallelly, in the beginning of 2000, Linninger and Chakraborty (2001) develop a deterministic mathematical modelling of WM with three different strategies to identify best plant-wide policies. The discussion was based on simplifying assumptions such as linearized cost models, residual computation and varying waste loads at unchanging compositions. Further, literature shows an increase in publication concerning WM methods, policies and pharmacovigilance programs at the same time specific publication on RL of pharmaceuticals also increases (Figures 3 and 4).

Daughton and Ruhoy (2008) first bring the term PharmaEcovigilance to unify needs for protecting both human and ecological health. After, Antai and Mutshinda (2010) and Daughton and Ruhoy (2011) suggest the use of data on medical reverse supply chain to infer changes of a population's health status with regard to a focal disease. Thus, researchers glimpse an interchange between the pharmacovigilance and RL subjects.

The content analysis of SLR papers also reveals a complex system concerning pharmaceutical RL. First, RL of products disposal may solve only part of the entire problem because there are several sources of environmental contamination other than the inadequate disposal. For instance, the broad human and animal metabolization of medicines and manufacturers' effluents in diverse pharmaceutical segments (human, veterinary, hygiene, and cosmetics). If considered only the improper disposal of EOL or EOU medicines, these products may depart from different sites such as houses, pharmacies, hospitals, clinics, retailers, manufacturers and government stores, where they are under the responsibility of different stakeholders such as end users, pharmacists, physicians, nurses and other professionals.

This may explain the publication on policies (Linninger and Chakraborty, 2001; Abahussain *et al.*, 2012; Huang *et al.*, 2015), engagement of stakeholders for RL (Xie and Breen 2014), client compliance (Breen, 2006) and the need of awareness of professionals from the PSC (Kotchen *et al.*, 2009; Vellinga *et al.*, 2014), as described in Figure 4 and exemplified next.

Ortner and McCullagh (2010), after highlighting the environmental impact of pharmaceutical agents in the water, indicate gaps and recommendations for hospice nursing practice. Guirguis (2010) suggests that pharmacists are in a good position either to collect unused medications and to educate patients. Abahussain *et al.* (2012) assess the pharmacist practice and awareness regarding the disposal or returned unused medication by the public. Moreover, Eissen and Backhaus (2011) developed an educational material that corresponds to series of worksheets (online resource) for gaining knowledge about the occurrence, fate and removal of pharmaceuticals in the environment.

The terms used in SLR returned subjects described in Section 4.1.1 due to the strong interdependency existent among them and RL. They have been kept in the discussion because they are part of a systemic view of the matter. Papers

that focused primarily on pharmaceutical RL (Figure 3) is described next.

4.1.2 Reverse logistics practices

The purpose of this section is to describe what practices – concerning recycling, reusing, reducing or other alternatives – are implemented for the EOL and EOU products by the pharmaceutical industry. As mentioned before, the number of papers increased from 2006 on, although they are still timid in number (24 out of 39) (Figure 3). The analysis of them revealed an evolution from financial evaluations and managerial practices towards mathematical and technological solutions, facing different segments of the value chain as pharmaceutical and chemical industries (14), hospital (4), pharmacies (3), national health systems (2) and household (1). While these segments belong to the broad chain, evidences show that studies on pharmaceutical RL are fragmented across the network of value delivery and fewer studies attempt to develop systemic solutions (Linninger and Chakraborty, 2001; Amaro and Barbosa-Póvoa, 2008; Kumar *et al.*, 2009; Xie and Breen, 2012). Danese *et al.* (2006) and Narayana *et al.* (2014b) reinforce this perception and suggest that as supply networks of pharmaceutical companies can be complicated, researchers tend to focus on parts of the chain.

4.1.2.1 Pharmaceutical and chemical industries reverse logistics. Narayana *et al.* (2014b) developed a systematic review of research on management in the PSC, and RL is one of the major themes identified in collated literature. They argue that there is an emerging interest in pharmaceutical RL. They reinforce our findings related to product recalls and safety, the innovation in health-care prediction depicted through the analysis of product returns, recycling, disposal, scheduling and planning in the context of designing effective distribution networks and healthcare logistics. These research efforts illustrate the prevalence and scope for sustainable practices in the PSC that is also present in Xie and Breen (2012). These results are synergic with the emphasis of literature in WM, which is a recurrent subject in this group of papers. Despite it is not properly an RL method, it meets part of the problematic manufacturers' effluents contamination.

Linninger and Chakraborty (2001) address the problem of finding optimal WM policies for entire manufacturing sites in the presence of uncertainty. Ngwuluka *et al.* (2011) researched industries in Nigeria and detected a scenario of inefficiency. They suggest practices for improving WM, including government incentives, staff training and water recycling, reinforcing the findings of this paper. Xie and Breen (2012) bring the concept of designing a green community PSC using a cross boundary approach that requires every participant in the PSC to take environmental practices.

Costs and revenues are also themes associated with RL papers. Despite the motivations for RL in pharmaceutical industry are more related to environmental matters, Kabir (2013) claims that RL is now following a trend where it is seen as a competitive advantage and a source of potential revenue. Kongar *et al.* (2015), who suggest that EOU drugs that are in usable condition and with extended shelf life are eligible for sale, confirm this idea. However, this revenue strategy, either for drugs or other pharmaceutical correlated products, may be impaired by regulatory policies and quality standards. Breen (2006), viewing costs reduction, adopts a focus on recycling of distribution equipment used to transport outbound and returned products because for both, B2B and B2C relationships, there is evidence of suppliers suffering financial loss due to customer non-compliance.

Considering that process efficiency is relevant for a successful RL, Kongar *et al.* (2015, pp. 55-56) state that:

> [. . .] high testing costs, liability - caused by significant risk to human health, and rules and regulations limiting the proper utilization of EOL pharmaceutical products are conceived as three major factors contributing to the lack of efficiency of the reverse logistics operations.

These authors propose a theoretical RL system considering these setbacks. The system is modeled as a supply chain that includes institutional targets, RL operations and an RFID-based IT infrastructure required for the EOL operations.

Studies in industry also focus models and mathematical modeling. Narayana *et al.* (2014a) developed a systemic analysis of the complex interaction of factors affecting the RL processes in a PSC. The findings suggest a strong linkage between RL network design and key activities in management of returns. The study lays a platform for developing a simulation model.

Another study, from Amaro and Barbosa-Póvoa (2008), presents an integrated approach for the planning and scheduling of forward and reverse flows and different operational policies are contemplated, not only at the production and storage levels, as traditionally, but also at the distribution and recovery levels.

Finally, Kumar *et al.* (2009) make a diagnostic using DMAIC process. This study is a first look at the forward and RL processes for the pharmaceutical industry supply chain and analysis of potential improvements. The tool helps in understanding gaps, suggesting measures to reduce them and providing directions for improvements related to the quality of service existing between logistics users, logistics service provider, pharmaceutical firm and customers. Aspects related to SC control, governance, relationship management, partnerships, broad use of technology as such as RFID, shared costs and others arise from this study.

4.1.2.2 Hospital segment. The main concern of RL thematic in hospital research is related to the amount of types, quantities and monetary value of drugs which are disposed of by patients, focused on cost reduction (Guirguis, 2010; Giacchetta and Marchetti, 2013). A survey from Sasu *et al.* (2012) showed that more than half of the respondents confirmed having unused, leftover or expired medicines at home, and over 75 per cent of pharmaceutical waste being disposed through the normal waste bins, which end up in the landfills or dump sites. The role of pharmacists in promoting the safe disposal of drug waste and reducing medication cost is reinforced in these studies.

Giacchetta and Marchetti (2013) performed a measurement campaign for assessing the waste flow in a pilot hospital of a region in central Italy, and Abahussain *et al.* (2012) attempt to assess pharmacists' awareness toward the impact of improper disposal on the environment and, to investigate whether pharmacists agree to have their pharmacies as collection points for future take-back programs.

The RL subject in the hospital segment seems more homogenous than in industry. In spite of it, the studies do not

go further in RL operationalization efforts. In fact, they confirm the opportunity for RL of unused products and reinforce the importance of professional education and commitment, already described in Section 4.1.1.

4.1.2.3 Pharmacy segment. Mackridge and Marriott (2007) developed a pilot RL of unused products although the practice is currently considered unethical in the UK. They suggest reopening the debate because their results revealed that unused medicines are returned in substantial quantities and have considerable financial value.

Manojlović *et al.* (2015), on the opposite side, focus the potential source of poisoning by drugs, due to improper disposal of unused medicines worldwide. They researched pharmacies to assess the current situation of pharmaceutical WM in the sector and results demonstrate that pharmacies have not started to implement their legal obligation of collecting pharmaceutical waste from the citizens yet, at least not in the full range.

Studies in the pharmacy segment are aligned with those described for hospitals, but they somehow emphasize the importance of the site in the reverse flow, striving for operationalization. Huang *et al.* (2015) argue that it is necessary for the government to select the right recycling stations and treatment stations to optimize the expired drug recycling logistics network and minimize the total costs of recycling and disposal. They establish a tri-level programming model to study how the government can optimize an expired drug recycling logistics network and the appropriate subsidy policies. The Hybrid Genetic Simulated Annealing Algorithm has proven to have the ability to converge on the global optimal solution and to act as an effective algorithm for solving the optimization problem of expired drug recycling logistics network and government subsidies.

4.1.2.4 National health systems segment. Studies reinforce the importance of RL to National Health Service (NHS) in UK. Ritchie *et al.* (2000) identify opportunities for reducing waste and proactive reducing stocks of the Manchester Royal Infirmary. Other insights include the need for training, awareness of professionals and patients, responsibilities definition, schedules and processes establishment.

Xie and Breen (2014) determine the best way to reduce, reuse and dispose of household waste medicines in the NHS (UK). By combining literature review and empirical work, this research investigates the existing household waste medicines RL system and makes recommendations for improvement by benchmarking it against RL of household waste batteries. As the RL system for batteries appears to be more structured and effective, best practices are recommended to be incorporated into the waste medicines RL system, including recapturing product value, revised processing approaches, system cooperation and enforcement, drivers and motivations and system design and facilitation.

4.1.2.5 Household segment. Specific studies in this segment are rare. Musson *et al.* (2007) developed a five-month "self-serve" pilot project to properly disposal of old and unwanted prescription and nonprescription medications. Obstacles found during the program included reluctance by major drug store chains to participate, regulatory and legal restrictions on pharmaceutical handling and collection of detailed data from participants. A research with the participants indicated that the discard of pharmaceuticals to the sanitary sewer is a common practice, and the primary purpose cited for its disposal was that the medication had exceeded its expiration date.

4.1.3 Considerations on systematic literature review

The purpose of this paper is to provide an overview in the literature about pharmaceutical RL. One first finding is that the RL thematic in the pharmaceutical field is intimately associated to at least two other themes: risk of harm and regulatory stakeholder's education, as depicted in Section 4.1.1. Three groups of papers are highlighted in the review (Figures 2-4). They portray the need of parallel actions concerning RL:

- precise, efficient technology to assess and control of drug contaminants in the environment (water, soil, animals); and
- the support of a meticulous but flexible pharmacovigilance service on the collection, detection, assessment, monitoring and prevention of adverse effects of pharmaceuticals.

The technology provided by universities and research institutes would provide environmental surveillance indicators for monitoring WM and RL processes' efficiency-efficacy in the entire system. The pharmacovigilance, provided by regulatory agencies, should go beyond its traditional activities, incorporating the concept of "pharmaEcovigilance", as claimed by Daughton and Ruhoy (2008), to unify protection of both human and ecological health. Safeguarded the necessary rules, the role of regulatory agencies should be a system's partner, being flexible in case-to-case analysis. The current barriers imposed to RL by regulations are a frequent complain in the revised literature, thickening the typical barrier lines already mentioned to forward logistics, at the beginning of this paper. Other players, not clearly mentioned, would include city governments, responsible for house effluent treatment and the role of universities in preparing health professionals to educate populations across the entire RL system.

Advancing to the pharmaceutical RL group of papers analyzed, in the beginning of 2000s, WM emerges as if it was a preliminary formalization effort toward RL development. Nevertheless, WM differs from RL. The waste management focuses on the collection and treatment of waste products that have no other use, what would include the traditional incineration of EOL products. On the other hand, RL concept focuses on the addition of value to a product to be recovered, as stated to EOU products. The literature does not explore the fact that pharmaceuticals and correlates include large variety classes of products and chemical substances, what adds complexity for WM and RL.

Literature also revealed that EOU products are a concern in studies performed in hospitals, pharmacies, NHS centers and household, what is expected because these stakeholders are the natural owners or keepers of these products. Nevertheless, the surveys and data collection for proving that economical value may be recovered from unused products, prevail in relation to those that deal with developing managerial or technical solutions. Notwithstanding, the awareness and role of professionals from these sites was reinforced and meets the

directions observed in papers on the pharmacovigilance timeline.

Most papers related to industry focused on solutions to post-consumption RL. Post-sale RL was better discussed in the B2B and B2C studies from Breen (2006). Further studies concerning this subject are necessary because it represents costs to the entire logistic system. Costs are recurrently mentioned in pharmaceutical RL, as they are related to forward logistics. The difference is that emphasis is given in an efficient management of forward logistics aiming cost reduction, whereas organizations fear RL due to increase of costs. Integration of both logistics, forward and reverse, in a systemic approach was observed in Narayana *et al.* (2014a) and Amaro and Barbosa-Póvoa (2008) aiming more efficiency because post consumption and EOL products are current mandatory practices in the pharmaceutical industry.

Papers have revealed distinct initiatives that are useful toward this integration as diagnostic tools (Kumar *et al.*, 2009), system and mathematical modeling (Linninger and Chakraborty, 2001; Li and Tee, 2012; Narayana *et al.*, 2014a; Amaro and Barbosa-Póvoa, 2008), information technologies (Kongar *et al.*, 2015). Narayana *et al.* (2014b) and Kumar *et al.* (2009) also mention in PSC the importance of Information Systems (IS) and Kongar *et al.* (2015); the communication between the SC parties in RL, corroborating literature on SC and RL of other industries (Section 2). In fact, Kongar *et al.* (2015) advocate that accurate inventory information, like the one that may be provided by RFID technology, for instance, lowers overall costs by facilitating in-house activities for many members of the SC involved in the EOL RL process.

Another aspect mentioned in studies is commitment and cooperation among actors along the entire production and consumption chains. This context has been highlighted mainly in the pharmacovigilance papers of the timeline and also in Narayana *et al.* (2014b) and Kongar *et al.* (2015).

The full RL process is complex and the literature brought insights in some of its operations such as collection, packaging, storage, sorting, transaction processing, delivery and integration and/or correct disposal. Sustainable development and economic viability are decision-making criteria to guide managers on their efforts toward pharmaceutical RL. The main gaps and research opportunities will be presented in Section 4.3.

4.2 Bibliometric mapping of *SCMij* publication – Step 2

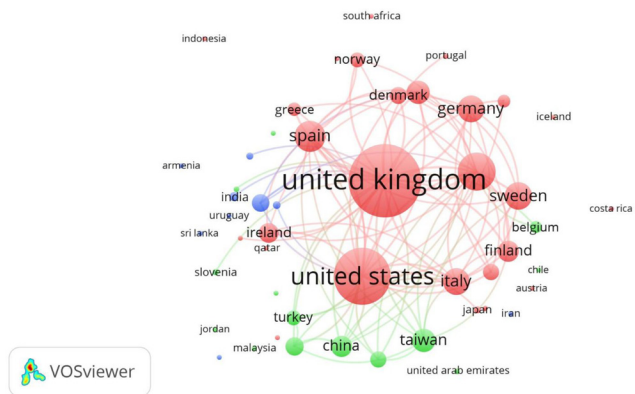
Step 2 of the method consisted in assessing the journal *SCMij* and build a bibliometric mapping related to its publications. The 39 papers identified for the systematic review are an evidence of a gradual evolution on the theme but still can be considered as timid. The analysis of the citations, according to countries on the 748 references published in the period of 20 years, considering the scope that covers all interfaces of integrated logistics was done. According to Govindan and Soleimani (2017), the review studies for a specific journal can give researchers and journal managers a comprehensive overview of the past and a useful insight into future research opportunities. In this context, both researchers and journal managers can use the results: the first ones can elevate the scope of research focusing the identified gaps, and the latter can revise or expand journal strategies. For the total number of publications (748), 63 countries were detected. The software VOSviewer® was configured to calculate only one publication by country. Based on the relationships set by the software, 51 countries were studied (Figure 5).

Figure 5 reveals the presence of three clusters. The red cluster is composed of 23 countries, the green cluster consists of 14 countries, the blue cluster consists of six countries. Countries with the largest volume of publications are in the center of the map, represented by the bigger circles. Table I presents the distribution of documents and citations by country. Not surprisingly, UK is the most referred country in the papers from SLR from Section 4.1.1, mainly those regarding the environmental risk timeline, RL in hospital, pharmacy, NHS and household.

Within the *SCMij* periodical, a volume of 8,861 sources was identified. Among them, 500 cited sources were considered for the elaboration of the map. Figure 6 presents the maps of journals.

For the set of 500 sources cited, 4 clusters of journals were generated, which are the red cluster composed of 146 periodicals; the green one composed of 118 periodicals; the blue one composed of 115 periodicals; and the yellow one

Figure 5 Network considering the nationalities of the authors within the 1996-2015 period

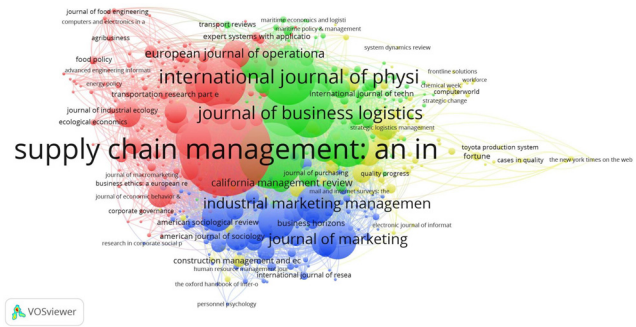


Source: This map can be web-started at: goo.gl/X61Ti3

Table I Distribution of publications, by country

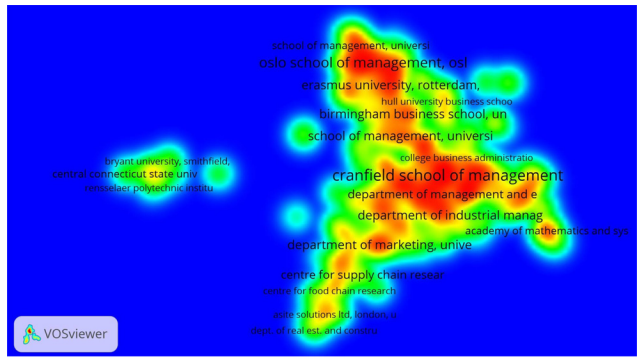
Country	Documents	Citations	Country	Documents	Citations
UK	244	1,236	IRL	19	142
US	183	808	NO	16	90
AU	60	421	KOR	15	101
SPA	38	296	IND	12	40
NLD	36	183	GRE	10	72
SWE	34	248	DEN	9	111
CAN	32	116	SUI	9	99
FIN	30	160	TUR	9	87
TW	27	183	NZL	8	27
GER	24	227	BEL	7	63
CHN	23	155	BRA	6	39
HKG	21	125	MAS	4	16
IT	21	235	SIN	4	10

Figure 6 Co-citation network of the journals within the 1996-2015 period



Source: This map can be web-started at: goo.gl/pA8p2Y

Figure 7 Density of universities in the period (1996-2015)



Source: This map can be web-started at: goo.gl/RCnSIs

composed of 111 periodicals. The distribution of the first ten periodicals that presented the largest number of citations can be observed in Table II. Additional information about the periodicals are detailed in the Appendix.

Considering the type of analysis "Citations" and the unit of analysis "Organizations", representing the universities of origin of the authors, a volume of 1,204 universities was considered. Then, 500 universities, more active and dynamic in the SCMij, were selected. These universities presented one to nine papers published, revealed in the density map on Figure 7.

Universities with higher number of articles and volume of citations are displayed in the orange area. Among them are the universities mentioned in Table III.

To identify the keywords used in the *SCMij* journal to subsequently draw up a guide for future studies, the "Co-occurrence" and "All Keywords" options were used in the VOSviewer® software. It was possible to identify 1,790 words among the 748 publications. Figure 8 presents the words cited.

Considering the existence of 19 clusters, we noticed that the network is supported by four major themes: *SCM* (372 occurrences); *Industrial Management* (143 occurrences); *Customer Satisfaction* (107 occurrences) and *Marketing* (99 occurrences). In Figure 8, it is possible to identify evidences

Table II Volume of citations and citations by periodicals

Periodicals	Citation	Co-citation
Supply Chain Management	1,960	95,311
Journal of Operations Management	1,121	67,307
International Journal of Physical Distribution & Logistics	853	43,003
International Journal of Production Economics	731	43,602
Journal of Business Logistics	684	35,697
Journal of Operations and Production Management	666	34,849
Harvard Business Review	551	25,215
Industrial Marketing Management	461	23,991
Journal of Marketing	461	20,570
Strategic Management Journal	410	23,406

Table III Documents and citations, by universities

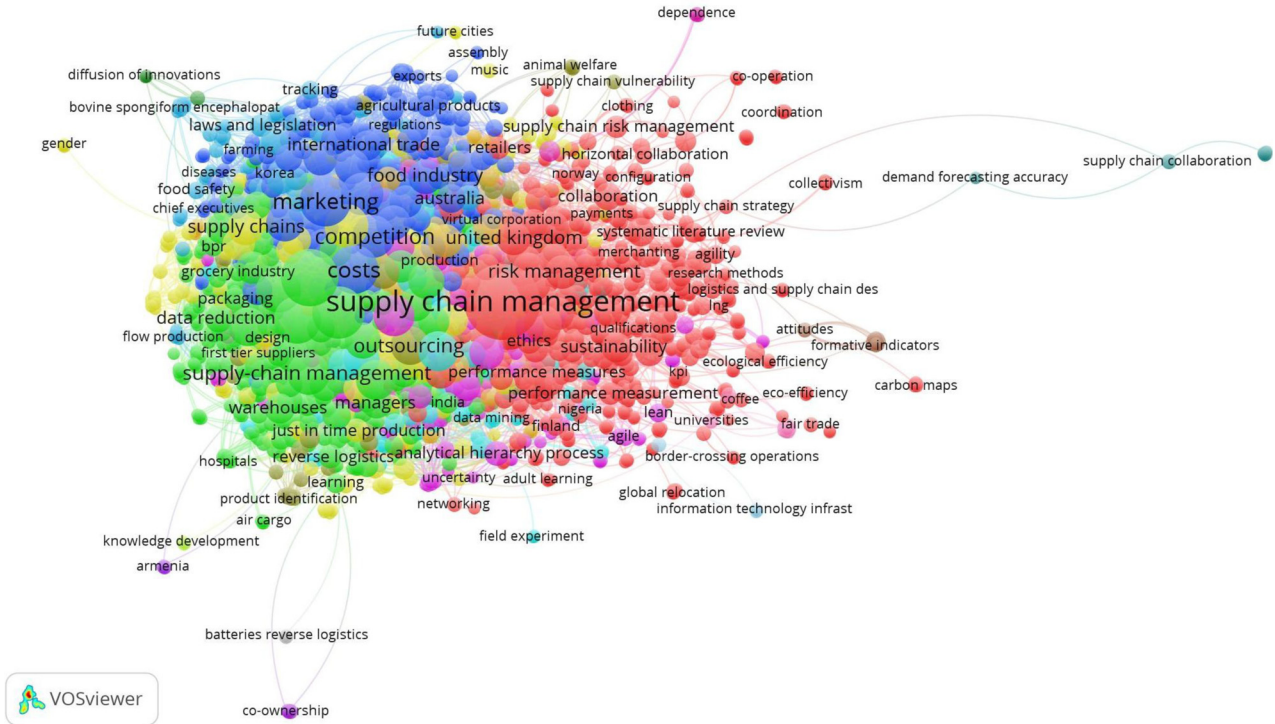
University	Documents	Citation
Cranfield University	9	124
Oslo School of Management	7	72
Birmingham Business School	4	20
Cardiff Business School	4	50
Linköping University	4	42
University of Stirling	4	42
Copenhagen Business School	4	78
Erasmus University	4	51
Kent Business School	4	18
Cardiff University	4	28
Leeds University Business School	4	37
Manchester Business School	4	12

that there is a centrality ratio and hence a higher density among the topics that have a higher volume of occurrences. Consequently, more dispersed terms indicate the low incidence of studies covering subjects that are less discussed.

From a perspective of integration with other phases of the logistics process, there is still much to do in terms of research on RL. The term RL presented nine occurrences and 85 co-occurrences, confirming that there is a gap in understanding the industry from the aspect of RL and that it is an emerging theme. Similarly, to what was observed in Section 4.1, the papers cover a broad spectrum of themes related to RL, but nothing much different from which was discussed in Section 4.1, in terms of practices and tools. Seven papers were published from 2006 to 2015 considering RL in other segments. Three of the papers mentioned in Section 4.1, specifically about pharmaceutical RL were also in this bibliometry. The term RL is not present in one of these papers, reason why the bibliometry counted nine occurrences instead of ten.

The social role of *SCMij* might be questioned (considering that it is an expressive journal of the SCM area that has in its subject areas: operations, logistic and quality) in the sense of stimulating more publications with special editions that focus on themes such as RL in diverse segments, including the pharmaceutical sector. Why not? Pharmaceutical industry generates revenues of trillions of dollars a year, with proportional investments, and it is responsible for a significant

Figure 8 Network of keyword co-occurrence within the period (1996-2015)



Source: This map can be web-started at: goo.gl/KypTwl

impact in all the world's populations lives, both directly in their health and indirectly in the environment balance, as demonstrated in this paper. Additionally, RL applied to the pharmaceutical sector can be identified as a possible source of study in which integration is possible with themes that appear on the map, such as *Strategic Elements of the Supply Chain Management, Vision of Sustainability, Eco-efficiency, Cooperative Relations and Horizontal Relations in SC*, among others.

This might be the main point of insertion of new studies that consider RL analyzing its application in various sectors and also applied to the pharmaceutical industry. The data obtained regarding the use of keywords may be important for the researchers to have a reference regarding the themes related to RL for future works.

4.3 Identification of gaps and opportunities

This topic makes a summary of the findings from Steps 1 and 2 (Sections 4.1 and 4.2). RL is a relatively new thematic, and a horizon of 10 years is small to present a large number of studies revealing opportunities of investigation.

Figure 9 attempts to provide a systemic view of the value delivery network that is fragmented across the literature. It summarizes the authors, the RL practices and the players (managerial segments) that were mentioned by these authors, such as the manufacturer (either of drugs, pharmaceuticals, veterinary, cosmetic or correlate products), government agency (policy makers and/or agencies responsible for the National Health System), pharmacies, houses and hospitals. The players directly mentioned by the authors in the studies are marked in the table with (✓). Nevertheless, other players that are potentially responsible or part of the chain were included in the picture to reveal the complexity of the system and to reinforce that such players might also perform the RL practices (gray cells).

Figures 9-11 include more than 20 different practices, most of them originally described to be implemented by manufacturers. The practices were arranged into in three groups. First the operations and managerial practices, most of them under the responsibility of manufacturers (Figure 9).

Product recall and WM, for instance, are current RL practices in pharmaceutical organizations. Effluent treatment is a mandatory practice that is not typical from RL, but it is related to WM and must be performed by almost all the players in the chain, to assure a systemic environmental impact reduction.

Second, the strategic and decision-making related practices include both the strategies that might be implemented by any player of the value chain, as well as those strategies that are pertinent of policy makers. Regulatory, Health Agencies, Town Halls and other government institutions must be in synergy with the entire chain to provide incentives and to control the different players' actions. Scheduling and planning in RL, considering the adequate adaptations, were originally mentioned by the authors as a practice for manufacturers, but it would be performed by distribution and acquisition organizations, as well as by other players in the chain. The demand for professional education is another strategic practice which was primarily mentioned in a hospital study, but that should be leaded by Universities to prepare experts to act in the entire value chain, as can be seen in Figure 10.

The third group, technological practices, was less expressive, concentrating IT solutions, RFID applications and

Figure 9 Practices described in the 39 articles (operational and managerial practices)

	Players											
OPERATIONAL AND MANAGERIAL PRACTICES	Extraction Transformation	Manufacturer	Government Agencies	Distribution	Retailer	Pharmacy	Government Stores	Houses	Clinic	Hospital	Universities	Town hall
-Product recall		✓										
-Recycling		✓*										
-Waste management	•	✓*							•	•	•	
-Expired Drugs Recycling logistic (incineration)						✓						
-Disposal		✓	✓					✓				
-Reuse EOU drugs		✓				✓				✓		
-Effluents treatment	•	•							•	•		•
-Scheduling and planning		✓	*		*	*	*		*	*		*
-Schedules and processes establishment			✓	✓								
-SC Control		✓				✓			✓	✓		
-Collection of medicines by pharmacies						✓						
-DMAIC process		✓										
-Donation of unexpired medicines						✓		✓				
Authors	Kabir (2013); Bravo and Carvalho (2013); Narayana *et al.,* (2014a); Khan and Subzwari (2009); Huang *et al.,* (2015); Kumar *et al.,* (2009); Guirguis (2010).											

Legend: Potential Player: **[grey cell]** / Player mentioned ✓/ Scheduling and planning at distributions and acquisition organizations: */ Effluent treatment in addition to waste management: •

Figure 10 Practices described in the 39 articles (strategic and decision-making related practices)

STRATEGIC AND DECISION MAKING RELATED PRACTICES	Extraction Transformation	Manufacturer	Government Agencies	Distribution	Retailer	Pharmacy	Government Stores	Houses	Clinic	Hospital	Universities	Town hall
-Government incentives and policies			✓									
-Community collection programs		✓						✓				
-Green Community pharmacies (PSC)		✓										
-System design and facilitation		✓										
-System cooperation		✓										
-Recapturing product value		✓										
-Shared costs		✓										
-Responsability definition		✓										
-Relationships management		✓										
-Staff training		✓	✓									
-Partnership		✓										
-Awareness of professionals and patients										✓		
-Professional education										✓		
Authors	Kumar *et al.,* (2009); Khan and Subzwari (2009); Kongar *et al.,* (2015); Ritchie *et al.,* (2000); Narayana *et al.,* (2014ab); Guirguis (2010); Eissen and Backhaus (2011); Abahussain, *et al.,* (2012); Ngwuluka *et al.,* (2011); Xie and Breen (2012); Daughton and Ruhoy (2008); Xie and Breen (2014).											

Legend: Potential Player: **[grey cell]** / Player mentioned ✓/ Scheduling and planning at distributions and acquisition organizations: */ Effluent treatment in addition to waste management: •

Figure 11 Practices described in the 39 articles (technological practices)

TECHNOLOGICAL PRACTICES	Extraction Transformation	Manufacturer	Government Agencies	Distribution	Retailer	Pharmacy	Government Stores	Houses	Clinic	Hospital	Universities	Town hall
-IT like practices and RFID		✓										
-Innovation in healthcare (demand forecasting suported by RL and other innovations)			✓									
Authors	Narayana *et al.,* (2014ab); Kumar *et al.,* (2009); Kongar *et al.,* (2015).											

Legend: Potential Player: **[grey cell]** / Player mentioned ✓/ Scheduling and planning at distributions and acquisition organizations: */ Effluent treatment in addition to waste management: •

innovation healthcare. Besides the use of information from RL to forecast the demand, as mentioned originally for Government agencies, other innovative solutions may be developed by every player of the chain (Figure 11).

Some players that were not directly mentioned but would make a difference if involved are: universities, town hall, distribution/logistic organizations and retailers. The retailers were not formally mentioned in the SLR but they were cited in

the bibliometric RL papers. The practices mentioned in Figures 9-11 serve as inspiration for researchers and practitioners who intent to explore the theme in a systemic approach, along with gaps and opportunities detailed below:

1 Opportunity of investigation
- chemical analytical technologies;
- governance of the RL system;
- integration of WM e RL to better address the environmental risk of chemical in environment;
- innovation in health care prediction aiming to reduce prescriptions and customization of treatments;
- innovation in recycling, disposal, scheduling and planning;
- aspects related to SC control, governance, relationship management, partnership, broad use of technology as RFID, shared costs and others;
- testing of mathematical models in real cases;
- on the role of professionals from hospital, pharmacies, end users in the EOU RL;
- cooperation and interface of stakeholders and manufacturing sites;
- post-sale RL studies, especially because they represent costs to the system;
- IT supporting accurate information flows, customer relationship management, forecasting, inventory and transport management;
- risk management;
- cooperation and commitment of stakeholders;
- RL economic viability methods; and
- treating RL as a new business unit and a management strategy.

2 Gaps
- studies not only in developed countries, but on a global level;
- development of global policies;
- integration among regulatory agencies, managers, professional and users;
- Integration of researchers from related areas like biology, environment, and others;
- policies review and new policies development to attend the pharmaceutical industry specificities on different EOL or EOU products, living beings and environment;
- research on upstream value chain, including chemical industries that synthetize drugs and excipients;
- education for value chain stakeholders;
- preparation of professionals for designing effective systemic distribution networks and health-care logistics;
- integration of logistics elements, such as RL and market performance, RL and "green" practices for the efficient management of EOL or EOU drugs as a marketing strategy, or yet RL to meet the legal demands; and
- horizontal collaborations logistics (HCL) elements to RL.

5. Final considerations

When a pharmaceutical product is not adequately manufactured, used or discarded, different chemicals may cause impact on human health and/or environment. It is reasonable that managers from the entire pharmaceutical value chain demand from RL the same efficiency and effectiveness obtained from direct flow logistics. This SLR indicates that researchers and practitioners have to work together to find systemic solutions.

An analysis of the past 20 years of publications reveals that it lacks topics related to social and environmental aspects, which could be stimulated by influent specialized Journals in their special issues. Direct logistics has a responsibility related to RL, since it reflects the maturity of SCM.

Specifically related to the research questions, we highlighted the main findings:

RQ1. How is RL evolving in the pharmaceutical industry? What are the practices concerning recycling, reusing, reducing or other alternatives, implemented for the EOL and EOU products by the pharmaceutical industry?

For this purpose, considering the period from 1996 to 2015, it was elaborated a timeline related to the evolution of RL. This timeline provides an overview covering three main classification topics:

1 *The environmental risk*: The papers approach the strong unknown impact of the presence of pharmaceuticals products and metabolites in environment.
2 *The regulatory/educational perspective*: The papers discuss policies, engagement of stakeholders for RL, client compliance and the need of awareness of professionals from the PSC.
3 *The formal RL evolution*: It was found that in the beginning of 2000's WM emerges as if it was a preliminary formalization effort toward RL development (Figures 2-4).

Regarding to the practices, our analysis showed an evolution from financial evaluations and managerial practices, toward mathematical and technological solutions. The operations practices are widely implemented, such as product recall, WM, effluent treatment, reuse, recycling, donation, incineration, among others. Regarding strategic and decision-making practices, we found shared prices, relationship management, responsibility definition, community programs, government incentives, green practices, staff training, partnerships, among others. In addition, we found that the technological practices are still scarce and are limited to use of RFID and demand forecasting solutions. We approached it according the practices of following segments: hospitals, pharmacies, national health systems and household. These segments are considered as part of value chain as pharmaceutical and chemical industries.

RQ2. What research gaps in RL can be identified from bibliometric maps of the papers published from 1996 to 2015 that would drive studies in the pharmaceutical industry?

We found some research gaps, which can be developed by studies in future studies, as well, considered by practitioners related to implementation of RL. Some of them are detached:

- the need of global studies on RL of pharmaceuticals covering developed and developing countries;
- policies development and reformulation;
- integration among different research areas related to residues and, among regulatory agencies, companies and final users;
- education of stakeholders, professionals and consumers; and
- integration of activities from direct logistics and RL and collaboration practices.

This study led to the identification of gaps and the notion that RL in the pharmaceutical industry field still relies on specific and localized actions, such as:

- diagnostics from surveys;
- studies about management of disposal impacts; and
- fewer studies considering RL with the goal of product reuse (under special safety rules), or with the goal of remanufacturing product ingredients, such as packages, for instance.

Moreover, studies on RL in the pharmaceutical field are also still focused on the finished goods but would also present a broader context of application, such as raw materials, in-process inventory and related issues.

Related to the limitations of the study, other organization categories could be created from the content analysis effort. Other limitations include the presentation of research gaps based on information available in the papers gathered. Besides that, the consideration of *SCMij* for the second part of the research limits the analysis to the scope of this journal.

5.1 Implications of the research (practical, theoretical, methodological)

In this section, we reported the implications of the study, which are relevant to the effective management of RL in pharmaceutical segment, despite many others may be depicted from Section 4.3.

First, regarding the *practical implications*, we emphasize that the formalization of policies and regulations can affect the structuration of RL networks, considering that many companies implement RL reactively.

In the case of "consumed products", to reduce the costs involved in RL process, mainly related to transportation of low volumes, joint initiatives among the companies involved in the supply chain of pharmaceutical industry can be implemented, in which the point-of-sale, units from national health systems and hospitals can receive the consumed or expired medicines from consumers.

It is important to emphasize that, although the delivery of expired and used medicines by consumers in point-of-sale is already a common practice in developed countries, as USA and EU (Daughton, 2003; Vollmer, 2010; Gray and Hagemeier, 2012), it is still considered a challenge and an innovative practice in developing countries, such as Brazil. Third-party logistics will collect the amount of residues discarded in point-of-sale, units from national health systems and hospital to increase the quantity to be transported to incineration plants (drugs) or recyclers (external packages). The costs involved can be shared with the supply chain members.

In some countries, in other segments such as electronics, the consumers pay a fee related to RL, making the process clearer for the consumer. However, in most countries, the costs related to RL are not clear to consumers, being embedded in general logistics costs and added to purchasing cost. Some legislation in European countries, such as Germany and Portugal, and in Brazil, advocates the shared responsibility in RL, which requires collaborative practices to manage residues and share costs related to it. In addition, in some countries, a manager company is created to manage RL, so the stakeholders share the costs to support it. In addition, programs of awareness and environmental education aimed to consumers should be developed, to stimulate the consumers to discard correctly the medicines or drugs in the point-of-sale.

Currently, there are some initiatives from pharmaceutical laboratories, in which they incentive the point-of-sales to receive the used or expired medicines in exchange for discounts of purchasing of medicines. However, in developing countries practices in this context are still scarce.

In the case of "not consumed products", the third-party logistics can be involved to collect the amount of medicines/drugs from retailers, at the same time they collect the consumed products, so the supply chain can take advantage in terms of transportation costs.

Second, in terms of *theoretical implications*, this research identified some aspects that can be developed in future studies. Future studies can investigate the management of RL and its complex differences compared to forward distribution in pharmaceutical industry. Additionally, the mapping of the practices of RL worldwide through a survey could be relevant. The inclusion of third party logistics providers (3PLs) in the process of RL in pharmaceutical industry can be also studied, in terms of criteria to select them and the certifications required.

Studies comparing legislations and restrictive policies affecting pharmaceutical segment in terms of returns of products would be useful, as well as studies comparing the practices of RL conducted in different segments, including the pharmaceutical one. So further investigation expanding to a cross-industry perspective is suggested.

Third, in terms of *methodological implications*, this paper used specific protocols to conduct a systematic literature review on RL in pharmaceutical segment. Further studies can use the protocols proposed on Pagani *et al.* (2015), among others. Studies using other protocols can find different results when compared to this research.

Besides that, case studies can be carried out to probe some aspects related to formalization and the implementation of reverse practices in pharmaceutical segments. Studies with PSC also can be conducted to map practices related to RL.

In addition, studies comparing the developed and developing countries practices related to RL of medicines would be useful to identify the benchmarking practices. Furthermore, studies applying the MCDA approach and PSM can be useful to structure and systematize decisions related to the implementation of RL in this segment.

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Appendix

Table AI Classifications of portfolio by the *Australian business deans' council (ABDC)* and impact factor

Journals	No. of papers	Ranking ABDC 2016	Impact factor 2015
SCMij	3	A	2.731
Computers & Chemical Engineering	2	–	2.581
Environment. Science and Pollution Research	2	–	2.760
Environment International	2	–	5.929
African Journal of Biotechnology	1	–	0.573
Drug Safety	1	–	3.206
Environmental Chemistry Letters	1	–	2.918
Environmental Health Perspectives	1	–	8.44
Expert Review of Clinical Pharmacology	1	–	2.488
Independent Journal of Management & Production (IJM&P)	1	–	0.876
Indian Journal of Pharmaceutical Education and Research	1	–	0.219
Information Technology Management	1	B	0.600
International Journal of Supply Chain Management	1	–	–
International Journal of Environmental Research and Public Health	1	–	2.035
International Journal of Procurement Management	1	C	–
International J. P. Perf. Manag.	1	B	–
International Journal of Physical Distribution & Logistics Management	1	–	2.101
Journal of Environmental Management	1	A	3.131
Journal of Hospice & Palliative Nursing	1	–	0.475
Journal of Purchasing and Supply Management	1	B	2.562
Journal of Public Health	1	–	2.019
Journal of the Air & Waste Management Association	1	–	1.613
Management Research News	1	C	–
Management Research Review	1	C	–
Pharmacy World & Science	1	–	1.339
Process Safety and Environ. Protection	1	–	2.078
Saudi Pharmaceutical Journal	1	–	2.233
Science of the Total Environment	1	–	3.976
South Asian Journal of Management Sciences	1	C	–
Strategic Outsourcing: an International Journal	1	B	–
International Journal of Procurement Management	1	A	0.917
Trends in Biotechnology	1	–	12.065
Vitae Revista Facultad de Quim Farmacéutica	1	–	–
Waste Management & Research	1	–	1.338
Total	39	–	

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