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TESE DE DOUTORADO

Elaine Aparecida Regiani de Campos

ANÁLISE DOS FATORES CRÍTICOS NA GESTÃO DE MEDICAMENTOS VISANDO À LOGÍSTICA REVERSA ENTRE INSTITUIÇÕES DE SAÚDE DO SETOR PÚBLICO

Porto Alegre
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Tese submetida ao Programa de Pós-Graduação em Engenharia de Produção da Universidade Federal do Rio Grande do Sul como requisito parcial à obtenção do título de Doutora em Engenharia, na área de concentração Sistemas de Produção.

Orientadora: Profa. Carla Schwengber ten Caten, Dra.

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Esta tese foi julgada adequada para a obtenção do título de Doutora em Engenharia e aprovada em sua forma final pelo Orientador e pela Banca Examinadora designada pelo Programa de Pós-Graduação em Engenharia de Produção da Universidade Federal do Rio Grande do Sul.

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Albert Einstein

RESUMO

No processo de gestão de medicamentos, visando à logística reversa (LR), os gestores das instituições de saúde do setor público se deparam com diferentes fatores críticos e que se não forem gerenciados, podem se tornar barreiras ao processo de implementação eficiente da LR. Esta tese teve como objetivo geral analisar o impacto dos fatores críticos na gestão de medicamentos visando à logística reversa entre instituições de saúde do setor público. Para isso seu objetivo geral foi desdobrado em quatro capítulos, sendo estes (*i*) desenvolvimento de uma revisão sistemática de literatura que permitiu a identificação de conceitos e práticas de LR aplicadas ao end-of-life (EOL) e ao fim de uso (EOU) de medicamentos; (*ii*) mapeamento dos fluxos reverso e de remanejo de medicamentos que fazem parte do processo de Assistência Farmacêutica em nível de Atenção Primária de Saúde (APS) no município de Porto Alegre, no Brasil; (*iii*) com o uso do método de abordagem multicritério - grey-DEMATEL foi estruturada uma avaliação da inter-relação dos principais fatores críticos na implementação das práticas de gestão de medicamentos, visando a logística reversa, e por fim, (*iv*) é apresentada uma análise da influência dos fatores críticos sobre a performance logística da PCP. Os resultados desta tese são de suma importância no aspecto teórico e gerencial vislumbrando para a importância da gestão efetiva de medicamentos EOL/EOU visando à logística reversa, sendo que os resultados apresentados são considerados como uma importante ferramenta que permite aos gestores e tomadores de decisões uma visão ampla dos fatores críticos e demonstrando quantitativamente o impacto na performance logística da APS.

Palavras-chave: Logística Reversa; Fatores Críticos; Medicamentos End-of-Life; Atenção Primária de Saúde.

ABSTRACT

In the medication management process, aimed at reverse logistics (RL), managers of public sector health institutions are faced with different critical factors which, if not managed, can become barriers to the efficient implementation process of RL. The general objective of this thesis was to analyze the impact of critical factors in the management of medications aimed at reverse logistics among public sector health institutions. For this, its general objective was divided into four chapters, these being (i) the development of a systematic literature review that allowed for the identification of RL concepts and practices applied to the end-of-life (EOL) and end of use (EOU) of medicines; (ii) mapping of the reverse flow and reassignment of drugs that are part of the Pharmaceutical Assistance process at the Pharmaceutical Care Process (PCP) level in the city of Porto Alegre, in Brazil; (iii) using the multi criteria approach - grey-DEMATEL, an assessment of the interrelation of the main critical factors during the implementation of drug management practices was structured, aimed at reverse logistics, and finally, (iv) an analysis of the influence of critical factors on the logistics performance of the PCP is presented. The results of this thesis are of paramount importance to the theoretical and managerial aspect, glimpsing at the importance of the effective management of EOL/EOU medications aimed at reverse logistics, and the results presented are considered to be an important tool that provides managers and decision makers with a broader view of the critical factors and quantitatively demonstrating the impact on the performance logistics of PHC.

Key words: Reverse Logistics; Critical Factors; End-of-Life Medicines; Pharmaceutical Care Process

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LISTA DE ABREVIATURAS E SIGLAS

AHP – Analytic Hierarchy Process

ANVISA – Agencia Nacional de Vigilância Sanitária

APS – Atenção Primária de Saúde

AVE – Average Variance Extracted

B2B – Business to business

B2C – Buss Business to Consumer

BEC – Bidding Evaluation Committee

COORAF – Coordenação de Assistência Farmacêutica

CF – Collaboration Factor

CFs – Critical Factors

CR – Composite Reliability

DDC/PSC – Drug Distribution Center/Pharmaceutical Supply Center

DEMATEL – Decision-Making Trial and Evaluation Laboratory

DIS – Sistema de Dispensação de Medicamentos

EOU – End-of-Use

EOL – End-of-Life

EOL-MP – End-of-life/Management Practices

FAHP – Fuzzy Analytic Hierarchy Process

FC – Fator Crítico

FEF – Financial and Economic Factor

GMAT – Sistema de Gestão de Materiais

HCL – Horizontal Collaborations Logistics

HU – Health Unit

IF – Infrastructure Factor

ISM – Interpretive Structural Modeling

ITF – Information Technology Factor

LPF – Logistics Performance Factor

LR – Logística Reversa

MCDA – Multi-criteria Decision Analysis

MCDM – Multiple-Criteria Decision Making Methods

MF – Management Factor

MP – Municipal Pharmacy

NHS – National Health Service

PA – Pronto Atendimento

PC – Pharmaceutical Care

PCP – Pharmaceutical Care Process

PEV – Pontos de Entrega Voluntária

PF – Politic Factor

PLS-SEM – Partial Least Square-Structural Equation Modeling

PNRS – Política Nacional dos Resíduos Sólidos

PNUMA – Programa das Nações Unidas para o Meio Ambiente

PPCP – Pharmaceuticals and Active Ingredients in Personal Care Products

PSC – Pharmaceutical Supply Chain

RDC – Resolução da Diretoria Colegiada

REMUME – Relação Municipal de Medicamentos

RENAME – Relação Nacional de Medicamentos Essenciais

RFID – Radio Frequency Identification

RL – Reverse Logistics

RSL – Revisão Sistemática de Literatura

SCM – Supply Chain Management

SCU – Still in Conditions of Use

SLR – Systematic literature review

SPAADD - Seleção, Programação, Aquisição, Armazenamento, Distribuição e Dispensação

SUS – Sistema Único de Saúde

TOPSIS – Technique for Order of Preference by Similarity to Ideal Solution

TPC – Therapeutic Pharmacy Commission

UBS – Unidade Básica de Saúde

WM – Waste Management

SUMÁRIO

1. INTRODUÇÃO

Nas últimas décadas, os esforços dos gestores das organizações privadas e também do setor público têm sido no sentido de incluir em suas tarefas, ações que envolvam práticas voltadas para a sustentabilidade. Autores como Jindal e Sangwan (2011) consideram que tratar a sustentabilidade dentro do escopo de atividades é fundamental para as organizações do século XXI, e uma abordagem para a sustentabilidade se dá por meio da introdução da Logística Reversa (LR) como uma prática sistêmica.

Rogers e Tibben-Lembke (1998) definem a LR como o processo de planejamento, implementação e controle do fluxo eficiente e econômico, de matéria-prima, estoque em processo, produtos acabados e informações do ponto de consumo ao ponto de origem com o objetivo de recuperar o valor ou dispor adequadamente o produto.

A partir da definição, entende-se que a LR é uma parte fundamental no processo da gestão da cadeia de suprimentos (WAQAS et al., 2018). Aksoylu e Demirel (2018) citam as principais atividades de logística direta, sendo elas: transporte, armazenagem, gestão da informação, gestão de inventário, aquisição, previsão de demanda, manuseio de material, embalagem, planejamento de produção, localização da instalação, atendimento ao cliente, seguro e desembaraço aduaneiro.

Para Srivastava e Srivastava (2006) desenvolver e melhorar os conceitos de LR, reflete o quão preparadas as organizações estão para fazer com que as principais atividades da logística direta sejam tão eficazes quanto os processos de retorno dos produtos por elas distribuídos, respondendo assim às questões econômicas, às pressões do consumidor e às normas regulatórias.

Nos países desenvolvidos, a LR é considerada uma das partes mais significativas da cadeia de suprimentos. Já em se tratando dos países em desenvolvimento, sua implementação encontra-se em estágios iniciais, e o processo de implementação de ações de LR pode enfrentar barreiras substanciais (GONZÁLEZ-TORRE et al., 2010; WAQAS et al., 2018).

No processo de implementação de LR, as organizações enfrentam barreiras, que pode ser influenciado pelo setor, dentre eles, podem ser citados os setores: eletrônico (KUMAR e DIXIT 2018; GEETHAN et al., 2011), construção civil (CHILESHE et al., 2018), automobilístico (PHUC et al., 2017), resíduos da saúde (COLE et al., 2018; XIE e BREEN 2013), e ainda o de medicamentos (SCAVARDA et al., 2019; CAMPOS et al., 2017; RITCHIE et al., 2000).

Erol et al. (2010) apontam que algumas das dificuldades na implementação de LR são causadas pela infraestrutura tecnológica inadequada, como a falta de sistema de informação e tecnologia para o desenvolvimento de uma cadeia reversa eficiente e de gestão dos retornos.

Com relação ao descarte dos produtos farmacêuticos, Kelly et al. (2018) e Manojolović et al. (2015) apontam que uma das grandes preocupações permeia na prática que o consumidor adota em relação ao descarte dos produtos indesejados, e essa é uma questão de saúde pública. O potencial de contaminação e envenenamento é alto, além disso uma das formas mais comuns de descarte se dá pelo lixo doméstico ou em esgotos. No entanto, existem preocupações globais sobre a extensão, o impacto ambiental, os riscos para a saúde, e também em relação à incapacidade de monitorar o armazenamento e o descarte dos medicamentos que estão em posse dos usuários.

No Brasil, o usuário de produtos farmacêuticos tem acesso aos medicamentos, tanto pelas farmácias comerciais quanto em farmácias do Sistema Único de Saúde (SUS), que mantém em seu estoque os medicamentos da lista básica, definidas pela Relação Nacional de Medicamentos Essenciais (RENAME). Na Relação Municipal de Medicamentos (REMUME), os medicamentos são disponibilizados por meio da Política Nacional de Medicamentos (PNM) instituída a partir de 1998 (BRASIL, 1998). O SUS é um dos maiores e mais complexos sistemas de saúde pública do mundo (MINISTÉRIO DA SAÚDE, 2019).

O contexto desta tese é o sistema público de saúde, do município de Porto Alegre, RS, na Secretaria Municipal de Saúde, que, por meio da Coordenação de Assistência Farmacêutica (COORAF). Para a realização da pesquisa, inicialmente foi submetido o projeto de estudo para o Comitê de Ética em Pesquisa (CEP), os documentos pertinentes a autorização para a realização da pesquisa (parecer consubstanciado e Termo de Consentimento Livre e Esclarecido - TCLE), encontram-se nos Apêndices A, B e C deste capítulo.

A COORAF, administra o estoque de dez farmácias distritais (denominado – farmácia municipal - em outros estados brasileiros) e mais de cento e quarenta pontos de atendimentos entre as Unidades Básicas de Saúde (UBS) e Pronto Atendimento (PA).

Representado em nível municipal pelas secretarias de saúde que desempenham a gestão das atividades de logística direta: seleção, programação, aquisição, armazenamento, distribuição e dispensação (SPAADD) dos medicamentos, o ciclo logístico faz parte de um ciclo mais abrangente denominado Assistência Farmacêutica (AF).

O medicamento disponibilizado na rede SUS percorre um processo logístico intenso e grandioso, desde o fornecedor até o usuário final. Neste intenso processo logístico, as AF, de

cada estado brasileiro e de cada município desempenham uma função intermediadora, de modo a prover o acesso da população aos medicamentos essenciais, por meio das unidades de dispensação de medicamentos. É importante ainda mencionar que todos os fluxos do processo logístico desempenham uma função importante para que o medicamento chegue nas mãos do usuário na quantidade e na qualidade certa (SERAFIM, 2010).

Tendo uma estrutura complexa, os gestores enfrentam desafios administrativos que vão desde os fluxos de informação e físicos que percorrem as operações logísticas do fluxo SPAADD que, no âmbito da AF é tratado em nível de Atenção Primária de Saúde no setor público de medicamentos.

Sobretudo, os fluxos logísticos diretos da AF também devem dar integral destino a medicamentos que não estão mais no prazo de validade, *end-of-life* (EOL), nos estabelecimentos da rede de saúde, farmácias e/ou pontos de distribuição. Como nem sempre o usuário adere ao tratamento pode haver retenção de medicamentos nas residências, pontos de tratamento ou ainda medicamentos dentro da validade, *end-of-use* (EOU).

Uma lacuna antecedente vem no fato do usuário não ter local adequado ou instituição suficiente para descartar medicamentos EOL/EOU. Tecnicamente, existe uma discussão sobre "quem?" e "como?" deve ser gerenciado o medicamento EOL/EOU originário do retorno de qualquer ponto da rede de saúde (seja do usuário final ou de instituições do sistema de saúde – farmácias, hospitais, UBS, etc.).

Entende-se que o papel desempenhado pelos gestores farmacêuticos é de fundamental importância para que o processo logístico tenha eficiência e eficácia. Neste caso, também se reconhece a participação do setor público, no processo de implementação das atividades de logística reversa.

Neste sistema coordenado de provisão de medicamentos pelo SUS, uma intensa discussão se dá em relação à função majoritária das farmácias e unidades básicas de saúde. Tal função consiste em apenas prover o medicamento? Ou deve ser papel dela também recolher o medicamento que está em posse do paciente e que se encontra vencido ou não? Diferentes autores chamam a atenção para a importância desse movimento, sobretudo para a importância da triagem do medicamento que o paciente tenta devolver, dado que seu estado de conservação é desconhecido e difícil de ser revalidado (AQUINO et al., 2018).

Para Tong et al. (2011) o descarte adequado de medicamentos que não são utilizados pode ser uma prática que permite aos pacientes retornar de forma consciente o medicamento não utilizado para uma farmácia. Do ponto de vista do autor, isso pode ser essencialmente

importante em países que oferecem medicamentos gratuitos ou subsidiados. Um ponto importante e reflexivo, é que algumas farmácias em todo o mundo se recusam a aceitar medicamentos não utilizados ou desencorajam tal prática.

Diante da discussão que permeia a LR de medicamentos no setor de saúde, destacam-se diferentes tipos de resíduos que podem ser gerados a partir do atendimento ao paciente. Resíduos estes que estão previstos na Resolução da Diretoria Colegiada - RDC 222 de 2018 da Agência Nacional de Vigilância Sanitária (ANVISA) (BRASIL, 2018). A RDC 222 traz em suas seções orientações de boas práticas de gerenciamento de resíduos da saúde de acordo com as suas especificidades e a forma de tratamento, sendo estes: Grupo A: de risco biológico, Grupo B: risco associado à periculosidade de resíduo químico; Grupo C: apresenta risco radioativo, Grupo D: Resíduos que não apresentam risco biológico, químico ou radiológico à saúde ou ao meio ambiente e Grupo E: risco biológico e perfuro cortante (vide Anexo A – Capítulo 3).

Esta tese destaca um caso específico sob uma perspectiva particular do setor de medicamentos e foca nos resíduos do Grupo B, medicamentos, pois apresenta um grande desafio para a logística reversa na área da saúde, dada a sua complexidade de estimativa de qualidade do produto que retorna – *end-of-use* (EOU) e seus impactos ambientais na esfera, *end-of-life* (EOL).

As práticas mais comuns são pontos de entrega voluntária (PEV) instalados nas farmácias comerciais. Cole, Lindsay e Barker (2018) destacam a importância de aprimorar o fluxo reverso nas cadeias de suprimentos de assistência médica sendo que este é um passo importante para melhorar os processos sustentáveis para o serviço público. Todavia, Cole, Lindsay e Barker (2018) relatam que a falta e inconsistência da legislação sobre a reutilização é problemática na área da saúde, embora tenha recebido foco crescente de discussões, ainda se têm deficiências substanciais em como lidar com o retorno e reutilização de produtos.

A partir da contextualização apresentada, chega-se a seguinte questão de pesquisa:

Quais são os fatores críticos na gestão de medicamentos EOL/EOU, com foco na performance logística e como estes fatores se inter-relacionam?

1.1 TEMA

O descarte de medicamentos não utilizados ou pós prazo de validade, tem sido uma preocupação em muitos países. A principal questão é que a presença de substâncias de produtos

farmacêuticos pode causar sérios problemas ambientais (ABAHUSSAIN et al., 2012; SEBASTINE e WAKEMAN, 2003).

Serviços públicos em todo o mundo, incluindo setores governamentais e de saúde, precisam ser mais proativos estabelecendo diretrizes específicas (TONG et al., 2011). Em alguns países do mundo, o descarte adequado de medicamentos EOU pode incluir projetos que permitem os pacientes retornar de forma consciente o medicamento não utilizado a uma farmácia (GLASSMEYER et al., 2009). Isso pode ser importante em países que oferecem medicamentos gratuitos.

Devido à crescente demanda por produtos verdes e também devido a pressões governamental, social e econômica, os gestores dos setores industriais começaram a perceber a importância de aplicar conceitos de gerenciamento verde em suas atividades. Há uma necessidade de aumentar a conscientização no meio privado e público sobre a questão do descarte de medicamentos e os vários impactos no meio ambiente (TONG et al., 2011). Sobretudo, a prática de LR é uma das estratégias importantes para fornecer uma utilização eficiente dos recursos e minimizar os resíduos dos produtos EOL (SRISAWAT e KIATCHAROENPOL, 2018).

1.2 OBJETIVOS

O objetivo geral desta tese consiste em, analisar o impacto dos fatores críticos na gestão de medicamentos, visando à logística reversa, entre instituições de saúde do setor público.

Para que seja possível alcançar o objetivo geral, esta tese é norteada pelos seguintes objetivos específicos:

a) Identificar conceitos e práticas de logística reversa (LR) aplicadas ao *end-of-life* (EOL) e ao fim de uso (EOU) de medicamentos;
b) Mapear os fluxos de logística reversa e de remanejo de medicamentos que fazem parte do processo de Assistência Farmacêutica em nível de Atenção Primária de Saúde (APS) no município de Porto Alegre, no Brasil;
c) Avaliar a inter-relação dos principais fatores críticos na implementação das práticas de gestão de resíduos de medicamentos, visando a logística reversa;
d) Determinar a influência dos fatores críticos sobre a performance logística da APS.

1.3 JUSTIFICATIVA, RELEVÂNCIA E ORIGINALIDADE DO ESTUDO

A indústria farmacêutica constantemente trabalha no desenvolvimento de medicamentos para as mais diversas patologias. O desenvolvimento de produtos ocorre a partir de longas pesquisas envolvendo um sistema complexo de moléculas químicas e demandando tempo até que possa ser consolidado (BUSETTI et al., 2009). Por essa análise, se reconhece que o comportamento, o impacto e o desgaste das propriedades naturais do solo, é muito mais veloz em relação ao processo de desenvolvimento do medicamento.

Comumente, os principais resíduos de fármacos encontrados no solo, ou na água são as substâncias ativas como: ácido clorídrico, ácido salicílico, diclofenaco, ibuprofeno (Ternes 2001), os xenobióticos (Payan et al. 2010), dentre outros. A presença destes é encontrada em efluentes de estações de tratamento de esgoto entrando no ciclo da água por meio de fontes domésticas, eliminação de produtos vencidos ou em desuso. E, muitas vezes o resíduo fármaco ainda pode ser ingerido por seres humanos via ingestão de água tratada (SEBASTINE e WAKEMAN, 2003; BUCHBERGER, 2011).

No Brasil, a Lei Federal 12.305 instituiu a Política Nacional de Resíduos Sólidos (PNRS) a partir de agosto de 2010, que determina que todos os envolvidos na cadeia produtiva sejam responsáveis pela destinação final do produto, instituindo assim a responsabilidade compartilhada dos geradores de resíduos (BRASIL, 2010). Nesse intuito, espera-se a redução na geração de resíduos sólidos e consequentemente reduzindo os danos ao meio ambiente. Por esse princípio de ecoeficiência, as empresas tornam-se competitivas a medida em que se comprometem em desenvolver mecanismos de retorno do produto em desuso.

Na atualidade, a sociedade é consumista de recursos que são escassos e que de alguma forma acabam impactando o meio ambiente, tanto para as gerações atuais como para as gerações futuras. No mundo, o consumo de medicamentos é crescente, e gradativamente, as pessoas fazem uso de medicamentos para diferentes patologias. Uma das preocupações, reside em compreender o que os usuários farão com o medicamento caso não seja integralmente consumido (GLASSMEYER et al., 2009). Dados da Organização Mundial da Saúde - *World Health Organization*, confirmam que 50% da população não adere integralmente ao tratamento com medicamentos (WHO, 2003).

Diante deste cenário, como controlar um estoque de medicamentos de tal forma que seja possível prover as necessidades de uma população, mas também não gerar número extenso de cifras de perdas de medicamentos por vencimentos ou por falhas na prescrição ou não adesão ao tratamento? (AQUINO et al., 2018). Todavia, a gestão cuidadosa dos fármacos está

diretamente relacionada à capacidade de um país em responder às preocupações de saúde pública (UTHAYAKUMAR e PRIYAN, 2013).

Um dos limiares concentra-se na questão dos medicamentos e produtos oriundos dos setores médico-hospitalares, resíduos que necessitam de um cuidado específico tanto na segregação como na destinação que será dada, de modo a preservar as fontes de recursos naturais (COLE, LINDSAY e BARKER, 2018).

Também uma das maiores necessidades das empresas, tanto em âmbito público como privado quer seja por força da lei ou pressão econômica e social, reside em como tornar-se responsável pelo resíduo por ela gerado?. Nesse sentido, cabe à academia realizar estudos nas diferentes realidades que retratem essa problemática e que tenha como objetivo apontar soluções para o curto, médio e longo prazo. A tomada de decisão dos gestores não deve ficar à mercê das decisões políticas (MUDULI et al., 2013; DIABAT et al., 2013).

Todavia, todo o sistema é dependente de recursos para realizar as atividades que competem à logística reversa, recursos estes: financeiro, recursos humanos e tecnológicos. Tais recursos, muitas vezes, podem ser entendidos como fatores críticos à implementação de um sistema de logística reversa eficiente e eficaz e que se não tratados podem se tornar uma barreira (TAVANA et al., 2016; KAVIANI et al., 2020).

A tese em questão implica na apresentação e análise de um problema atual no âmbito da ciência e por se tratar de um sistema intrincado que é o SUS, sob uma perspectiva de sustentabilidade e em particular a logística reversa de medicamentos e seus insumos. Sobretudo, sendo de suma importância no contexto multidisciplinar e principalmente para a Engenharia de Produção. Todavia, a carência de estudos publicados ao longo dos anos revela um campo atual e relevante de estudos. Ainda cabe destaque para a ausência de ferramentas que tenha como propósito auxiliar os gestores na tomada de decisões o que traz consigo a relevância e a originalidade desta tese que busca suprir esta lacuna.

1.4 DELINEAMENTO DO ESTUDO

A partir da definição dos objetivos da tese e apresentadas a justificativa, a relevância e a originalidade da pesquisa, esta seção apresenta o delineamento do estudo pelo qual os objetivos foram alcançados, considerando o método de pesquisa e o método de trabalho que foram utilizados.

1.4.1 Método de Pesquisa

Pela caracterização do *ponto de vista do seu objeto*, a pesquisa é classificada como pesquisa de campo, sendo que a coleta de dados é efetuada onde ocorrem espontaneamente os fenômenos. Do *ponto de vista da sua natureza*, é considerada como pesquisa aplicada prática, dirigida à solução de problemas específicos, envolvendo verdades e interesses locais. Na pesquisa aplicada o investigador é movido pela necessidade de contribuir para fins práticos mais ou menos imediatos, buscando soluções para problemas concretos (MARCONI e LAKATOS, 2003).

Pela caracterização da *abordagem do problema*, a pesquisa proposta para esta tese é classificada como *Mix Method*, integrando coleta e análise de dados qualitativos e quantitativos. O uso de métodos mistos tem várias vantagens, dentre elas possibilitar a comparação dos dados qualitativos e quantitativos. Métodos mistos são especialmente úteis para entender contradições entre resultados quantitativos e descobertas qualitativas, refletindo o ponto de vista dos participantes. As junções de ambos os métodos têm grande flexibilidade e são adaptáveis a muitos desenhos de estudo fornecendo um resultado mais completo em comparação com qualquer método utilizado de forma individual (VENKATESH, et al., 2016; WISDOM e CRESWELL, 2013).

Entende-se que a coleta de dados quantitativos envolve entrevistas estruturadas, *check lists* de observação analisados por meio de procedimentos estatísticos descritivos e inferenciais. Os dados qualitativos consistem em entrevistas semiestruturadas e observações de campo, que são analisadas usando codificação para desenvolver temas e categorias. A coleta dos dados ocorreu simultaneamente e sequencialmente (BARDIN, 1977; BAUER e GASKELL, 2000).

Para Creswell et al. (2004) e Venkatesh et al. (2016), este tipo de abordagem ainda são recomendados para criação de modelos de construção de instrumentos, triangulação e transformação de dados para projetos de métodos mistos como estrutura útil para adicionar rigor às investigações.

Do *ponto de vista dos seus objetivos* é classificada como explanatória. De acordo com Saunders et al. (2009) a pesquisa explanatória busca estabelecer, a partir da natureza dos relacionamentos de um conjunto de diferentes variáveis, as relações de causa-efeito e como tais relações ocorrem.

Do *ponto de vista dos procedimentos técnicos* é considerada como levantamento do tipo *survey*. O levantamento pode ser descrito como a obtenção de dados ou informações sobre características, ações ou opiniões de determinado grupo de pessoas, indicado como

representante de uma população alvo (amostra), por meio de um instrumento de pesquisa, normalmente um questionário. As conclusões obtidas com base nessa amostra são projetadas para a totalidade do universo, levando em consideração a margem de erro, que é obtida mediante cálculos estatísticos. Ainda pode ser considerada como pesquisa-ação. Lindgrenet al. (2004) caracterizam a pesquisa-ação como um método intervencionista que possibilita ao pesquisador testar hipóteses sobre o fenômeno implementando, acessando as mudanças no cenário real. Neste tipo de pesquisa, o pesquisador assume a responsabilidade não apenas de assistir os atores envolvidos através da geração de conhecimento, mas também de aplicação deste conhecimento.

1.4.2 Método de Trabalho

A construção da tese compreende na análise do impacto dos fatores críticos na gestão dos resíduos de medicamentos visando a logística reversa entre instituições de saúde do setor público. A proposta compreende quatro importantes fases, como pode ser observado no Quadro 1- 1.

Estudos desenvolvidos	Questões de Pesquisa	Resultados obtidos	Metodologia empregada
Artigo 1 ([a])	QP1. Como a LR está evoluindo na indústria farmacêutica? Quais são as práticas de reciclagem, reutilização, redução ou alternativas implementadas para os produtos EOL e EOU pela indústria farmacêutica? QP2. Quais lacunas de pesquisa na LR podem ser identificadas a partir de mapas bibliométrico dos artigos publicados de 1996 a 2015 que orientariam estudos na indústria farmacêutica?	✓ Identificação do tema como uma oportunidade para pesquisa; ✓ Compilação de evidências sobre LR farmacêutica nos grupos: risco ambiental, a evolução da LR e a perspectiva educacional regulatória e dos *stakeholders;* ✓ A LR para a indústria farmacêutica precisa ser abordada de forma mais completa e abrangente.	Revisão Sistemática de Literatura (RSL)
Artigo 2 ([b])	QP1. Quais são os fluxos de logística reversa e de remanejo de medicamentos que fazem parte da Atenção Primária de Saúde (APS) na opinião de especialistas? QP2. Quais são os fatores críticos para realização das atividades dos fluxos de logística reversa e de remanejo de medicamentos no contexto das operações logística da Atenção Primária de Saúde (APS)?	✓ Mapeamento dos fluxos de logística reversa e de remanejo; ✓ Identificação dos fatores críticos para implementação de logística reversa; ✓ Triangulação dos dados (teoria e entrevistas) para criar o modelo teórico.	Estudo de Caso
Artigo 3 ([c])	QP1. Quais são os fatores críticos para a implementação de logística reversa de medicamentos na APS? QP2. Quais são as relações de causa-efeito entre esses fatores críticos?	✓ Avaliação dos fatores críticos na implementação de logística reversa de medicamentos; ✓ Apresentação dos fatores seguindo ordenação causa-efeito.	Multicriteria Decision Analysis Grey Decision-Making Trial and Evaluation Laboratory (Grey-DEMATEL
Artigo 4 ([d])	QP1. Como os fatores críticos influenciam a implementação de práticas de gestão de medicamentos *End-of-Life*, e como esta última pode relacionar-se com a performance logística da APS?	✓ Identificação da influência que os fatores críticos exercem na adoção práticas de gestão de medicamentos *end-of-life*, determinando o impacto dos mesmos sobre a performance logística da APS.	Modelagem de Equações Estruturais – Partial Least Square (PLS)

Quadro 1-1 Estrutura das etapas da pesquisa desenvolvida

([a]) Artigo publicado no periódico *Supply Chain Management: An International Journal*
([b]) Artigo em avaliação no periódico *Environmental Science and Pollution Research*
([c]) Artigo em avaliação no periódico *Environmental Science and Pollution Research*
([d]) Artigo em avaliação no periódico *Journal of Cleaner Production*

1.5 DELIMITAÇÕES DO ESTUDO

Em muitos países desenvolvidos, a LR é parte integrante da cadeia de suprimentos (ABDULRAHMAN et al., 2014). Para esta tese algumas delimitações podem ser elencadas para definir o escopo e a sua contribuição. As delimitações teóricas e empíricas são descritas na sequência.

Delimitação Teórica: Considerando os diferentes tópicos que contemplam a sustentabilidade, desde elementos estratégicos na Gestão da Cadeia de Suprimentos como, por exemplo, Green Supply Chain Management, Ecoeficiência, Relações Cooperativas Horizontais e Verticais na cadeia de suprimentos, Avaliação do Ciclo de Vida de produtos; e mais atualmente, a transição para a Economia Circular (EC) como um fenômeno emergente (Fischer e Pascucci, 2017), dentre outros tópicos. Pretende-se nesta tese limitar a investigação para aspectos relacionados aos fatores críticos na gestão de medicamentos, visando o estabelecimento da logística reversa. Portanto, a discussão sobre os aspectos relacionados a outros aspectos não serão discutidos com maior profundidade.

Delimitação Empírica: Uma das delimitações da tese reside no escopo de aplicação, sendo que os dados foram obtidos apenas na realidade do sistema público de saúde da região Metropolitana de Porto Alegre - RS e profissionais de municípios da região da 8ª Coordenadoria de Saúde. Conceitualmente, a logística reversa envolve toda cadeia, percorrendo o ciclo do consumidor final ao fabricante. Entende-se que os resultados aqui apresentados não permitem extrapolar diretamente para outros contextos, e que seria necessária uma continuidade neste campo de estudo para outros estados e municípios com suas peculiaridades em termos de gestão. Na Figura 1- 1, é apresentado o mapa conceitual da tese com o desdobramento da mesma nos 6 capítulos.

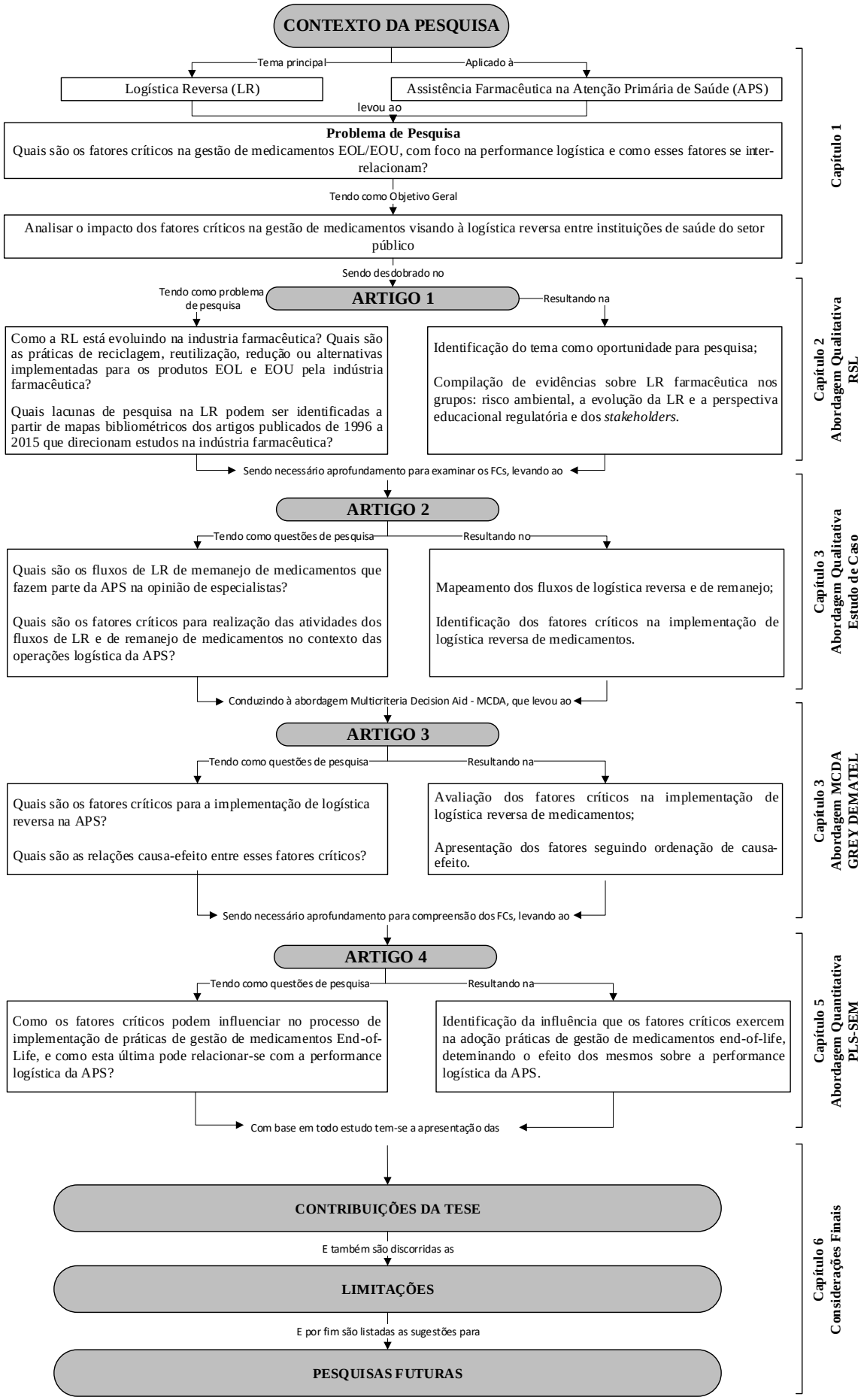

Figura 1-1 Desdobramentos da tese e relações entre os artigos e a análise proposta

1.6 CONCEITOS CHAVES E DEFINIÇÕES

Nesta seção serão apresentados os principais conceitos chaves que foram utilizados nesta tese e suas respectivas definições.

Conceito	Definição
Fatores Críticos	*Visando à implementação da logística reversa os fatores críticos foram listados a partir de conceitos oriundos da literatura, e referem-se aos elementos que precisam ser bem gerenciados para que não se tornem uma barreira à gestão da logística reversa de medicamentos.*
Logística direta	*Faz menção ao fluxo da cadeia de suprimentos de medicamentos, que se inicia com a matéria-prima até a produção, e prossegue com a distribuição até a entrega do produto ao usuário final.*
Logística de remanejo	*Diz respeito aos medicamentos e insumos, que estão dentro do prazo de validade, e que fazem parte de um processo de redistribuição e/ou realocação de uma unidade com um consumo mensal menor para uma unidade onde o consumo é maior. Os objetivos do remanejo são para evitar perdas de medicamentos por vencimento e desabastecimento.*
Performance Logística	*Considerado o desempenho por trás das atividades logísticas. No processo de logística farmacêutica, a distribuição de medicamentos aos pacientes deve ser realizada, valorizando a qualidade do atendimento e a rapidez do processo. Outros elementos também podem ser abordados, como o controle de estoque, que fará com que a distribuição seja executada com eficiência ou não.*
Assistência Farmacêutica	*Um conjunto de ações voltadas à promoção, proteção e recuperação da saúde, por meio da promoção do acesso aos medicamentos e uso racional são desenvolvidas pelo Ministério da Saúde. A oferta de medicamentos no SUS é organizada em três componentes que compõem o Bloco de Financiamento da Assistência Farmacêutica - Básico, Estratégico e Especializado, além do Programa Farmácia Popular. Com exceção do Farmácia Popular, em todos os outros componentes o financiamento e a escolha de qual componente o medicamento fará parte é tripartite, ou seja, a responsabilidade é da União, dos estados e os municípios.*
Atenção Primária de Saúde	*Refere-se ao primeiro nível de complexidade em atenção em saúde e se caracteriza por um conjunto de ações, no âmbito individual e coletivo, que abrange a promoção e a proteção da saúde, a prevenção de agravos, o diagnóstico, o tratamento, a reabilitação, a redução de danos e a manutenção da saúde com o objetivo de desenvolver uma atenção integral que impacte positivamente na situação de saúde das coletividades. No Brasil, a Atenção Primária é constituída pelas Unidades Básicas de Saúde (UBS), pelos Agentes Comunitários de Saúde (ACS), pela Equipe de Saúde da Família (ESF) e pelo Núcleo de Apoio à Saúde da Família (NASF). Estas estratégias atendem aos atributos essenciais da APS, a atenção no primeiro contato, a longitudinalidade, a integralidade e a coordenação. Tem como atributos derivados a orientação familiar e comunitária e a competência cultural.*
Maleta de Emergência	*Trata-se de um estoque reserva de medicamentos básicos, controlados e de uso ambulatorial que são disponibilizados em cada unidade de saúde, sendo utilizados em casos de urgência e emergência.*
End-of-Life	*Diz respeito aos medicamentos ou insumos que estão no fim de sua vida útil, fora do prazo de validade.*
End-of-Use	*Diz respeito aos medicamentos que os usuários não utilizam mais por razões distintas como, por exemplo, término, substituição do tratamento ou falta de adesão ao tratamento, dentro do prazo de validade.*

Quadro 2-2 Conceitos chaves e definições

1.7 REFERÊNCIAS

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APENDICE A – Parecer Consubstanciado do Comitê de Ética em Pesquisa (CEP) – Projeto

UFRGS - PRÓ-REITORIA DE PESQUISA DA UNIVERSIDADE FEDERAL DO RIO GRANDE DO

PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: Modelo para diagnóstico e acompanhamento do desempenho logístico da Assistência Farmacêutica pela perspectiva dos profissionais da rede multidisciplinar e das Farmácias Distritais de Porto Alegre

Pesquisador: Istefani Carísio de Paula

Área Temática:

Versão: 2

CAAE: 82571018.6.0000.5347

Instituição Proponente: Universidade Federal do Rio Grande do Sul

Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 2.532.199

Apresentação do Projeto:

Trata-se do projeto de pesquisa que tem como pesquisador responsável Istefani Carísio de Paula, intitulado "Modelo para diagnóstico e acompanhamento do desempenho logístico da Assistência Farmacêutica pela perspectiva das Farmácias Distritais de Porto Alegre" a ser executado de 03/2018 a 03/2019 e que pretende desenvolver um modelo para análise dos fluxos físicos, fluxos de informação e acompanhamento dos serviços logísticos da Assistência Farmacêutica pela perspectiva dos profissionais que trabalham na rede multidisciplinar de atendimento ao usuário na Assistência Farmacêutica das Farmácias Distritais de Porto Alegre.

Como justificativa, os pesquisadores informam que "pretende-se dar atenção à qualidade e melhoria dos processos logísticos da AF pela perspectiva das unidades de dispensação, por meio do diagnóstico e proposição de melhoria dos fluxos de informação e fluxos físicos (fluxos do medicamento) dentro e entre tais unidades."

Ainda, enfatizam quem a Assistência Farmacêutica (AF), "por ter uma estrutura complexa, os gestores enfrentam desafios administrativos dos fluxos de informação e físicos que perpassam as operações logísticas da AF de: seleção, programação, aquisição, distribuição e dispensação(S-P-A-D-D), que resultam muitas vezes em perdas econômico-financeiras da ordem de milhões, sem

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Bairro: Farroupilha **CEP:** 90.040-060
UF: RS **Município:** PORTO ALEGRE
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mencionar outras perdas intangíveis como aquelas que afetam a saúde do usuário final ou a imagem dos governantes e dos profissionais de saúde. Esta proposta de projeto tem por ênfase a qualidade destas operações logísticas (S-P-A-D-D).

Trata-se de um projeto avaliado pelo CEP/UFRGS (Instituição Proponente) e também pelo CEP/SMS de Porto Alegre, cadastrada como Instituição Coparticipe.

Objetivo da Pesquisa:

O objetivo da pesquisa é desenvolver um modelo para análise dos fluxos físicos, fluxos de informação e acompanhamento dos serviços logísticos da Assistência Farmacêutica pela perspectiva dos profissionais que trabalham na rede multidisciplinar de atendimento ao usuário na Assistência Farmacêutica das Farmácias Distritais de Porto Alegre.

Como objetivos específicos:

a. Mapear as operações de seleção, programação, aquisição, distribuição e dispensação, com ênfase nos fluxos de informação e físicos direto e reverso, necessários a uma AF eficiente;

b. Compreender as principais barreiras e facilitadores dos fluxos de informação e físicos do medicamento, a partir de diagnóstico que identifique perdas potenciais e reais;

c. Propor métricas e indicadores para os fluxos de informação e físico;

d. Estruturar um modelo de avaliação continuada dos fluxos de informação e físico para a Assistência Farmacêutica em Farmácias Distritais, a partir de práticas do Lean Healthcare e da Logística Reversa.

e. Proporcionar redução de perdas nos processos logísticos da AF.

Avaliação dos Riscos e Benefícios:

Como riscos, os pesquisadores informam que "É uma pesquisa de risco mínimo, pois a entrevista que será realizada não fará nenhuma intervenção ou modificação intencional nas variáveis fisiológicas ou psicológicas e sociais dos indivíduos que participam no estudo. Os riscos que podem ser gerados são: desconforto pelo tempo de entrevista, interrupção de tarefas importantes para participação na pesquisa e possibilidade de quebra de sigilo e vazamento de informações. Para minimizar esses riscos será realizada uma entrevista de no máximo meia hora que será agendada previamente para garantir que tarefas importantes da rotina de trabalho dos envolvidos não sejam interrompidas. Será garantida a segurança dos dados gerados. A entrevista será gravada

e posteriormente transcrita, sendo desgravada após sua transcrição. Os formulários em papel serão codificados e serão arquivados com segurança,
não sendo identificados com o nome de profissionais envolvidos e as planilhas eletrônicas serão armazenadas em computadores com acesso restrito. Serão garantidas a privacidade e confidencialidade dos dados utilizados preservando integralmente o anonimato. As informações geradas não serão utilizadas em prejuízo dos profissionais envolvidos.."

Como benefícios, os pesquisadores relatam que "a identificação de pontos críticos nos fluxos de informação e físicos da Assistência Farmacêutica. Além da aplicação de ferramentas que trarão melhorias que irão refletir no processo como um todo e consequentemente, no atendimento ao usuário."

Comentários e Considerações sobre a Pesquisa:
Segundo os pesquisadores, "foi escolhido o município de Porto Alegre, onde serão estudadas as 10 Farmácias Distritais. Em relação ao mapeamento, pretende-se usar uma Farmácia Distrital como estudo piloto, estendendo a análise para as demais."

Na nova versão do projeto, foi justificado o número amostral de 200, considerando que "o escopo dessa pesquisa são as 10 farmácias distritais do município de Porto Alegre e que as entrevistas irão abranger diferentes profissionais que atuam nessas farmácias, além dos profissionais que atuam na coordenação da Assistência Farmacêutica, estima-se que o instrumento de pesquisa será aplicado a pelo menos 20 profissionais por farmácia, totalizando 200 indivíduos (PENDÊNCIA ATENDIDA)

Para o levantamento dos dados necessários para atender os objetivos desta pesquisa serão utilizados roteiros de entrevistas destinados aos profissionais, presentes nos Apêndices A, B e C.

Os formulários de coleta de dados estão apresentados e adequadamente redigidos. Para o formulário B, foi incluída a identificação alfa-numérica. (PENDÊNCIA ATENDIDA)

Etapas previstas:
(A) Levantamento bibliográfico;
(B) Diagnóstico das operações logísticas da AF nas unidades de dispensação (Farmácias Distritais);

(C) Análise do sistema e proposição de soluções;
(D) Definição de diretrizes de gestão dos fluxos operacionais da AF.

O cronograma está apresentado e prevê coleta de dados a partir de maio de 2018.

Na segunda versão todos os pesquisadores listados no projeto foram ser incluídos na PB. (PENDÊNCIA ATENDIDA)

Foram ainda apresentados o TCUD e Termo de Autorização do coordenado da AF no Município de Porto Alegre.

Na nova versão foi incluido orçamento no projeto e previsão de fonte de financiamento com a justificativa "Este pesquisa não conta com financiamento de instituições de fomento, nem qualquer outro tipo de financiamento externo. As despesas serão custeadas pelos próprios pesquisadores. Ressalta-se que a responsabilidade do financiamento é exclusiva do pesquisador responsável. (PENDÊNCIA ATENDIDA)

Considerações sobre os Termos de apresentação obrigatória:
Foram apresentados o projeto completo e folha de rosto assinada.

Na nova versão, todas as solicitações relacionadas ao TCLE foram atendidas. (PENDÊNCIA ATENDIDA)

Conclusões ou Pendências e Lista de Inadequações:
O projeto de pesquisa encontra-se em condições de aprovação, de acordo com os aspectos éticos (CNS Resolução 466/12).

Considerações Finais a critério do CEP:
Aprovado.

Este parecer foi elaborado baseado nos documentos abaixo relacionados:

Tipo Documento	Arquivo	Postagem	Autor	Situação

Informações Básicas do Projeto	PB_INFORMAÇÕES_BÁSICAS_DO_PROJETO_1064138.pdf	21/02/2018 11:03:45		Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	APENDICE_D_TCLE_v2.pdf	21/02/2018 11:01:34	André Teixeira Pontes	Aceito
Outros	APENDICES_A_B_C_v2.pdf	21/02/2018 10:59:52	André Teixeira Pontes	Aceito
Parecer Anterior	PB_PARECER_CONSUBSTANCIADO_CEP_2492126.pdf	21/02/2018 10:55:48	André Teixeira Pontes	Aceito
Recurso Anexado pelo Pesquisador	CartaResposta.pdf	21/02/2018 10:53:23	André Teixeira Pontes	Aceito
Projeto Detalhado / Brochura Investigador	Projeto_Completo_v2.pdf	21/02/2018 10:51:28	André Teixeira Pontes	Aceito
Projeto Detalhado / Brochura Investigador	ProjetoCompleto.pdf	28/01/2018 08:44:00	André Teixeira Pontes	Aceito
Outros	Termo_Istefani.pdf	28/01/2018 08:42:51	André Teixeira Pontes	Aceito
Cronograma	Cronograma.pdf	25/01/2018 17:52:37	André Teixeira Pontes	Aceito
Outros	Apendices_A_B_C_Questionarios.pdf	23/01/2018 08:24:33	André Teixeira Pontes	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	APENDICE_D_TCLE.pdf	23/01/2018 08:21:15	André Teixeira Pontes	Aceito
Outros	ANEXO_A_TermoSMSPA_Assinado.pdf	23/01/2018 08:20:07	André Teixeira Pontes	Aceito
Outros	ANEXO_B_indicadores.pdf	23/01/2018 08:18:56	André Teixeira Pontes	Aceito
Folha de Rosto	folhaDeRosto_Assinada.pdf	23/01/2018 08:09:24	André Teixeira Pontes	Aceito

Situação do Parecer:
Aprovado

Necessita Apreciação da CONEP:
Não

PORTO ALEGRE, 08 de Março de 2018

Assinado por:
José Artur Bogo Chies
(Coordenador)

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APENDICE B – Parecer Consubstanciado do Comitê de Ética em Pesquisa (CEP) – Emenda

UFRGS - PRÓ-REITORIA DE PESQUISA DA UNIVERSIDADE FEDERAL DO RIO GRANDE DO

PARECER CONSUBSTANCIADO DO CEP

DADOS DA EMENDA

Título da Pesquisa: Modelo para diagnóstico e acompanhamento do desempenho logístico da Assistência Farmacêutica pela perspectiva dos profissionais da rede multidisciplinar e das Farmácias Distritais de Porto Alegre

Pesquisador: Istefani Carísio de Paula

Área Temática:

Versão: 3

CAAE: 82571018.6.0000.5347

Instituição Proponente: Universidade Federal do Rio Grande do Sul

Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 3.260.151

Apresentação do Projeto:

Trata-se do projeto de pesquisa que tem como pesquisador responsável Istefani Carísio de Paula, intitulado "Modelo para diagnóstico e acompanhamento do desempenho logístico da Assistência Farmacêutica pela perspectiva das Farmácias Distritais de Porto Alegre" a ser executado de 03/2018 a 03/2019 e que pretende desenvolver um modelo para análise dos fluxos físicos, fluxos de informação e acompanhamento dos serviços logísticos da Assistência Farmacêutica pela perspectiva dos profissionais que trabalham na rede multidisciplinar de atendimento ao usuário na Assistência Farmacêutica das Farmácias Distritais de Porto Alegre.

Como justificativa, os pesquisadores informam que "pretende-se dar atenção à qualidade e melhoria dos processos logísticos da AF pela perspectiva das unidades de dispensação, por meio do diagnóstico e proposição de melhoria dos fluxos de informação e fluxos físicos (fluxos do medicamento) dentro e entre tais unidades."

Ainda, enfatizam quem a Assistência Farmacêutica (AF), "por ter uma estrutura complexa, os gestores enfrentam desafios administrativos dos fluxos de informação e físicos que perpassam as operações logísticas da AF de: seleção, programação, aquisição, distribuição e dispensação (S-P-A-D-D), que resultam muitas vezes em perdas econômico-financeiras da ordem de milhões,

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sem mencionar outras perdas intangíveis como aquelas que afetam a saúde do usuário final ou a imagem dos governantes e dos profissionais de saúde. Esta proposta de projeto tem por ênfase a qualidade destas operações logísticas (S-P-A-D-D).

Trata-se de um projeto avaliado pelo CEP/UFRGS (Instituição Proponente) e também pelo CEP/SMS de Porto Alegre, cadastrada como Instituição Coparticipe.

Tramita pela emenda de ampliação do cronograma com a justificativa: "A coleta e a análise dos dados requerem mais tempo do que o previsto no cronograma original, devido ao acesso aos atores entrevistados e à complexidade encontrada na pesquisa. O projeto original previa 6 meses de coleta de dados, mas a rotina de trabalho e a escala de férias dos atores entrevistados dificultaram o cumprimento desse prazo. Da mesma forma, a complexidade dos cenários encontrados demanda mais tempo para análise dos dados, com eventuais necessidades de retornar aos atores. Essa dificuldade operacional justifica a ampliação do período de coleta de dados em 6 meses e do período de análise dos dados em 9 meses, totalizando 9 meses de ampliação total do cronograma do projeto. Ressalta-se que não houve alterações além da atualização do cronograma e que mantém-se os mesmos sujeitos recrutados, sem mudança essencial nos objetivos e na metodologia do projeto original."

Objetivo da Pesquisa:

O objetivo da pesquisa é desenvolver um modelo para análise dos fluxos físicos, fluxos de informação e acompanhamento dos serviços logísticos da Assistência Farmacêutica pela perspectiva dos profissionais que trabalham na rede multidisciplinar de atendimento ao usuário na Assistência Farmacêutica das Farmácias Distritais de Porto Alegre.

Como objetivos específicos:

a. Mapear as operações de seleção, programação, aquisição, distribuição e dispensação, com ênfase nos fluxos de informação e físicos direto e reverso, necessários a uma AF eficiente;

b. Compreender as principais barreiras e facilitadores dos fluxos de informação e físicos do medicamento, a partir de diagnóstico que identifique perdas potenciais e reais;

c. Propor métricas e indicadores para os fluxos de informação e físico;

d. Estruturar um modelo de avaliação continuada dos fluxos de informação e físico para a Assistência Farmacêutica em Farmácias Distritais, a partir de práticas do Lean Healthcare e da

Logística Reversa,
e. Proporcionar redução de perdas nos processos logísticos da AF.

Avaliação dos Riscos e Benefícios:
Como riscos, os pesquisadores informam que "É uma pesquisa de risco mínimo, pois a entrevista que será realizada não fará nenhuma intervenção ou modificação intencional nas variáveis fisiológicas ou psicológicas e sociais dos indivíduos que participam no estudo. Os riscos que podem ser gerados são: desconforto pelo tempo de entrevista, interrupção de tarefas importantes para participação na pesquisa e possibilidade de quebra de sigilo e vazamento de informações. Para minimizar esses riscos será realizada uma entrevista de no máximo meia hora que será agendada previamente para garantir que tarefas importantes da rotina de trabalho dos envolvidos não sejam interrompidas. Será garantida a segurança dos dados gerados. A entrevista será gravada e posteriormente transcrita, sendo desgravada após sua transcrição. Os formulários em papel serão codificados e serão arquivados com segurança, não sendo identificados com o nome de profissionais envolvidos e as planilhas eletrônicas serão armazenadas em computadores com acesso restrito. Serão garantidas a privacidade e confidencialidade dos dados utilizados preservando integralmente o anonimato. As informações geradas não serão utilizadas em prejuízo dos profissionais envolvidos.,"

Como benefícios, os pesquisadores relatam que "a identificação de pontos críticos nos fluxos de informação e físicos da Assistência Farmacêutica. Além da aplicação de ferramentas que trarão melhorias que irão refletir no processo como um todo e consequentemente, no atendimento ao usuário."

Comentários e Considerações sobre a Pesquisa:
Segundo os pesquisadores, "foi escolhido o município de Porto Alegre, onde serão estudadas as 10 Farmácias Distritais. Em relação ao mapeamento, pretende-se usar uma Farmácia Distrital como estudo piloto, estendendo a análise para as demais.

Na nova versão do projeto, foi justificado o número amostral de 200, considerando que "o escopo dessa pesquisa são as 10 farmácias distritais do município de Porto Alegre e que as entrevistas irão abranger diferentes profissionais que atuam nessas farmácias, além dos profissionais que atuam na coordenação da Assistência Farmacêutica, estima-se que o instrumento de pesquisa será

aplicado a pelo menos 20 profissionais por farmácia, totalizando 200 indivíduos.

Para o levantamento dos dados necessários para atender os objetivos desta pesquisa serão utilizados roteiros de entrevistas destinados aos profissionais, presentes nos Apêndices A, B e C.

Os formulários de coleta de dados estão apresentados e adequadamente redigidos. Para o formulário B, foi incluída a identificação alfa-numérica.

Etapas previstas:
(A) Levantamento bibliográfico;
(B) Diagnóstico das operações logísticas da AF nas unidades de dispensação (Farmácias Distritais);
(C) Análise do sistema e proposição de soluções;
(D) Definição de diretrizes de gestão dos fluxos operacionais da AF.

Na segunda versão todos os pesquisadores listados no projeto foram ser incluídos na PB.

Foram ainda apresentados o TCUD e Termo de Autorização do coordenado da AF no Município de Porto Alegre.

Na nova versão foi incluido orçamento no projeto e previsão de fonte de financiamento com a justificativa "Este pesquisa não conta com financiamento de instituições de fomento, nem qualquer outro tipo de financiamento externo. As despesas serão custeadas pelos próprios pesquisadores. Ressalta-se que a responsabilidade do financiamento é exclusiva do pesquisador responsável.

Considerações sobre os Termos de apresentação obrigatória:
Foram apresentados o projeto completo, folha de rosto assinada e TCLE.

Na tramitação da emenda, foi apresentado novo cronograma com previsão de término de coleta de dados em dezembro de 2019.

Conclusões ou Pendências e Lista de Inadequações:
O projeto de pesquisa encontra-se em condições de aprovação, de acordo com os aspectos éticos (CNS Resolução 466/12).

Considerações Finais a critério do CEP:

Aprovado,

Este parecer foi elaborado baseado nos documentos abaixo relacionados:

Tipo Documento	Arquivo	Postagem	Autor	Situação
Informações Básicas do Projeto	PB_INFORMAÇÕES_BÁSICAS_1328011_E1.pdf	03/04/2019 14:00:23		Aceito
Cronograma	Cronograma.pdf	03/04/2019 13:49:32	André Teixeira Pontes	Aceito
Outros	Justificativa_.pdf	03/04/2019 13:47:30	André Teixeira Pontes	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	APENDICE_D_TCLE_v2.pdf	21/02/2018 11:01:34	André Teixeira Pontes	Aceito
Outros	APENDICES_A_B_C_v2.pdf	21/02/2018 10:59:52	André Teixeira Pontes	Aceito
Parecer Anterior	PB_PARECER_CONSUBSTANCIADO_CEP_2492126.pdf	21/02/2018 10:55:48	André Teixeira Pontes	Aceito
Recurso Anexado pelo Pesquisador	CartaResposta.pdf	21/02/2018 10:53:23	André Teixeira Pontes	Aceito
Projeto Detalhado / Brochura Investigador	Projeto_Completo_v2.pdf	21/02/2018 10:51:28	André Teixeira Pontes	Aceito
Projeto Detalhado / Brochura Investigador	ProjetoCompleto.pdf	28/01/2018 08:44:00	André Teixeira Pontes	Aceito
Outros	Termo_Istefani.pdf	28/01/2018 08:42:51	André Teixeira Pontes	Aceito
Outros	Apendices_A_B_C_Questionarios.pdf	23/01/2018 08:24:33	André Teixeira Pontes	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	APENDICE_D_TCLE.pdf	23/01/2018 08:21:15	André Teixeira Pontes	Aceito
Outros	ANEXO_A_TermoSMSPA_Assinado.pdf	23/01/2018 08:20:07	André Teixeira Pontes	Aceito
Outros	ANEXO_B_indicadores.pdf	23/01/2018 08:18:56	André Teixeira Pontes	Aceito
Folha de Rosto	folhaDeRosto_Assinada.pdf	23/01/2018 08:09:24	André Teixeira Pontes	Aceito

Situação do Parecer:
Aprovado

Necessita Apreciação da CONEP:
Não

PORTO ALEGRE, 11 de Abril de 2019

Assinado por:
MARIA DA GRAÇA CORSO DA MOTTA
(Coordenador)

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APENDICE C – Modelo Termo de Consentimento Livre e Esclarecido (TCLE)

TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO PARA PARTICIPAÇÃO DOS PROFISSIONAIS DESTE PROJETO

TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO

Estamos convidando você para participar da pesquisa intitulada "Modelo para diagnóstico e acompanhamento do desempenho logístico da Assistência Farmacêutica pela perspectiva das Farmácias Distritais de Porto Alegre", desenvolvida por pesquisadores do Laboratório de Otimização de Produtos e Processos (LOPP) da Universidade Federal do Rio Grande do Sul (Av. Osvaldo Aranha, 99 - 5º andar – Porto Alegre). O pesquisador responsável é Istefani Carísio de Paula, a quem você pode contatar a qualquer momento que julgar necessário através do telefone nº (51) 3359-4298.

O objetivo geral desta pesquisa é o desenvolvimento um modelo inovador para análise dos fluxos físicos, fluxos de informação e acompanhamento do desempenho logístico da Assistência Farmacêutica pela perspectiva das unidades de dispensação (Farmácias Distritais). Entender a perspectiva dos profissionais envolvidos com os processos da Assistência Farmacêutica no município de Porto Alegre amplia nossa compreensão sobre o tema. Assim, pretendemos realizar uma entrevista abordando questões referentes à sua experiência como profissional envolvido diretamente ou indiretamente com os processos relacionados aos medicamentos no âmbito da Atenção Primária à Saúde de Porto Alegre. Buscamos identificar fatores positivos e negativos em seu atendimento. A entrevista será realizada presencialmente, em caráter reservado, com a sua presença e a dos pesquisadores do projeto.

O tempo estimado para a realização da entrevista é de 30 minutos, nas dependências das Unidades de Saúde de Porto Alegre, especialmente as Farmácias Distritais, durante seu período de trabalho, com agendamento prévio, para garantir que tarefas importantes da rotina de trabalho dos envolvidos não sejam interrompidas. A entrevista será gravada e posteriormente transcrita, sendo desgravada após sua transcrição. A transcrição não será identificada com o seu nome e serão arquivados com segurança.

A participação nesta pesquisa não trará benefícios diretos a você. Porém, este estudo pretende contribuir para a melhoria dos processos relacionados aos serviços logísticos da Assistência Farmacêutica no município de Porto Alegre. Não são conhecidos riscos decorrentes da sua participação nessa pesquisa.

O acesso e a análise dos dados coletados serão realizados apenas pelos pesquisadores e seus orientadores. A divulgação dos resultados da pesquisa será realizada somente em meio acadêmico e científico, sem identificação dos participantes. Dessa forma, os pesquisadores se comprometem com a confidencialidade dos dados de identificação dos participantes em todas as etapas da pesquisa. As informações geradas não serão utilizadas em prejuízo dos profissionais envolvidos.

A sua participação é voluntária. Em qualquer momento do estudo você poderá se recusar participar da pesquisa, sem sofrer quaisquer sanções ou constrangimentos, assim como nenhum prejuízo nas suas atividades profissionais.

Sendo assim, ao assinar este termo, você afirma que aceita participar por sua própria vontade, sem receber qualquer incentivo financeiro ou ter qualquer ônus e com a finalidade exclusiva de colaborar para o sucesso da pesquisa.

Se você tiver dúvidas em relação aos seus direitos como participante de pesquisa, poderá entrar em contato com o comitê de ética em pesquisa do Município de Porto Alegre pelo telefone (51)

3289-5517, localizado na Rua Capitão Montanha, 27 – 7º andar (Centro Histórico), das 8h às 14h.

Uma cópia assinada deste Termo de Consentimento Livre e Esclarecido será entregue a você.

Porto Alegre, _____ de _____ de _____.

_____	_____
Nome do Participante	Assinatura do Participante
_____	_____
Nome do Pesquisador	Assinatura do Pesquisador

2. ARTIGO 1 - REVERSE LOGISTICS FOR THE END-OF-LIFE AND END-OF-USE PRODUCTS IN THE PHARMACEUTICAL INDUSTRY: A SYSTEMATIC LITERATURE REVIEW

Artigo publicado no periódico: Supply Chain Management: An International Journal
Elaine Aparecida Regiani de Campos, Istefani Carísio de Paula, Regina Negri Pagani
Patricia Guarnieri

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). 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®. 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. 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. 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

2. 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 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.

2. 2 LITERATURE REVIEW

2.2.1 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 has two main duties:

a) It is responsible for value added processes to cover customers' demand.

b) 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 embryonic 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.

2.2.2 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 low 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).

2.3 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.

2.3.1 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 2- 1).

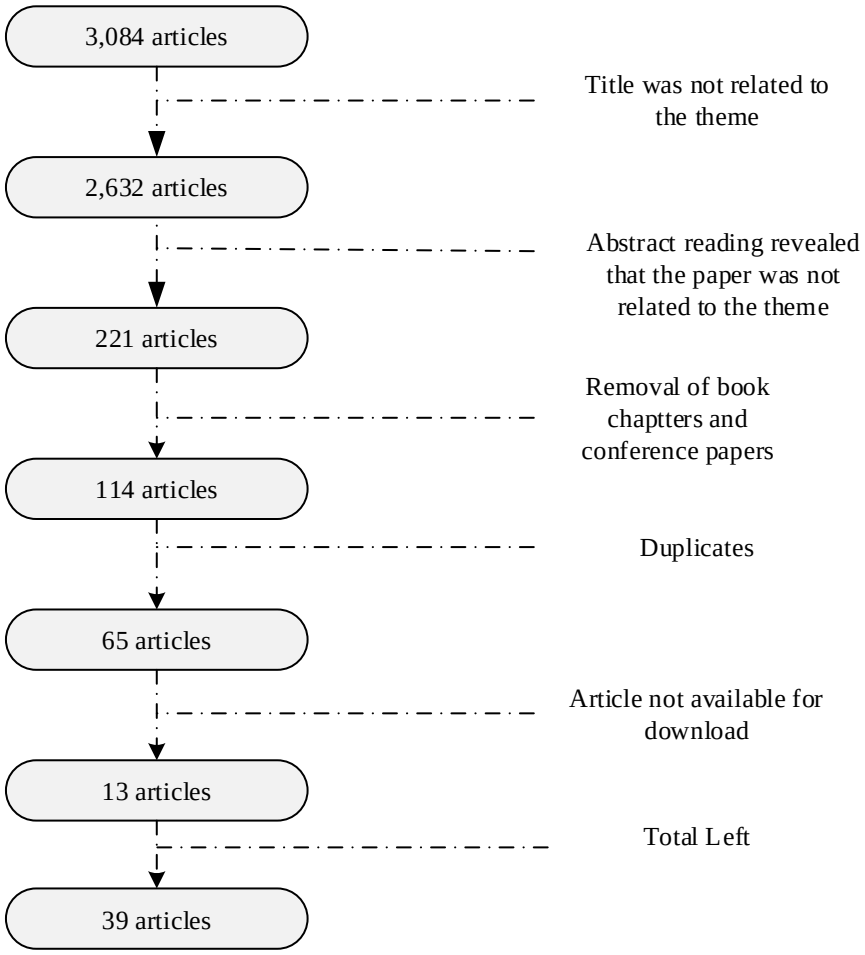

Figure 2-1 Number of papers discarded by the filtering procedures

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.

2.3.2 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;
- 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 A). 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).

2.4 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 2.4.1. Subsequently, bibliometric maps developed with publications from 1996 to 2015 are presented.

2.4.1 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- 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 2.4.1.1 due to the complementarity of the themes. Section 2.4.1.2 presents the deployment of the specific pharmaceutical RL thematic, clearing the RL practices found in literature.

2.4.1.1 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 2-2). On the contrary of the other segments, as electronic industry, which has a well-established regulation related to disposal of residues (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- 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).

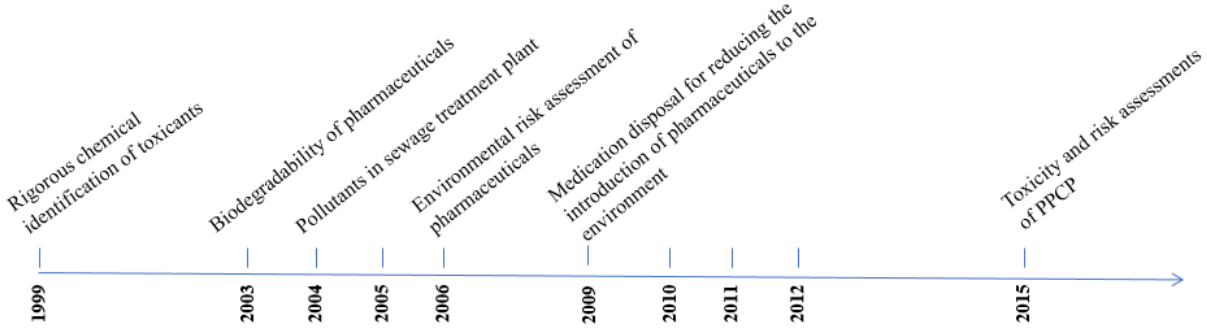

Figure 2-2 Timeline of publications – focus the environmental risk of pharmaceuticals

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- 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 2- 3 and 2- 4).

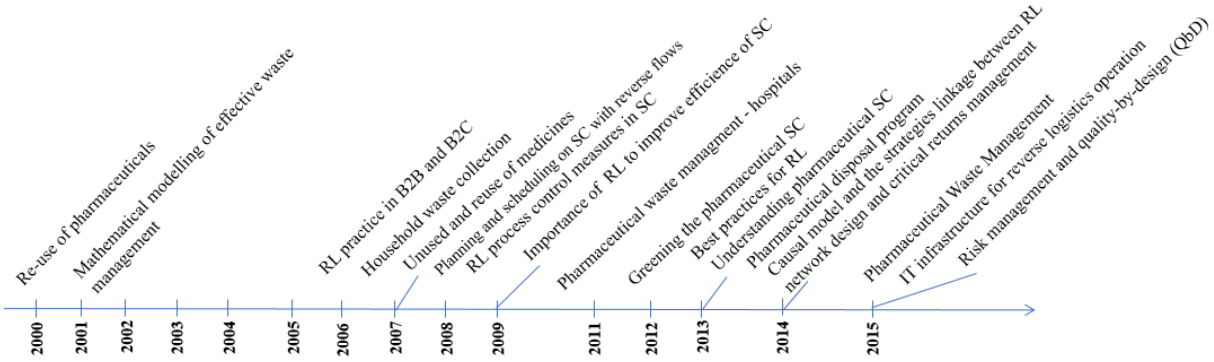

Figure 2-3 Timeline of publications – focus the RL evolution in pharmaceutical industry

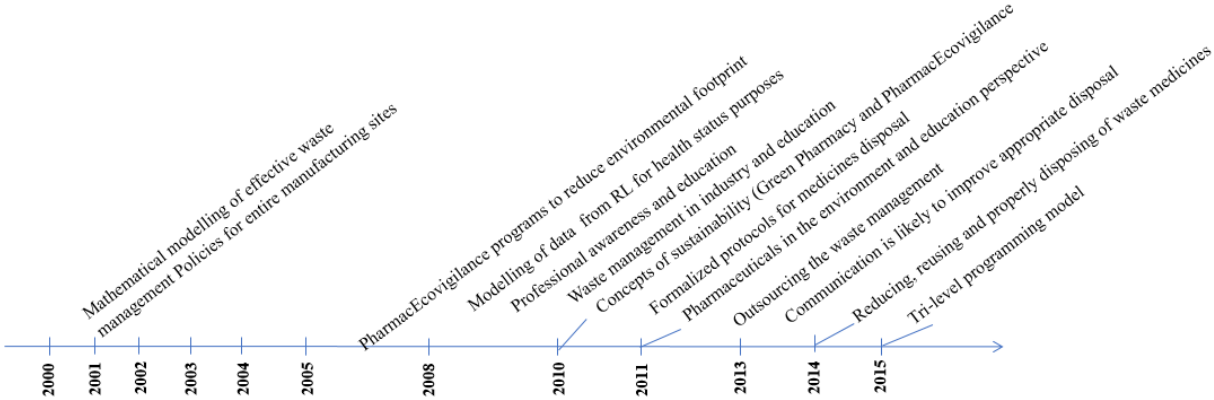

Figure 2-4 Timeline of publications - focus on regulatory and stakeholder's educational perspective

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 2- 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 2.4.1.1 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 2- 3) is described next.

2.4.1.2 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 2- 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.

2.4.1.2.1 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.

2.4.1.2.2 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 2.4.1.1.

2.4.1.2.3 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.

Manojlovic´ 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.

2.4.1.2.4 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.

2.4.1.2.5 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.

2.4.1.3 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 2.4.1.1. Three groups of papers are highlighted in the review (Figures 2-2 to 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 2-2). 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 2.4.3.

2.4.2 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 later 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 2- 5).

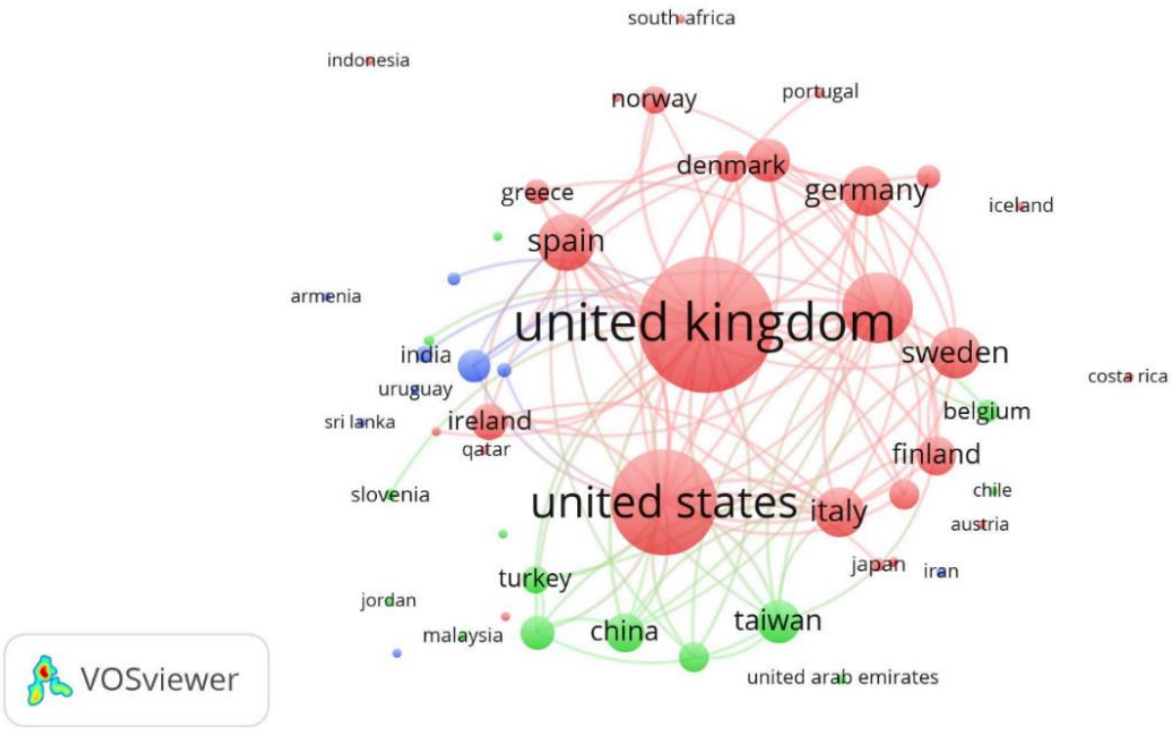

Figure 2-5 Network considering the nationalities of the authors within the 1996-2015 period

Figure 2-5 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 2-1 presents the distribution of documents and citations by country. Not surprisingly, UK is the most referred country in the papers from SLR from Section 2.4.1.1, mainly those regarding the environmental risk timeline, RL in hospital, pharmacy, NHS and household.

Country	Documents	Citations	Country	Documents	Citations
UK	244	1236	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

Table 2- 1 Distribution of publications, by country

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 2- 6 presents the maps of journals.

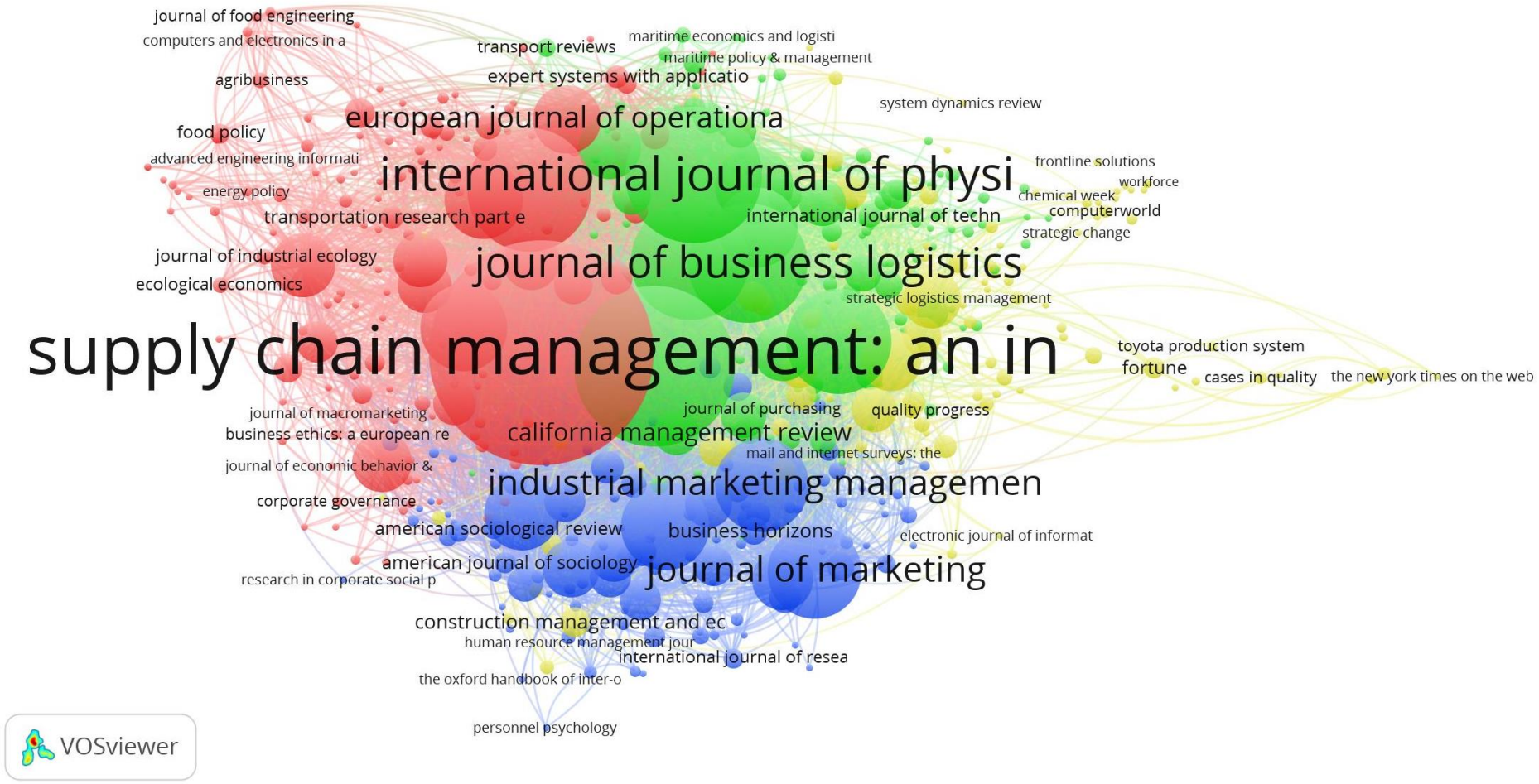

Figure 2- 6 Co-citation network of the journals within the 1996-2015 period

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 composed of 111 periodicals. The distribution of the first ten periodicals that presented the largest number of citations can be observed in Table 2-2. Additional information about the periodicals are detailed in the Appendix A.

Periodicals	Citation	Co-citation
Supply Chain Management	1960	95311
Journal of Operation Management	1121	67307
International Journal of Physical Distribution & Logistics	853	43003
International Journal of Production Economics	731	43602
Journal of Business Logistics	684	35697
Journal of Operations and Production Management	666	34849
Harvard Business Review	551	25215
Industrial Marketing Management	461	23991
Journal of Marketing	461	20570
Strategic Management Journal	410	23406

Table 2-2 Volume of citations and citations by periodicals

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 2-7.

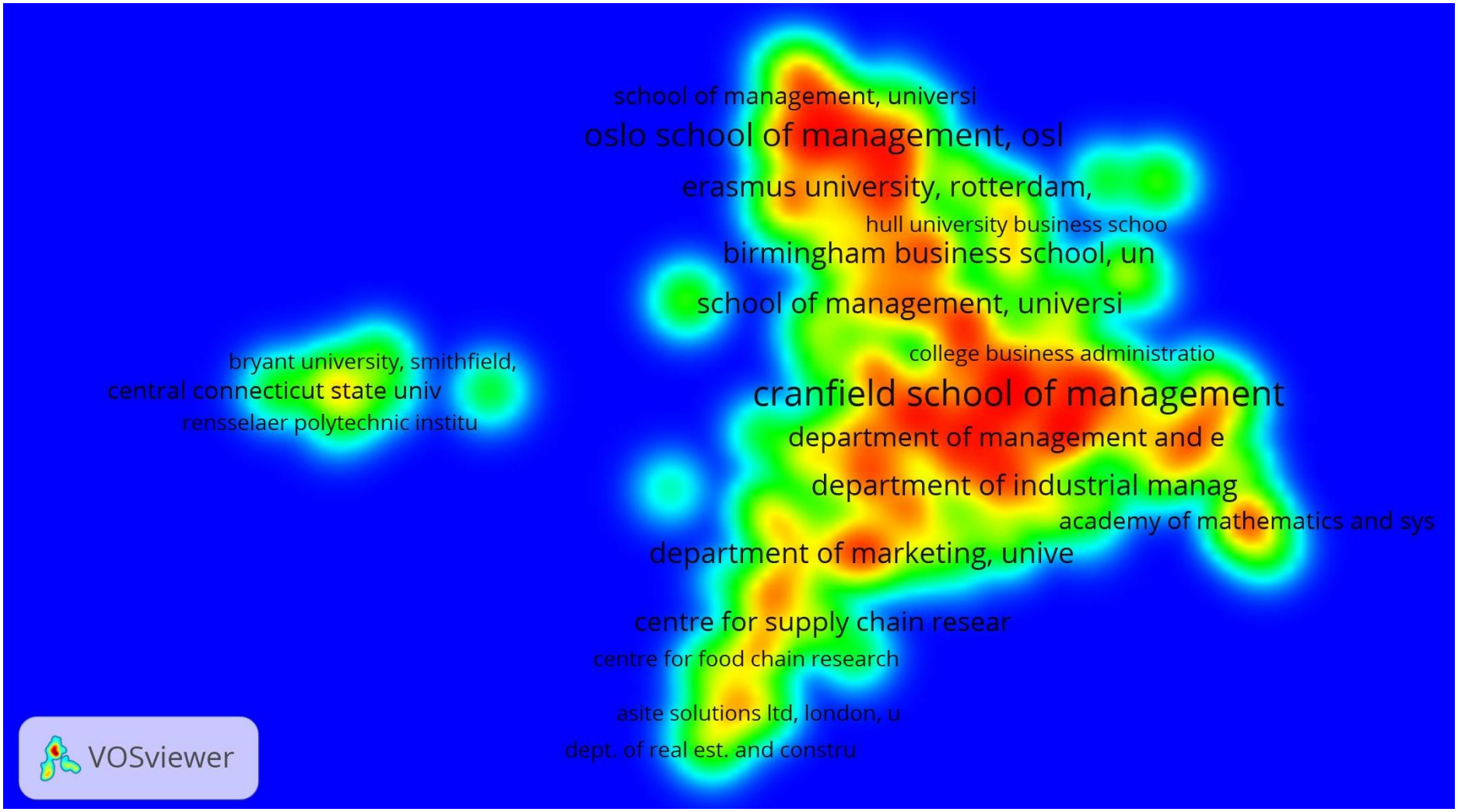

Figure 2-7 Density of universities in the period (1996-2015).

Universities with higher number of articles and volume of citations are displayed in the orange area. Among them are the universities mentioned in Table 2-3.

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

Table 2-3 Documents and citations, by universities

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 2- 8 presents the words cited.

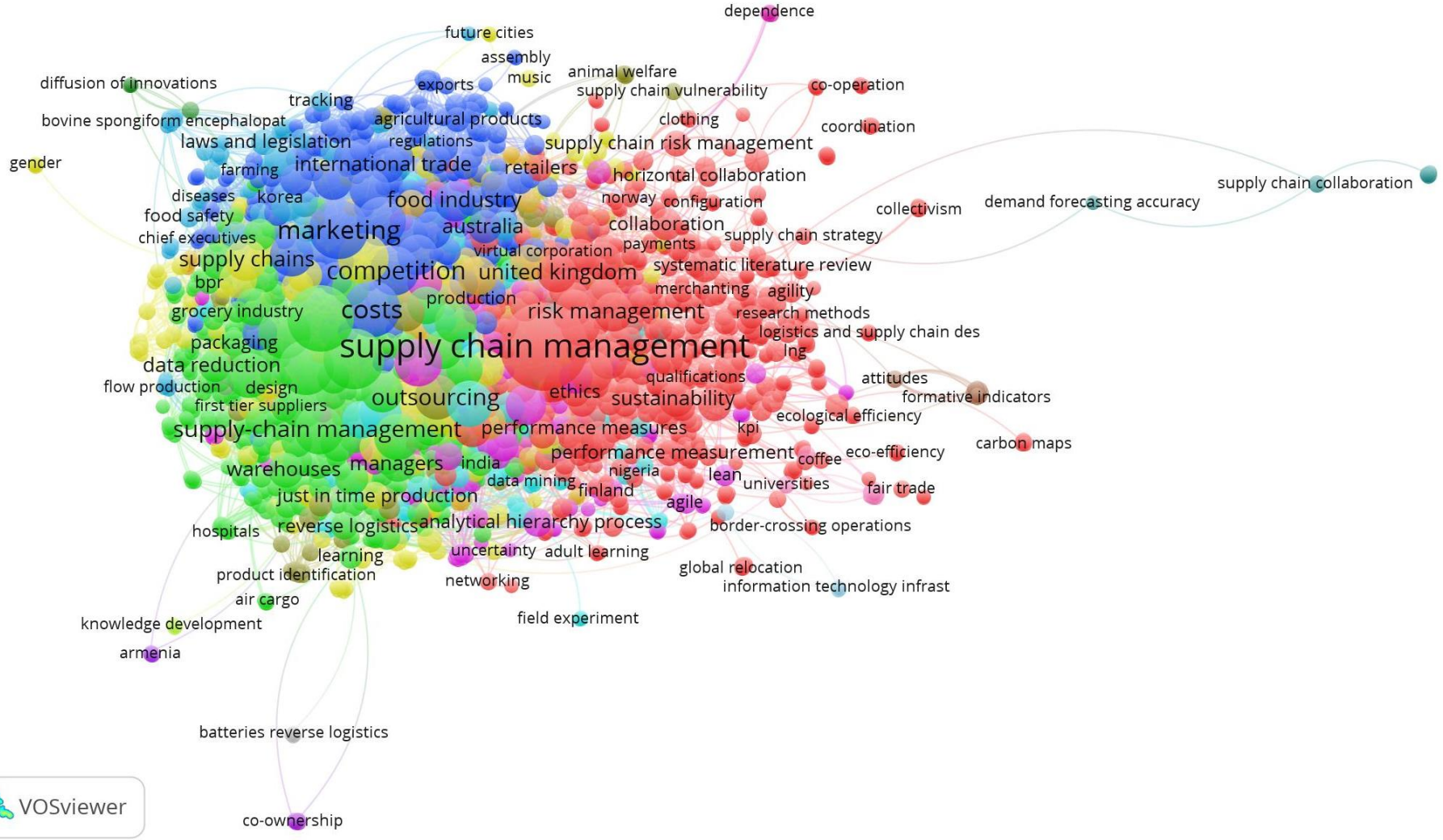

Figure 2-8 Network of keyword co-occurrence within the period (1996-2015).

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 2- 8, it is possible to identify evidences 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 2.4.1, the papers cover a broad spectrum of themes related to RL, but nothing much different from which was discussed in Section 2.4.1, 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 2.4.1, 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 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.

2.4.3 Identification of gaps and opportunities

This topic makes a summary of the findings from Steps 1 and 2 (Sections 2.4.1 and 2.4.2). 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 2- 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).

OPERATIONAL AND MANAGERIAL PRACTICES	Players											
	Extraction Transformation	Manufacturer	Government Agencies	Distribution	Retailer	Pharmacy	Government Stores	Houses	Clinic	Hospital	Universities	Town hall
-Product recall		✓										
-Recycling		✓*										
-Wast 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 2-9 Practices described in the 39 articles (Operational and Managerial Practices)

Figures 2- 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 2- 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 2- 10.

The third group, technological practices, was less expressive, concentrating IT solutions, RFID applications and 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 2- 11).

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		✓										
-Responsabilit 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 2-10 Practices described in the 39 articles (Strategic and Decision-Making Related Practices)

TECHNOLOGICAL PRACTICES	Extraction Transformation	Manufacturer	Government Agencies	Distribution	Retailer	Pharmacy	Government Stores	Houses	Clinic	Hospital	Universities	Town hall
-IT lke 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: **•**

Figure 2- 11 Practices described in the 39 articles (Technological Practices)

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 2- 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.

2.5 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 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.

2.5.1 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 2.4.3.

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 A - 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 J. of Biotech.	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 J. of Manag. (IJM&P)	1	-	0.876
Indian J. of Pharm. Educ. and Research	1	-	0.219
Information Technology Management	1	B	0.600
Int. J Sup. Chain. Mgt	1	-	-
Int. J. Environ. Res. Public Health	1	-	2.035
Int. J. Procurement Management	1	C	-
International J. P. Perf. Manag.	1	B	-
International J. of P. 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 & W. M. Association	1	-	1.613
Management Research News	1	C	-
Management Research Review	1	C	-
Pharm 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 J. of Manag. Sciences	1	C	-
Strategic Outsourcing: an International Journal	1	B	-
The Int. J. of Log. Manag.	1	A	0.917
Trends in Biotechnology	1	-	12.065
Vitae Rev. Facultad de Quim. Farmaceutica	1	-	-
Waste Management & Research	1	-	1.338
TOTAL	**39**		

3. ARTIGO 2 - END-OF-USE AND END-OF-LIFE MEDICINES - INSIGHTS FROM PHARMACEUTICAL CARE PROCESS INTO WASTE MEDICINES MANAGEMENT

Artigo em avaliação no periódico: Environmental Science and Pollution Research

Abstract: End-of-Use and End-of-Life medicines (EOU/EOL-M) waste management has been a challenge for public and private managers in different countries. Reverse logistics is a waste management strategy whose application to public EOU/EOL-M pharmaceutical care processes is still permeated with incertitude. Therefore, this study has two purposes: (1) to map reverse logistics and reassignment of medicine included in the Pharmaceutical Care Process (PCP) in the city of Porto Alegre, State of Rio Grande do Sul, Brazil; (2) to identify the most relevant critical factors for implementing medicine waste management in PCP, focused on reverse logistics of pharmaceuticals. Considering the characteristics of the issue at hand, we designed a qualitative study. We collected data through semi-structured interviews. We interviewed ten key individuals who work directly with the process - from administering medicine to patients to managing waste at the end of the medicine's lifespan or after its use. Results from this study allowed us to map reverse logistics and reassignment flows. We also identified the most critical factors in implementing those strategies, such as: aspects pertaining to management, information technology, infrastructure, government, etc. Our results further clarify the literature on EOU/EOL-M reverse logistics and provide managers a perspective on the most relevant critical factors involved in their decision-making process.

Keywords: Pharmaceutical Care Process; waste management; End-of-Use and End-of-Life medicines; Reverse logistics; medicine disposal

3.1 INTRODUCTION

Products with a shorter lifespan, which quickly become waste, have led to the changes on how institutions work. They make an effort to change product design to make those products less damaging to the environment at the end of their lifecycle. Managers have also changed their production processes, to include sustainable management of resources and assets and investments in reverse logistics - which is deemed an essential part of direct logistics (Aksoylu and Demirel, 2018; Geethan et al., 2011; Rogers and Tibben-lembke, 2001).

For different industries throughout the world, the commitment to crate effective logistical processes is increasingly important (Ding, 2018), with both the bottom line and the environment in mind (Geethan et al., 2011; Kabir, 2013; Viegas et al., 2019).

Reverse logistics practices, which seek to return products at the end of their lifespan, allow value to be accrued and those products to be reverted into new technical and/or biological cycles, as advocate circular economy (Bernon et al., 2018; Fischer and Pascucci, 2017) and green supply chain (Govindan et al., 2014; Luthra et al., 2011).

As for pharmaceuticals, waste creation is even more concerning given the growing consumption of medications caused by factors such as: development of new drugs, increase in life expectancy, search for a better quality of life. They create greater dependency of the use of medicines (Massoud et al., 2016; Tong et al., 2011). Estimates show a global growth trend for

the pharmaceutical industry, which is associated with greater consumption of medicaments, population growth and aging, easier access to drugs, and other factors. Further estimates for the future indicate the global worth of the pharmaceutical industry will reach around USD 1.57 trillion by 2023 (Navadhi, 2019).

Linked to the growth of this industry, different agencies in the public and private sectors have been paying more attention to the increase in the level of active pharmaceutical ingredients (APIs) in the environment (Lees et al., 2016), as well as to user practices (Massoud et al., 2015; Vellinga et al., 2014). This has led to public health concerns, as medicines may have economic and environmental impacts if discarded incorrectly (Bekker et al., 2017; Lees et al., 2016). Active pharmaceutical ingredients (APIs) are omnipresent environmental contaminants created mainly from unused drugs discarded by users in sewers or by healthcare facilities in landfills (Lees et al., 2016; Daughton and Ruhoy, 2011).

Furthermore, the presence of chemicals - which frequently are a result of pharmaceutical activities themselves - particularly in potable water has boosted discussions and debates on the best practices for discarding End-of-Use and End-of-Life Medicines (EOU-EOL-M) (Campos et al., 2017; Daughton and Ruhoy, 2011; Glassmeyer et al., 2009; Medeiros et al., 2014; Viegas et al., 2019).

Despite the reuse of EOU medicines would encourage patients to return unused medicines instead of unsafe disposal practices, there is always the risk of the improper storage of unused medicines in terms of the temperature, humidity or cleanliness of the storage environment. Inadequate storage practices may impact on the safety of unused medicines. Safety was conceptualised as inadvertent contamination or deliberate tampering (Alhamad et al, 2018). Apart this discussion, the management of EOU-EOL-M calls for reverse flows processes.

Reverse logistics for medicaments has its own particularities if compared to other industries. For example, recycling returned material, which can be a source of income, is a difficult strategy to adopt for pharmaceuticals. That and other particularities make proactive implementation more difficult, as reverse logistics of medicines is limited by external and internal barriers (Murillo-Luna et al., 2011). For example, Murillo-Luna et al. (2011) have identified 25 barriers deemed “significant” in 240 industries in Spain: external barriers, endemic limitation in the company, environmental motives, lack of employee training or limited expertise, and inertia in operations. Different authors highlight the greater difficult in implementing reverse logistics due to incertitude on product quantity and quality (Badenhorst

2016; Prakash and Barua, 2015; Sirisawat and Kiatcharoenpol, 2018), and to the lack of information technology systems (Abahussain et al., 2012; Narayana et al., 2014).

Considering that the use of medicaments is intrinsic to certain treatments, thus their use is inevitable and necessary for individuals' health and well-being, it is essential to understand how different factors affect the effective implementation of reverse logistics (Luthra et al., 2017; Mangla et al., 2016). However, different actors - such as manufacturers, distributers, and retailers - must work with inefficiencies to make product return viable (Massoud et al., 2015).

Considering the distinct interests Alhamad et al., (2018, p. 237) mention that "[…] pharmaceutical companies and their employees (or others with an interest in these companies) were considered amongst the groups that would disapprove medicines reuse because of a potential of reducing financial profits". If in one hand reverse flows of medicines are not attractive to pharmaceutical companies, on the other hand, government would take advantage of the savings that the take back of EOU medicines would bring. This would be very attractive at the pharmaceutical care process level managers' point of view, for instance.

Management of medicament processes, including the promotion of their rational use, is called Pharmaceutical Care (PC). PC is defined as a set of actions and services that seek to ensure full treatment assistance and promotion, protection and recovery of health in public and private institutions that undertake pharmaceutical activities; medicaments are the fundamental input, while access to them and their rational use are the purposes (Brasil, 2007).

In the context of Brazilian universal public healthcare, which is under study in this research, each municipality is responsible for managing healthcare waste under a reverse logistics chain perspective (Pereira et al., 2012). However, the main factors that lead to adopting such practices are proportional to the barriers that exist to it, which leads to a low level of adherence that is rarely discussed in literature and, most importantly, complex in nature (Abdullah and Yaakub, 2014).

In Brazil, primary healthcare is the first level of an individual's access to the Universal Healthcare System (*Sistema Único de Saúde – SUS*). This health network operates hierarchically: municipal managers are responsible for less complex healthcare with greater demand as it may be accessed by every citizen (Brasil, 2007). Municipalities are also responsible for managing the fundamental flow of direct logistics for medicaments in PC processes, which includes six operations: selecting, scheduling, acquiring, storing, distributing, and administering (*SPAADD*, in the acronym in Portuguese). This study emphasizes this set of

logistical PC operations in primary healthcare. Higher complexity levels (secondary, tertiary, and quaternary care) are not in the scope of this research. Thus, in primary healthcare, the last operation in the direct logistics of pharmaceutical care (*SPAADD*), administering, refers to the delivery of medicaments to the population, free of charge, in government-ran pharmacies and in health centers.

Operations in the *SPAADD* cycle have been implemented and managed based on SUS' management guidelines (Brasil, 2007), which means those processes have reached some management maturity, especially in larger cities. However, this maturity has not yet been reached for reverse flows. Return of EOU-EOL-M drugs from the population is prohibited by Normative Ordinance no. 344, dated May 12, 1998 (Brasil, 1998). However, reverse flows of medicaments which are still in good condition happen between pharmacies and health centers and are called "reassignment flows". Even though Law 12.305 and Resolution 222/2018 (Brasil, 2018) set forth the implementation of reverse flows, even for the pharmaceutical industry, those flows must be designed for the whole supply chain, including the part pertaining to *SPAADD* operations in PC.

Therefore, it is relevant to explore which flows refer to reverse logistics of drugs that are still in good condition to be used (EOU) and of drugs that shall be handled are unserviceable (EOL) in PC contexts. Therefore, the first research question (RQ1) we seek to answer with this study is:

> *RQ1* - What medicament reverse logistics and reassignment flows comprise the pharmaceutical care process (PCP) according to the experts?

Literature often deals with different sectors and economic, political, social, and cultural contexts - for example, the study by Chauhan et al. (2018); Prakash et al. (2015) and Sharma et al. (2011), which observes the barriers inherent to the Indian context.

Institutions must indistinctively overcome those barriers to effectively adopt RL (Daughton and Ruhoy, 2011; Massoud et al., 2015). However, albeit the importance of exploring reverse waste management issues in healthcare, given its importance for the environment, there are few studies dealing with the topic of pharmaceuticals. The number of studies is even smaller regarding PCP logistics in public healthcare.

Considering that the logistics operations (*SPAADD*) in the PCP cycle also contribute to generating medicine waste and that managers are potentially responsible for dealing with such residue, we propose the following research question, *RQ2*:

RQ2 - What are the critical factors for undertaking reverse logistics flow and reassignment activities for medicines in the context of PCP operations?

Therefore, this study has two purposes: (1) to map reverse logistics and reassignment of medicine included in the Pharmaceutical Care Process in the city of Porto Alegre, Brazil; (2) to identify the most relevant critical factors for implementing medicine waste management, focused on reverse logistics of pharmaceuticals. Porto Alegre is the capital of the State of Rio Grande do Sul (Brazil) and has 1.6 million inhabitants who have access to medicines through PCP *SPAADD* operations. Those operations are managed by the Pharmaceutical Care Process Coordination (*COORAF*, in the acronym in Portuguese) of the city's Municipal Department of Health. The complexity of the process of distributing medicaments may be grasped by the fact that there are 10 government-ran pharmacies and over 140 health centers where healthcare professionals administer pharmaceuticals and offer guidance on how to correctly use them. EOU-EOL-M reverse flows from the public that is served by those processes is not yet authorized.

The main academic contribution from this qualitative study is to improve the understanding about critical factors for the implementation of reverse logistics of medicines in Pharmaceutical Care Processes. In practice, managers from over 5,000 Municipalities in Brazil will have more bases for making decisions about how to organize LR processes in the context of PCP.

3.2 THEORETICAL FRAMEWORK

3.2.1 Reverse Logistics of Medicaments

Developing countries around the world face several problems that impact or degrade the environment (Nakyanzi et al., 2010). Managing reverse supply chains is particularly challenging for perishable products (Abbas and Farooquie, 2013).

Reverse logistics has been understood as a part of sustainable development, becoming increasingly important during the last few years. This is a reflex of the search for lower costs, for extracting value from waste in a circular economy, and for environmentally friendly ways of discarding products after consumption (Bernon et al., 2018; Guarnieri et al., 2020; Khan and Subzwari, 2009; Prakash et al., 2015).

Conceptually, Rogers and Tibben-Lembke (1998, p. 2) define RL as:

> [...] 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.

In Brazil, the National Policy on Solid Waste (*Política Nacional de Resíduos Sólidos, PNSRS*) was established by Law 12.305/2010. It is based on the principle of shared responsibility among the actors of the supply chain aimed at managing waste (Brazilian Policy of Solid Waste, 2010).

In general, one of the reasons company managers adopt RL practices at first is to comply with legislation that make manufacturers responsible for products they sell and distribute. However, there are other benefits such as minimizing environmental impacts, saving natural resources, and consumers' inevitable return (Abbas and Farooquie, 2018; Prakash et al., 2015).

Alongside other residue generated in healthcare operations in hospitals, clinics, and homes, medicaments are complex waste, as their handling required destructing the active substance (chemical ingredient or drug) (Daughton and Ruhoy, 2011; Glassmeyer et al., 2009; Le Corre et al., 2012). Consequently, their discard has been of concern for professionals in public and private healthcare (Aquino et al., 2018; Kelly et al., 2018; Vellinga et al., 2014).

Environmental issues cannot be left aside: it is a well-known fact that pharmaceutical waste from manufacturing and discarding drugs enter ecosystems, affecting human health (Thach et al., 2013; Tong et al., 2011; Vellinga et al., 2014). Barring residue from ending up in direct contact with nature is a great challenge (Le Corre et al., 2012; Blankenstein and Junior, 2018).

There is global awareness that inadequate disposal of medicaments that were not used may harm the environment (Braund et al., 2009), especially those originating in industrial activities. Toxicity analyses from the study by Zhou et al. (2018) indicated that some diseases - even cancer - may be linked to exposal to certain chiral pharmaceuticals. Disposal of EOL/EOU-M in water also hinders the development of aquatic beings (Bound and Voulvoulis, 2005). Furthermore, due to increased consumption by the population, medicine components have been frequently detected in water, which has several consequences for the environment (Tewari et al., 2013). However, waste management must be adapted to the involved manufacturers and consumers, as it is highly dependent on economies of scale and requires high levels of cooperation between all the links in the chain (Wiel et al., 2012).

Literature indicates that undertaking reverse logistics practices requires collaborative, concrete, economic, technological, and political human structures capable to responding to all the challenges inherent to each industry (Bernon et al., 2018; Mahadevan, 2019; Paula et al., 2019). Solid coordination between retailers in different industries and their clients is required

to harmonize sales and consumption. Likewise, vertical programs must be in place to avoid duplicated purchases (Nakyanzi et al., 2010).

3.2.2 Critical Factors in Implementing Reverse Logistics

Regardless of the industry under analysis, there are several critical factors in RL implementation. There are those internal of the processes of an institution, while others are external to it. This section will present the following aspects: Management Factor (MF); Collaboration Factor (CF); Information Technology Factor (ITF); Infrastructure Factor (IF); Political Factor (PF); Financial and Economic Factor (FEF).

3.2.2.1 Management Factor (MF)

The implementation process for reverse logistics in institutions depends on many internal factors, such as the behavior of managers and how they perceive RL as an integral part of direct logistics (Abdulrahman et al., 2014; Jindal et al., 2013; Ravi et al., 2005).

Not only are managers resistant to change, institutions often adopt restrictive policies that lead to lack of environmental awareness (Chileshe et al., 2015; Prakash and Barua, 2015). (Govindan et al., 2014; Moktadir et al., 2018) also consider commitment from higher management as a barrier. Another relevant issue that may hinder RL implementation is the lack of human resources and/or qualified workforce available and with the required expertise on reverse logistics (Muduli et al., 2013; Sharma et al., 2011; Shen et al., 2015).

3.2.2.2 Collaboration Factor (CF)

In general, collaboration between the links in the supply chain is discussed regarding direct logistics, as the study by (Pakdeechoho and Sukhotu, 2018; Soosay and Hyland, 2015). In a systematic literature review, Paula et al. (2019) consider collaboration and trust inseparable elements to implement reverse logistics.

Furthermore, lack of trust may inhibit information sharing, just as lack of communication abilities may hinder the transfer of information. This weakens the commitment to the environment in all levels of organizations, especially if better communication could support them in implementing sustainable activities (Bernon et al., 2011).

Information sharing does not mean a company discloses all its information to partner companies. However, it is important that participants provide necessary information to each other (Chan, 2007).

3.2.2.3 Information Technology Factor (ITF)

Benefits resulting from the use of information and communication technology are seen in a positive light. However, regarding quality assurance for products returning for recycling or remanufacturing, lack of technology has a significant impact, as important data on those products may be lost (Agarwal et al., 2016; González-Torre et al., 2010; Janse et al., 2010; Kongar et al., 2015; Laribi and Dhouib, 2015; Ravi et al., 2005; Sharma et al., 2011; Xia et al., 2015). Furthermore, (El Baz et al., 2018; Govindan et al., 2014; Jabbour et al., 2016; Jindal et al., 2013; Luthra et al., 2011; Pumpinyo and Nitivattananon, 2014) have reported low data security and even lack of big data that provides more precise information to base decision-making are barriers to RL implementation.

Traditional measures, such as waste processing technologies that are used to handle hazardous waste are deemed inadequate to integrate managing, collection, storage, distribution, and transportation activities comprising broad reverse logistics operational strategies (Shi et al., 2012).

3.2.2.4 Infrastructure Factor (IF)

Some studies debate the infrastructure required to undertake waste management practices (Cline et al., 2015; Sivakumar et al., 2018). However, infrastructure is often assessed within a technological framework, as mentioned by (Erol et al., 2010; Waqas et al., 2018).

Within the infrastructure factor itself, this study considered aspects pertaining to transport and storage of items intended for RL processes, as pointed out in previous studies by (Abdulrahman et al., 2014; Diabat et al., 2013; Prakash and Barua, 2015). According to Beh et al. (2016), products intended for recycling pose a greater challenge as they are far from their suppliers, resulting in challenges for transportation and complexity for international logistics.

Meyer et al. (2017), in turn, argue that many suppliers do not specialize in transportation and choose cheaper alternatives without considering their possible consequences. According to them, managers frequently subcontract transportation providers whose drives do not understand the stages required for RL processes, which results in losses.

3.2.2.5 Political Factor (PF)

Among other relevant factors for effective RL processes in different industries, the political factor plays a major role as action and participation from governments in all levels are required to develop policies and pass legislation that contemplate the particularities of each of those industries. According to Bouzon et al. (2018), issues pertaining to legislation are still not mature in emerging economies such as Brazil. Whenever legislation is flawed or non-existent, legal and political factors may become an external barrier to the implementation of reverse logistics.

Rahman and Subramanian (2012) argue that public legislation is one of the main forces driving environmental efforts that managers may or may not adopt. Support from municipal government, for example, allows different sectors, both public and private, as well as industries, to have guidelines on how to return products they produce and distribute.

3.2.2.6 Financial and Economic Factor (FEF)

Organization managers are often unable to implement RL activities due to the lack of financial resources (Ali et al., 2018). Sharma et al. (2011) highlight cost as one of the main challenges for recycling. Economic aspects also affect implementation of improvements to IT systems, as they require more resources and without them it is impossible to track and recover products through several processes such as reutilization, remanufacturing, recycling, and others. Personnel training is also relevant for managing waste and ultimately to make reverse logistics profitable. However, this requires financial support (Sharma et al., 2011).

Economic challenges to adopt waste management practices pertain to circumstances beyond the control of companies, but that affect their priorities, especially concerning the environment. This situation is even worse for companies that are not sure of the value of green practices (Hillary, 2004).

3.3 METHODOLOGY

3.3.1 Study Subject

The subject for this study was the Pharmaceutical Care Process of the city of Porto Alegre, State of Rio Grande do Sul, Brazil, under the Pharmaceutical Care Process Coordination (COORAF, in the acronym in Portuguese). The municipality's public assistance network has ten regional pharmacies and 145 health centers. It is also responsible for the city's central

medicament stock, servicing a population of 1.6 million people. In the context of the public health system, drugs are procured by bidding, based on the Municipal List of Essential Drugs. After receiving care, patients present their prescriptions at public pharmacies and health centers, where they receive their medicines free of charge.

After this research was approved by the ethics committee, we collected data from professionals who work with the PCP in the city through a semi-structured script seeking to answering the research questions posed by this study (see Appendix A). Interviews were then scheduled according to the availability of the ten key-participant interviewees (see section 3.3.2). At the interview, participants received information about the project and requested to read the Informed Consent Form, in which they were informed data would be used for research purposes only. We also requested their authorization to record the interviews, which would allow information obtained in them to be duly transcribed.

Interviews were individual and lasted for about 40 minutes each. The script used for the interview was divided into three major sections: (*i*) characteristics of the respondent and their knowledge on RL practices and on the National Policy on Solid Waste; (*ii*) mapping direct and reverse logistics flows; (*iii*) identifying what were the factors each interviewee perceived as critical in direct and reverse flow management.

Interviews were recorded and transcribed. Units for study emerged from analyzing their contents - especially types of reverse logistics operations that are already in place. Questions from the script were compared internally among respondents and externally to data from studies from academic literature.

3.3.2 Interviewee Profile

The pharmaceutical supply center is where medicaments are stored and distributed, while municipal pharmacies and health centers receive them. To collect qualitative data, eight of the selected key-interviewees were directly involved with coordinating different sectors responsible for *SPAADD* operations: Health Unit (HU) - dispensation, DDC/PSC (Drug Distribution Center/Pharmaceutical Supply Center) storage and distribution; TPC (Therapeutic Pharmacy Commission); MP= (Municipal Pharmacy); BEC (Bidding Evaluation Committee) programming and acquisition. Two other individuals who did not work at the Municipal Department of Health were also interviewed. They actively participated in the working group (WG) responsible for creating the Healthcare Solid Waste Management Plan for the city of Porto Alegre. One of them was from the Public Urban Cleaning Company and the other from

the Health Surveillance Agency. Table 3- 1 shows the profile of the respondents, who received codes from Interv_1 to Interv_10.

Interviewee Code	Sector	Gender	Position
Interv_001	HU	Female	Nurse
Interv_002	PSC/DDC/PSC	Male	Coordinator
Interv_003	DDC/PSC	Male	Manager/PSC
Interv_004	DDC/PSC	Female	Manager/Technical Responsible Pharmacist
Interv_005	CTP	Female	Manager/Technical Responsible Pharmacist
Interv_006	SG	Female	Manager/Technical Responsible Pharmacist
Interv_007	BEC	Female	Manager/Technical Responsible Pharmacist
Interv_008	HU	Female	Manager/Technical Responsible Pharmacist
Interv_009	Public Urban Cleaning Company	Male	Chemical Engineer
Interv_010	Sanitary Surveillance	Male	Chemical Engineer

Table 3-1 Interviewee profile
HU= Health Unit HU; DDC/PSC= Drug Distribution Center/Pharmaceutical Supply Center; TPC= (Therapeutic Pharmacy Commission); MP= Municipal Pharmacy; BEC= Bidding Evaluation Committee

3.4 RESULTS AND DISCUSSION

The next sections (3.4.1 to 3.4.2) will present the reassignment and reverse logistics flows for medicaments in accordance with the purposes of this study as state above.

3.4.1 Logistical flows of medicines reassignment

The interviews analysis revealed a practice of reassignment of exceeding stocks of medicines among the Pharmacies and Health Units, that was called in this text as “Reassignment Logistics”. This is also considered a reverse logistics. Extra stock of medicines in a given HU or MP is caused by the fact that the citizens are allowed to pick his medicine up in any HU or MP of the city. As some MP are very well located in the city, near urban transportation stations, that makes it easier to the consumer to pick the medicine up in his/her way in direction to work, more than picking it up in the HU or MP nearest his/her living address. Moreover, some types of medicines are only dispensed in the presence of a pharmacist professional, like antimicrobial medicines and those that act in central nervous system. Pharmacist professionals work only in the ten MP, concentrating the delivery of specific medicines in these sites. The bidding process, that sometimes is very bureaucratic, is another cause of medicine stock shortage or accumulation. Therefore, even considering the monthly medicines stock forecast it is frequent to have a medicine accumulation in one site or another. The “reassignment logistics” is the best practice developed among HU and MP managers of exchanging products to face the fluctuating demand.

After analyzing the contents of interviews, we were able to identify which flows were included in medicament reassignment logistics between pharmacies and healthcare centers: (a) drug dose to expiration in condition of use; (b) excess medications in use condition (still in condition of use - SCU); (c) donations; (d) Lend of medicines, and; (e) exchange.

After transcribing the interviews, we also identified another flow: Emergency suitcases or strategic medicines (highlighted in Fig. 3-1 in a light color). Emergency suitcases or strategic medicines include drugs and other consumables used in emergency situations in Health Centers. They comprise both medicaments for the treatment of out-patients and controlled, injectable drugs.

As mentioned above, this stage was identified at a later stage of our research and was not included as one of the activities among the critical factors of (Fig. 3- 2 and Fig. 3- 4). Fig. 3-1 below, details the flows described.

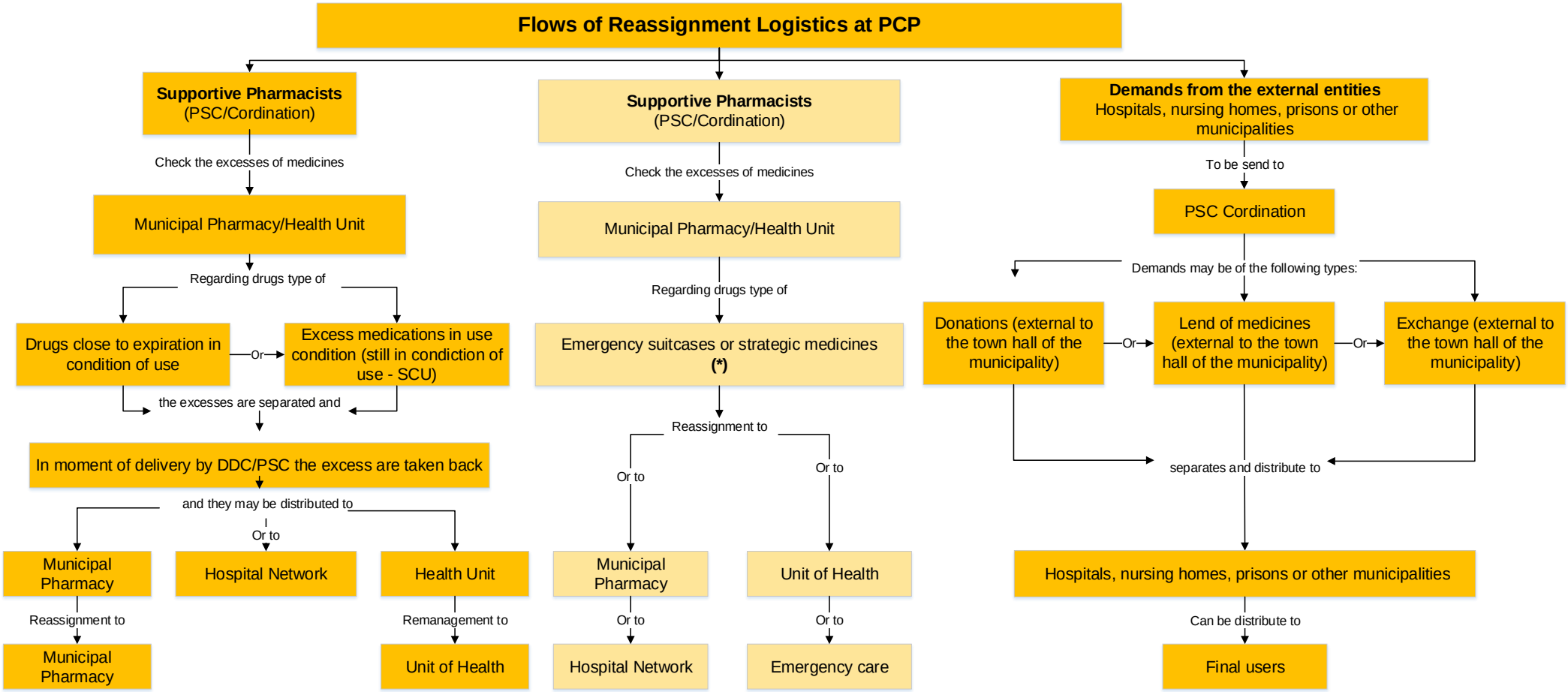

Figure 3-1 Flows of Reassignment Logistics

PCP=Pharmaceutical Care Process; PSC= Pharmaceutical Supply Chain; DDC= Drug Distribution Center

(*) Emergency Suitcases comprise drugs for the treatment of out-patients as well as controlled, injectable drugs

The reassignment flow in Figure 3.1 was created together with the interviewees and they validated it. It intends to provide a visualization of what they perceive to be the most relevant steps in their effort to avoid medicines to expire as well as to regain value from them.

As state on purpose (2) of this study, we were also able to identify some of the most relevant factors by analyzing the contents from the interviews. Below (section 3.4.1.1), we present critical factors for medicines reassignment logistics.

3.4.1.1 Critical Factors in the Medicines Reassignment Logistics

Interviewees were shown a list of previously identified critical factors during their interviews about medicines reassignment logistics. They could indicate if there was more than one critical factor in each activity in the reassignment logistics flow. Fig 3-2. presents the frequency of critical factors identified by each interviewee at each stage of the reassignment flows.

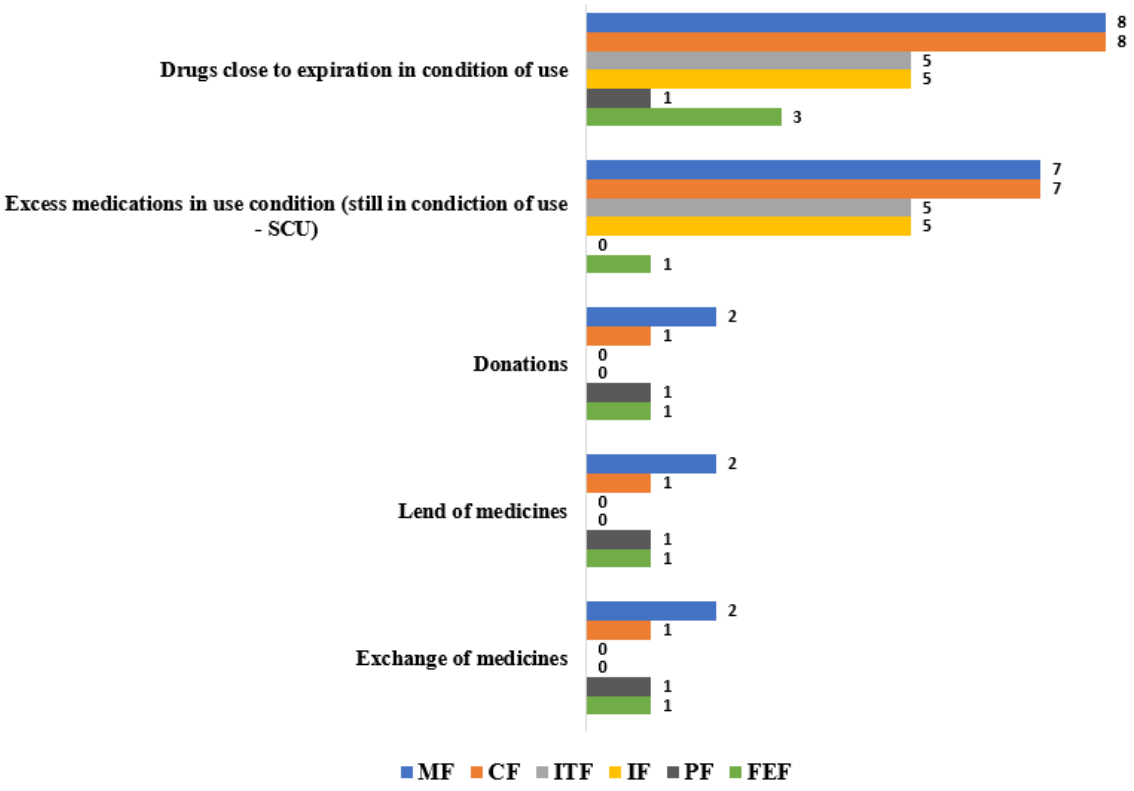

Figure 3-2 Critical factors in reassignment logistics

Management Factor (MF); Collaboration Factor (CF); Information Technology Factor (ITF); Infrastructure Factor (IF); Political Factor (PF); Financial and Economic Factor (FEF)

As we can see on Fig. 3-2, interviewees considered the management factor and the collaboration factor as the most important for drug reassignment flows. They were identified by 8 out of 10 respondents.

The management factor included aspects pertaining to the number of public civil servants available to undertake those activities, expertise and technical knowledge, worker motivation and training. This is in line with studies by Ali and Abdelsalam (2017; Xia et al., 2015), who affirm that lack of qualified professionals for remanufacturing, lack of support to workers, and lack of personnel training are relevant barriers. Although the practice of "reassignment logistics of medicines" among the sites is much less time consuming than the "remanufacture of a product" in a typical RL, it is expected that every reverse flow is out of the current routine of the SPAADD direct flow. Considering that, the entire infrastructure of the pharmaceutical care process is designed to attend the several activities of the direct flow, it is reasonable that every extra activity exceeds capacity, revealed in voice of interviewees demanding for more "people" for reassignment purposes.

The collaboration factor includes aspects pertaining to information sharing and exchange, reliability in information exchange, as well as cooperation and collaboration between parties involved in the process. Lack of cooperation was the focus of Mathiyazhagan et al. (2013).

The second and the third most relevant critical factor for reassigning excess medicaments that are still in good condition were Infrastructure and Information Technology, which were identified by 5 out of 10 interviewees.

The infrastructure factor includes facilities for storing reassigned medicaments. In fact, the current PSC area available is already accommodating stocks of reassignment, but it is very close of its space limit. According information from interviewees a group of researchers from the local Federal University are analyzing the PSC layout and processes, viewing the optimization of the infrastructure in the place.

In the reassignment flow for drugs whose expiration date was approaching, but that could still be used, once again the most relevant factors mentioned were the management factor and the collaboration factor. They were identified by 7 out of 10 interviewees.

Unsurprisingly, the infrastructure factor also appeared as one of the most relevant, as lack of space in facilities restricts drug storage.

The Information Technology factor was identified by 5 out of 10 interviewees. It includes aspects pertaining to information systems used to record reassigned medicaments and

consumables. The information system currently implemented at healthcare centers has been important to make drug administration for users faster.

According to Gyanendra et al. (2011), the quantity and cost of unused prescribed medicines increases, and they must be discarded. Drugs that are not used are a relevant source of waste in healthcare systems around the world (Toh and Chew, 2017). On that issue, a statement by one of the interviewees on the implementation of the information system in healthcare units helps us to understand the importance of the Information Technology factor in regaining value:

> *"[...] Losses from the number of products lost because they expired multiplied by their unit prices are currently at 19,577 Brazilian reais. However, 223 thousand were recovered by transferring medicaments from places where they would expire to places where they would not. We are able to recover 10 times what we lose. They expire mostly at health centers. They hardly do at regional pharmacies [resp_002]. "There are more visits every two months, and at the same time they are reassigned more often, which means they do not expire [Interv _002]."*

The Financial and Economic Factor, in turn, was identified by 3 out of 10 interviewees. This factor includes aspects pertaining to financial and economic amounts that could be recovered via reassigned medicaments. In 2018 there was a reorganization of metrics and indicators and the data collected revealed that a significant amount of money for bidding was saved due to "reassignment" among sites.

For other medicament reassignment flows (Donations/Loans of medicines/Exchange of medicines), critical factors were mentioned less often, by 2 out of 10 interviewees.

3.4.2 Reverse Logistics Flows for Medicines

By analyzing the content from interviews, we were also able to identify cycles pertaining to reverse logistics: (a) expired medicines delivered by the population; (b) expired medicines from health units; (c) medicines overdue in own stock; (d) drug for return to supplier, and (e) Defective medicine or with breakdown. Fig. 3-3 details the flows described.

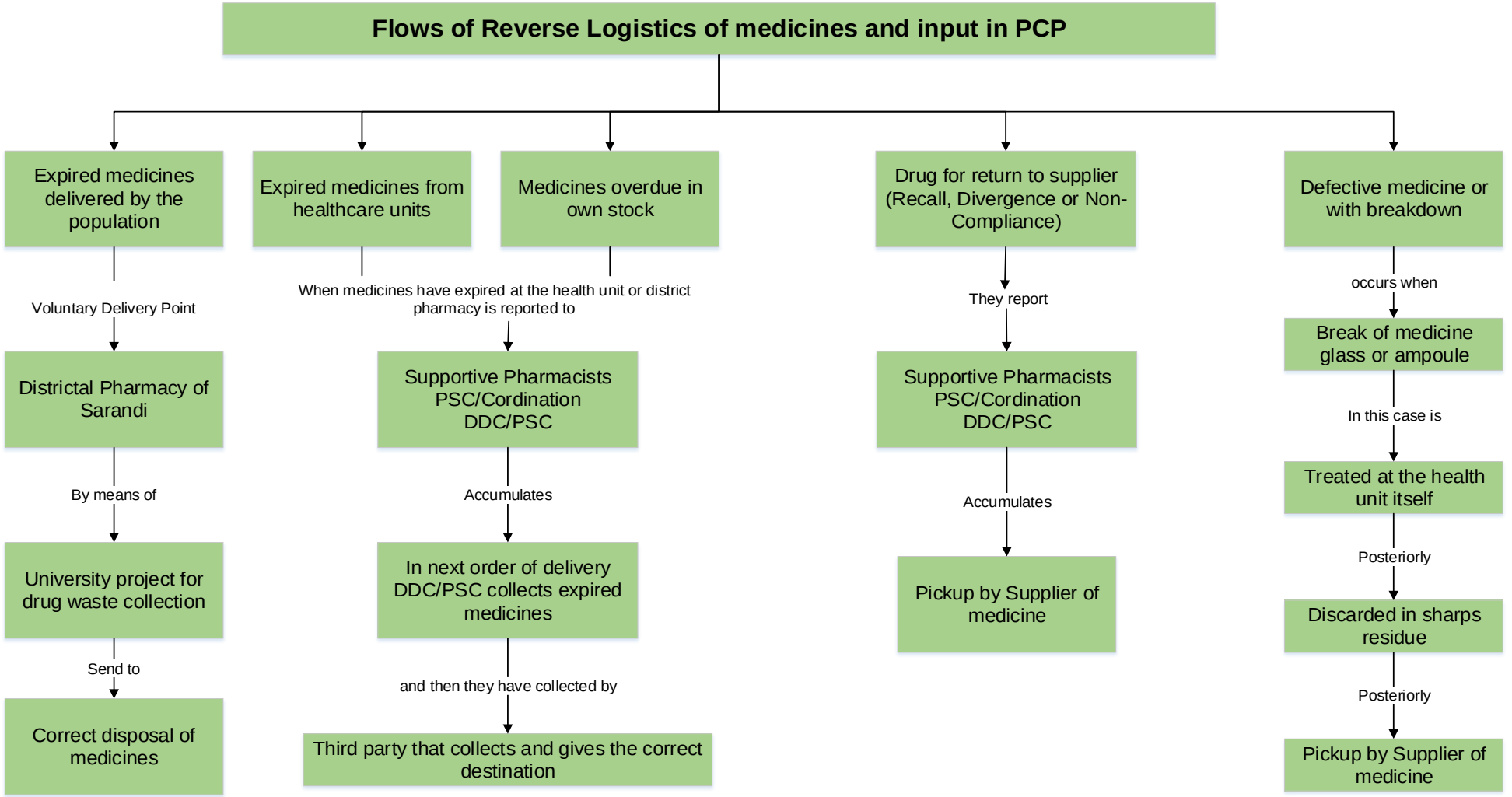

Figure 3-3 Flows of Reverse Logistics of medicines

PCP=Pharmaceutical Care Process; PSC= Pharmaceutical Supply Chain; DDC= Drug Distribution Center

The flowchart in Figure 3-3 was created together with the interviewees and they validated it. It intends to provide a visualization of what they perceive to be the most relevant steps in their effort to avoid medicines to expire as well as to regain value from them.

As state on purpose (2) of this study, we were able to identify critical factors by analyzing contents from interviews. Section 3.4.2.1, presents the critical factors for the reverse logistics of medicaments.

3.4.2.1 Critical Factors in Reverse Logistics of Medicines

As mentioned in section 3.4.1.1, interviewees were shown a list of previously identified critical factors during their interviews about the reverse logistics of medicines. They could indicate if there was more than one critical factor in each activity in the reverse logistics flow of medicaments. Fig. 3-4 shows the frequency of critical factors identified by each interviewee in each step of the reverse logistics process for medicaments.

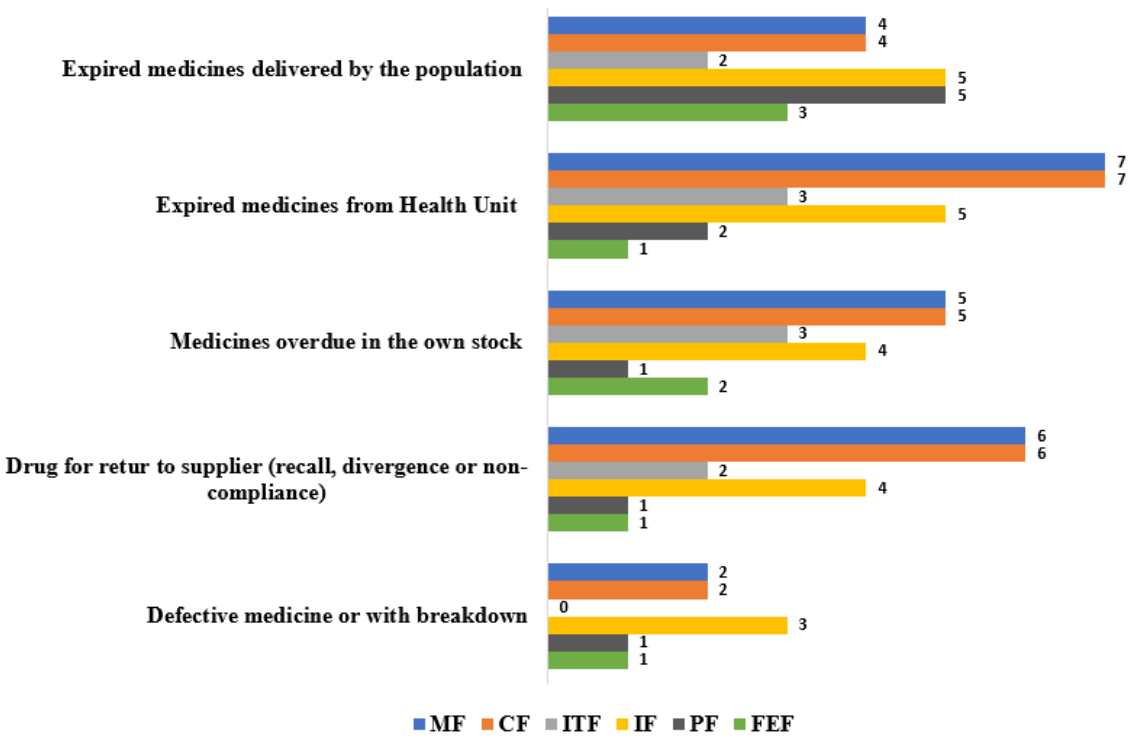

Figure 3-4 Critical Factors in reverse logistics

Management Factor (MF); Collaboration Factor (CF); Information Technology Factor (ITF); Infrastructure Factor (IF); Political Factor (PF); Financial and Economic Factor (FEF)

As we can see on Fig. 3-4, there is a greater prevalence of critical factors identified by the interviewees in reverse logistics flows. In the flow for medicines overdue in the own stock,

critical factors Management Factor and Collaboration Factor were identified by 5 out of 10 respondents each.

We notice that there is initial concern with the lack of human resources available for administering drugs. This refers to managing drugs that expire while they are the stocks of health centers and pharmacies, as well as to those coming from other healthcare units. This is in line with the results from (Glassmeyer et al., 2009; Sharma et al., 2011).

The Information Technology critical factor was mentioned by 3 out of 10 interviewees. Lack of information systems for reverse logistics was also identified by (Jabbour et al., 2016; Laribi and Dhouib, 2015; Waqas et al., 2018).

Still concerning infrastructure, we can notice a lack of facilities to store expired drugs and consumables that must be submitted to DDC/PSC. The Infrastructure Factor was mentioned by 4 out of 10 respondents. Lack of appropriate facilities to handle returns was also identified by (Muduli et al., 2013; Shaharudin et al., 2015; Waqas et al., 2018).

In the flow for expired medicine in health units, interviewees indicated the prevalence of the following critical factors: The Management Factor and the Collaboration Factor were identified by 7 out of 10 respondents. When questioned about what they understood as an RL process, one interviewee clearly indicated the need for collaboration to create reverse processes:

> *Collaborative logistics process to return a logistics distribution process seeking to appropriately handle each item to reduce losses so drugs are adequately available for people [Interv_002].*

We also notice a lack of human resources available to perform those tasks. This is noticeable in a statement by one of the interviewees:

> *This is a place where human resources make all the difference. It's not about reducing costs, on the contrary, you have more people [...] so there is less workload on each of them, less errors, which are different types of errors... If you make an error in the batch or in the quantity, we can fix that because we correct any non-compliance... But what if you give the wrong drug to a patient? [Interv_004]."*

The next most relevant critical factors were Infrastructure, with 5 mentions, and Information Technology, with 3 mentions. As for medicaments returned by the population, interviewees most often identified the Infrastructure and the Political Factors, which were mentioned 5 times each. The main purpose of the PCP is to administer drugs. Due to infrastructure and legal issues, the PCP does not receive back those two types of medicine -

expired and/or in good condition for use. Section 3.4.2.1.1 includes a more thorough discussion on those issues.

As for critical factors, the Management Factor and the Collaboration Factor were identified by 4 out of 10 respondents. Next was the Financial and Economic Factor, mentioned by 3 out of the 10 interviewees, and Information Technology, identified by 2 out of 10 respondents.

In the flow of drugs that are returned to the manufacturer due to recall, critical factors Management Factor and Collaboration Factor were identified by 6 out of 10 interviewees. Next was the Infrastructure Factor, mentioned by 4 out of the 10 interviewees, and Information Technology, identified by 2 out of 10 respondents.

In the flow of defective medicine or with breakdown, the most significant critical factor was Infrastructure, identified by 3 out of 10 interviewees. Next, the Collaboration Factor, which were identified by 2 out of 10 respondents each.

These are the steps in direct logistics: *Selecting* medicine attributed to the TPC; *Scheduling*, which is based on consumption history and in services offered, managed by DDC/PSC; *Acquiring* via bidding processes or judicial orders, managed by COMEL/CELIC; *Storing* at the central unit responsible for storing and distributing the drugs, managed by DDC/PSC and pharmaceutical care units, that focus on providing quality care to patients in pharmacies and health centers. Reverse logistics activities include, in general, only certain, specific sectors, as we can conclude from an answer from one of the interviewees: *"[...] Reverse logistics is in place, in general, between* DDC/PSC*, health centers and regional pharmacies, and CAF/COORAF [Interv_002]".*

3.4.2.1.1 Medicines Returned by Patients

The public tries to return medicines for different reasons, such as: death of a patient who was using them, interruption in treatments, new treatments, and other reasons.

When patients seek out a health center or a regional pharmacy to return drugs and find out that is not possible, sometimes they will leave medicines at the healthcare units anyway. This is noticeable in statements by several interviewees:

> *"[...] We instruct the public to discard the drugs in other places, but sometimes they are not able to go somewhere else or refuses to do so. They often leave those drugs at the hallways, in benches, or in the restroom [...]. In those cases, we collect them to make sure they are adequately discarded. However, we do inform the population often adequate places to discard drugs, especially as we do not*

> *have appropriate discard recipients at regional pharmacies. To avoid having to reassign them to* DDC/PSC*, we try to inform the public about some places for discard, such as private drugstores, pharmacy departments in universities, etc. [Interv_008], [Interv_004], [Interv_002], [Interv_005].”*

Currently, as we can see on Fig. 3- 3, only one regional pharmacy collects expired medicine via a partnership with the local Federal University. In that case, drugs are collected and correctly discarded. In most cases, patients try to return medicine received from other sources, i.e. drugs not listed among those distributed by the public system.

On one hand, this shows lack of knowledge by the public, and on the other, communication issues between patients and pharmacists, who should inform them on how to correctly proceed if medicaments are not used anymore. According to (Braund et al., 2009; Campos et al., 2017), appropriately educating the public about disposal may minimize eventual impacts on the environment and to reduce the excess of medicaments wasted. Saravanan and Manoj (2016) argue that the public is often not aware of the impacts drugs have on the environment. Patients who are aware of those impacts are more likely to seek adequate ways to discard medicaments.

However, when pharmacies refuse to accept unused medicaments, they discourage users from doing so (Tong et al., 2011). According to Abbas and Farooquie (2013), often patients do not know the actual reason why pharmacies and health centers refuse to collect those drugs.

On that issue, Glassmeyer et al. (2009) highlight the need for the creation of strategies that include opportunities for users to send or take unused medicines to several collection points, such as pharmacies or other places to be correctly discarded. (Campos et al., 2017; Law et al., 2015), in turn, argue that pharmacists may play an important role in educating patients about adequate use and disposal of medicaments. Often, most people dispose of medicines improperly due to lack of clarity about the matter, not aware of actual effects on the environment (Pinto et al., 2014). This may be observed in a statement by one of the interviewees:

> *“[...] We normally do not provide that information. However, when they show up saying they will no longer use them, or that the person has died, then we instruct them, provide them with an address where they can donate it. Sometimes there are drugs that are not even on our list [Interv_006].”*

There is a drug bank in the city, created with the purpose of receiving non-expired medicaments that for some reason are not used by patients anymore. The banks receive those drugs and then give them to people in need free of charge when they seek it. Different studies

mention the need to create take-back programs or national collection programs (Gracia-Vásquez et al., 2015; Thach et al., 2013; Pereira et al., 2017). However, this requires a great level of organization, as well as significant time, funding, and human resources commitment (Glassmeyer et al., 2009).

According to Abbas and Farooquie (2013), the process of returning medicaments also faces several barriers throughout the reverse supply chain. Even though it complies with return policy conditions, refusal to accept returned medicaments from clients indicates there are factors that hinder the appropriate operation of return processes. Clients may decide to discard drugs declared non-returnable by themselves or by those responsible for keeping stock due to being expired or having their integrity compromised.

According to Bekker et al. (2017) and McRae et al. (2016), waste is partially unavoidable, but may be reduced by redistributing drugs not used by patients. However, they also indicate there is no knowledge about stakeholders' opinion on medicine redistribution. Stakeholders consider drug redistribution desirable if implementing this process is viable and if the requirements for safe redistribution are met. Drug redistribution or recycling raises a relevant debate about saving costs and reducing waste. However, safety and product integrity issues generally block healthcare centers to recycle donated drugs (Toh and Chew, 2017).

Due to Brazilian sanitary legislation, the public healthcare sector is prohibited from redistributing drugs, as it cannot verify the conditions in which they were stored while patients held them.

3.4.2.1.2 Implementing an Information Technology System to Administer Medicines in Healthcare Centers

In the recent effort to streamline the Brazilian Universal Healthcare System (SUS), there have been initiatives in place to implement a computerized patient care and medicine distribution system in all healthcare centers in cities that participate in the PCP.

Implementation of such system in regional pharmacies and virtually all municipal healthcare centers allowed excess medicaments from one unit to be reassigned to units that had greater demand for them.

The outcome was positive as it streamlined the process of delivering drugs to patients, but it was also important to monitor and analyze stock in healthcare units. Managers are thus able to monitor their stocks on a daily basis, as may be gathered from a statement by one of the interviewees: *"I think implementation of the system was positive [Interv_004]."*

The need for improving the system was also noted, to include warning systems for expiration dates, which would make it easier for managers to see in the system itself what drugs are close to expiring:

> *"[...] We actually have the system in place here, which does not have a warning (a popup saying "they will expire in one month"), but it does monitor them and allow you to monitor them as well [Interv_004]."*

Advancements in technology must be considered in creating and reviewing disposal routines. It is also relevant to understand and disclose factors that lead to certain principles being adopted. This information helps decision-makers (Nakyanzi et al., 2010; He et al. 2016). This may be observed in a statement by one of the interviewees:

> *"[...] By implementing the DIS (administration system) in healthcare units, we received may drugs that could still be used and that were expiring soon [Interv_006]."*

After a system allowing precise information pertaining to quantity in stock was implemented, drugs could be reassigned. Then, all stock was audited by supporting pharmacists and included in the system, which started operating drug administration activities exclusively via computerized system.

3.4.2.1.3 Supporting Pharmacists

Another point that came up during the interviews was the fundamental role played by supporting pharmacists, who have been working effectively in managing and in implementing drug administration practices via the computerized system. The PCP currently has three supporting pharmacists who support the whole system. This may be observed in statements by the interviewees:

> *"There should be more pharmacists that could offer support to units more often [...] the number of pharmacists for those support tasks is too small and way less than what we actually need [Interv_008]."*

Nonetheless, the role of supporting pharmacists is important to avoid expiration of medicaments at healthcare centers without reassigning them to other units to avoid losses:

> *"[...] that change had a significant impact in the last few months, and we can see the volume has decreased... because the drugs were not administered, so I was not going to ask for them anyhow, as before. So, I think this will happen less often [Inter_004]. "In-loco visits cannot stop happening in places that have been visited or where the DIS was implemented, as there are still excess drugs.*

> *Currently, the system does not show who transferred the most. Places visited by supporting pharmacists return drugs. We still have problems with the car used for those visits [...] currently it is cheaper to employ a driver than letting drugs expire [Interv_002]."*

Drug backlog or undesired left-over drugs result in three major concerns: (i) APIs discarded in sewers or in the garbage, which are a complex source of potential chemical release to the environment; (ii) drug backlog presents a greater potential of being unduly diverted, risking poisoning and non-intentional abuse; (iii) drug backlog are also a waste of health resources and represent lost opportunities of medical treatment (Ruhoy and Daughton, 2008).

3.4.2.1.4 Waste Sorting Practices

Inadequate storage, use, and/or disposal of medicines lead to public health concerns, especially for returned drugs. Healthcare professionals must deal with user misconception about keeping, storing, and discarding them (Kelly et al., 2018). On that subject, a statement by one of the interviewees shows the concern for adequate temporary storage areas for medicaments:

> *"We do not have a separate place for that, they are left in boxes labeled 'expired' [Interv_008]."*

> *"[...] If they expire, healthcare units sort them and informs a supporting pharmacist, who then informs DDC/PSC. In the next delivery it collects those drugs, which means drugs accumulate at DDC/PSC. Once a year, a contracted company collects them from health centers and regional pharmacies. When the car delivers the drugs, if the unit has excess or expired medicine, instead of having 140 drug collection points as intended, we centralize collection by another organ in distribution centers [Interv_002]."*

As for infrastructure to store expired drugs and consumables destined to be collected by third parties, all interviewees mentioned those drugs are left in a common area where non-expired drugs to be administered to patients are also kept. Lack of facilities in some units means storage is in a common place until expired drugs are sent to DDC/PSC:

> *"[...] Consumables that cannot be used, such as broken ampoules or glasses, for example, are handled by the healthcare unit itself. They are discarded as sharp residue, just like bottles of injectable dipyrone. I cannot carry something broken in a box for other people to handle [Interv_002]."*

Lack of an industry-wide agreement for reverse logistics of medicaments causes environmental and economic issues that pose great challenges for public healthcare in several Brazilian municipalities (Pereira et al., 2017).

3.5 FINAL REMARKS

The main purposes of this study were: (1) to map reverse logistics and reassignment of medicine included in the Pharmaceutical Care Process (PCP) in the city of Porto Alegre, State of Rio Grande do Sul, Brazil; and (2) to identify the most relevant critical factors for implementing medicine waste management in pharmaceutical care processes, focused on reverse logistics of pharmaceuticals.

By means of qualitative analysis of data collected from interviews, this case study on APS provided relevant insights for the public health sector as we were able to identify reassignment and reverse logistics flows that were not identified before.

Once activities comprising each flow were identified and verified by managers, we were able to identify their most relevant critical factors. This solved purposes (1) and (2). From interviews, we observed the fundamental role played by the implementation of a computerized system for medicine administration in healthcare units throughout the city in those two cases. These medicaments can now be reassigned to other units with greater demand for them, avoiding their expiration. Another fundamental point raised in this study was the role played by supporting pharmacists in the context of PCP.

Finally, partnerships with the University have been positive. Not only does it provide scientific support for projects, it also encourages research, data collection on medicine disposal, demand, and costs, as well as on the reasons for disposal. It also adequately disposes of returned drugs and consumables.

There is still no pharmaceutical industry-wide agreement in Brazil - as is the case for packaging, for example, which provides guidelines for that industry (Guarnieri et al., 2020). As is the case for other Brazilian municipalities, the city of Porto Alegre faces several challenges in implementing reverse logistics. In light of that, each Brazilian municipality, together with teams from different healthcare sectors can use Porto Alegre’s solid waste management plan, set forth in accordance with Law 12.305 and Resolution 222/2018 (Brasil, 2018), as a reference. That legislation categorizes waste generated by the public healthcare sector in groups A to E, listed on the annexes to Resolution 222/2018. Medicines are listed in group B, biohazard waste, which leads those teams to put greater efforts in creating health solid waste management programs.

The most relevant contribution from this study was showing - via a case study of the public healthcare system - the main flows and critical factors identified in each stage of those

reassignment and reverse logistics flows, which sheds light on a sector that the literature has only marginally discussed.

The research allowed us to identify factors Management, Collaboration, Information Technology, and Infrastructure as critical in the following flows: Drugs close to expiration in condition of use and medications in use conditions (Still in Conditions of Use – SCU) in reassignment logistics.

As for reverse logistics of medicaments, the factors most often mentioned by interviewees were: Management, Collaboration, Infrastructure, and Political. Results from this qualitative study are important for PCP managers' decision-making and for improving current waste management practices, as managers may develop strategies based on them.

As suggestions for future studies, these results could be quantitively validated with the use of statistics and multicriteria approach methods to confirm or refute them.

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APPENDIX A - Questionnaire for the interviews

Personal Information

Gender: ( ) Female ( ) Male

Where do you work? _____

What is your position? _____

1. Have you ever heard about the National Policy on Solid Waste? If affirmative, how would you describe your knowledge about it?

( ) Very low ( ) Low ( ) Adequate ( ) Good ( ) Very Good

2. How would you define Reverse Logistics? *(After the answer, show the definition below)*

According to the National Policy on Solid Waste (set forth by Law 12.305, dated August 02, 2010), reverse logistics can be defined as a "social and economic development tool characterized by a set of actions, procedures and means allowing the gathering and return of solid waste to companies so they may reuse it, either on their own production cycle or in other production cycles, or give it any other environmentally adequate final destination."

3. Are you aware of the environmental impacts caused by improper disposal of medicine and other materials used in pharmacies?

a) What would you change in the system (DIS or GMAT) to meet the needs of expired items control?
b) How are they transported?
c) Do you know what medicines were subject to this LR flow?
d) Did you identify any other products besides drugs?

4. Are patients informed about the medicaments they use, particularly in terms of what to do with excess drugs, their expiration, or where to discard them? *How to proceed in case of excess or expired drugs?*

5. What types or waste are generated at the regional pharmacy (drugs and/or other)?

6. What happens with expired drugs at regional pharmacies?

7. What do you think could be done to improve expired medicaments management processes?

Is any analysis done on causes of expiration?

What information is recorded on expired medicine? For example:

- Source (patient, stock, etc.)
- Quantity expired

- Cost of expired medicaments

Does the quantity of expired medicaments affect the following request? (*Does the quantity of expired medicaments influence the quantity of medicaments requested in the following request?*)

Are expired medicaments excluded from the system (DIS and GMAT)? How? *(Both medicaments excluded due to approaching expiration date and those actually expired.)*

Where are medicaments sent?

How are expired medicaments transported? When?

Is there an area to store expired medicaments?

Is there any procedure in place to remove medicaments from stock before they expire?

a. How long before expiring are, they removed?

b. How controls that?

c. What is the destination of those medicaments?

d. Are they already considered waste?

(According to legislation, no medicament that may expire during its use period may be administered to patients. E.g., patient treatment will last two months and the expiration date in stock is in one month. In that case, only the quantity for one month may be administered.)

8. What do you see as the positive aspects in the current drug disposal process or in the process of sorting them from other material to be incinerated? And what do you see as their negative aspects?

ANEXO A – GRUPOS E SUBGRUPOS DE RESÍDUOS DA SAÚDE

Grupo A	É identificado, no mínimo, pelo símbolo de risco biológico, com rótulo de fundo branco, desenho e contornos pretos, acrescido da expressão RESÍDUO INFECTANTE	**Subgrupo A1** - Culturas e estoques de micro-organismos; resíduos de fabricação de produtos biológicos, exceto os medicamentos hemoderivados; descarte de vacinas de microrganismos vivos, atenuados ou inativados; meios de cultura e instrumentais utilizados para transferência, inoculação ou mistura de culturas; resíduos de laboratórios de manipulação genética. - Resíduos resultantes da atividade de ensino e pesquisa ou atenção à saúde de indivíduos ou animais, com suspeita ou certeza de contaminação biológica por agentes classe de risco 4, microrganismos com relevância epidemiológica e risco de disseminação ou causador de doença emergente que se torne epidemiologicamente importante ou cujo mecanismo de transmissão seja desconhecido. - Bolsas transfusionais contendo sangue ou hemocomponentes rejeitadas por contaminação ou por má conservação, ou com prazo de validade vencido, e aquelas oriundas de coleta incompleta. - Sobras de amostras de laboratório contendo sangue ou líquidos corpóreos, recipientes e materiais resultantes do processo de assistência à saúde contendo sangue ou líquidos corpóreos na forma livre. **Subgrupo A2** - Carcaças, peças anatômicas, vísceras e outros resíduos provenientes de animais submetidos a processos de experimentação com inoculação de microrganismos, bem como suas forrações, e os cadáveres de animais suspeitos de serem portadores de microrganismos de relevância epidemiológica e com risco de disseminação, que foram submetidos ou não a estudo anatomopatológico ou confirmação diagnóstica. **Subgrupo A3** - Peças anatômicas (membros) do ser humano; produto de fecundação sem sinais vitais, com peso menor que 500 gramas ou estatura menor que 25 centímetros ou idade gestacional menor que 20 semanas, que não tenham valor científico ou legal e não tenha havido requisição pelo paciente ou seus familiares. **Subgrupo A4** - Kits de linhas arteriais, endovenosas e dialisadores, quando descartados. - Filtros de ar e gases aspirados de área contaminada; membrana filtrante de equipamento médico-hospitalar e de pesquisa, entre outros similares. - Sobras de amostras de laboratório e seus recipientes contendo fezes, urina e secreções, provenientes de pacientes que não contenham e nem sejam suspeitos de conter agentes classe de risco 4, e nem apresentem relevância epidemiológica e risco de disseminação, ou microrganismo causador de doença emergente que se torne epidemiologicamente importante ou cujo mecanismo de transmissão seja desconhecido 54 ou com suspeita de contaminação com príons. - Resíduos de tecido adiposo proveniente de lipoaspiração, lipoescultura ou outro procedimento de cirurgia plástica que gere este tipo de resíduo. - Recipientes e materiais resultantes do processo de assistência à saúde, que não contenha sangue ou líquidos corpóreos na forma livre. - Peças anatômicas (órgãos e tecidos), incluindo a placenta, e outros resíduos provenientes de procedimentos cirúrgicos ou de estudos anatomopatológicos ou de confirmação diagnóstica. - Cadáveres, carcaças, peças anatômicas, vísceras e outros resíduos provenientes de animais não submetidos a processos de experimentação com inoculação de microrganismos. - Bolsas transfusionais vazias ou com volume residual pós-transfusão. **Subgrupo A5** - Órgãos, tecidos e fluidos orgânicos de alta infectividade para príons, de casos suspeitos ou confirmados, bem como quaisquer materiais resultantes da atenção à saúde de indivíduos ou animais, suspeitos ou confirmados, e que tiveram contato com órgãos, tecidos e fluidos de alta infectividade para príons. - Tecidos de alta infectividade para príons são aqueles assim definidos em documentos oficiais pelos órgãos sanitários competentes.
Grupo B	É identificado por meio de símbolo e frase de risco associado à periculosidade do resíduo químico.	Resíduos contendo produtos químicos que apresentam periculosidade à saúde pública ou ao meio ambiente, dependendo de suas características de inflamabilidade, corrosividade, reatividade, toxicidade, carcinogenicidade, teratogenicidade, mutagenicidade e quantidade. - Produtos farmacêuticos - Resíduos de saneantes, desinfetantes, desinfetantes; resíduos contendo metais pesados; reagentes para laboratório, inclusive os recipientes contaminados por estes. - Efluentes de processadores de imagem (reveladores e fixadores).

		Efluentes dos equipamentos automatizados utilizados em análises clínicas. - Demais produtos considerados perigosos: tóxicos, corrosivos, inflamáveis e reativos.
Grupo C	É representado pelo símbolo internacional de presença de radiação ionizante (trifólio de cor magenta ou púrpura) em rótulo de fundo amarelo, acrescido da expressão MATERIAL RADIOATIVO, REJEITO RADIOATIVO ou RADIOATIVO.	Qualquer material que contenha radionuclídeo em quantidade superior aos níveis de dispensa especificados em norma da CNEN e para os quais a reutilização é imprópria ou 55 não prevista. - Enquadra-se neste grupo o rejeito radioativo proveniente de laboratório de pesquisa e ensino na área da saúde, laboratório de análise clínica, serviço de medicina nuclear e radioterapia, segundo Resolução da CNEN e Plano de Proteção Radiológica aprovado para a instalação radiativa.
Grupo D	Deve ser identificado conforme definido pelo órgão de limpeza urbana.	Resíduos que não apresentam risco biológico, químico ou radiológico à saúde ou ao meio ambiente, podendo ser equiparados aos resíduos domiciliares. - papel de uso sanitário e fralda, absorventes higiênicos, peças descartáveis de vestuário, gorros e máscaras descartáveis, resto alimentar de paciente, material utilizado em antissepsia e hemostasia de venóclises, luvas de procedimentos que não entraram em contato com sangue ou líquidos corpóreos, equipo de soro, abaixadores de língua e outros similares não classificados como A1; - sobras de alimentos e do preparo de alimentos; - resto alimentar de refeitório; - resíduos provenientes das áreas administrativas; - resíduos de varrição, flores, podas e jardins; - resíduos de gesso provenientes de assistência à saúde; - forrações de animais de biotérios sem risco biológico associado. - resíduos recicláveis sem contaminação biológica, química e radiológica associada. - pelos de animais
Grupo E	É identificado pelo símbolo de risco biológico, com rótulo de fundo branco, desenho e contorno preto, acrescido da inscrição de RESÍDUO PERFUROCORTANTE.	Materiais perfurocortantes ou escarificantes, tais como: lâminas de barbear, agulhas, escalpes, ampolas de vidro, brocas, limas endodônticas, pontas diamantadas, lâminas de bisturi, lancetas; tubos capilares; ponteiras de micropipetas; lâminas e lamínulas; espátulas; e todos os utensílios de vidro quebrados no laboratório (pipetas, tubos de coleta sanguínea e placas de Petri) e outros similares.

Fonte: Brasil, Agência Nacional de Vigilância Sanitária (2018).

4. ARTIGO 3 - A GREY-DEMATEL APPROACH FOR ANALYZING FACTORS CRITICAL TO THE IMPLEMENTATION OF REVERSE LOGISTICS IN THE PHARMACEUTICAL CARE PROCESS

Artigo em avaliação no Periódico Environmental Science and Pollution Research

Abstract: There is an increasing interest in product recovery, closed-loop supply chains, and reverse logistics (RL) for mitigating environmental impairment. Although RL is becoming a mandatory policy in developed countries, it is still in an embryonic stage in some industrial sectors of emerging economies, such as Brazil. We propose a grey decision-making trial and evaluation laboratory (DEMATEL) approach to identify and evaluate the critical factors and their interrelationship, contributing to the successful implementation of RL in the pharmaceutical care process. We consider expert opinions and construct a net cause-effect structure with management factor (MF), collaboration factor (CF), information technology factor (ITF), infrastructure factor (IF), policy factor (PF), financial and economic factor (FEF), end-of-life management practices (EOL-MP), and logistics performance factor (LPF). The study identified FEF, MF, PF, and ITF as the major causal factors. Moreover, EOL-MP was identified as the most critical factor, followed by LPF as the second most critical factor in the implementation of RL.

Keywords: reverse logistics; grey system theory; DEMATEL; implementation barriers; pharmaceutical care process.

4.1 INTRODUCTION

The sustainable management and conservation of resources require sustainable strategic initiatives by business and government (Scavarda et al., 2019; Prakash and Barua, 2016). Reverse logistics (RL) is a strategic initiative that contributes to the conservation of natural resources. Guarnieri et al. (2020) have argued RL improves competitiveness, reduces waste, provides greater profitability, and improves customer relationships. Other seminal publications reinforce the economic and social values provided by RL (Rogers and Tibben-lembke, 2001; Prahinski and Kocabasoglu, 2006).

Paula et al. (2019) highlighted the environmental impacts of the pharmaceutical supply chains as solid waste and wastewater generation (caused by incorrect discharges), human well-being (increased aging and demographic change leading to an escalating dependency on medicines), and social equality (contrasting with lack of access, high prices, and losses in supply chains). RL practices have been an integral part of sustainable development strategies, and it is an important approach for the efficient use of resources, minimizing waste from end-of-use/end-of-life (EOU/EOL) products, and being driven by regulatory issues (Viegas et al., 2019). Although many countries face difficulties in RL implementation, the problem is more serious in developing countries (Chauhan et al. 2018; Scavarda et al. 2019), where the rate of economic growth and urbanization is quickly increasing while the legislation is often incipient (Bouzon et al., 2016).

When it comes to health waste, especially concerning the disposal of EOU/EOL medicine not completely used in treatment, disposal has been a high priority problem and a concern for public health professionals, governments and society (Aquino et al. 2018; Kelly et al. 2018; Vellinga et al., 2014). Pharmaceutical waste has undesirable effects with significant economic and environmental consequences, particularly when it is discarded illegally in landfills, rivers, or oceans. Thus, the implementation of collection strategies requires greater attention (Bungau et al., 2018; Guirguis, 2010). With regard to the disposal of unused and expired EOU/EOL medicine, a study conducted by Al-Shareef et al. (2016) in Saudi Arabia, revealed that 79.15% of medication users dispose of their unwanted medication through household waste; 7.04% dispose of them into the toilet or sink; 4% do not know what to do with them; 3.71% send them for hazardous waste collection; 1.70% returned them to their doctor; 1.70% return them to the pharmacy; 1.60% give them to someone else; 0.70% never dispose them, and 0.60% discarded them some other ways. Similar results were found in Illinois, in a study by (Wieczorkiewicz et al., 2013).

Pinto et al. (2014) conducted a behavior survey with undergraduate students to understand what practices are adopted for the disposal of EOU/EOL medicine in Brazil. 62% of the students disposed of their unwanted medicine as ordinary garbage, 19% have a habit of discarding them in running water, 10% return the medication to a health center, pharmacy, or community center, 4% dispose of everything as recyclable waste, and 5% adopt other disposal practices. In many cases, pharmaceutical professionals recognize health waste collection as a new pharmaceutical service in addition to their daily responsibilities (Manojlović et al., 2015).

The pharmaceutical care process (PCP) implemented by the Brazilian Health Ministry is a structured set of procedures, part of the broader pharmaceutical supply chain, which includes selection, programming, acquisition, storage, distribution, and dispensation (SPASDD), supplying medicines to Brazilian citizens (Brazil, 2001). While the recovery of EOU/EOL medicine is forbidden in the PCP, many professionals, government workers, and system users have questioned it for a long time. The 12.305/10 Solid Residues Act (Brazilian Solid Waste Policy, 2010) has played an important role in maintaining the subject on the front burner. The disposal of medicines may be a complex discussion, albeit necessary, that requires efforts from the entire society, as well as various private and public sectors. There is an urgent need to accelerate the discussion and implement pilot drug collection programs (Medeiros et al., 2014). Campos et al. (2017) have identified regulatory and stakeholders' educational perspective by calling attention to the need for professional awareness throughout the

pharmaceutical supply chain. These authors mention that, ideally, pharmacists occupy a privileged position in the PCP for collecting unused medications and educating the population.

Due to its complexity, different countries do not have guidelines for the proper disposal of unused medicines (Tong et al., 2011). Moreover, RL management becomes challenging as medication use increases, and the pharmaceutical return process encounters several barriers along the reverse supply chain (Yazdani et al., 2020; Abbas and Farooquie, 2013; Viegas et al., 2019; Wiel et al., 2012). According to Pereira et al. (2017), the lack of agreement for the pharmaceutical sector may lead to serious environmental and public health challenges. Therefore, the identification and classification of these critical factors are prerequisites to the successful implementation of RL (Kumar and Dixit, 2018; Prakash and Barua, 2016).

Different issues may inhibit effective healthcare solid waste management, such as political, governmental, financial, and technological issues, among others (Yazdani et al., 2020). The rationale behind this study is to empirically understand the critical factors that prevent the implementation of pharmaceutical waste management in the public health sector, specifically in the PCP, so that it is possible to create guidelines for addressing these barriers. We formulate the following research questions in this study:

- RQ1 – What are the critical factors to the implementation of RL in the PCP?
- RQ2 – What are the cause-and-effect relationships among these critical factors?

For this purpose, we propose a multi-criteria decision analysis (MCDA) model using the grey decision-making trial and evaluation laboratory (grey-DEMATEL).

The remainder of this manuscript is organized as follows. Section 4.2 presents the literature review on the RL critical factors. Section 4.3 presents an explanation of the grey-DEMATEL method. Section 4.4 shows the application of the proposed method, and Section 4.5 discusses the results. Finally, Section 4.6 closes the paper by presenting the concluding remarks and suggestions on future research directions.

4.2 THEORETICAL REFERENCES

Abbas and Farooquie (2013) and Prajapati et al. (2019) argue every RL implementation faces obstacles, and it is vital to identify and eliminate these berries for a successful application, especially in the pharmaceutical supply chains comprising the disposal of unused medicine. They also show that MCDA tools and techniques are most uniquely effective in identifying the barriers to the successful implementation of RL. In this section, we review the MCDA applications in RL.

4.2.1 MCDA Application in RL

Rahman and Subramanian (2012) proposed a framework for EOL computer recycling operations by identifying the critical factors in implementing recycling operations. They investigated the causal relationship between factors that influence recycling operations using DEMATEL. The results indicate that resource availability, coordination and integration of recycling tasks, and volume and quality of recyclables are critical to computer recycling operations. Factors such as government legislation, incentive, and customer demand were identified as the main drivers.

Prakash et al. (2015) proposed a fuzzy analytic hierarchy process (FAHP) to identify and weigh the importance of the barriers to RL implementation. They also used the technique for order of preference by similarity to ideal solution (TOPSIS) to classify these barriers and formulate strategies for their elimination. Prakash and Barua (2016) presented a FAHP-based MCDA method for prioritizing barriers to the adoption of RL in the electronics industry. They identified 38 barriers through literature review and expert opinions. These barriers were classified into seven main categories. The result of the study indicated that customer acuity in RL, lack of coordination/collaboration with third-party logistics providers, and uncertain quality and return time are the three most significant barriers to RL adoption. Xia et al. (2015) employed the grey-DEMATEL method to analyze the internal barriers in the automotive parts industry. They showed the cause-effect relationships could be used by the remanufacturers to eradicate the main internal barriers and increase productivity.

Govindan et al. (2016) investigated the key barrier to remanufacturing and addressed crucial inter-relations and interdependencies in this industry. The data obtained were processed using two solution methodologies, interpretive structural modeling (ISM), and fuzzy analytic network process. They showed the higher cost and the lack of acceptance by the customer were the key barriers in the automotive industry. Chauhan et al. (2018) used the combination of MCDA, ISM, and DEMATEL to identify the barriers that deter the establishment of waste recycling units. Their study suggests that the lack of financial resources, raw material, and government subsidies are the most critical barriers to the successful implementation of waste recycling infrastructure. Agrawal et al. (2016) reviewed and prioritized the critical success factors (CSFs) for the successful implementation of RL in the electronics industry. Twelve CSFs were identified through a literature review and a discussion with industry experts. The authors employed the TOPSIS to prioritize the CSFs. The results indicate that most of the identified factors are crucial to RL implementation. Top management awareness, resource

management, economic factors, and contract terms and conditions are the four priority factors, while process capacities and worker qualification are the less prioritized factors. Similarly, Mangla et al. (2016) used the AHP and DEMATEL methods to evaluate the CSFs in the adoption of RL in manufacturing. Their results show the importance of global competitiveness in RL.

Waqas et al. (2018) studied the barriers to RL implementation in the manufacturing industry by combining the Delphi methodology and structural equation modeling. They identified high cost of RL adoption, lack of skilled professionals, lack of supporting policies, lack of organizational culture, lack of human resources, lack of knowledge of environmental laws, lack of community pressure, and company policies as the most critical barriers. Sivakumar et al. (2018) used DEMATEL to evaluate the barriers to sustainable practices for EOL products. They evaluated the strength of the relationships between 18 barriers in the used plastic industry and identified the most prevalent barrier. Sirisawat and Kiatcharoenpol (2018) focused on the classification and ranking of barriers to RL implementation in the electronics industry and proposed a methodology based on fuzzy AHP and fuzzy TOPSIS, in which fuzzy AHP was used to obtain the weights of each barrier and TOPSIS was used for the final ranking of the RL implementation barriers. Kumar and Dixit (2018) used DEMATEL to identified the barriers that should be addressed urgently to manage the waste issue in consumer electronics. They also recommended that a combination of the method with structural equation modeling could be used to validate the proposed model statistically. Bouzon et al. (2018) evaluated the barriers to RL implementation in the Brazilian consumer electronics industry from the stakeholders' perspective. They used grey-DEMATEL and identified organizational barriers as the most dominating barrier in the Brazilian consumer electronics industry. RL can no longer be treated as an auxiliary strategy, especially in industries susceptible to product recall and perishable products such as the pharmaceutical industry (Ali & Abdelsalam, 2017). We summarize by emphasizing on the importance of RL in the pharmaceutical industry with EOU/EOL medical products and medicine.

4.2.2 Critical Factors in the Implementation of Pharmaceutical RL

Abdulrahman et al. (2014) and Mangla et al. (2016) argue that "critical barriers" and "critical factors" are synonymous in the context of RL implementation of RL. We use the term critical factors in this study. We use a literature review with the construction of a bibliographic portfolio to identify the critical factors in the PCP. Initially, a literature review is conducted for

the period between 2000 and 2019 with the keywords "*reverse logistics*" AND "*critical barriers*" OR "*critical factors*"; "*reverse logistics"* AND "*implementation*" in the following databases: Web Science, Science Direct, Emerald, and Google Scholar. We used the Snowball procedure (Biernacki & Waldorf, 1981; Wohlin, 2014) and selected a portfolio of 78 papers related to the implementation of RL in different sectors. We pooled the following eight factors by using the classification proposed by Abdulrahman et al. (2014) and Mangla et al. (2016) in the deductive form: management factor (MF), collaboration factor (CF), information technology factor (ITF), infrastructure factor (IF), policy factor (PF), financial and economic factor (FEF), EOL management practices (EOL-MP), and logistics performance factor (LPF). Table 4- 1 below shows a brief description and the support found in the consulted literature (see Appendix A).

Factors	Description	Authors
Management Factor (MF)	This factor considered the human skills available to pharmaceutical care for waste management regarding the personnel who performs activities and their motivational aspects, reflecting the level of training and engagement of the human capital and the commitment of the senior management to RL practices	[50; 16; 65; 34; 1; 68; 64; 78; 60; 67; 17; 54; 48; 30; 62; 28; 3; 71; 53; 61; 29; 44; 47; 39; 38; 75; 4; 36; 31; 9; 72; 45; 25; 66; 33; 76; 18; 49]
Collaboration Factor (CF)	This concerns the level of collaboration of those involved and how much these are willing to collaborate and cooperate in terms of communications and information sharing about reverse logistics processes. It also includes the extent to which information is reliable to help with the management process as a whole.	[77; 69; 11; 59; 62; 60; 13; 1; 12; 4; 36; 45; 34; 15; 76; 18; 19; 43]
Information Technology Factor (ITF)	The technology system is important to direct logistics cycles, allowing dispensing to take place effectively, ensuring thus inventory control and logistic effectiveness. From the perspective of reverse logistics, not only does the information system allow for the recording of expired items, but also for the generation of available data, which allows the management of big data, helping managers possess greater decision-making reliability.	[52; 22; 73; 24; 1; 61; 27; 29; 44; 32; 37; 75; 4; 26; 36; 9; 45; 19; 48; 54; 55; 33; 76; 18; 20; 5; 2]
Infrastructure Factor (IF)	The infrastructure reflects aspects of the physical structure, that is, adequate storage sites and a facility for storing returned items, as well as transport infrastructure.	[58; 13; 70; 54; 56; 55; 52; 51; 73; 29; 44; 75; 4; 26; 9; 45; 19; 15; 40]
Policy Factor (PF)	Legal issues involve governmental decisions, both at municipal, state and federal levels, for the creation of laws and regulations aimed at enabling waste management policies in order to establish a pharmaceutical reverse logistics process as a required action. Policy issues have a major influence on the process of RL implementation in different sectors.	[72; 13; 23; 51; 30; 22; 62; 10; 42; 28; 46; 71; 1; 53; 61; 8; 29; 44; 47; 12; 38; 75; 4; 31; 36; 19; 48; 15; 33; 18; 57; 63; 43; 6; 2]
Financial and Economic Factor (FEF)	This reflects the economic capabilities for the implementation of waste management practices. All implementation and improvement is dependent on financial resources. In this regard, financial resources can be decisive for the accomplishment of RL activities.	[68; 13; 23; 54; 55; 48; 51; 50; 10; 28; 42; 73; 3; 46; 71; 53; 61; 27; 44; 14; 39; 37; 75; 4; 25; 31; 72; 45; 21; 34; 18; 43; 6]
End-of-life Management Practices (EOL-MP)	This concerns effective practices carried out for the management of expired products and waste from treatments conducted in health facilities. Their implementation also focuses on preventing the generation of expired drugs within the health facility by monitoring the expiry date of drugs and supplies available in the stock of each clinic, district pharmacy and hospital.	[78; 14; 70; 55; 54; 12; 22; 42; 73; 41; 61; 74; 48; 34; 7; 66; 15; 76; 57; 35; 21; 39; 38; 75; 4]
Logistics Performance Factor (LPF)	In the pharmaceutical logistic process, the dispensing of drugs to patients has to be carried out valuing quality of care and process expeditiousness. Other elements may also be addressed, such as inventory control, which will make dispensing be performed efficiently or not.	[30; 61; 14; 38; 4; 45; 2]

Table 4-1 Description of critical factors

4.3 PROPOSED FRAMEWORK

In this section, we present the grey-DEMATEL framework proposed in this study to analyze the barriers to the implementation of RL in the PCP. The proposed framework depicted in Figure 4- 1 is composed of three distinct steps. In Step 1, we identify a comprehensive list of the critical factors through literature review (snowball procedure) and qualitative interviews with experts. In Step 2, we use the grey-DEMATEL approach to select the most critical factors for the successful implementation of RL in the pharmaceutical care process. In Step 3, we analyze and synthesize our findings and propose the managerial and practical implications of our study.

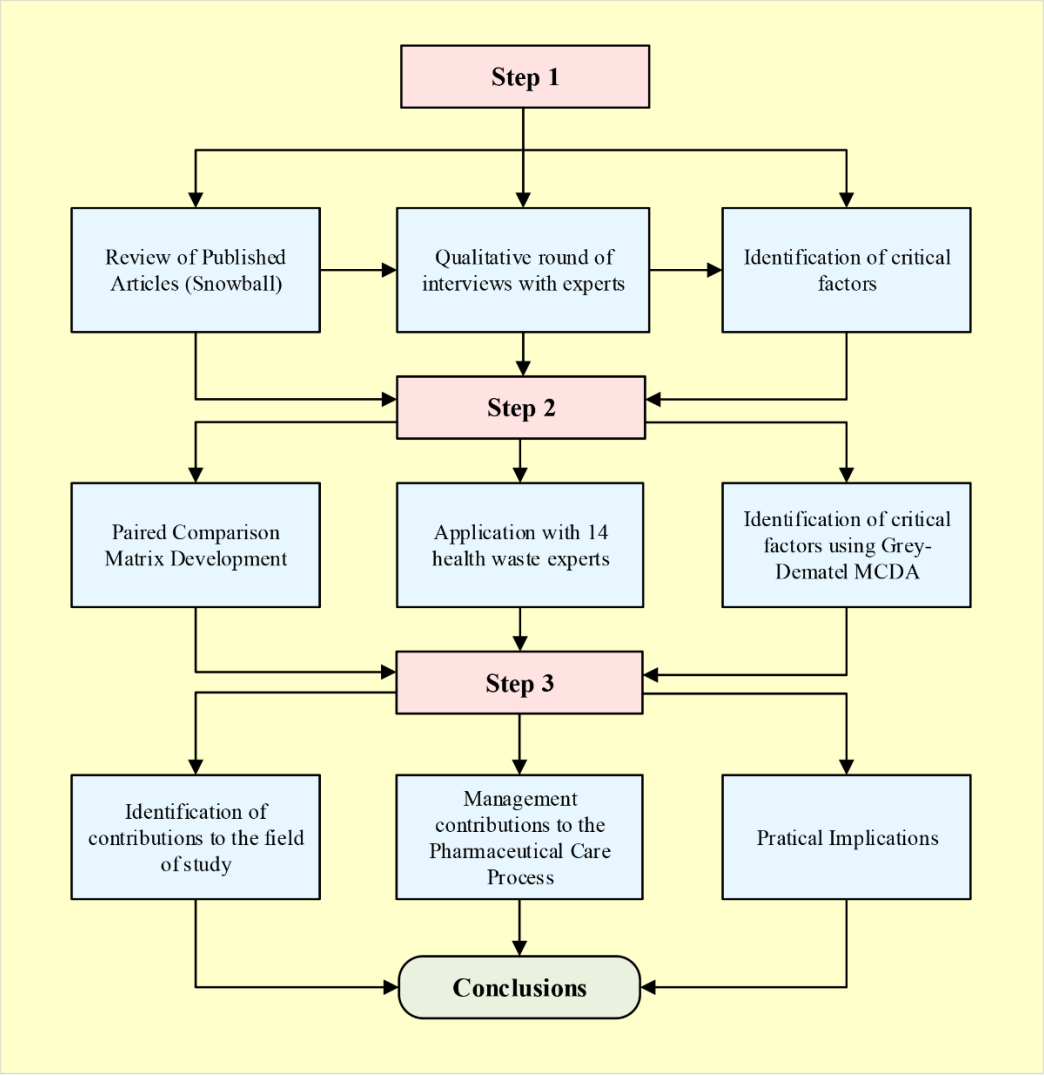

Figure 4-1 Steps of study

4.3.1 Context of Application

The Brazilian Unified Health System - Sistema Único de Saúde (SUS) is one of the most intricate public health systems in the world, with services ranging from simple treatment to more complex cases (Brazilian Ministry of Health, 2019). This healthcare network is structured with the primary health care (PHC), which consists of basic health units, mobile care service community agents, emergency care units or Unidade de Pronto Atendimento (UPA), and medium and high complexity care provided in hospitals. The secondary and tertiary care levels are generally provided in hospitals and consist of services with greater technological density and greater complexity (Mendes, 2011). There is a clear need for efficiency in the regional health management systems (Zare et al. 2019).

The PCP cycle is a component of the pharmaceutical supply chain and comprises drug selection, scheduling, procurement, storage, distribution, and dispensing operations to serve the citizens by the entire network of UPAs, but also public and private hospitals. The city of Porto Alegre in Brazil has 1.6 million citizens with access to medications, for free, at ten municipal pharmacies and 145 UPAs, which receive medications from the city inventory called Pharmaceutical Supply Center. In the context of the public health system, drugs are procured by bidding, based on the municipal list of essential drugs, buy means of the PCP cycle.

4.3.2 Data Collection

In the first step of data collection (see Fig. 4- 1) was the interviewing of the pharmacists who coordinate each district pharmacy and on-site observations to become familiar with PHC direct and reverse flows. In the second step, after the development of the critical factor’s matrix, new interviewees who were involved with the working group for the development of the solid waste management plan for the municipality were contacted and, if these were available, interviews were scheduled with 14 experts. We limited the size of the decision-making group to a minimum of five and a maximum of fifty members, as suggested by Ranjan et al. (2016), and used the data collection instrument presented in Appendix B.

The members of the working group for the development of the Solid Waste Management Plan for the municipality were contacted, and interviews were scheduled with 14 experts. The complete team of experts was made up of managers from different municipal pharmacy and health clinics in the public health system, waste managers from public hospitals,

the municipal public cleaning department, and the sanitary surveillance of the city of Porto Alegre, Brazil. More information on these experts is provided in Table 4- 2.

Unit of Work	No. of Respondents	Function
Pharmaceutical Assistance	1	Coordinator
Municipal Pharmacy	1	Nurse
	3	Pharmaceutical
Central Warehouse	2	Pharmaceutical
Public Hospital	1	Nurse/Waste Manager
	3	Waste Manager
Sanitary Surveillance	1	Chemical Engineer
Public Urban Cleaning Company	1	Chemical Engineer
	1	Civil Engineer

Table 4-2 Description of experts

All the interviewees and responding experts in the pairwise comparison matrix have direct or indirect experience in pharmaceutical or hospital waste management, and most of them were involved with the working group. The sample was considered a reasonable representative of the PCP since each expert performed a different role in the system. The interviews were administered face-to-face and on an individual basis within two months, depending on the availability of the interviewees. The representatives from the public urban cleaning company were included in the process to represent the opinions of this stakeholder group that impacts the reverse flow of medicine in the PCP cycle.

4.3.3 Justification for Choosing the Grey-DEMATEL Method in the Study Context

Bai and Sarkis (2013) argue DEMATEL is a useful method for uncovering causal knowledge from the causal analysis. The uncovered causal knowledge is instrumental in advancing the quality of decision-making and thus enabling the process of converting strategic objectives into practical actions. DEMATEL is a powerful MCDA method developed by the Geneva Research Centre of the Battelle Memorial Institute (Gabus and Fontela, 1972) for collecting knowledge from a group of experts and visualizing the interrelationships with a cause/effect relationship diagram. Shaik and Abdul-Kader (2014) justify the applications of DEMATEL by highlighting its strengths as:

a. providing a graphical output and presenting the reciprocal relationship of the factors under study numerically,
b. visualizing the feedback relationships among the factors at every level (the same, upper, and lower levels), and
c. presenting the importance weight of each factor in comparison with the influence of all

other factors in the system.

We integrated the grey system theory with DEMATEL in this study because RL is not currently used in the PCP flows due to legal and safety reasons, and the experts' opinions are naturally uncertain. The integration of the grey system theory with DEMATEL allows for the representation of vague, imprecise, and incomplete information (Xia et al., 2015). Thus, grey-DEMATEL is used in scenarios where there is uncertainty in expert responses concerning the relationships among the factors. The grey-DEMATEL steps are described in the next section:

4.3.4 Steps of the Grey-Dematel Approach

The mathematical theory known as "grey theory" was initially proposed by (Deng, 1982). The grey-based DEMATEL method comprises the following major stages and steps (Xia et al., 2015; Zhu et al., 2011).

Step 1: Once the factors that were found in the literature were defined and validated by waste management experts, the experts were asked to indicate the influence exerted by each critical factor when compared with another critical factor, using a scale ranging from 0 to 4: (0) no influence, (1) low influence, (2) medium influence, (3) high influence, and (4) very high influence. In this case, *n* represents the total number of experts. The grey scales for these linguistic values are defined in Table 4- 3.

Linguistic terms	Grey numbers	Normal values
No influence (N)	[0, 0]	0
Very low influence (VL)	[0. 0.25]	1
Low influence (L)	[0.25, 0.5]	2
High influence (H)	[0.5, 0.75]	3
Very high influence (VH)	[0.75, 1]	4

Table 4-3 The grey linguistic scale for evaluation of respondents
Source: Adapted from (Bouzon et al., 2018; Xia et al., 2015)

Step 2: An 8 x 8 grey-direct relation matrix *X* was defined for the grey pairwise influence relation comparison ($\otimes x_{ij}^{k}$) which was answered by the experts, generating 14 matrices with 64 comparisons of each expert. The diagonal of the matrix is always represented by number zero as there is no interrelation of the factor with itself. To illustrate the structure of each matrix, $\otimes x_{ij}^{k}$ the following is presented:

$$\otimes X_{ij}^{k} = \begin{bmatrix} [0,0] & \otimes X_{12}^{k} & \cdots & \otimes X_{1n}^{k} \\ \otimes X_{21}^{k} & [0,0] & \cdots & \otimes X_{2n}^{k} \\ \vdots & \vdots & \ddots & \vdots \\ \otimes X_{n1}^{k} & \otimes X_{n2}^{k} & \cdots & [0,0] \end{bmatrix}$$

Each expert was given a brief explanation described (in the body of each pairwise matrix) of the elements that were present in each critical factor, which resulted in the building of the classic DEMATEL matrix. Zhu et al. (2011) proposed a three-stage procedure that convert the grey numbers into crisp numbers using the modified-CFCS method, as demonstrated in the following equations (Eq.1 to Eq.5):

Step 1: Normalize the values:

$$\underline{\otimes}\,\overline{x}_{ij}^{k} = \left(\underline{\otimes}\,x_{ij}^{k} - \min_{j}\underline{\otimes}\,x_{ij}^{k}\right)/\Delta_{min}^{max} \tag{1}$$

$$\overline{\otimes}\,\overline{x}_{ij}^{k} = \left(\overline{\otimes}\,x_{ij}^{k} - \min_{j}\overline{\otimes}\,x_{ij}^{k}\right)/\Delta_{min}^{max} \tag{2}$$

$$\text{where } \Delta_{min}^{max} = \max_{j}\overline{\otimes}\,x_{ij}^{k} - \min_{j}\underline{\otimes}\,x_{ij}^{k} \tag{3}$$

Step 2: Determine the total normalized crisp value:

$$Y_{ij}^{k} = \frac{\underline{\otimes}\,\overline{x}_{ij}^{k}\left(1 - \underline{\otimes}\,\overline{x}_{ij}^{k}\right) + \overline{\otimes}\,\overline{x}_{ij}^{k} * \overline{\otimes}\,\overline{x}_{ij}^{k}}{1 - \underline{\otimes}\,\overline{x}_{ij}^{k} + \overline{\otimes}\,\overline{x}_{ij}^{k}} \tag{4}$$

***Step 3*:** Determine the final crisp value:

$$z_{ij}^{k} = \min_{j}\underline{\otimes}\,x_{ij}^{k} + Y_{ij}^{k}\,\Delta_{min}^{max} \tag{5}$$

Step 3: Develop a crisp direct-relation matrix for each expert and transforming Matrix *X* into a crisp matrix denominated *Z*. It is possible to derive an average matrix *N* from a group of experts' direct matrices.

Step 4: Obtain the direct-relation matrix *N* from Eqs. (6) and (7)

$$N = s \cdot Z \tag{6}$$

$$S = Min\left[\frac{1}{\max\limits_{1\le i\le n}\sum_{j=1}^{n} Z_{ij}}, \frac{1}{\max\limits_{1\le i\le n}\sum_{i=1}^{n} Z_{ij}}\right] \tag{7}$$

Step 5: Determine the total relation matrix (*T*) by using Equation (Eq. 8)

$$T = N(I - N]^{-1} \tag{8}$$

where *I* is denoted as an identity matrix and total- relation matrix *T*.

Step 6*:* Determine the row R_i and column D_j sums for row *i* and column *j* in the total-relation matrix using Eqs. (9) and (10):

$$R_i = \left[\sum_{j=1}^{n} t_{ij}\right]` \quad \forall_i \tag{9}$$

$$D_j = \left[\sum_{i=1}^{n} t_{ij}\right]` \forall_i \quad (10)$$

Step 7: Determine the overall importance or prominence (P_i) and net effect (E_i) of each critical factor. In this case P_i, the overall prominence or importance of critical factor *i*, is described regarding the overall relationships with other critical factors. According to Tzeng et al. (2007), the larger the value of P_i is, the greater the overall prominence of critical factor *i* will be. If the net effect $E_i > 0$, then critical factor *i* is a net cause for the other critical factor. If the net effect $E_i < 0$, the critical factor relies on the (net effect of) operation of the other critical factor.

Step 8: To determine the strongest relationships between the critical factors, the digraph relationship for each critical factor in relation with the other critical factor using the total relation matrix *T*, a threshold value θ is calculated. In this case, the relations with threshold value plus one standard deviation, plotted on the digraph as can may be seen in bold in Table 4- 5, were considered to build the digraph.

4.4 RESULTS

This section presents the results of each step of the grey-DEMATEL method, which was applied considering the perspectives of 14 experts in the context of PCP.

4.4.1 Interrelations of the Group of Factors

Bearing in mind the context of PCP cycle selection, scheduling, procurement, storage, distribution, and dispensing operations, the experts should analyze how the critical factors presented might have impacted pharmaceutical RL in this process. Data related to the opinion of each expert were obtained in the form of an 8 x 8 matrix, using a pairwise comparison matrix. The total and non-negative matrices of the experts consulted are presented in Appendix C.

The factors presented for analysis were the following: Management Factor (MF), Collaboration Factor (CF), Information Technology Factor (ITF), Infrastructure Factor (IF), Policy Factor (PF), Financial and Economic Factor (FEF), End-of-life Management Practices (EOL-MP), and Logistics Performance Factor (LPF). Table 4- 4 shows the values that were derived from the normalized direct influence matrix (step 1, explained in section 4.3.4).

Factors	MF	CF	ITF	IF	PF	FFE	EOL-MP	LPF
MF	0	0.1293	0.0738	0.0920	0.0710	0.0882	0.1559	0.1703
CF	0.1065	0	0.0791	0.0441	0.0520	0.0646	0.1521	0.1384
ITF	0.0837	0.0973	0	0.0586	0.0849	0.0882	0.1247	0.1338
IF	0.1156	0.1110	0.0555	0	0.0355	0.0555	0.1247	0.1247
PF	0.1384	0.1285	0.1004	0.1331	0	0.1148	0.1475	0.1240
FFE	0.1612	0.0837	0.1065	0.1658	0.0862	0	0.1521	0.1521
EOL-MP	0.0875	0.0875	0.0738	0.1057	0.0646	0.1110	0	0.1110
LPF	0.0821	0.0601	0.1019	0.1011	0.0697	0.1156	0.1430	0

Table 4-4 Mean values of the normalized direct influence matrix D

MF = Management Factor; CF = Collaboration Factor; ITF = Information Technology Factor; IF = Infrastructure Factor; PF = Policy Factor; FEF = Financial and Economic Factor; EOL-MP = End-of-life Management Practices; LPF = Logistics Performance Factor.

Subsequently, to develop the cause and net effect diagram, the sum of the values of matrix *T* was calculated and multiplied by the number of factors squared. To create the causal diagram, relations with a threshold θ greater than 0.4083 were considered. These relations can be seen in Table 4- 5 highlighted in **bold**.

Factors	MF	CF	ITF	IF	PF	FEF	EOL-MP	LPF
MF	0.2615	0.3525	0.2787	0.3284	0.2335	0.3109	**0.4750**	**0.4709**
CF	0.3124	0.1974	0.2480	0.2469	0.1902	0.2537	**0.4151**	0.3912
ITF	0.3088	0.2987	0.1860	0.2726	0.2270	0.2845	**0.4099**	**0.4036**
IF	0.3139	0.2926	0.2214	0.1951	0.1700	0.2378	0.3846	0.3726
PF	**0.4219**	0.3874	0.3284	0.3963	0.1898	0.3623	**0.5141**	**0.4785**
FEF	**0.4442**	0.3547	0.3367	**0.4285**	0.2719	0.2636	**0.5234**	**0.5073**
EOL-MP	0.3046	0.2828	0.2464	0.3045	0.2026	0.2933	0.2873	0.3746
LPF	0.3099	0.2694	0.2781	0.3111	0.2143	0.3070	**0.4250**	0.2865

Table 4-5 Total relation matrix (T)

MF = Management Factor; CF = Collaboration Factor; ITF = Information Technology Factor; IF = Infrastructure Factor; PF = Policy Factor; FEF = Financial and Economic Factor; EOL-MP = End-of-life Management Practices; LPF = Logistics Performance Factor.

The relationship $R_i + D_j$ represents the total influence that a criterion exerts and receives in relation to the others The relationship $R_i - D_j$, represents the net influence that a criterion exerts on the set of criteria, that is, the causal relationship Positive values indicate that the critical factor exerts more influence than it receives from other factors. If this value is negative, it indicates that it receives more influence than exerts on the others. Table 4- 6 shows the degrees of prominence and net cause/effect.

Factors	*Ri*	*Dj*	*Ri + Dj*	*Ri - Dj*	Weight	Prominence Ranking	Impact
MF	2.7113	2.6771	5.3885	0.0342	0.1317	4	Cause
CF	2.2549	2.4355	4.6904	-0.1805	0.1147	6	Effect
ITF	2.3910	2.1238	4.5147	0.2672	0.1104	8	Cause
IF	2.1879	2.4834	4.6713	-0.2955	0.1142	7	Effect
PF	3.0788	1.6993	4.7780	1.3795	0.1168	5	Cause
FEF	3.1303	2.3130	5.4432	0.8173	0.1331	3	Cause
EOL-MP	2.2962	3.4345	5.7307	-1.1383	0.1401	1	Effect
LPF	2.4013	3.2852	5.6865	-0.8839	0.139	2	Effect
			40.9033			Threshold value = 0.4083	

Table 4-6 Degree of prominence and net cause/effect values

MF = Management Factor; CF = Collaboration Factor; ITF = Information Technology Factor; IF = Infrastructure Factor; PF = Policy Factor; FEF = Financial and Economic Factor; EOL-MP = End-of-life Management Practices; LPF = Logistics Performance Factor.

These critical factors, listed according to their relative weight and order of classification, are EOL-MP> LPF> FEF> MF > PF> CF> IF> ITF>. Figure 4- 2 shows the interrelationship map, and the relationships that were plotted on the graph were those previously highlighted in bold. In Table 4- 5, the critical factors that exert greater influence were identified from the established threshold value, and it was possible to filter the effects that had an irrelevant importance. The results from Figure 4- 2 are discussed in the next section.

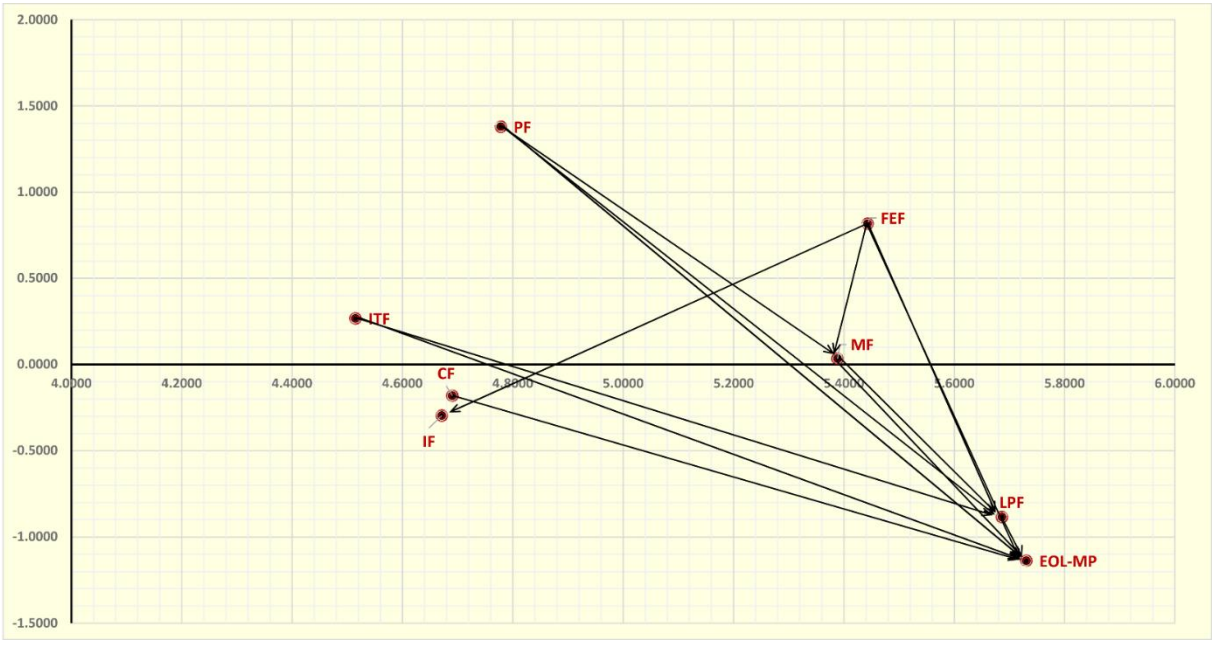

Figure 4-2 Digraph for causal relationship among factors

MF = Management Factor; CF = Collaboration Factor; ITF = Information Technology Factor; IF = Infrastructure Factor; PF = Policy Factor; FEF = Financial and Economic Factor; EOL-MP = End-of-life Management Practices; LPF = Logistics Performance Factor.

4.5 DISCUSSION

Through the Grey-DEMATEL steps, the critical RL implementation factors can be organized into two groups: cause and effect clusters, as can be seen in Table 4- 6 and also in Fig. 4- 2.

The first major cause is “financial and economic factor.” This finding is consistent with the previous studies conducted by Abdulrahman et al. (2014), Agrawal et al. (2016), Kumar and Dixit (2018), Mangla et al. (2016), and Sivakumar et al. (2018). This critical factor represents the economic aspects of RL implementation, including the level of economic resources required to make improvements to the pharmaceutical care information system. Aspects regarding the availability of financial resources for sorting out, collecting, and properly disposing of pharmaceutical waste were also surveyed and presented in Appendix D. Considering the reality of the PCP in which resources are scarce, this can be a major inhibitor, making it difficult to implement pharmaceutical RL. In a study by Chauhan et al. (2018), the lack of funds was considered to exert the greatest influence in RL in the waste disposal industry.

The second major cause is the “management factor.” This critical factor represents the management collaboration with the RL initiative and activities, technical knowledge of the management in motivating and leading the employees in this initiative, and the ability and familiarity of the management with capacity building and training. The number of employees to perform the PCP direct flow is already limited, and the RL flow might be the target of outsourcing strategies. This finding is consistent with Prakash and Barua (2016) which found the lack of management coordination and collaboration as the most important barriers, Abdulrahman et al. (2014) which found the lack of RL management expertise and commitment most impactful, and Agrawal et al. (2016) which found the top management awareness plays an important role in the implementation of RL.

The third major cause is the “policy factor.” This critical factor represents government policies, laws, and legislation on public health waste management, as well as the supervision of waste management practices by the municipal bodies. This finding is consistent with the studies by Kumar and Dixit (2018), Mangla et al. (2016), Sirisawat and Kiatcharoenpol (2018), and Abdulrahman et al. (2014) which found policy and regulatory barriers are the most important barriers to the implementation waste in electrical and electronic equipment management. The difficulties in implementing the sectoral agreement on pharmaceutical RL illustrate the importance of this barrier.

The fourth major cause is “information and technological factor.” This factor

represents the information systems used in the pharmaceutical care for daily activities such as dispensing, relocation, registration of expired drugs, or registration of expired drugs delivered by patients in the public health system. This finding is consistent with the studies conducted by Kumar and Dixit (2018) and Sivakumar et al. (2018), which found the technological factors as one of the main causes of RL implementation.

Our study found two major effects. The first major effect is "EOL-MP." This effect represents the daily actions of professionals in "sorting waste, monitoring the expiry date of drugs" and "stock supplies" and "the practices related to third parties hired to collect and properly dispose of the waste generated within the pharmaceutical health process." The second major effect was the critical factor connected with logistic performance. This effect represents elements related to drug dispensation to the public health patients, drug relocation, when there are cases of excess in health facilities, inventory control, amount of expired medicines, and order delivery times are considered for this critical factor. As the reverse flow process is not structured and, considering the current direct flow, an entirely new group of management practices (EOL-MP) and logistic performance factors (LPF) would be necessary. The collaboration factor (CF), including information exchange and sharing, reliability, and cooperation among the parties involved, are frequently associated with ITF, as demonstrated by Paula et al. (2019); but was not revealed similarly in this study. The last major effect was infrastructure (IF). Considering the overall rankings presented in Table 4-6, CF>IF>ITF are the bottom-ranked factors.

4.5.1 Practical Implications

The Brazilian case of pharmaceutical waste is extraordinary because of the availability of medicine through the public PCP network, a large number of pharmacies and drugstores, judicialization of healthcare, and self-medication. Despite these forms of access to medications, only local return programs run by private companies or institutions, called voluntary delivery points are available to the public without a nationwide return program (Gracia-Vásquez et al., 2015; Pereira et al., 2012 and Thach et al., 2013). In addition, there is a lack of awareness about the impact of medication on the environment when disposed of incorrectly (Glassmeyer et al., 2009; Saravanan & Manoj, 2016; Vellinga et al., 2014).

Another issue that is also related to drugs provided by the public health system is that the major concern is often with drug dispensation only. Pharmacists are often aware of the impact of drugs on the environment, but there is no structure in place for drug collection to

become a reality. As a result, from the perspective of the interviewed public health sector experts, findings of this research may help managers to understand the critical factors that need to be addressed before RL implementation throughout the pharmaceutical health process.

Practicing managers should take into consideration the barriers identified in this study to create alternatives to bypass the financial and economic policies and management causes. Possible outsourcing of PCP RL is an example of a mitigating strategy. Nevertheless, the third-party should be selected carefully, considering its ability to efficiently and effectively collect unwanted medicine. An adequate information technology infrastructure and performance indicators are prerequisites to the successful RL implementation in the PCP.

4.6 CONCLUDING REMARKS

This study was conducted with the PCP cycle in the city of Porto Alegre, Brazil. The study used a grey-DEMATEL approach to consider a group of eight factors and identify the critical barriers to the RL implementation in the PCP. The major factors identified in this study are financial and economic factors (FEF), management factor (MF), policy factor (PF), and information technology factor (ITF).

The contribution of this study is twofold: (1) We identified and prioritized the critical factors to RL implementation in the PCP by considering each step of the SPASDD cycle. Therefore, the municipal PCP coordinator may use this knowledge to formulate strategies and articulate actions to eliminate these barriers, and (2) The results suggests how the PCP sector, which plays an important role in the Brazilian health system, can efficiently and effectively address and eliminate these barriers to the successful implementation of RL in the PCP.

The scope of this investigation is limited to the understanding of the critical factors hindering RL implementation from the perspective of the public health sector experts. Encouraged by the growth of the pharmaceutical industry and the excessive drug consumption worldwide, future endeavors may include studying the problem from an inside points of view within the pharmaceutical industry who supply the PCP with medicines in a broader scope of the pharmaceutical supply chain. Other critical factors may rise from the complex relationship between the pharmaceutical industry and the government agencies in charge of the public health. Subsequently, it is important to confirm the results by means of an analysis of the critical factors equipped with statistical validation empowered by structural equation modeling.

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APPENDIX A - **Portfolio of studies consulted**

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APPENDIX B – Relationship matrix

Matrix of relationships		1					2					3					4					5					6					7					8				
		Management Factor (MF)					Collaboration Factor (CF)					Information Technology Factor (ITF)					Infrastructure Factor (IF)					Policy Factor (PF)					Financial and Economic Factor (FEF)					End-of-Life Management Practices (EOL-MP)					Logistics Performance Factor (LPF)				
		0	1	2	3	4	0	1	2	3	4	0	1	2	3	4	0	1	2	3	4	0	1	2	3	4	0	1	2	3	4	0	1	2	3	4	0	1	2	3	4
1	**MF**	-																																							
2	**CF**						-																																		
3	**ITF**											-																													
4	**IF**																-																								
5	**PF**																					-																			
6	**FEF**																										-														
7	**EOL-MP**																															-									
8	**LPF**																																				-				

APPENDIX C – Expert response matrix

$$E^1 = \begin{bmatrix} 0 & 2 & 2 & 2 & 0 & 2 & 4 & 4 \\ 2 & 0 & 1 & 3 & 0 & 2 & 4 & 3 \\ 2 & 4 & 0 & 3 & 0 & 2 & 3 & 4 \\ 1 & 3 & 1 & 0 & 0 & 2 & 3 & 3 \\ 4 & 4 & 4 & 4 & 0 & 3 & 2 & 3 \\ 3 & 1 & 2 & 4 & 1 & 0 & 4 & 4 \\ 3 & 3 & 3 & 4 & 0 & 4 & 0 & 1 \\ 1 & 2 & 4 & 2 & 2 & 2 & 4 & 0 \end{bmatrix}, \quad E^2 = \begin{bmatrix} 0 & 3 & 2 & 3 & 3 & 3 & 4 & 4 \\ 3 & 0 & 3 & 3 & 3 & 1 & 1 & 2 \\ 2 & 2 & 0 & 4 & 1 & 2 & 2 & 2 \\ 2 & 2 & 4 & 0 & 3 & 3 & 2 & 2 \\ 4 & 3 & 3 & 1 & 0 & 1 & 1 & 1 \\ 2 & 2 & 2 & 3 & 2 & 0 & 1 & 3 \\ 4 & 4 & 3 & 3 & 2 & 2 & 0 & 4 \\ 4 & 3 & 3 & 2 & 0 & 1 & 4 & 0 \end{bmatrix}, \quad E^3 = \begin{bmatrix} 0 & 2 & 3 & 2 & 3 & 3 & 3 & 3 \\ 3 & 0 & 3 & 2 & 2 & 1 & 3 & 3 \\ 3 & 3 & 0 & 3 & 3 & 1 & 3 & 3 \\ 2 & 3 & 1 & 0 & 1 & 1 & 3 & 3 \\ 2 & 3 & 3 & 4 & 0 & 4 & 4 & 4 \\ 4 & 3 & 3 & 4 & 4 & 0 & 3 & 3 \\ 3 & 3 & 3 & 3 & 2 & 2 & 0 & 3 \\ 3 & 2 & 3 & 3 & 2 & 2 & 3 & 0 \end{bmatrix}$$

$$E^4 = \begin{bmatrix} 0 & 3 & 4 & 1 & 1 & 2 & 4 & 4 \\ 3 & 0 & 2 & 0 & 0 & 2 & 4 & 3 \\ 2 & 2 & 0 & 1 & 0 & 2 & 3 & 3 \\ 3 & 2 & 3 & 0 & 0 & 1 & 3 & 3 \\ 3 & 3 & 0 & 3 & 0 & 0 & 3 & 3 \\ 3 & 2 & 2 & 3 & 3 & 0 & 3 & 3 \\ 0 & 2 & 1 & 3 & 0 & 1 & 0 & 4 \\ 0 & 2 & 1 & 1 & 0 & 1 & 3 & 0 \end{bmatrix}, \quad E^5 = \begin{bmatrix} 0 & 1 & 0 & 0 & 0 & 1 & 4 & 4 \\ 3 & 0 & 1 & 0 & 0 & 0 & 4 & 4 \\ 2 & 2 & 0 & 2 & 3 & 1 & 2 & 2 \\ 3 & 1 & 2 & 0 & 0 & 4 & 4 & 4 \\ 1 & 2 & 1 & 2 & 0 & 1 & 4 & 4 \\ 4 & 3 & 4 & 4 & 0 & 0 & 4 & 4 \\ 1 & 3 & 1 & 4 & 4 & 4 & 0 & 4 \\ 1 & 1 & 2 & 4 & 4 & 4 & 4 & 0 \end{bmatrix}, \quad E^6 = \begin{bmatrix} 0 & 3 & 1 & 1 & 1 & 2 & 4 & 4 \\ 1 & 0 & 1 & 2 & 1 & 3 & 3 & 4 \\ 2 & 1 & 0 & 1 & 3 & 3 & 4 & 4 \\ 2 & 3 & 1 & 0 & 2 & 2 & 3 & 4 \\ 3 & 3 & 2 & 4 & 0 & 4 & 4 & 4 \\ 4 & 4 & 3 & 4 & 2 & 0 & 4 & 4 \\ 1 & 0 & 3 & 3 & 3 & 2 & 0 & 1 \\ 0 & 1 & 3 & 4 & 2 & 3 & 1 & 0 \end{bmatrix}$$

$$E^7 = \begin{bmatrix} 0 & 3 & 2 & 2 & 2 & 1 & 3 & 4 \\ 1 & 0 & 3 & 1 & 2 & 2 & 3 & 3 \\ 4 & 3 & 0 & 2 & 4 & 2 & 2 & 2 \\ 2 & 3 & 0 & 0 & 1 & 2 & 4 & 4 \\ 4 & 4 & 3 & 4 & 0 & 4 & 4 & 4 \\ 3 & 2 & 1 & 3 & 4 & 0 & 4 & 4 \\ 2 & 2 & 1 & 2 & 1 & 1 & 0 & 4 \\ 4 & 4 & 3 & 3 & 2 & 4 & 4 & 0 \end{bmatrix}, \quad E^8 = \begin{bmatrix} 0 & 3 & 1 & 3 & 3 & 4 & 4 & 3 \\ 3 & 0 & 3 & 1 & 3 & 3 & 4 & 4 \\ 1 & 2 & 0 & 2 & 1 & 3 & 3 & 3 \\ 2 & 2 & 1 & 0 & 0 & 1 & 1 & 1 \\ 4 & 3 & 3 & 3 & 0 & 3 & 4 & 3 \\ 3 & 2 & 1 & 3 & 1 & 0 & 3 & 3 \\ 2 & 1 & 3 & 3 & 1 & 3 & 0 & 1 \\ 2 & 1 & 3 & 1 & 1 & 3 & 3 & 0 \end{bmatrix}, \quad E^9 = \begin{bmatrix} 0 & 3 & 2 & 4 & 3 & 1 & 3 & 4 \\ 3 & 0 & 4 & 1 & 0 & 3 & 4 & 4 \\ 2 & 3 & 0 & 1 & 3 & 3 & 4 & 2 \\ 4 & 4 & 2 & 0 & 2 & 2 & 3 & 4 \\ 2 & 4 & 4 & 4 & 0 & 4 & 3 & 1 \\ 4 & 2 & 4 & 4 & 2 & 0 & 3 & 1 \\ 1 & 3 & 2 & 1 & 1 & 3 & 0 & 2 \\ 2 & 3 & 2 & 4 & 3 & 3 & 3 & 0 \end{bmatrix}$$

$$E^{10} = \begin{bmatrix} 0 & 4 & 1 & 4 & 1 & 4 & 3 & 3 \\ 4 & 0 & 1 & 2 & 1 & 1 & 3 & 1 \\ 1 & 1 & 0 & 0 & 1 & 3 & 4 & 4 \\ 3 & 2 & 3 & 0 & 1 & 2 & 3 & 3 \\ 4 & 1 & 3 & 3 & 0 & 3 & 4 & 4 \\ 4 & 2 & 3 & 4 & 2 & 0 & 4 & 4 \\ 3 & 3 & 2 & 2 & 2 & 4 & 0 & 4 \\ 3 & 0 & 2 & 2 & 2 & 4 & 4 & 0 \end{bmatrix}, \quad E^{11} = \begin{bmatrix} 0 & 3 & 1 & 3 & 1 & 3 & 0 & 3 \\ 3 & 0 & 1 & 0 & 0 & 1 & 3 & 2 \\ 2 & 1 & 0 & 0 & 0 & 1 & 1 & 1 \\ 3 & 3 & 1 & 0 & 0 & 0 & 2 & 2 \\ 2 & 0 & 0 & 0 & 0 & 3 & 2 & 0 \\ 3 & 1 & 3 & 3 & 0 & 0 & 3 & 3 \\ 3 & 2 & 0 & 0 & 0 & 3 & 0 & 1 \\ 1 & 1 & 1 & 0 & 0 & 3 & 2 & 0 \end{bmatrix}, \quad E^{12} = \begin{bmatrix} 0 & 3 & 2 & 3 & 2 & 2 & 3 & 3 \\ 3 & 0 & 2 & 1 & 1 & 1 & 3 & 3 \\ 3 & 3 & 0 & 1 & 2 & 2 & 3 & 3 \\ 2 & 3 & 1 & 0 & 1 & 1 & 3 & 3 \\ 3 & 3 & 1 & 3 & 0 & 3 & 3 & 3 \\ 3 & 3 & 2 & 3 & 2 & 0 & 3 & 3 \\ 2 & 1 & 1 & 1 & 1 & 2 & 0 & 2 \\ 2 & 1 & 1 & 2 & 1 & 2 & 3 & 0 \end{bmatrix}$$

$$E^{13} = \begin{bmatrix} 0 & 4 & 3 & 1 & 1 & 1 & 3 & 3 \\ 2 & 0 & 2 & 0 & 3 & 2 & 3 & 3 \\ 2 & 4 & 0 & 2 & 3 & 3 & 2 & 3 \\ 3 & 2 & 1 & 0 & 2 & 1 & 2 & 2 \\ 4 & 3 & 2 & 3 & 0 & 1 & 3 & 2 \\ 4 & 1 & 2 & 4 & 1 & 0 & 3 & 3 \\ 2 & 1 & 1 & 2 & 2 & 2 & 0 & 2 \\ 2 & 1 & 1 & 2 & 2 & 2 & 2 & 0 \end{bmatrix}, \quad E^{14} = \begin{bmatrix} 0 & 3 & 2 & 2 & 2 & 2 & 3 & 3 \\ 1 & 0 & 2 & 2 & 1 & 3 & 3 & 3 \\ 2 & 2 & 0 & 0 & 1 & 3 & 3 & 3 \\ 3 & 3 & 2 & 0 & 0 & 1 & 3 & 3 \\ 3 & 3 & 3 & 2 & 0 & 2 & 3 & 2 \\ 3 & 2 & 3 & 3 & 2 & 0 & 3 & 3 \\ 3 & 2 & 3 & 3 & 2 & 3 & 0 & 3 \\ 3 & 2 & 3 & 3 & 1 & 3 & 3 & 0 \end{bmatrix}$$

APPENDIX D – Description of Critical Factors

Factors	Description of critical factors
Management Factor (MF)	• Number of employees to perform RL activities • Expertise and technical knowledge • Employees' motivation • Capacity building and/or training for performing RL activities • Managers' awareness about pharmaceutical RL
Collaboration Factor (CF)	• Information exchange and sharing • Reliability in information exchange • Cooperation to perform RL activities • Collaboration between the parties involved
Information Technology Factor (ITF)	• IT system for dispensing • IT system for relocating • IT system for registering expired drugs • IT system for registering medications delivered to the population treated by the public health system
Infrastructure Factor (IF)	• Physical structure to receive relocated drugs • Physical structure to receive expired drugs and supplies • Physical structure to store expired drugs • Physical structure to store drugs still under use condition returned by patients • Drug transportation from one unit to another
Policy Factor (PF)	• Laws/legislation for RL of medicines and supplies produced by the municipality • Failures in public sector waste management law and regulations • Inspection of RL practices • Economic policies for reducing RL implementation costs in the public sector
Financial and Economic Factor (FEF)	• Financial resource to improve the information system • Financial resource for waste sorting practices • Financial resource for waste collection • Financial resource for waste storage, handling and transportation • Financial resource for disposal of medications and waste
End-of-life Management Practices (EOL-MP)	• Waste sorting practices • Monitoring of the expiry date of medicines and stock supplies • Monitoring of expired medications and supplies • Collection of medications delivered by the population • Third parties that collect pharmaceutical and supply waste generated in healthcare facilities • Third parties that properly dispose of drugs and supplies
Performance Logistics Factor (LPF)	• Dispensing of drugs and supplies to patients • Relocation of excess drugs • Inventory Control • Control of drugs about to expire • Control of the amount of expired medicines in one's own stock • Order Delivery Times

5. ARTIGO 4 - CRITICAL FACTORS IN IMPLEMENTATION OF END-OF-LIFE MANAGEMENT PRACTICES IN PHARMACEUTICAL CARE PROCESS: THE EFFECTS ON LOGISTICS PERFORMANCE

Artigo em análise no Journal of Cleaner Production

Abstract: One of the many difficulties faced by the public health sector involves the correct management of health-care waste and End-of-Life (EOL) medication originating from the population. Within the waste management process, aimed at implementing reverse logistics, several factors may be considered critical and inhibitive and, if left unmanaged, may become obstacles. The aim of this study is to assess the effect that critical factors exercise in the adoption of EOL management practices for medication and determining the effect on logistics performance. Critical factors were then selected based on studies of literature and include the following: Management Factor (MF), Collaboration Factor (CF), Information Technology Factor (ITF), Infrastructure Factor (IF), Policy Factor (PF), Financial and Economic Factor (FEF), End-of-life Management Practices (EOL-MP), and Logistics Performance Factor (LPF). A theoretical model was applied with 67 professionals from public health sector pharmacies. Analysis were conducted using Partial Least Square-Structural Equation Modeling (PLS-SEM) com software WarpPLS 4.0. With the theoretical structural test, eleven of the fifteen hypotheses tested were confirmed. Results show that the critical factors have a positive and direct effect on EOL-MP, with a direct influence on logistics performance. The direct effect of ITF on EOL-MP was also confirmed, though the moderation effect was not. The results of this study contribute to the literature by providing deeper insight for health managers concerning EOL management practices, aimed at providing support EOL pharmaceutical waste management, through reverse logistics in the public health sector.

Keywords: reverse logistics; pharmaceutical care process, critical factors, medicine residues, partial least square

5.1 INTRODUCTION

At a global level, the managers of organizations, governments and society as a whole have been privy to an array of discussions regarding environmental and ecological issues, involving numerous uncertainties with respect to industries and companies (Kannan et al., 2012).

Several studies have highlighted these concerns, with a focus on topics ranging from climate change, experienced around the world, the carbon footprint based on reverse logistics aimed at the adoption of environmental friendly supply chain management (SCM) (Kannan et al., 2012) and touching on the green supply chain management (Govindan et al., 2014; Zhu et al., 2007).

More recently, the world has been coping with the impact of the COVID-19 pandemic, which has been challenging societies on varying levels, including resources, logistics operations, and especially waste management (Sarkis et al. 2020). And this is especially prevalent in the terms of improper handling of health-care waste, which facilitates the spread of the virus. Meanwhile, direct and reverse logistics operations for medication at a Pharmaceutical Assistance level have found themselves completely overwhelmed during this pandemic.

In an attempt to trigger the least environmental impact for future generations, issues like Reverse Logistics (RL) and principally the transition towards a Circular Economy (CE) in association with the arrival of Industry 4.0 (I4.0) are treated as emerging and which permit a disruptive transformation of organizational activities by means of several technological innovations (Kouhizadeh, et al. 2019). The exploration of emerging technologies in the pharmaceutical industry 4.0 is based on the premise of creating sustainable value through agile, disruptive and intelligent operations, in the sense that a sustainable pharmaceutical supply chain offers the conditions to correspond to pharmaceutical product operations and management throughout the entire life cycle (Ding, 2018).

However, other studies have also been looked at, with a focus on subsidizing sustainable management tools for companies and also for the industrial sectors (Fischer and Pascucci, 2017; Viegas et al., 2019) aimed at adding value to materials and products, maximizing the life cycle, regeneration of the end-of-life and, thereby, introducing precepts of value recovery (Kouhizadeh, et al. 2019).

Generally speaking, RL activities are now used widely for a variety of reasons, such as a means of product recovery, due to environmental issues. They are dealt with according to levels of importance, and on a wider scale, by existing environmental legislation and regulations in countries, through raising global awareness on the consequence of exhausted resources and a degraded environment (Abdulrahman et al., 2014; Kannan et al., 2012). It is also considered a competitive edge, influencing the economic, social and environmental performance of organizations (Ali et al., 2018; Govindan et al., 2015).

Considering the high rates of medicine consumption around the world as clearly shown by Vellinga et al. (2014) and market expectations that the global pharmaceutical industry will be worth 1.57 trillion dollars by 2023 (Navadhi, 2019). Meanwhile, the Pharmaceutical Supply Chain (PSC) is seen as largely responsible for considerable environmental impacts(Viegas et al., 2019), and considered one of the most complex and harmful (Abbas and Farooquie, 2020). This study examines waste management within the health-care sector, and more specifically the management of pharmaceutical waste.

It is understood that one of the forms of contaminating the environment is through the incorrect disposal of medicine by users, which ends up generating a high financial cost for national government (Glassmeyer et al., 2009; Langley et al., 2005). Not to mention the environmental impact to which human beings and aquatic life are exposed (Daughton and Ternes, 1999; Ekedahl, 2007). Medicine that is not wholly consumed represents a huge source

of waste in terms of volume and cost to health systems around the world (Gyanendra et al., 2011; Toh and Chew, 2017), and also forming a major threat to the supply chains of developing nations (Nakyanzi et al., 2010). Factors associated to high costs, time consumption, a lack of experience and training of those involved, scarcity of commercial incentives, collaborations and ineffective coordination are all considered obstacles to the entire PSC (Ding, 2018).

Despite a stated conceptual transition from RL to a CE (Fischer and Pascucci, 2017; Genovese et al., 2017; Guarnieri et al., 2020), very often managers from companies, industry and also the public sector are unable to implement or even manager RL efficiently, and an attempt to promote the practices end up failing or coming too late (De Sousa Jabbour et al., 2014; Tavana et al., 2016). Above all, there are different factors that can be considered as critical to the implementation of RL and can very often become barriers to the process (Abdulrahman et al., 2014).

Brazilian Law n. 12.305 established the National Policy on Solid Waste (PNRS, Portuguese abbreviation), based on the premise of greater shared responsibility among waste generators, including: manufacturers, importers, distributors, traders, citizens and those overseeing urban solid waste management(Brazilian Policy of Solid Waste, 2010).

RDC 222/2018 (Brasil, 2018) is of particular importance, assisting managers to articulate guidelines for the creation of a management plan for waste generated by the health-care sector in each Brazilian municipality. However, as point out by Pereira et al. (2012), in Brazil, a sectorial agreement is still needed, with clear guidelines for all those involved in the supply chain, including each entity, as is described in the RL concept. A lack of disposal standardization was also highlighted by Tong et al. (2011), as many countries still have no protocols for disposing of medicine.

Given the importance of managing the understanding of critical factors in the implementation of EOL management practices for medication, this study seeks to fill a critical gap in the literature, developing a theoretical model to understand critical factors in RL implementation, supported by the theory of resource-based view (RBV).

Based on this, this study is justified by several different reasons:

- The 17 sustainable development goals cited by the UN must be fulfilled by nations (United Nations, 2015). Considering the idiosyncrasies, especially those inherent to each country and each sector, many barriers must still be overcome to ensure successful implementation of RL.

- There is a conceptual transition from reverse logistics to a circular economy, which presents a second life for products;
- Complexity of RL implementation in the pharmaceutical sector;
- Studies by the public health sector and/or distribution of medication are scarce or multifaceted.
- The global crisis linked to the COVID-19 pandemic, especially prevalent within health-care residue management and chiefly the transformation to a sustainable system, and;
- A lack of quantitative studies geared specifically towards the pharmaceutical sector.

The following factors were identified based on a theoretical review and categorized into eight dimensions, namely: Management Factor (MF), Collaboration Factor (CF), Information Technology Factor (ITF), Infrastructure Factor (IF), Policy Factor (PF), Financial and Economic Factor (FEF), End-of-life - Management Practices (EOL-MP), and Logistics Performance Factor (LPF). These are used to present the following research question (RQ) for this study:

RQ: How do the critical factors influence the implementation of End-of-Life management practice for medication, and how said management be related to Pharmaceutical Care Process logistics performance?

The variables included in the Logistics Performance Factor (LPF) and used for this study cover three logistics cycles: (*i*) direct logistics: referring to the distribution of medication; (*ii*) reallocation logistics: medication and inputs that are still within their valid date and that are part of a redistribution and/or reallocation process from one unit with a lower monthly consumption to a unit with a higher consumption. The goal of reallocation is to prevent loss of medicine due to expiry and depleted stocks and; *(iii)* reverse logistics: medication at the end of its useful life.

Thus, the aim of this study is to assess the influence of critical factors in the adoption of End-of-Life management practices for medication and to determine the effect on Pharmaceutical Care Process logistics performance.

The contributions of this study develop into two perspectives. Once the critical factors are known for the implementation of EOL-MP and its influence on Logistics Performance, this study further contributes practically with the presentation of an important tool for decision making among health-care managers; the theoretical contribution comes by the way of

confirming the validity and quality of the represented model, considering a scenario underrepresented in scientific studies.

This study is organized into 5 sections. Following the Introduction (Section 5.1), the theoretical model and that for developing the hypothesis is presented (Section 5.2). Methodological details are provided in (Section 5.3), with the results and analyses in (Section 5.4). Finally, (Section 5.5) presents the main conclusions, contributions and theoretical and practical implications.

5.2 LITERATURE REVIEW

The implementation of EOL practices, aimed at reverse logistics, involve several stakeholders that run the system. This situation is particularly evident for external practices, as a specification for suppliers within environmental requirements, auditing of supplier environmental management systems, ecological design and handling products returned by clients (Sarkis et al., 2011).

To Govindan and Bouzon (2018), the implementation and management of RL are dependent on the support and participation of the main parties interested in shared responsibility for the supply chain through the reverse flow of EOL products and in resources that will be necessary for RL operations.

Nevertheless, the literature suggests the importance of considering a theoretical base to explain issues related to product recovery (Kumar and Dixit, 2018). From this perspective, certain studies employ different theories, such as, for example, the theory of economic transaction costs, institutional theory and stakeholder theory, among others. A study by (Lau and Wang, 2009) suggests a combination of these theories to help companies select a system for managing the recovery of EOL products. This study applied the resources-based view theory, presented in section 5.2.1.

5.2.1 Resource-Based View Theory (RBV)

The theory of a resource-based view allows for an assessment of the structure and behaviour of a company (Grant, 1996). The theory suggests that companies can generate above average rates of return and obtain sustainable competitive results over its competition when well supported by its competencies and essential resources at an organizational level - tangible assets (Barney, 1991).

According to the RBV outlook, a company is seen as an exclusive package of characteristic resources and capacities, wherein the main task of management is to maximize value through the ideal implementation of existing resources and capacities, while developing the company's resource base for the future (Barney, 2001; Grant, 1996).

The theory assumes that the resources and capacities of organizations are valuable and difficult to copy, as they provide the leading sources of sustainable competitive edges (Barney, 2001). Resources are considered assets, capacities, company attributes, organizational processes, expertise and information that allows a company to conceive and implement strategies with the aim of improving competitiveness (Barney, 2001; Sarkis et al., 2011).

According to this view, a company should be concerned not only with profitability in the present and mid-term growth, but also its future position and the source of its competitive edge. This view calls for explicit strategies about how the company will compete when its current strategy configuration is copied or becomes obsolete (Hart, 1995).

Barney (2001) suggests that resources should be heterogeneous among companies and that some valuable resources are rare, difficult to imitate or not replaceable, with companies having specific essential resources. Supported by the theory of contingent resource-based view, Bag and Gupta (2019) note that the availability of green human capital positively influences the adoption of reverse logistics and performance in remanufacturing operations.

5.2.2 Critical Factors in Implementation of Reverse Logistics in Pharmaceutical Care Process (CFIRL-PCP)

Each sector has a specific factor considered critical and that needs to be overcome to ensure the effective implementation of reverse logistics. Examples include studies by Erol et al., (2010); Kumar and Dixit, (2018) involving the electric and electronics sector, mentioning that the lack of an information system prevents the attainment of scales of economy, in such a way that it significantly reduces the value captured through the recovery of products, not to mention political and regulatory barriers, a lack of legislation and economic incentive. Similarly, a lack of expertise or infrastructure are also considered critical and mentioned by Massoud et al. (2015).

Within the medicine sector, Yang, Doshi and Mason (2015) mention that a lack of information and expertise concerning environmental impacts, a lack of more conservative medication prescriptions and not means of safe disposal are also considered hurdles to the management of pharmaceutical residues.

Based on a literature studies, to follow is a brief presentation of the eight critical factors mentioned previously (section 5.1).

5.2.2.1 Management Factor (MF)

Critical factors that involve the management factor are those regarding managerial aspects and/or the behavior of senior management in the implementation of RL activities. In many cases, a lack of expertise among managers regarding the benefits generated (Sirisawat and Kiatcharoenpol, 2018) or a lack of interest among senior management may become a major barrier to the implementation of RL (Sirisawat and Kiatcharoenpol, 2018).

Aspects related to technical knowledge and/or expertise among employees and strategic planning are also cited by (Massoud et al., 2015; Muduli et al., 2013; Ravi et al., 2005). Literature further cites as an important element the number of employees for executing activities, as, oftentimes, employees end up with a higher number of activities to perform (El Baz et al., 2018; Xia et al., 2015).

To Sarkis et al. (2011), the interdependence of supply chain partners, as well as the quality and efficiency of their collaboration determines the success of the implementation of a green supply chain and, as such, cannot be ignored. The following hypotheses are based on this context:

- Hypothesis 1a. Management Factor has a direct effect in EOL-MP.
- Hypothesis 1b. Management Factor has a direct effect in Logistics Performance Factor.
- Hypothesis 1c. Management Factor has a direct effect in Infrastructure Factor.

5.2.2.2 Collaboration Factor (CF)

In direct logistics, organizations need to create a collaborative environment among the different links or levels of the supply chain, and collaboration becomes essential to the successful performance of the supply chain (Chen et al., 2007). To Luthra et al., (2020) and Mahadevan (2019), companies require solid coordination and collaboration among members of the supply chain and to extend these principles to the reverse flow of products.

Said collaboration noted within the supply chain is highly critical and may contribute to interorganizational dynamics, bolstering the capacity to absorb knowledge, share information, structure solutions and driving the implementation of activities around problems related to environmental issues, cleaner production and reverse logistics (Van Hoof and Thiell, 2014).

Wagner et al. (2011) point out that collaboration can be looked at as an intangible resource for organizations and may present positive impacts on organizational performance. As such, greater attention is being paid to the creation of ways to encourage supply chain operators to work collaboratively, in production, logistics and other operations, to attain ecological objectives, as RL processes based on a collaborative network will increase performance and productivity for reverse flow operations (Mahadevan, 2019; Ramanathan et al., 2014). The following hypotheses are based on the presented context:

- Hypothesis 2. Collaboration Factor has a direct effect in EOL-MP.

5.2.2.3 Information Technology Factor (ITF)

Within the scope of technological innovations resulting from I4.0, emerging technologies are being explored in the hopes of creating sustainable value, allowing companies to gain a competitive edge and make the direct and reverse supply chain more sustainable throughout the product life cycle (Ding, 2018).

Certain pieces of technology have been highlighted in the fields of RL and CE, such as the use of blockchain technology for reliable and secure information tracking. And the automation provided by blockchain can effectively leverage circular economy initiatives (Kouhizadeh et al. 2019).

Within the health-care environment technological tools that bolster automation are of the utmost importance to the performance of daily tasks, reducing errors and costs. IT is a major ally and has eliminated the need for manual transcription of medication prescriptions; fostered greater speed in health-care; identification of doses prescribed by doctors; medicine labeling containing all necessary identification, practicality and safety in optic verification based on barcodes for requested and dispensed medicine (Serafim et al., 2010).

When complying with issues related to RL, companies that invest in improving their competencies and technological abilities consequentially enjoy direct and positive effects on direct and reverse logistics performance (Morgan et al., 2016). And, generally speaking, a high level of innovation among organizations allows for the creation of the right conditions to improve their capacity to respond to sustainability related issues (García-Sánchez et al., 2019; Morgan et al., 2016).

In studies such as those by Chauhan et al. (2016; Mathiyazhagan et al., 2013; Pérez-Belis et al., 2015), one notes just how the lack of technology can trigger difficulties in the implementation of RL. In a study by Costa and Guarnieri (2018), the main difficulties are linked

to limitations in purchase management software as well as inventory. The following hypotheses are based on this context:

- Hypothesis 3a. Information Technology Factor has a direct effect in EOL-MP.
- Hypothesis 3b. Information Technology Factor has a moderating effect on the relationship between Collaboration and EOL-MP.
- Hypothesis 3c. Information Technology Factor has a moderating effect on the relationship between Management Factor and EOL-MP.
- Hypothesis 3d. Information Technology Factor has a direct effect in Collaboration Factor.
- Hypothesis 3e. Information Technology Factor has a direct effect in Management Factor.

5.2.2.4 Infrastructure Factor (IF)

This topic considers physical aspects and storage, with one of the critical points in the execution of RL activities is related to infrastructure. Organizational managers must provide a suitable location to temporarily store EOL products that are to be returned to their point of origin. Studies point out that a lack of infrastructure may present a barrier to the RL implementation process (Kumar and Dixit, 2018; Massoud et al., 2015; Meyer et al., 2017; Prakash and Barua, 2015).

The reality faced by many public and private organizations is that they need to find specific third-party companies, according to the characteristics of the product, in order to correctly recycle and process EOL products (Sivakumar et al., 2018). This also ends up generating transport costs for organizations and, very often, the hurdle of finding third-party logistics providers (3PLs) ends up discouraging this practice (Prakash and Barua, 2015; Sivakumar et al., 2018). The following hypotheses are based on the presented context:

- Hypothesis 4. Infrastructure Factor has a direct effect in EOL-MP.

5.2.2.5 Politics Factor (PF)

From a regulatory perspective, political issues are fundamental, given that based on political guidelines, regulations and laws, managers are charged with articulating and responding to legal issues and those related to protecting the environment. Authors like Abdulrahman et al. (2014), Govindan et al., (2016) and Luthra et al., (2011) highlight a lack of government support for economic policies that include EOL products, complicating the RL implementation process.

Aquino et al. (2018) There is also concern surrounding reverse logistics for medication, as Brazil still has no specific legislation regarding disposal by end users and the resulting environmental contamination from expired or obsolete medication is growing steadily. The following hypotheses are based on this context:

- Hypothesis 5a. Politic Factor has a direct effect in EOL-MP.
- Hypothesis 5b. Politic Factor has a direct effect in Management Factor.

5.2.2.6 Financial and Economic Factor (FEF)

The Financial and Economic Factor refers to economic and financial issues that often interfere in reverse logistics implementation. A lack of financial resources is mentioned by Chileshe et al. (2015; Govindan et al., 2014; Shaharudin et al., 2015) as being an important issue in RL implementation.

In general, organizations require financial resources to execute activities like: training teams to oversee EOL management activities; provide computerized systems to manage returns. Abdulrahman et al. (2014) point out that a lack of funds for return monitoring systems is a critical barrier to the RL implementation process. Given the setup of public institutions, a collaborative relationship with green suppliers is often limited by restrictive budgets (Costa and Guarnieri, 2018). The following hypotheses are based on this context:

- Hypothesis 6a. Financial and Economic Factor has a direct effect in EOL-MP.
- Hypothesis 6b. Financial and Economic Factor has a direct effect in Infrastructure Factor.

5.2.2.7 End-of-life - Management Practices (EOL-MP)

Despite the major importance of correct practices for pharmaceutical residue, there is very little awareness regarding the right ways of disposing of medicines (Vellinga et al., 2014). Abbas and Farooquie (2018) posit that it is necessary to prioritize attention to the return flow of medicine to the point of origin, with the aim of recovering value but, also, to ensure suitable disposal.

According to Viegas et al. (2019), most studies on reverse flow do not cover the diverse EOL-MP routes and present restrictions on how supply chain processes and operations affect reverse flows. A more sustainable pharmaceutical supply chain (PSC) must be implemented to

correspond to future operations and management of pharmaceutical products during the entire life cycle (Ding, 2018).

The EOL-MP construct was defined based on a series of elements from the literature, with contemplations including the practices used to monitor medicine expiry dates; communication and delivery of expired medicines; requests for the collection of expired medication; inputs, and; separation of medication that is returned by the population.

5.2.2.8 Logistics Performance Factor (LPF)

The process of caring for patients in the health-care sector involves a series of operational activities, including the management of inventory and distributions of supplies to points of care. Storage and distribution operations for items throughout the entire health-care supply chain are of the utmost importance to efficient and quality care (Moons et al., 2019).

There is constant pressure to increase quality and productivity without having to increase investments in organizations. Logistics planning, especially in the pharmaceutical sector, is fundamental to ensuring the supply of medication and medical equipment. This make the use of a rational medicine distribution system imperative (Serafim et al., 2010).

The capacity to offer efficient health-care services with acceptable performance, catering to the needs of society, depends on managerial capacity and the coordination of logistics activities, included within a health-care system, in a systemic and effective manner (La Forgia and Couttolenc, 2008; Longaray et al., 2018).

Despite patient care being the primary concern within health-care sectors, activities related to logistics are critical to ensuring supply security, availability and accessibility. The interaction among the clinical, material and information flows are now essential to improved operational performance for logistics processes and to obtaining an integrated supply chain (Moons et al., 2019).

Correct and rational distribution must guarantee that the delivery process is efficient, based on a pre-established flow chart, preventing delays and ensuring products will reach users in the correct volumes and with the desired quality (Moons et al., 2019). An efficient information and control system means that distribution is monitored constantly, providing updated information at any time regarding the “physical and financial” position of inventory, the volumes received and distributed, consumption and demand data for each product, maximum and minimum stock, replacement points, volumes acquired and other information necessary to optimal management (Serafim et al., 2010).

The LPF construct considered variables relative to: medicine and input delivery time to patient; control of checking and receiving in the material management system for medication and input orders; time required for reallocating surplus medication and inputs; reduction in medication and input loss due to expiration; control of medicine and input expiration dates in stock; control of medication and inputs not in stock; control of medication and inputs close to their expiration dates; delivery times for medication and inputs orders through the medication dispensary; suitable storage of medication and inputs.

The following hypotheses are based on this context:

- Hypothesis 7. EOL-MP has a direct effect in Logistics Performance Factor.

To follow, Table 5-1 presents the constructs reported in the literature and adapted to the work process identified in the Pharmaceutical Care Process (PCP).

Construct	ID	Description
Management Factor (MF)	MF1	Workers in sufficient numbers to perform RL activities for medication and inputs
	MF2	Workers with technical knowledge/expertise involving RL for medication and inputs
	MF3	Workers with the capacities and/or trained with regards to separating expired medication and inputs
	MF4	Workers committed to/motivated by issues related to pharmaceuticals and input waste management
	MF5	Capacity building and/or training for workers on separation practices for expired medication and inputs
	MF6	Coordination support for RL involving medication and inputs
	MF7	Coordination support to reallocate surplus medication and inputs among basic health units
	MF8	Support partner pharmaceutical companies for RL involving medication and inputs
	MF9	Support partner pharmaceutical companies in reallocating surplus medication and inputs among units
	MF10	Support from NDM-CAF for RL involving medication and inputs
	MF11	Support from NDM-CAF to reallocate surplus medication and inputs among basic health units
Collaboration Factor (CF)	CF1	Sharing of information
	CF2	Reliability in sharing information
	CF3	Collaboration among workers involving RL activities for medication and inputs
	CF4	Coordination collaboration for RL activities involving medication and inputs
	CF5	Collaboration of partner pharmaceutical companies in reallocating surplus pharmaceuticals
	CF6	Collaboration of partner pharmaceutical companies for returning expired medication or sanitary collection.
Information Technology Factor (ITF)	ITF1	Deliver medication to patients using the DIS system
	ITF2	Reallocate surplus medication to partner pharmaceutical companies using the GMAT system
	ITF3	Monitor medication expiry dates via the GMAT system
	ITF4	Generate information on expired medication and input volumes via the GMAT system
	ITF5	Return expired medication to the NDM/CAF in (SOP 10) via the GMAT system
	ITF6	Return medication for sanitary waste collection NDM/CAF in *(SOP 10)* via the GMAT system
Infrastructure Factor (IF)	IF1	Receive reallocated medication in a usable condition
	IF2	Store expired medication or inputs delivered by the population
	IF3	Temporarily store expired medication or that no longer suited to use, which shall be returned to NDM/CAF
	IF4	Transport medication in conditions suitable for use from one unit to another, planned by partner pharmaceutical companies
	IF5	Store medication in conditions suited to use which has been returned by patients that left my stock
Politic Factor (PF)	PF1	I know pertinent health-care solid waste legislation
	PF2	I fulfil the task of raising awareness among the population regarding rational use of medication and inputs
	PF3	I fulfil the task of raising awareness among the population regarding disposal of medication and inputs
	PF4	There are flaws in the law/regulations regarding health-care solid waste in the public sector
	PF5	Auditing occurs with regards to correctly managing health-care solid waste generated by the city
	PF6	There are public policies for the implementation of reverse logistics for medication in the public health-care sector
	FEF1	Make improvements to the GMAT system

Financial and Economic Factor (FEF)	FEF2	Hire outsourced services to ensure correct collection and disposal of all waste generated
	FEF3	Tender the purchase of materials for permanent education actions (trash cans, adhesives with symbols, plastic bags, etc.)
	FEF4	Store and handle waste until it is sent to the NDM-CAF
	FEF5	Improve medication and input storage areas
	FEF6	Improve medication and input separation areas
	FEF7	Improve medication and input delivery areas
EOL Management Practices (EOL-MP)	EOL-MP1	Monitoring the validity of medication and inputs in stock via the GMAT system
	EOL-MP2	Notification of expired medication sent to partner pharmaceutical companies and the NDM-CAF
	EOL-MP3	Request the collection of expired medication and inputs from partner pharmaceutical companies/NDM-CAF
	EOL-MP4	Delivery of expired medication to NDM-CAF employees
	EOL-MP5	Separation of medication and inputs returned by the population
Logistics Performance Factor (LPF)	LPF1	Delivery time for medication and inputs to patients
	LPF2	Check and receipt control in the GMAT system for medication and input orders
	LPF3	Time required for reallocation of surplus medication and inputs
	LPF4	Reduction in medication and input loss due to expiration
	LPF5	Expiry control of medication and inputs in stock
	LPF6	Control of medication and inputs not in stock
	LPF7	Control of medication and inputs close to expiry
	LPF8	Order delivery time for medication and inputs by NDM-CAF
	LPF9	Suitable storage of medication and inputs

Table 5-1 Constructs and variables

Note: GMAT= Material Management System; DIS= Medicine Dispensing System; NDM/CAF= Medicine Distribution Center of the Pharmaceutical Assistance Coordination; SOP=Standard Operation Procedure.

5.3 METHOD

5.3.1 Constructs and Hypotheses

To follow, Figure 5-1 presents the constructs together with the study hypotheses.

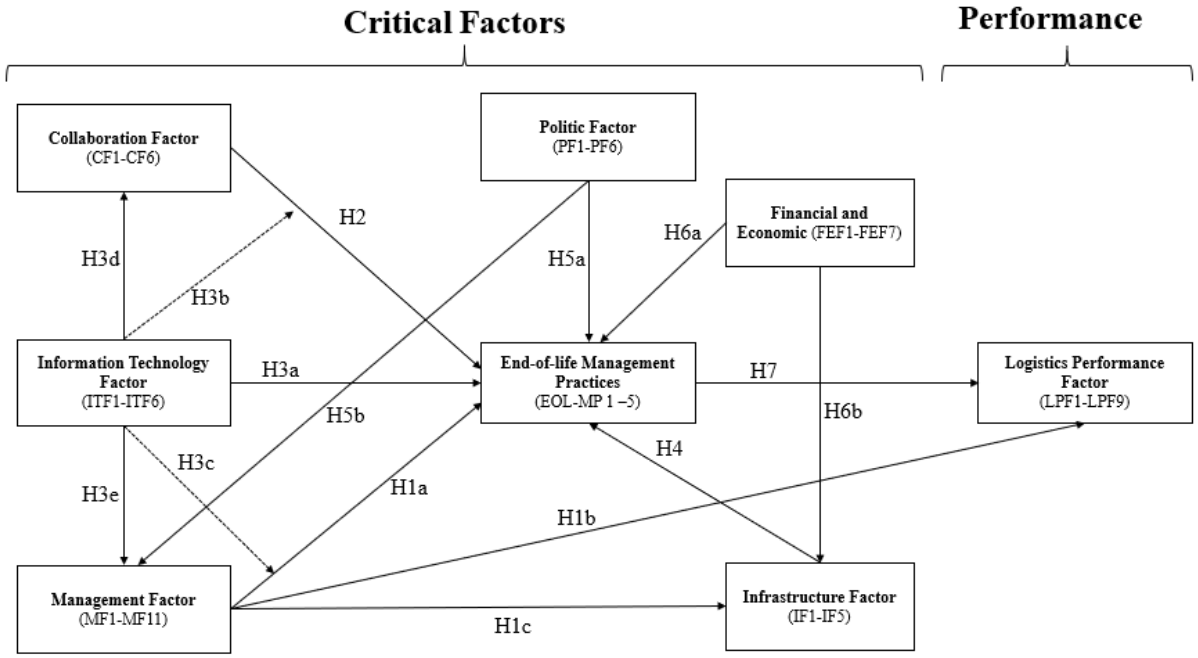

Figure 5-1 Model propose to this research, with direct and moderate effects
Note: continuous line = direct effect; broken line = moderator effect

5.3.2 Data collection instrument

Aimed at understanding the critical factors in waste management and geared towards reverse logistics implementation for medication in the Pharmaceutical Care Process (PCP), the construct variables and hypotheses created for the study were developed based on previously consulted literature.

Initially, the variables studied and later validated with the five principal managers involved in the process and three external specialists. After adjusting the items according to the suggestions, an online form was made available using the Google Forms® platform. Each respondent had the option of attributing the level of agreement with each statement presented, considering a 7-point Likert scale (1= totally disagree and 7= totally agree).

The form, containing 55 items (Table 1), was available for approximately four months, in order to allow pharmaceutical professionals to respond. Initially, the research instrument was planned to be responded by 145 health-care units in the city of Porto Alegre, in Brazil. However, due to political issues that involved outsourcing health unit work teams, the number of respondents was restricted to just 10 local district pharmacies in the city. The reason behind the

decisions to not involve the new work team as possible respondents was due to the newly outsourced team not possessing sufficient expertise and experience in the activities in order to complete the form, which would jeopardize the results obtained.

As such, the form was adjusted once again and sent to other municipalities in the region, with both centralized and non-centralized dispensary characteristics. This included 68 additional respondents, totalling 78 in all. Of these, 67 were completed and the others were removed. Table 5-2 presents the profile of respondents.

Characteristics	Frequency (f)	Percentage (%)
Gender		
Male	10	14,9
Female	57	85,1
Experience		
De 3 a 6 meses	4	6
De 6 meses a 1 ano	5	7,5
De 1 a 4 anos	16	23,9
De 5 a 9 anos	25	37,3
De 10 a 14 anos	8	11,9
De 15 a 20 anos	5	7,5
Mais de 20 anos	4	6
Age		
21-30	15	22,4
31-40	36	53,7
41-50	14	20,9
>50	2	3
Education		
Graduação	61	91
Especialização	3	4,5
Mestrado	3	4,5

Table 5-2 Profile of respondents

Despite being low, the number of respondents is not considered a limiting factor to the study. A similar number of respondents was previously identified in the study by Chileshe et al., (2018) with 48 respondents.

5.4 RESULTS

This study employed Structural Equation Modeling (SEM) using Partial Least Squares (PLS) and the software WarpPLS 6.0 (Kock, 2013). The PLS statistic is justified as it is a model built on the theoretical framework consulted and the items from each construct were considered reflexive and with a restricted sample.

The model was initially estimated to include 55 items. Following an analysis of factor loads for the items, four were excluded for presenting a factor loading below 0.5, as recommended by Hair et al. (2017).

The items removed were the following: In the ITF construct, the *"ITF1 - Deliver medication to patients via DIS"* item was excluded. In the PF construct, *"PF4 - Flaws in law/regulations regarding solid health-care waste in the public sector"* item was excluded. In the EOL- MP construct the *"EOL-MP4 - Deliver expired medication to NDM-CAF employees"* item was excluded. In the LPF construct, the *"LPF1 - Delivery time for medication and inputs to patients"* item was excluded.

Table 5-3 presents the results for convergent validity, following the removal of the aforementioned items. All items maintained, present factor loading higher than the recommended 0.5. To assess internal consistency, Average Variance Extracted (AVE) and Composite Reliability (CR) were used as parameters. To be representative, this index must be higher than 0.7 and the values for Cronbach's Alpha to estimate measurement error and true composite weights. Thus, as can be seen in Table 5-3, all the indexes were satisfactory.

Constructs	Item	Cross Loading	SE	AVE	CR	Cronbach's Alpha
Management Factor (MF)	MF1	0.770	0.095	0.740	0.969	0.964
	MF2	0.839	0.092			
	MF3	0.814	0.093			
	MF4	0.811	0.093			
	MF5	0.727	0.096			
	MF6	0.892	0.091			
	MF7	**0.938**	**0.089**			
	MF8	**0.932**	**0.090**			
	MF9	0.899	0.091			
	MF10	**0.929**	**0.090**			
	MF11	0.883	0.091			
Collaboration Factor (CF)	**CF1**	**0.782**	**0.094**	0.573	0.889	0.849
	CF2	0.717	0.096			
	CF3	0.697	0.097			
	CF4	0.704	0.097			
	CF5	**0.832**	**0.093**			
	CF6	**0.798**	**0.094**			
Information Technology Factor (ITF)	ITF2	0.638	0.099	0.539	0.853	0.783
	ITF3	**0.735**	**0.096**			
	ITF4	0.683	0.097			
	ITF5	**0.834**	**0.093**			
	ITF6	**0.766**	**0.095**			
Infrastructure Factor (IF)	**IF1**	**0.824**	**0.093**	0.669	0.910	0.875
	IF2	**0.871**	**0.091**			
	IF3	0.809	0.093			
	IF4	**0.856**	**0.092**			
	IF5	0.722	0.096			
Politics Factor (PF)	**PF1**	**0.778**	**0.094**	0.582	0.874	0.820
	PF2	**0.794**	**0.094**			
	PF3	0.763	0.095			
	PF5	0.686	0.097			
	PF6	**0.789**	**0.094**			
Financial and Economic Factor (FEF)	FEF1	0.849	0.092	0.741	0.952	0.941
	FEF2	0.773	0.095			
	FEF3	0.886	0.091			
	FEF4	0.752	0.095			
	FEF5	**0.919**	**0.090**			
	FEF6	**0.923**	**0.090**			
	FEF7	**0.906**	**0.090**			
EOU/EOL Management Practices	**EOL-MP1**	**0.742**	**0.095**	0.643	0.876	0.809
	EOL-MP2	**0.877**	**0.091**			
	EOL-MP3	**0.898**	**0.091**			
	EOL-MP5	0.666	0.098			
	LPF2	0.743	0.095	0.612	0.925	0.905

Logistics Performance Factor (LPF)	LPF3	0.792	0.094
	LPF4	0.806	0.093
	LPF5	**0.910**	**0.090**
	LPF6	**0.851**	**0.092**
	LPF7	**0.891**	**0.091**
	LPF8	0.526	0.103
	LPF9	0.667	0.098

Table 5-3 Convergent validity and internal consistency reliability results
Notes: Loadings are unrotated and cross-loadings are oblique-rotated. SEs and P values are for loadings.

In each construct, when analyzing the item with the higher factor loading highlighted in bold in (Table 5-3), there are certain findings: in the Management Factor construct, items with the higher factor loading include “MF7 - Support from COORAF in reallocating surplus medication and inputs among units”, “MF8 - Support from partner pharmaceutical companies for RL involving medication and inputs”, “MF10 - Support from NDM-CAF for RL involving medication and inputs”.

In the Collaboration Factor construct, items with higher factor loading were “CF5 - Collaboration of partner pharmaceutical companies in reallocating surplus medication”, “CF6 - Collaboration of pharmaceutical companies in returning expired medication or for sanitary collection”, “CF1 - Sharing of information”.

In the Information Technology Factor construct, items with a higher factor loading included: “ITF5 - Return expired medication to the NDM-CAF in (SOP 10) via GMAT”, “ITF6 - Return medication for sanitary collection in (SOP 10) via GMAT” and “ITF3 - Monitor medication expiry dates via the GMAT”.

For the Infrastructure Factor construct, items with a higher factor loading included: “IF2 - Store expired medication or inputs delivered by the population”, “IF4 - Transport medication in conditions suitable for use from one unit to another, planned by partner pharmaceutical companies” and “IF1 - Receive reallocated medication in a usable condition”.

For the Politics Factor construct, items with a higher factor loading included: “PF2 - I fulfil the task of raising awareness among the population regarding rational use of medication and inputs”, “PF6 - There are public policies for the implementation of reverse logistics for medication in the public health-care sector” and “PF1 - I know pertinent health-care solid waste legislation”.

For the Financial and Economic Factor construct, items with a higher factor loading included: “FEF6 - Improve medication and input separation areas”, “FEF5 - Improve medication and input storage areas”, “FEF7 - Improve medication and input delivery areas”

For the EOU/EOL Management Practices construct, items with a higher factor loading included: “EOL-MP3 - Request the collection of expired medication and inputs from partner pharmaceutical companies/NDM-CAF”, “EOL-MP2 - Notification of expired medication sent to partner pharmaceutical companies and the NDM-CAF” and “EOL-MP1 - Monitoring the validity of medication and inputs in stock via the GMAT system”.

In the Logistics Performance Factor construct, items with a higher factor loading included: “LPF5 - Expiry control of medication and inputs in stock”, “LPF7 - Control of medication and inputs close to expiry” and “LPF6 - Control of medication and inputs not in stock”.

Table 5-4 presents the correlation results for discriminant validity. In the diagonal (**in bold**) the values show that the square root of the average variances extracted (AVEs) are higher than the other correlation values, in conformity with that recommended in the literature.

	MF	CF	ITF	IF	PF	FEF	EOL-MP	LPF
MF	**(0.860)**							
CF	0.652	**(0.757)**						
ITF	0.457	0.426	**(0.734)**					
IF	0.528	0.434	0.314	**(0.818)**				
PF	0.667	0.486	0.458	0.529	**(0.763)**			
FEF	0.482	0.443	0.428	0.611	0.415	**(0.861)**		
EOL-MP	0.618	0.565	0.513	0.511	0.652	0.565	**(0.802)**	
LPF	0.509	0.536	0.606	0.363	0.510	0.494	0.650	**(0.782)**

Table 5-4 Results of discriminatory validity
Note: Square roots of AVEs are shown on diagonal
MF = Management Factor; CF = Collaboration Factor; ITF = Information Technology Factor; IF = Infrastructure Factor; PF = Policy Factor; FEF = Financial and Economic Factor; EOL-MP = End-of-life Management Practices; LPF = Logistics Performance Factor

Further considerations included adjustment indexes for the Average Path Coefficient (APC) = 0.357, $p < 0.01$; Average R-Squared (ARS) = 0.472, $p < 0.001$; Average Adjusted R-Squared (AARS) = 0.456, $p < 0.001$; Average Block VIF (AVFI) = 1.362, ideally acceptable if <=3.3; Average Full Collinearity VIF (AFCVIF) = 2.184, ideally acceptable if <= 3.3. The model also proved suitable in the indexes, Tenenhaus because GoF = GoF (GOF) = 0.549, considering that 0.10 is small, ≥0.25 is medium and ≥0.36 is large. Sympson’s Paradox ratio (SPR) = 1.000, acceptable if >=0.7 and ideally =1; R-Squared Contribution Ratio (RSCR) = 1.000, acceptable if >=0.9 and ideally = 1; Statistical Suppression Ratio (SSR) = 1, acceptable if >=0.7 and Nonlinear Bivariate Causality Direction Ratio (NLBCDR) = 1.000, acceptable if >= 0.7.

Figure 5-2 presents a model of the final path diagram, followed by a summary of the relationships among the constructs that were confirmed and refuted.

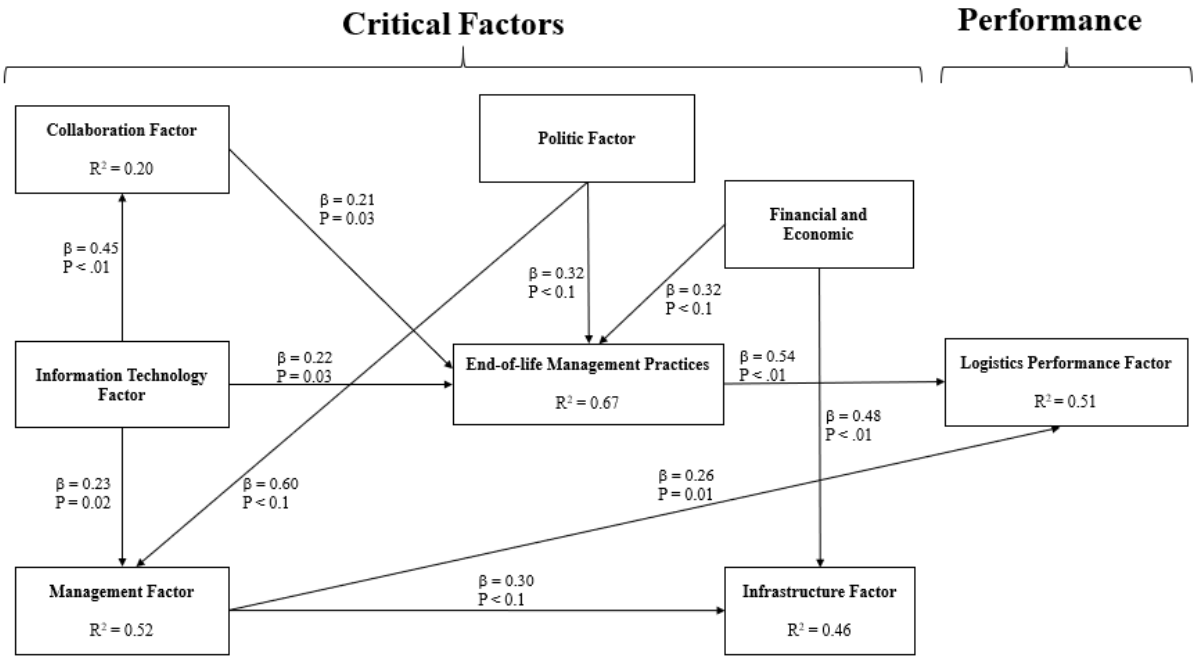

Figure 5-2 Result of the path diagram with confirmed hypotheses

Table 5-5 presents the hypotheses that were tested with the direct effect and also the moderator effect. Considering a value of $p<0.05$ was used as a baseline to determine the significance of direct and moderating relationships. A total of 15 hypotheses were tested, with thirteen having a direct effect and two a moderating effect, totaling eleven confirmed hypotheses and four that were rejected.

Hypotheses	Coef (β)	*p-Value*	Conclusion
H1a - MF → EOL-MP	-0.04	0.36	Reject
H1b - MF → LPF	0.26	0.01	**Accepted**
H1c - MF → IF	0.30	<.01	**Accepted**
H2 - CF → EOL-MP	0.21	0.03	**Accepted**
H3a - ITF → EOL-MP	0.22	0.03	**Accepted**
H3b - ITF → CF → EOL-MP	0.10	0.21	Reject
H3c - ITF → MF → EOL-MP	0.09	0.23	Reject
H3d - ITF → CF	0.45	<.01	**Accepted**
H3e - ITF → MF	0.23	0.02	**Accepted**
H4 - IF → EOL-MP	0.03	0.40	Reject
H5a - PF → EOL-MP	0.32	<.01	**Accepted**
H5b - PF → MF	0.60	<.01	**Accepted**
H6a- FEF → EOL-MP	0.32	<.01	**Accepted**
H6b - FEF → IF	0.48	<.01	**Accepted**

H7 - EOL-MP → LPF	0.54	<.01	**Accepted**

Table 5-5 Results of the hypotheses tests
MF = Management Factor; CF = Collaboration Factor; ITF = Information Technology Factor; IF = Infrastructure Factor; PF = Policy Factor; FEF = Financial and Economic Factor; EOL-MP = End-of-life Management Practices; LPF = Logistics Performance Factor

As can be seen in Figure 5-2 and also in Table 5-5, Management Factor had a negative effect on End-of-Life - Management Factor with a coefficient value of (β)=-0.04 and an MF→EOL-MP ratio of *p*=0.36, which means H1a was rejected. Management Factor had a positive effect on the Logistics Performance Factor with a coefficient value of (β)=0.259 and an MF→LPF ratio of *p*=0.001, meaning H1b was confirmed. Management Factor had a positive effect on Infrastructure with a coefficient value of (β)=0.302 and an MF→LPF ratio of *p*=0.001, meaning H1c was confirmed. Collaboration Factor had a positive effect on End-of-Life Management Factor with a coefficient value of (β)=0.210 and a CF→EOL-MP ratio of *p*=0.003, meaning H2 was confirmed. Information Technology Factor had a positive effect on End-of-Life Factor with a coefficient value of (β)=0.220 and an ITF→CF ratio of *p*=0.03, meaning H3a was confirmed. There was no moderating effect between ITF→CF→EOL-MP and ITF→CF→EOL-MP with a coefficient of (β)=0.10 and (β)=0.09, respectively, and presented *p*=0.21 and *p*=0.23, also respectively, which means that H3b and H3c were rejected. Information Technology Factor had a positive effect on Collaboration Factor with a coefficient value of (β)=0.448 and an ITF→CF ratio of *p*=<.01, meaning H3d was confirmed. Information Technology Factor had a positive effect on Management Factor with a coefficient value of (β)=0.228 and an ITF→CF ratio of *p*=0.02, meaning H3e was confirmed. Information Factor did not relate to End-of-Life Management Factor with a coefficient value of (β)=0.03 and an IF→EOL-MP ratio of *p*=0.40, meaning H4 was rejected. Politics Factor had a positive effect on End-of-Life Management Factor with a coefficient value of (β)=0.318 and a PF→EOL-MP ratio of *p*=<.01, meaning H5a was confirmed. Politics Factor had a positive effect on Management Factor with a coefficient value of (β)=0.596 and a PF→MF ratio of *p*=<.01, meaning H5b was confirmed. Financial and Economic Factor had a positive effect on End-of-Life Management Factor with a coefficient value of (β)=0.325 and an FEF→EOL-MP ratio of *p*=<.01, meaning H6a was confirmed. Financial and Economic Factor had a positive effect on Infrastructure Factor with a coefficient value of (β)=0.485 and an FEF→IF ratio of *p*=<.01, meaning H6b was confirmed. Finally, End-of-Life Management Factor had a positive effect on

the Logistics Performance Factor with a coefficient value of (β)=0.596 and an EOL-MP→LPF ratio of *p*=<.01, meaning H7 was confirmed.

With regards to the empirical test of the proposed structure, statistical indicators presented a suitable quality level, as per Table 5-6.

Latent variables	R-squared (R^2)	Adjusted (R^2)	Q^2 Predictive validity	Full collinearity VIF
MF	0.523	0.508	0.523	2.578
CF	0.201	0.188	0.201	1.988
ITF	-	-	-	1.719
IF	0.463	0.447	0.476	1.953
PF	-	-	-	2.334
FEF	-	-	-	1.997
EOL-MP	0.667	0.646	0.667	2.655
LPF	0.507	0.491	0.513	2.245

Table 5- 6 Inner model analysis results

MF = Management Factor; CF = Collaboration Factor; ITF = Information Technology Factor; IF = Infrastructure Factor; PF = Policy Factor; FEF = Financial and Economic Factor; EOL-MP = End-of-life Management Practices; LPF = Logistics Performance Factor

5.5 DISCUSSION

Results show that data adapted well to the structure of the theoretical model presented and in general represents the reality of the Pharmaceutical Care Process, where the study was applied. However, it is worth highlighting certain points that deserve attention and which are presented in topic 5.5.1.

5.5.1 Main Findings

In the process of EOL management for medication, managers have to cope with critical factors for the implementation of reverse logistics to be successful, as previously highlighted by (Abdulrahman et al., 2014; Tavana et al., 2016). The way that effective RL can positively affect economic, social and environmental sustainability of organizations (García-Sánchez et al., 2019).

Considering the theory of the resource-based view, human resources are considered an intangible and crucial resource in the development and maintenance of effective reverse logistics activities (García-Sánchez et al., 2019). Based on support from senior management and also the support of partner pharmaceutical companies in the three cycles of logistics (direct, reallocation and reverse), there is a major impact on logistics performance, which converges with the literature.

Despite surprisingly rejecting H1a, this result can initially be justified by the fact that most municipalities where the study was applied are places with lesser scope in terms of expired medication volumes. Furthermore, these practices do already exist, though partially, because EOL medication within the Pharmaceutical Assistance network/system is the responsibility of the actual network. However, there is still no decree regulating EOL medication coming from patients.

Under the current conditions of the studied network, only three well-qualified pharmaceutical professionals can handle EOL reverse logistics out of 145 health-care establishments (FD, UBS).

As these three professionals are part of coordination, and there is strong integration among coordination management professionals, EOL RL within the network operates well. But if all the complexity of collecting and disposing of EOL medication coming from the population becomes a reality, it would be exceedingly difficult for the structure to cope in its current form. That is because the core business of the Pharmaceutical Assistance network is direct logistics, which is well structured to deliver value in this format.

Taking effect in Brazil Federal Decree n. 10.388, dated June 5, 2020, instituted EOL/EOU reverse logistics for medication coming from the population, the issue of Management Factor should be reviewed and adapted to cater to this complexity. It is suspected that simply expanding the service already provided by partner pharmaceutical companies will not consider the peculiarities of the RL problem for medication coming from the population. As such, certain recommendations include: (create a new strategic unit within the network to deal solely with EOL/EOU RL; outsource RL requirements - developed in coordination, with support from or subordinate to the Pharmaceutical Assistance Coordination (CAF, Portuguese acronym) and the municipal health department.

The NDM-CAF, for example, as a necessary structure, is already at its resource limit in catering to the three logistics cycles (direct, reallocation and reverse) for the network. It would certainly fail to cope with medication coming from the population.

As shown in Table 5-5, the study confirmed eleven of the fifteen hypotheses tested with a direct effect. The two hypothesis with a moderating effect were rejected, which is contrary to the results presented in (Morgan et al., 2016) wherein IT moderated the relation between collaboration, geared towards RL practices. As there were elements of management in the construct, ITF moderation was also tested for Management Factor, with moderation not confirmed either.

The rejection of H3b and H3c is justified by the fact that collaboration and sharing of information provided by managers and also the support of partner pharmaceutical companies, for activities related to stock control, reallocation of surplus and expired medication, are sufficient. In this case, information technology did not moderate, with no effect on the intensity of how this happens, with trust seen as an important element for collaboration and effective communication among parties, as highlighted by Paula *et al.* (2019), and inseparable from collaboration.

On the other hand, the ITF construct variables with the highest factor loading are those dealing with information system functions related to RL for EOL medication. This construct had a positive and direct effect on MF, CF and EOL-MP constructs, in CF. This greater emphasis was expected, as the management system is actually a tool to support collaborative work in the Pharmaceutical Assistance network, geared towards EOL medication, in fact. The ITF moderation effect (a more operational character) on the MF (strategic character) on EOL-MP (operational character) was not observed. The ITF construct was prepared with an emphasis on the currently existing functionalities in the IT system of the studied Pharmaceutical Assistance network, which has highly operational characteristics. If the system has functionalities related to other aspects like capacity building, the collection and analysis of data for decision making and RL performance analysis, perhaps moderation could have been observed. Besides IT featuring as a major resource for organizations, and particularly the PCP, it interfered directly in EOL-MP, in the MF and CF constructs. The underlying literature shows that IT resources are necessary to effective decision making in RL (Mai *et al.*, 2012). The importance of IT to RL activities was highlighted earlier (Morgan et al., 2016; Kongar et al., 2015; Sarkis et al., 2020). Authors like (Lee and Lam, 2012) point out that technological resources and the improvement of IT systems for RL lead to a more sustainable result for environmental protection, social responsibility and economic performance, simultaneously.

The recent implementation of a system for dispensing medication at the Pharmaceutical Assistance offered benefits like stock control and agility in the process of dispensing medication to users. Standard operating procedures (SOP10) were also developed, whereby managers were able to register medication that would be returned to the medication dispensary and/or collected for sanitary disposal by means of a stock management system. Statistical results show a strong relation between IT facilitating expiry monitoring activities and the separation of medication to be returned.

Another challenged faced by the public health-care sector is the need to find specific outsourced companies, according to the product characteristics. These companies recycle and handle EOL products, which was pointed out by (Sivakumar *et al.*, 2018). This ends up generating costs and, very often, difficulty in finding third-party logistics providers (3PLs), discouraging this practice (Prakash and Barua, 2015; Sivakumar *et al.*, 2018).

Organizational managers must provide a suitable location to temporarily store products returned products by end users to their point of origin. Studies point out that a lack of infrastructure may present a barrier to the RL implementation process (Kumar and Dixit, 2018; Massoud et al., 2015; Meyer et al., 2017; Prakash and Barua, 2015). For this study, Infrastructure, formerly represented by physical aspects, reverse logistics and reallocation, did not present statistical results that alter EOL-MP.

With regards to political aspects, as discussed in the study by Pereira et al. (2012) and in Aquino et al. (2018), there is still not sectoral agreement for the pharmaceutical industry that establishes mandatory relations among different links of the chain. The main attributes of a sectoral agreement would be general guidelines for public and private sector managers, with goals and specific actions to structure the reverse logistics system.

One may affirm further that political issues related to legislation, considering the municipal health-care solid waste management plan prepared based on RDC 222/2018 (Brasil, 2018), is an important mechanism to guide managers keen to support the correct disposal of waste generated through medical and hospital care (Aquino et al., 2018). Study results show a strong relation with political aspects in EOL-MP.

Regarding political aspects, the line seems more technical than political when it comes to EOL medication and Still Condition of Use (SCOU), at a level of the Pharmaceutical Assistance network, which has existed for some time as part of the education skills of pharmaceutical professionals and sometimes other health-care professionals.

The political direction in relation to RL for health-care waste from the Pharmaceutical Assistance network, considering waste in ample forms, such as syringes, needles and even medicine, already exists due to the National Policy on solid Waste (PNRS, Portuguese abbreviation) and RDC 222/2018 (Brasil, 2018). However, health professionals continue discussing forms of operationalization, a complex discussion as it involves the type of waste, form of separation and disposal, need for professional capacity building and infrastructure (in-company or outsourced?)

Very recently, with the institution of Federal Decree 10.388, dated June 5, 2020, (Brazil, 2020) dealing with the disposal of medication and its packaging, regulating the environmentally correct disposal of medication from the production and consumption chains. Within this context, RL for EOL and EOU medication coming from the population should gain political strength and more actively influence the management of the Pharmaceutical Assistance network, in the sense of calling for adaptation within the public sector in the short term. This seeks to sway the old anxieties of the pharmaceutical sector, as well as concerns regarding care for the environment, especially at a time in which the world is dealing with a pandemic and even more so in Brazil, where health-care waste can become potential propagators of COVID-19.

The decree establishes 2 years for adaptation: “within two years, all capitals of Brazil and municipalities with populations higher than 500,000 shall implement collection points for expired medication. This deadline will be up to five years for municipalities with populations over 100,000.”

With regards to the political effect on inspection aspects, despite the decree, PNRS and RDC, there are elements that complicate inspection efforts. The question is, will inspection bodies (ANVISA - Brazilian Health Surveillance Agency) have the available infrastructure and human resources to meet demand?

Another point that should be highlighted lies in the financial and economic factor. If there were more resources, improvements could be made to the IT system, services could be outsourced and, in general, improvements could be made to separation and storage spaces and, lastly, though primary in role, dispensing medication and inputs among users of the Unified Health System (SUS, Portuguese acronym). These elements have had a major impact on EOL-MP, with the availability of financial resources also tending to result in considerable improvements to PCP infrastructure. A lack of resources was a barrier described by (Abdulrahman et al. 2014). Finally, with regards to EOL-MP, it was noted that implementing reverse logistics practices impacts PCP logistics performance, which converges with the findings presented by (Morgan et al. 2016).

According to the results described in this study, pharmacists from municipal pharmacies are clearly aware that EOL-MP have a positive and direct impact on the control of medication and input expiry, on medication close to expiry and also on medication not in stock. A study by Ding et al. (2018) also highlighted that activities involving reverse logistics have a major impact on logistics performance.

5.5.2 Theoretical Implications

From a theoretical point of view, the study held with PCP pharmacists showed congruence with respect to the influence of critical factors on the implementation of EOL practices, while interfering with logistics performance. In general, public health-care system managers must pay attention to critical factors so that these do not become barriers, further complicating the implementation of reverse logistics.

After the implementation of reverse logistics comes the circular economy, which has already shown promising results in developed nations. With the Covid-19 pandemic, issues related to direct and reverse logistics, and especially the management of health-care waste, has gained bother theoretical and practical relevance, given that there will soon be a higher demand due to waste generated, coupled with elevated potential to propagate disease.

On the other hand, the theory of a resource-based view provides mechanisms that guide managers of the supply chain in developing strategies to operationalize PCP reverse logistics activities, establishing the necessary resources, core capacities and operational routines.

5.5.3 Lessons for Policy Formulators and Professionals

Lesson 1: It is imperative that critical factors in the implementation of EOL management practices for medication are not ignored by public health-care sector managers, as they impact logistics performance.

Lesson 2: Medicine consumption is on the rise, globally, and in Brazil users have access to the Unified Health System (SUS) and commercial pharmacies, which is cause for concern among different entities regarding the final destination of this medication resulting from changes in treatment or failure to follow through with treatment. This is a short, medium and long-term concern for national governments.

Lesson 3: The exploration of emerging I4.0 technologies facilitate the creation of sustainable value, leading to agile and intelligent operations, in the sense that a sustainable pharmaceutical supply chain should extend to product operations and management in the reverse cycle.

Lesson 4: The current Covid-19 pandemic provides solid evidence of just how vital waste management is, while also highlighting the many vulnerabilities of nations, such as Brazil.

This study only considered medicine waste, which already presents a high level of complexity for decision makers. In the face of the Covid-19 pandemic, many other types of hazardous and infectious waste is being generated around the world, such as personal protection equipment (PPE), masks, gloves and other infected equipment. According to RDC 222/2018 (Brasil, 2018) classification, this type of waste is categorized as Group A and Subgroup A1 (Annex A), presenting biological risks (infectious).

According to the United Nations Environment Programme (UNEP) (PNUMA, 2020), incorrect management of this waste may have irreversible effects on human health and the environment. As such, safe handling and correct final disposal of this material are vital to an effective urgent response.

As discussed by Sarkis et al. (2020), the current global crisis also provides opportunities to transform into a sustainable supply and production system, catalysing the transition to sustainability and a circular economy post pandemic.

Lesson 4: Following the institution of the medication reverse logistics decree, public policies must be formulated government agencies to provide solutions for the management of waste generated by each municipality and especially that originating from the public health-care sector, which currently presents elevated potential to propagate diseases.

The Basel Convention Regional Centre for Asia and the Pacific (Basel Convention Regional, 2020) recently published a series of technical forms carrying guidelines to support the implementation of environmentally correct management of hazardous and other waste. With information about health-care waste management, the document suggests guidelines to guarantee that the management of this waste, including its handling and disposal, be consistent with the protection of human health and the environment, from the place of generation, treatment, storage, recovery and final disposal.

It also worth highlighting the importance of bolstering coordination between the health sector and other department, cooperating to promote the prevention and control of medical waste, through a joint effort.

5.6 CONCLUSIONS

Considering the resourced-based view, the aim of this study was to assess the influence of critical factors in the adoption of End-of-Life management practices for medication and to determine the effect on Pharmaceutical Care Process logistics performance.

The management of waste from health-care services is a complex and current issue, influenced by many aspects, like the economy, environment, technical and social, among others, and has become a core theme (Xiao, 2018).

There are certain limits to this study in terms of sample size. The first concerns the sample for this study, which may be considered small. A larger sample would be highly beneficial for future studies.

Regarding the results from this study, they are based on the context of the city of Porto Alegre, which is similar to other Brazilian municipalities in the context of the Unified Health System (SUS, Portuguese acronym). It is strongly suggested that a similar study framework to this one be applied in other countries so as to compare them with the reality of Brazil.

With the sudden onset of the Covid-19 pandemic, the management of waste from the health-care system has become vital due to the level of contamination and greater prorogation of the virus, in an attempt to find the silver lining in such an unusual moment in the world in order to discover mechanisms and how to then apply the sustainable concept of a circular economy, something already underway in developed nations.

Further to suggestion on future studies, research is encouraged to discuss the transition towards a circular economy and look at how organization resilience can reduce the impacts of Covid-19 and foster collaborative effort in efficient health-care waste management.

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Appendix A – Questionnaire applied

Collaboration Factor (CF)

Regarding aspects of Collaboration, indicate the degree of agreement considering (1 - totally disagree to 7 - totally agree)
It exists at my basic health unit ...

	1	2	3	4	5	6	7
Sharing of information among basic health units, partner pharmaceutical companies and/or NDM-CAF							
Reliability in sharing of information among basic health units, partner pharmaceutical companies and/or NDM-CAF							
Collaboration among workers at basic health units for RL activities for medication and inputs							
Collaboration from NDM-CAF for RL involving medication and inputs							
Collaboration of partner pharmaceutical companies in reallocating surplus medication							
Collaboration of partner pharmaceutical companies for returning expired medication or sanitary collection.							

Infrastructure Factor (IF)

Regarding aspects of Infrastructure, indicate the degree of agreement considering (1 - totally disagree to 7 - totally agree)
My basic health unit is equipped with suitable physical infrastructure to ...

	1	2	3	4	5	6	7
Receive reallocated medication in a usable condition							
Store expired medication or inputs delivered by the population							
Temporarily store expired medication or that no longer suited to use, which shall be returned to NDM/CAF							
Transport medication in conditions suitable for use from one unit to another, planned by partner pharmaceutical companies							
Store medication in conditions suited to use which has been returned by patients that left my stock							

Information Technology(IT)

Regarding aspects of Information Systems, indicate the degree of agreement considering (1 - totally disagree to 7 - totally agree)
My basic health unit uses the DIS/PROCEMPA and GMAT information systems to:

	1	2	3	4	5	6	7
Deliver medication to patients using the DIS system							
Reallocate surplus medication to partner pharmaceutical companies using the GMAT system							
Monitor medication expiry dates via the GMAT system							

Generate information on expired medication and input volumes via the GMAT system							
Return expired medication to the NDM/CAF in (SOP 10) via the GMAT system							
Return medication for sanitary waste collection in (SOP 10) via the GMAT system							

Management Factor (MF)

Regarding aspects of Management, indicate the degree of agreement considering (1 - totally disagree to 7 - totally agree)
My basic health unit has...

	1	2	3	4	5	6	7
Workers in sufficient numbers to perform RL activities for medication and inputs							
Workers with technical knowledge/expertise involving RL for medication and inputs							
Workers with the capacities and/or trained with regards to separating expired medication and inputs							
Workers committed to/motivated by issues related to pharmaceuticals and input waste management							
Capacity building and/or training for workers on separation practices for expired medication and inputs							
Support from COORAF for RL involving medication and inputs							
Support from COORAF to reallocate surplus pharmaceuticals and inputs among basic health units							
Support partner pharmaceutical companies for RL involving medication and inputs							
Support partner pharmaceutical companies in reallocating surplus medication and inputs among units							
Support from NDM-CAF for RL involving medication and inputs							
Support from NDM-CAF to reallocate surplus medication and inputs among basic health units							

Politics Factor (PF)

Regarding aspects of the Policies Factor, indicate the degree of agreement considering (1 - totally disagree to 7 - totally agree)
Considering that ...

	1	2	3	4	5	6	7
I know pertinent health-care solid waste legislation							
I fulfil the task of raising awareness among the population regarding rational use of medication and inputs							
I fulfil the task of raising awareness among the population regarding disposal of medication and inputs							
There are flaws in the law/regulations regarding health-care solid waste in the public sector							
Efficient auditing occurs with regards to correctly managing health-care solid waste generated by the city							

There are public policies for the implementation of reverse logistics for medication in the public health-care sector							

Financial and Economic Factor (FEF)

Regarding aspects of financial and economic issues, indicate the degree of agreement considering (1 - totally disagree to 7 - totally agree)

COORAF and/or the Municipal Health Department have financial resources to ...

	1	2	3	4	5	6	7
Make improvements to the Information (GMAT system)							
Hire outsourced services to ensure correct collection and disposal of all waste generated							
Tender the purchase of materials for permanent education actions (trash cans, adhesives with symbols, plastic bags, etc.)							
Store and handle waste until it is sent to the NDM-CAF							
Improve medication and input storage areas							
Improve medication and input separation areas							
Improve medication and input delivery areas							

End-of-life Management Practices (EOL-MP)

Regarding aspects of Reverse Logistics Implementation, indicate the degree of agreement considering (1 - totally disagree to 7 - totally agree)

My basic health unit performs...

	1	2	3	4	5	6	7
Monitoring the validity of medication and inputs in stock via the GMAT system							
Notification of expired medication sent to partner pharmaceutical companies and the NDM-CAF							
Request the collection of expired medication and inputs from partner pharmaceutical companies/NDM-CAF							
Delivery of expired medication to NDM-CAF employees							
Separation of medication and inputs returned by the population							

Logistics Performance Factor

Select a degree of performance for your basic health unit, following the implementation of DIS, based on the indicators presented below (1- extremely poor performance, 7 - excellent performance)

	1	2	3	4	5	6	7
Delivery time for medication and inputs to patients							
Check and receipt control in the GMAT system for medication and input orders							
Time required for reallocation of surplus medication and inputs							
Reduction in medication and input loss due to expiration							
Expiry control of medication and inputs in stock							
Control of medication and inputs not in stock							
Control of medication and inputs close to expiry							
Order delivery time for medication and inputs by NDM-CAF							
Suitable storage of medication and inputs							

6. CONSIDERAÇÕES FINAIS

Neste capítulo são apresentadas as conclusões da tese, juntamente com as principais contribuições teóricas e gerenciais no tópico 6.1, no tópico 6.2 as limitações e as sugestões para pesquisas futuras no tópico 6.3.

6.1 CONTRIBUIÇÕES DA TESE

O descarte de medicamentos EOL/EOU têm sido uma preocupação em muitos países e não diferente no caso brasileiro. Em geral, há uma necessidade de aumentar a conscientização no meio público e privado sobre a questão do descarte de medicamentos e os vários impactos do descarte incorreto no meio ambiente.

Tendo como objetivo geral, analisar o impacto dos fatores críticos na gestão de medicamentos visando à logística reversa entre instituições de saúde do setor público. A presente tese foi estruturada considerando um setor pouco explorado na literatura, que é a Atenção Primária de Saúde, sob uma perspectiva de logística reversa de medicamentos. Dessa forma a tese foi conduzida por meio dos quatro artigos (Capítulos 2, 3, 4 e 5).

Com o propósito de realizar o levantamento do estado da arte, subsidiando conteúdo para a delimitação do problema de pesquisa o que também permitiu uma síntese dos estudos na área de logística reversa na indústria farmacêutica. No Artigo 1, foi apresentada uma revisão sistemática de literatura, para construção de um portfólio de estudos. A RSL é considerada robusta, consistente, defensável e replicável sendo desenvolvida com uso de protocolo metodológico. Os principais resultados evidenciam para a identificação de conceitos e práticas de logística reversa (LR) aplicadas ao *end-of-life* (EOL) e ao fim de uso (EOU) de medicamentos. O artigo foi um importante balizador para constatação de um tema de suma importância, porém pouco explorado. Fato que pode ser comprovado pelo volume de estudos que foram sintetizados no Capítulo 2.

A partir da revisão sistemática de literatura, no Artigo 2, foi apresentado um estudo de caso que foi desenvolvido na Atenção Primária de Saúde (APS), no município de Porto Alegre. O estudo de caso teve como propósito o mapeamento dos fluxos de logística reversa e de remanejo de medicamentos que fazem parte do processo da APS. A partir do estudo de caso foi possível a identificação dos fatores críticos para implementação de logística reversa e também a construção dos fluxos de logística reversa e de remanejo.

Posteriormente à consolidação da triangulação dos dados (teoria e entrevistas) para criação do modelo teórico, no Artigo 3, utilizando abordagem MCDA – grey DEMATEL, os

fatores críticos na implementação de logística reversa de medicamentos, foram avaliados dentro de uma ordenação de causa-efeito dos fatores, demonstrando assim, as inter-relações dos principais fatores críticos na implementação das práticas de gestão de resíduos de medicamentos.

Finalmente, no Artigo 4, utilizando uma abordagem quantitativa PLS-SEM, com base nos oito fatores críticos identificados anteriormente no artigo 3, como causas-efeitos, foi determinada a influência dos mesmos sobre a performance logística da APS. Os resultados demonstram que os fatores críticos têm um efeito positivo e direto nas práticas de gerenciamento EOL-MP e influenciando diretamente na performance logística. Ainda foi confirmado o efeito direto de ITF sobre EOL-MP, mas não foi confirmado efeito de moderação. Os resultados fornecem uma compreensão mais aprofundada para os gestores de saúde no gerenciamento das práticas EOL, com vistas a apresentar subsídios para a gestão de medicamentos EOL, visando a logística reversa no setor público de saúde.

Em linhas gerais, com o uso da metodologia *Mix Method* foi realizada uma análise minuciosa que visou compreender os fatores críticos na gestão de medicamentos EOL/EOU e o impacto no desempenho logístico. Os resultados desta tese são de suma importância no avanço teórico o que vislumbra para a importância da gestão efetiva de medicamentos EOL visando à logística reversa. Ainda pode ser entendida como uma importante ferramenta com elementos gerenciais, permitindo aos gestores e tomadores de decisões uma visão ampla dos fatores críticos e demonstrando quantitativamente o impacto na performance logística da APS, sendo que estes fatores podem ser de ordem interna ou externa.

Espera-se que a partir dos resultados que foram apresentados e discutidos possa suscitar maior interesse por parte dos pesquisadores em desenvolver novas perspectivas de estudo sobre a temática. Um outro ponto que merece destaque, é também em razão à importância da gestão dos resíduos da saúde diante ao momento pandêmico que o mundo enfrenta com o COVID-19. O que faz com que um tema que antes era periférico e que se torne central, passando a ser um divisor de águas como suporte teórico para os gestores na busca pela transformação para um sistema sustentável no pós pandemia.

6.2 LIMITAÇÕES

As limitações pertinentes a essa tese são evidenciadas de acordo com os quatro artigos (Capítulos 2, 3, 4 e 5) que anteriormente foram apresentados.

- Na revisão sistemática de literatura, foi utilizado um *string* de busca abrangente em que foi possível capturar um volume de estudos para análise e síntese. De um modo geral a RSL desenvolvida e publicada no periódico *Supply Chain Management: An International Journal* foi representativa, apesar de lidar com um setor específico da indústria farmacêutica, os 39 estudos que foram selecionados podem ser considerados um volume relativamente pequeno se comparados com outros setores, além disso alguns estudos não foram incluídos devido a falta de acesso ao documento completo, bem como, houve uma limitação em relação as bases de dados direcionadas a engenharias III e desconsiderado publicações de bases da área da saúde como, por exemplo, PubMed, Lilacs e Medline.

- Uma limitação presente nesta tese diz respeito ao escopo de aplicação, o estudo poderia ter sido desenvolvido em toda a cadeia contemplada no conceito de logística reversa, ou seja, do consumidor ao fabricante. No entanto, o recorte desta tese deu-se apenas, no setor público de saúde com enfoque na dispensação de medicamentos.

- No artigo qualitativo e também no artigo em que foi utilizado o método de abordagem multicritério, Grey-DEMATEL, duas limitações podem ser elencadas, sendo que a primeira delas refere-se ao número de entrevistados no estudo qualitativo e o número de especialistas em que foi aplicado a matriz multicritério. O que não é justificado pela indisponibilidade dos farmacêuticos que foram inicialmente contatados, mas em alguns casos pela localização geográfica de algumas farmácias em áreas de risco do município, e que inviabilizou a aplicação com alguns gestores. Por outro lado, foram entrevistados participantes externos, sendo que inicialmente não faziam parte do escopo de aplicação da pesquisa, mas que foi obtido informações fundamentais para o ajuste dos objetivos, dado que os mesmos estavam atuando no desenvolvimento do programa de gerenciamento dos resíduos sólidos da saúde do município de Porto Alegre.

- Uma segunda limitação se dá no aspecto teórico, dado a dificuldade de enquadrar o setor de aplicação – Atenção Primária de Saúde, nas teorias complementares como por exemplo, Resource Based View (RBV), Social Network Theory (SNT), Information Theory (IT), Transaction Cost Economic (TCE) dentre outras.

- Por fim, no artigo quantitativo em que foi conduzido utilizando modelagem de equações estruturais, a maior limitação refere-se à quantidade de unidades farmacêuticas disponíveis para a aplicação, dado às mudanças gerenciais enfrentadas durante o período de aplicação, ou seja, a terceirização que o sistema enfrentou, o que acabou reduzindo

drasticamente o escopo de aplicação, tendo que ser ampliado para profissionais de outros municípios da 8ª Coordenadoria de Saúde.

- Uma das limitações da tese reside no escopo de aplicação, sendo que os dados foram obtidos apenas na realidade do sistema público de saúde da região Metropolitana de Porto Alegre – RS. Os resultados aqui apresentados não permitem extrapolar diretamente para outros contextos, o que seria necessária uma continuidade neste campo de estudo para outros estados e municípios com suas peculiaridades em termos de gestão.

6.3 PESQUISAS FUTURAS

A presente tese delimitou-se em compreender os fatores críticos na gestão resíduos de medicamentos, com vistas à implementação de logística reversa em um setor específico da cadeia de dispensação do setor público – Atenção Primária de Saúde (APS), no município de Porto Alegre, RS. Espera-se que a partir desta tese, novas perspectivas de estudos possam ser vislumbradas por pesquisadores da área. A seguir são apresentados alguns tópicos que podem ser úteis para criação de novos problemas de pesquisa com base nos artigos apresentados nos Capítulos 2, 3, 4 e 5.

- Compreender os fatores críticos na implementação de gestão de resíduos, visando a logística reversa de medicamentos, utilizando como base as percepções e perspectivas de outros elos da cadeia de logística reversa, conforme preconiza em seu conceito, ou seja, desde o fabricante até o consumidor final.

- Replicação do modelo multicriterial proposto no Capítulo 3, em setores da saúde de outros municípios e estados brasileiros ou comparando com a realidade internacional de países desenvolvidos e em desenvolvimento. Sabe-se das inúmeras dificuldades enfrentadas na gestão de resíduos de medicamentos e principalmente a gestão de resíduos da saúde em geral, considerando, o momento sem precedentes, que o mundo enfrenta com a pandemia do COVID-19. Sendo que se recomenda, ainda, o uso de métodos de abordagem híbrida como, por exemplo, a combinação do método de abordagem MCDM, Best Worst Method (BWM) com Weighted Influence Non-linear Gauge System (WINGS) o que permite uma avaliação híbrida das inter-relacão dos fatores apresentados anteriormente e que podem ser utilizados em várias fases do processo de tomada de decisões com vistas à implementação da logística reversa de medicamentos.

- Replicação do modelo teórico desenvolvido no Capítulo 5, em um contexto de transição para economia circular, com vistas na compreensão do papel da indústria farmacêutica

e fazendo um paralelo com as teorias complementares - Resource Based View (RBV), Social Network Theory (SNT), Information Theory (IT), Transaction Cost Economic (TCE) dentre outras. Sendo que recomenda-se fortemente a aplicação em amostras maiores.