UNIVERSIDADE D
COIMBRA

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LIFE CYCLE ASSESSMENT OF A NEW PACKAGING FOR LARGE VOLUME PARENTERALS

M.Sc. Dissertation

March 2021

Life cycle assessment of a new packaging for large volume parenterals

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Dissertation in the context of the Master in Energy for Sustainability presented to the Department of Mechanical Engineering of the University of Coimbra

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Coimbra
March 2021

Acknowledgements

I would like to express my sincere gratitude and appreciation to all those who, directly or indirectly, contributed to my personal and professional evolution, in the realization of this dissertation.

In particular, I am especially grateful to my supervisors, Professor Fausto Freire and Pedro Marques, for giving me valuable guidance, materials and support throughout this learning process. To Professor Fausto Freire, thank you for giving me your trust and the opportunity to carry out this project and receiving me in the Centre for Industrial Ecology. To Pedro Marques, thank you for your huge patience and availability to answer my many questions, for all the meetings and the time you dedicated helping me with the difficulties I had in each of the stages of this project.

I would like to thank Pedro Pacheco, for giving me the opportunity to conduct this study in the pharmaceutical company and for the support and trust shown, this was a very enriching experience for me on a professional level. To Bruno Pinto, João Laranjeira and Vanessa Corceiro, thank you for your patience and the availability to help me with the data collection.

I would also like to thank my friend and colleague Jade Müller, for helping me with several ideas to improve the text.

To my family who, even being in different parts of the world, their love and support have always been present despite the difficulties that have arisen, for all the incentive they have given me and trust, this would have been impossible without you.

To all my friends in Colombia, here in Portugal, and in other parts of the worlds for staying in touch despite the distance and giving me your support when I have needed it most and for making my days more pleasant.

Abstract

Polymers are the most common raw materials used in pharmaceutical packaging due to their excellent properties. However, it is increasingly important to address the environmental concerns of plastic packaging, promoting eco-design and selecting the options with lowest environmental impacts. Life cycle assessment (LCA) can be used to assess the environmental performance of pharmaceutical products from a holistic perspective.

The goal of this study is to assess the environmental life cycle of a new plastic packaging for large volume parenterals (injectable products designed for intravenous delivery applications) manufactured by a pharmaceutical company in Portugal, with the following specific objectives: (i) To analyze the environmental impacts and identify potential improvements for the manufacturing processes of the large volume parenterals (LVPs) at the pharmaceutical company; (ii) To analyze the environmental impacts of the production of materials and transport of final product for alternative hospital locations; (iii) To evaluate and compare different end-of-life options; (iv) To assess future production scenarios with reduction of losses and internal recycling of production losses.

The LCA included the production and transport of materials, production processes (solution preparation and packaging production) and waste management at the factory, transport of final product (LVPs) for alternative hospitals (in Portugal and Spain), end-of-life of waste materials collected from hospitals: (i) incineration of plastic packaging waste and (ii) valorization of tertiary packaging waste. It was also considered alternative end-of-life scenarios for plastic packaging waste (landfilling and recycling). The function unit is defined as 1 unit of LVPs to deliver 500 ml of solution to a patient for an intravenous therapy at hospitals. A life cycle model and inventory were implemented based on primary data collected at the pharmaceutical company. Two future scenarios for packaging production were proposed considering reduction of losses and internal recycling of production losses. Nine environmental impact categories were selected to perform the assessment: climate change, resource use (fossils), acidification, freshwater eutrophication, resource use (minerals and metals), ozone depletion, freshwater ecotoxicity, human toxicity cancer, and human toxicity non-cancer.

The results show that packaging production is important for all categories, especially for climate change, resource use (fossils), freshwater eutrophication and freshwater ecotoxicity (contributing more than 50% of the life cycle impacts), due to the consumption of electricity and natural gas. The plastic used to manufacture the packaging and the cardboard box are the

materials with the largest contributions, especially for resource use (fossils), acidification and resource use (minerals and metals). The transport of final product (LVPs) requires refrigerated transport (with controlled atmosphere), which results in important ozone depletion (due to consumption of coolant R134a), particularly for long transportation distances. Both future scenarios for packaging production presented reductions in impacts and total costs due to less consumption of plastic material. End-of-life scenarios showed that recycling outperform incineration and landfilling in all impact categories. Main recommendations for future work are proposed, including: i) update the life cycle model, ii) include a sensitivity analysis and iii) perform a comparison with other similar products available in the market.

Keywords: Large volume parenterals, Life Cycle Assessment, Packaging, Pharmaceutical industry, Polymer

Resumo

Os polímeros são das matérias primas mais utilizadas em embalagens farmacêuticas devido as suas excelentes propriedades. No entanto, é cada vez importante abordar as questões ambientais das embalagens plásticas, promover o ecodesign e selecionar as opções com os menores impactes ambientais. A avaliação do ciclo de vida (ACV) pode ser utilizada para avaliar o desempenho ambiental dos produtos farmacêuticos numa perspectiva holística.

O objetivo desta tese é fazer uma avaliação ambiental de ciclo de vida para uma nova embalagem plástica para soluções parenterais de grande volume (produtos injetáveis projetados para aplicações intravenosas) fabricadas por uma empresa farmacêutica em Portugal, com os seguintes objetivos específicos: (i) Analisar os impactes ambientais e identificar potenciais melhorias para os processos de fabrico das soluções parenterais de grande volume (SPGV) na empresa farmacêutica; (ii) Analisar os impactes ambientais da produção dos materiais e do transporte do produto final diferentes destinos hospitalares; (iii) Avaliar e comparar diferentes opções de final de vida; (iv) Avaliar dois cenários futuros de produção, um considerando redução nas perdas de material, e um segundo considerando redução nas perdas de material e reciclando internamente os resíduos de produção.

A ACV incluiu a produção e transporte das matérias-primas, processos de fabrico (preparação da solução e produção da embalagem) e gestão de resíduos na fábrica, transporte do produto final (SPGV) para hospitais alternativos (em Portugal e Espanha) e o final de vida dos resíduos dos hospitais: (i) incineração do resíduos da embalagem plástica e (ii) valorização dos resíduos da embalagem terciaria. Também foram considerados cenários alternativos de final de vida para os resíduos da embalagem plástica (aterro sanitário e reciclagem). A unidade funcional foi definida como 1 unidade de SPGV para fornecer 500 ml de solução a um paciente para uma terapia intravenosa em hospitais. O modelo e inventário de ciclo de vida foram implementados com dados primários recolhidos diretamente na empresa farmacêutica. Foram propostos dois cenários futuros de produção da embalagem, um considerando redução nas perdas de material, e um segundo considerando redução nas perdas de material e reciclando internamente os resíduos de produção. Nove categorias de impacte ambiental foram selecionadas para realizar a avaliação: mudanças climáticas, uso de recursos fósseis, acidificação, eutrofização de água doce, uso de recursos minerais e metais, depleção da camada de ozono, ecotoxicidade de água doce, toxicidade humana cancerígena e toxicidade humana não cancerígena.

Os resultados mostraram que a produção da embalagem é importante para todas as categorias, especialmente para mudanças climáticas, uso de recursos fósseis, eutrofização de água doce e ecotoxicidade de água doce (contribuindo com mais de 50% dos impactes de ciclo de vida), devido ao consumo de eletricidade e gás natural. O plástico utilizado para fabricar a embalagem e a caixa foram os que mais contribuíram para os impactes, especialmente para uso de recursos fósseis, acidificação e uso de recursos minerais e metais. O transporte do produto final (SPGV) utiliza transporte frigorifico (com atmosfera controlada), o que resulta em impactes significativos na depleção da camada de ozono, devido ao consumo de refrigerante R134a e à distância. Os dois cenários futuros de produção mostraram reduções nos impactes e custos totais devido ao menor consumo de plástico. Os cenários de final de vida mostraram que a opção de reciclagem apresenta benefícios significativos face à incineração de resíduos perigosos e ao aterro em todas as categorias de impacte. Como recomendação para trabalhos futuros: i) atualizar o modelo de ciclo de vida, ii) incluir uma análise de sensibilidade e iii) realizar uma comparação com outros produtos similares no mercado.

Palavras-chave:

Solução Parenteral de Grande Volume, Avaliação do Ciclo de Vida, Embalagem, Industria Farmacêutica, Polímero

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List of abbreviations

API - Active pharmaceutical ingredients

CTUe – Comparative toxic unit for ecosystems

CTUh – Comparative toxic unit for humans

EC – European Commission

JRC – Joint Research Center

kg CFC-11eq - kilogram chlorofluorocarbon-11 equivalent

kg CO2 eq – kilogram carbon dioxide equivalent

kg P eq – kilogram phosphorous equivalent

kg Sb eq – kilogram of antimony equivalent

LC – Life cycle

LCA – Life cycle assessment

LCIA - Life cycle impact assessment

LVPs – Large volume parenterals

MJ – Megajoules

mol H+ eq – equivalent molar concentration of the hydrogen ion

mPP-R – Modified polypropylene random copolymer

PCR – Product Category Rules

PEF – Product Environmental Footprint

PET - Polyethylene terephthalate

t.km – tonne-kilometers

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1. Introduction

1.1. Context and motivation

The pharmaceutical industry is essential to make possible a sustainable development in the global society, which has become even more evident in the context of the actual covid-19 pandemic. With the increasing improvement in healthcare systems around the world, demand for pharmaceutical products and the need to address global concerns about climate change, fast depletion of fossil fuels, waste management and social welfare; sustainability has become a subject of growing attention in the pharmaceutical industry due to greater environmental and social awareness of consumers, policymakers, and organizations (Hahladakis et al., 2018; Raju et al., 2016; Siegert et al., 2020). In addition, due to the dynamic development of the pharmaceutical industry in recent years, pharmaceutical packaging has become one of the driving forces in the packaging industry (Dobrucka, 2014).

Consequently, there is a tremendous pressure on the pharmaceutical industry to reduce the environmental impacts related to their activities, making it necessary to identify the environmental hotspots in the manufacturing processes in order to overcome environmental concerns (Sharma et al., 2020). Bringing with it, the adoption of more sustainable manufacturing practices: new products with lower environmental impacts, less water usage, greener manufacturing methods and recyclable packaging (Hahladakis et al., 2018; Raju et al., 2016; Sharma et al., 2020).

The environmental life cycle assessment (LCA) can be used to measure the environmental impact pharmaceutical products from “cradle to grave” (Sharma et al., 2020; Zurkirch, 2012). LCA is performed by quantifying all inputs (raw materials, resources, energy etc.) and outputs (emissions, wastes etc.) as well as the related potential environmental and health impacts (EC-JRC, 2012; Rajendran et al., 2012).

Given this context, LCA will be used to analyze a new plastic packaging for large volume parenterals (injectable products designed for intravenous delivery applications) manufactured by pharmaceutical company in Portugal. The production processes analyzed in the pharmaceutical company are relatively new (production lines started in August of 2019), incorporating a new production technology for large volume parenterals. However, the production processes are still in optimization phase when the study was performed in the

pharmaceutical company (September 2020) because they are still being improved to increase the production rate and reduce material losses.

1.2. Research objectives

The main objective of this thesis is to perform an environmental LCA of a new plastic packaging for large volume parenterals (LVPs) manufactured by pharmaceutical company in Portugal, aiming at identifying opportunities for material efficiency and environmental improvement, with the following specific objectives:

- To analyze the environmental impacts and identify potential improvements for the manufacturing processes of the LVPs at the pharmaceutical company.
- To analyze the environmental impacts of the production of materials and transport of final product (LVPs) for alternative hospital locations (Portugal and Spain).
- To evaluate the end-of-life based on the existing national regulation for hospital waste and considering the implementation of alternative scenarios for plastic packaging: landfill, and recycling.
- To assess future production scenarios with reduction of losses and internal recycling of production losses.

1.3. Thesis structure

This thesis is organized through five chapters, including this introduction. Chapter 2 identifies and examines relevant LCA studies on pharmaceutical products. Chapter 3 describes the materials and methods used to evaluate the environmental performance of a plastic packaging for large volume parenterals (LVPs). Chapter 4 presents and discusses the results obtained. Finally, Chapter 5 presents the conclusions and limitations of this study, as well as suggestions for future work.

2. Literature review

In this section, a literature review is conducted to identify and examine relevant LCA studies on pharmaceutical products that may contribute to the materials and methods implemented in this study. The literature review was build based on research using the search engines and database "Google Scholar", "Science Direct", "*Biblioteca do Conhecimento Online*" and "*Bibliotecas da Universidade de Coimbra (webOPAC)*", using a combination of the key word "Life Cycle Assessment" with others, such as "Pharmaceutical industry", "Polymer Packaging" and "Pharmaceutical Packaging". As a result, 8 papers were found on LCA of pharmaceutical products.

Table 1 presents the LCA studies on pharmaceutical products and summarizes them in the following characteristics: LCA notes, type of packaging, functional unit, system boundaries, end-of-life of packaging, life cycle impact assessment (LCIA) methods, impact categories and conclusion and main findings. Afterwards, the relevant points of each LCA study (e.g. packaging materials, end-of-life treatments, LCIA methods, impact categories and results) are further discussed.

Table 1. Literature review on LCA studies of pharmaceutical products.

Reference	LCA notes	Type of packaging	System Boundaries	Functional Unit	End-of-Life	LCIA method	Impact categories	Conclusion and main findings
Belboom et al., 2011	Comparative LCA of glass VS polymer packaging for injectable drugs.	Vials	Cradle-to-grave	One thousand vials.	Incineration	*IMPACT 2002+ *ReCiPe	GW, OD, EP, IR, TEC, PM, AP, LU, ADF, WW, CA, N-CA, RO, AEC, N-RE	*The use of polymers shows environmental benefits. *Vial production and transport are the environmental hotspots.
Dhaliwal et a., 2014	Comparative LCA of glass VS polymer packaging for contrast media.	Vials	Cradle-to-grave	Packaging of contrast media required to deliver one dose of 96 mL to a patient for an X-ray procedure.	*Incineration *Landfilling *Recycling	*ReCiPe *IPCC *CED *IMPACT 2002+ *USEtox	GW, OD, HTP, PCOF, IR, PM, Ecosystems, Resources, CED	*The use of polymers shows environmental benefits. *Vial production and transport are the environmental hotspots.
Loste & Puig, 2013	Comparative LCA of different types of packaging for Ibuprofen 600 mg.	*Sachet *Blister *Pots	Gate-to-grave	One container offered for sale.	Not reported	CML 2001	GW, HTP, EP, TEC, FEC	Sachets had higher impacts during the distribution stage due to heavier weight.

McAlister et al., 2016	Environmental LCA of intravenous morphine.	*Glass ampoules *Plastic bags	Cradle-to-gate	100 mg of bulk morphine.	Do not apply	ReCiPe	GW, OD, HTP, PCOF, TEC, MEC	Packaging had the largest carbon footprint.
Navajas et al., 2017	Eco-design and comparative LCA of glass VS polymer packaging for cough syrup.	Bottle	Cradle-to-grave	Container to supply the final consumer with 200 mL of syrup.	*Landfilling *Recycling	ILCD	GW, OD, HTP, PCOF, EP, IR, PM, FEC, AP, ADE, TEP, AMEP	*The use of polymers shows environmental benefits. *Bottle production is the environmental hotspot.
Raju et al., 2016	Comparative LCA of aluminum VS polymer packaging for paracetamol tablets.	Blister	Cradle-to-gate	Material required for packing 1 lakh (100,000), 500 mg of paracetamol tablets.	Do not apply	*CML 2001 *CED	GW, OD, EP, AP, ADE, ADF	The use of polymers shows environmental benefits in nine out of 11 impact categories considered.
Sharma et al., 2020	Environmental LCA of paracetamol tablets.	Blister	Cradle-to-gate	Active pharmaceutical ingredients required to produce 100,000 paracetamol tablets.	Do not apply	ReCiPe	GW, OD, HTP, PCOF, EP, IR, TEC, PM, FEC, LU, ADF, WW, MD	Blister packaging is the environmental hotspot.

Siegert et al., 2020	Environmental LCA of ibuprofen tablets.	Blister	Cradle-to-grave	Treatment of a patient with the purpose of pain relief for 4 days.	Incineration	*IPCC *USEtox *ADP model	GW, HTP, FEC, ADE, ADF	Production and distribution are the stages that most affect the environmental performance.

Legend: GW: Global warming; **OD:** Ozone Depletion; **HTP:** Human toxicity; **PCOF:** Photochemical ozone formation; **EP:** Eutrophication, freshwater; **IR:** Ionizing radiation; **TEC:** Terrestrial ecotoxicity; **PM:** Particulate matter; **FEC:** Freshwater ecotoxicity; **AP:** Acidification; **LU:** Land use; **ADE:** Abiotic depletion elements; **ADF:** Abiotic depletion fossil; **WW:** Water withdrawal; **MD:** Metal depletion; **TEP:** Terrestrial eutrophication; **AMEP:** Aquatic marine eutrophication; **MEC:** Marine ecotoxicity; **CED:** Cumulative energy demand; **CA:** Carcinogens; **N-CA:** Non-carcinogens **RO:** Respiratory organics; **AEC:** Aquatic ecotoxicity; **N-RE:** Non-renewable energy.

Belboom et al., 2011 compared the environmental performance of glass and polymer vials for injectable drugs, throughout the entire life cycle (cradle-to-grave). Polymer vials are made of cyclo-olefin-copolymer, which is a copolymer made of monomer polyethylene units (65%) and monomer norbornene units (35%). Incineration of plastic materials (with energy recovery) and glass components were considered. The results showed the following: (i) the environmental performance of polymer vials outperformed glass vials in 14 (out of 15) impact categories. (ii) Vial production and transport by plane had the largest environmental impacts for either materials.

Similarly, Dhaliwal et al., 2014 compared the environmental performance of glass and polypropylene vials for contrast media, throughout the entire life cycle (cradle-to-grave). A wide range of end-of-life scenarios were analyzed and compared with two approaches to allocate the environmental impacts (cutoff allocation approach and the market-based approach). The results showed the following: (i) the environmental performance of polypropylene vials outperformed glass vials in all impact categories, regardless of the end-of-life scenario. Compared to glass vials, polypropylene vials had lower greenhouse gas emissions (46%), lower impacts on ecosystem (39%), lower impacts on resources (59%) and lower impacts in the remaining impact categories between 24% and 43%. Dhaliwal et al., 2014 pointed out that the better environmental performance of polypropylene vials can be mainly attributed to the lower processed mass. (ii) Vial production presented the largest environmental impacts for either materials.

Navajas et al., 2017 implemented an eco-design methodology to replace glass bottles for cough syrup delivery with polymer bottles made of polyethylene terephthalate (PET). It was reported that some materials were recycled in a closed-loop (PET, glass, cardboard and aluminum), considering the standard commercial rates (e.g. 57% of PET is recycled and the rest is landfilled; 75% of cardboard waste and glass waste are recycled and the rest is landfilled), and all other materials are landfilled. The impact categories and methods used in the impact assessment are defined based on a set of recommended environmental indicators provided by EC-JRC, 2012. The results showed the following: (i) polymer bottles presented better environmental performance than glass bottles. (ii) Bottle production had the largest environmental impacts for either materials.

A recent study by Siegert et al., 2020 analyzed the entire life cycle of ibuprofen analgesic. The end-of-life considered the incineration of blister packaging with thermal energy recovery. The

impact categories and methods used in the impact assessment were defined based on the PCR for pharmaceutical products and processes (Siegert et al., 2019). The results showed the following: (i) the production stage had the greatest contributions on all impact categories, followed by transport. In contrast, the use stage and end-of-life presented minor contributions on all impact categories. (ii) Blister packaging had the largest human toxicity, cancer (30%). (iii) Information leaflet had a high contribution on ecotoxicity, freshwater (42%). (iv) Transport presented a considerable share of the impacts in resource use, fossils (22%) and climate change (25%). (v) Catalyst (API production) had the largest resource use, minerals and metals (55%). (vi) The production of silicon dioxide (Galenic formulation) and incineration of hazardous waste (mainly mercury emissions) presented a considerable share of the impacts in human toxicity, non-cancer (29% and 26%, respectively).

McAlister et al., 2016 and Sharma et al., 2020 analyzed the environmental performance of intravenous morphine and paracetamol tablets, respectively. It can be noted that McAlister et al., 2016 reported that morphine's packaging had the largest CO2 emissions (46%). Sharma et al., 2020 reported that blister packaging had a considerable contribution on 7 out of 13 impact categories, contributing more than 70 % to freshwater eutrophication and human toxicity.

Summarizing the information shown in above, it can be noted the following:

- Only three LCA studies have examined the environmental performance of drug production, including its packaging (McAlister et al., 2016; Sharma et al., 2020; Siegert et al., 2020)
- Global warming was the most common impact categories in the LCA studies, followed by ozone depletion, human toxicity and freshwater eutrophication.
- Comparative LCA studies of packaging materials have shown that the use of polymer presents environmental benefits compared to other materials (Belboom et al., 2011; Dhaliwal et al., 2014; Navajas et al., 2017; Raju et al., 2016).
- Five LCA studies have concluded that packaging production presented largest environmental impacts (Belboom et al., 2011; Dhaliwal et al., 2014; McAlister et al., 2016; Navajas et al., 2017; Sharma et al., 2020).

The literature review on LCA studies of pharmaceutical products revealed that there is no previous LCA studies of large volume parenterals (LVPs). Therefore, this study will contribute to the literature on LCA of pharmaceutical products, by analyzing a type of pharmaceutical

product that have not been previously addressed, as well as considering special plastic materials for healthcare packaging applications (e.g. modified polypropylene random copolymer).

3. Materials and methods

The following chapter presents the materials and methods used to evaluate the environmental performance of a plastic packaging for large volume parenterals (LVPs). First, Section 3.1 provides an overview of the assessment framework implemented in this study. This is followed by the goal and scope definition in Section 3.2, life cycle inventory and modeling in Section 3.3, alternative scenarios for plastic packaging waste in Section 3.4 and future scenarios for packaging production in Section 3.5. Finally, Section 3.6 presents the environmental impact categories used in the assessment.

3.1. Assessment framework

Figure 1 describes the assessment framework implemented for the environmental LCA performed in this study. It is based on the LCA ISO 14040 and 14044, 2006 (goal and scope definition, life cycle inventory analysis, life cycle impact assessment, and interpretation of results). The assessment framework includes steps that were carried out in the pharmaceutical company (characterization of the product and processes and production data). Finally, recommendations on the environmental performance of the plastic packaging are provided to the pharmaceutical company.

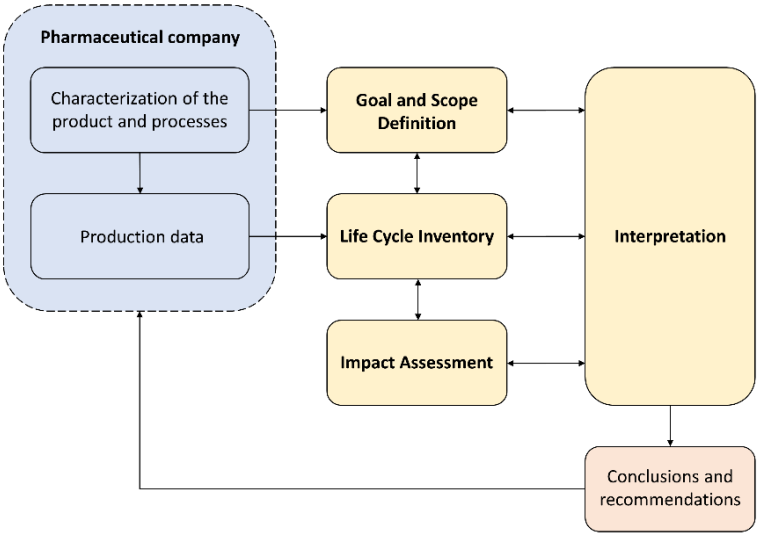

Figure 1. Assessment framework.

3.2. Goal and scope definition

The goal of this study is to assess the environmental performance of a plastic packaging for LVPs (Figure 2) manufactured by a pharmaceutical company in Portugal, aiming at identifying opportunities for material efficiency and environmental improvement.

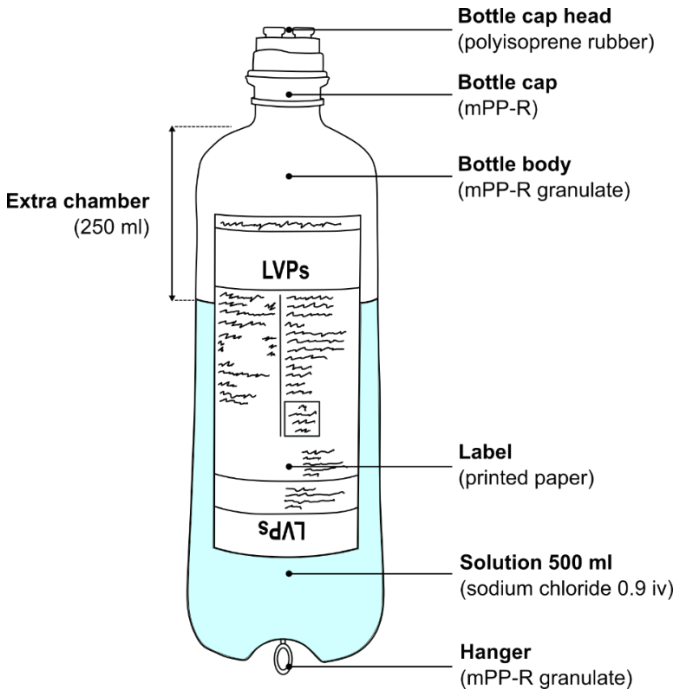

Figure 2. Plastic packaging for 500 ml large volume parenterals (LVPs).

Figure 2 presents the plastic packaging for LVPs. It is made of "modified polypropylene random copolymer" (mPP-R), which is typically used for healthcare packaging applications. The plastic packaging in addition to being used to protect and deliver the solution, also has an extra chamber that allows the addition of 250 ml of storable injectable drug. Furthermore, tertiary packaging is used for the distribution of the plastic packaging: a cardboard box to contain 20 plastic packaging units and an information leaflet.

Figure 3 shows the system boundaries (cradle-to-grave), which includes the following main stages:

- Production of materials (mPP-R granulate, bottle cap, labels, cardboard box, information leaflet, and sodium chloride) and their transport to the pharmaceutical company.
- LVPs production. For confidentiality reasons, the processes for manufacturing (packaging production and solution preparation) are presented as a black-box model.
- Waste management from the LVPs production: valorization of mPP-R waste (avoided materials: virgin polypropylene) and landfilling of rubber waste. It is also considered an alternative production scenario with internal recycling of mPP-R waste.
- Transport of final product (LVPs) from the pharmaceutical company to alternative hospitals located in Portugal (Coimbra, Faro, Lisbon, Porto) and Spain (Catalonia, Galicia, Madrid, Seville).

- End-of-life of final waste materials from hospitals: (i) incineration of plastic packaging waste in a specialized incinerator for hazardous waste and (ii) valorization of tertiary packaging waste (avoided materials: linerboard and fluting medium (raw materials of a cardboard box), and tissue paper). Alternative end-of-life scenarios for plastic packaging waste are considered: landfilling and recycling (avoided materials: virgin polypropylene, rubber, and tissue paper). The allocation at the point of substitution is used to allocate the environmental impacts.

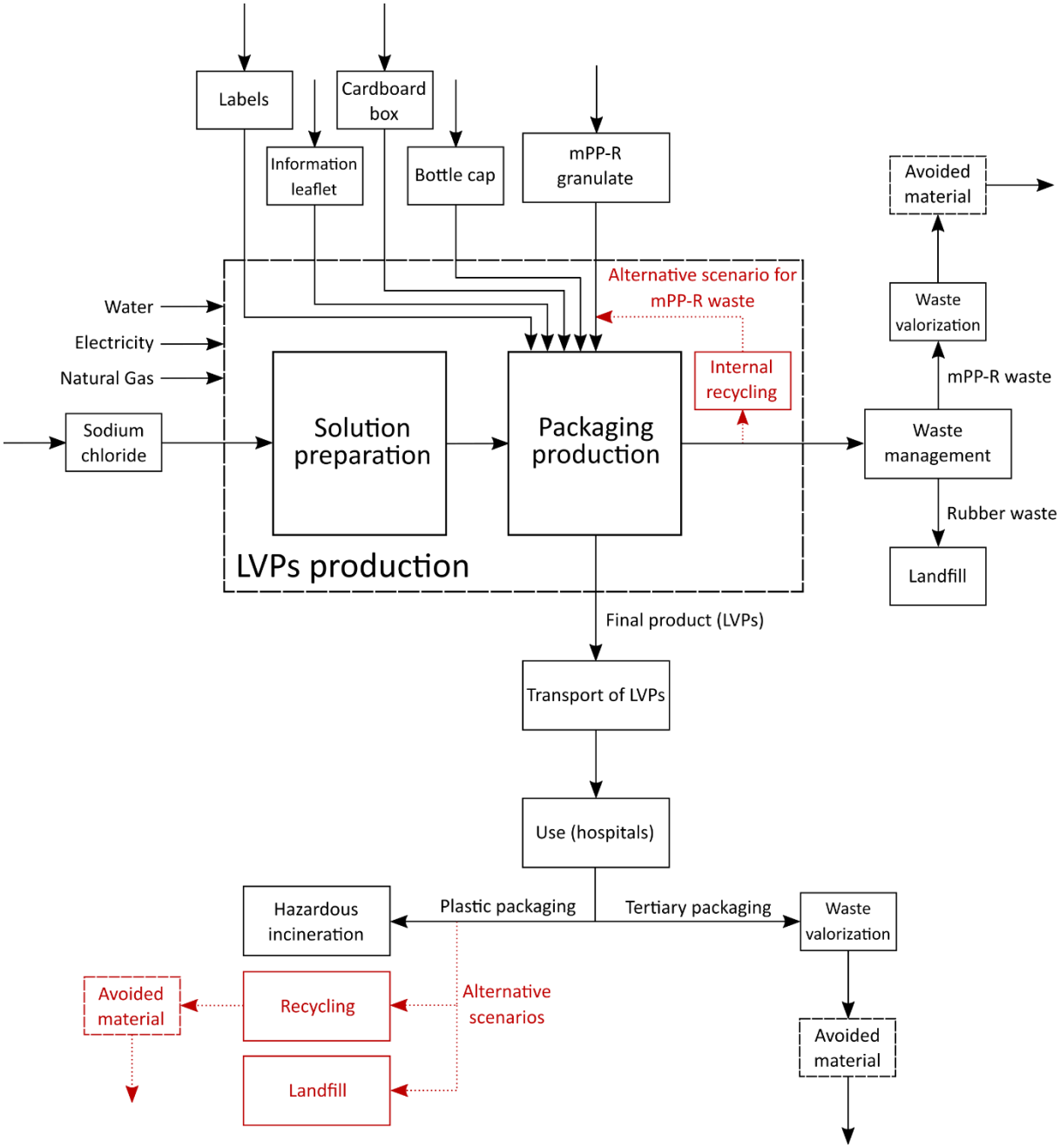

Figure 3. System boundaries (cradle-to-grave). The red mark represents alternative scenarios.

The functional unit is defined to provide a reference to which all inputs and outputs in the system boundaries are normalized; in this study, the functional unit is defined as 1 unit of LVPs to deliver 500 ml of solution to a patient for an intravenous therapy at hospitals. Based on this, the reference flow is defined as 1 unit of LVPs.

3.3. Life cycle inventory and modeling

The implementation of life cycle models and inventories was performed based on primary data collected at the pharmaceutical company for the processes involved in the LVPs production. Primary data was obtained for the quantity and cost of materials, manufacturing processes (energy demand), and as well as transportation of raw materials and distribution of final product (type of transport, distances, location of origin, and transport load). Secondary data include material production, transport models, and end-of-life were obtained and modelled from Ecoinvent 3.1 LCI database and Ecoinvent node (Data on Production of Chemicals created for the EU Product Environmental Footprint (PEF) pilot phase implementation) (ecoinvent, 2017).

3.3.1. Production primary data

Data collection from the pharmaceutical company was carried out through visits to the company, followed by a series of interviews with the production operators responsible for the LVPs production, measurements on the electrical panels and filling out inventory sheets (material and energy). The material and energy inventory in the LVP production consists of average production values from September 2020. According to the production operators, the LVPs production worked under normal operational conditions in September 2020.

i) Material inventory

Figure 4 illustrates the mass balance of mPP-R for one LVPs packaging production unit with following inputs: (i) mPP-R granulate that is used to manufacture the bottle body and the hanger; (ii) the bottle cap is also made of mPP-R. The final plastic packaging is made of 25.28 ± 0.51 [g] of mPP-R, but to manufacture one unit, on average 31.0 [g] of mPP-R is consumed with 18.4% of material loss, which corresponds to 5.7 [g] of mPP-R waste. In addition, the worst (Max) and the best (Min) production batch in September 2020 were identified in Figure 4, to understand the variability of the LVPs production and how much material losses can be reduced in future scenarios for packaging production. Detailed data used to build Figure 4 are presented in Table A1 in Appendix A.

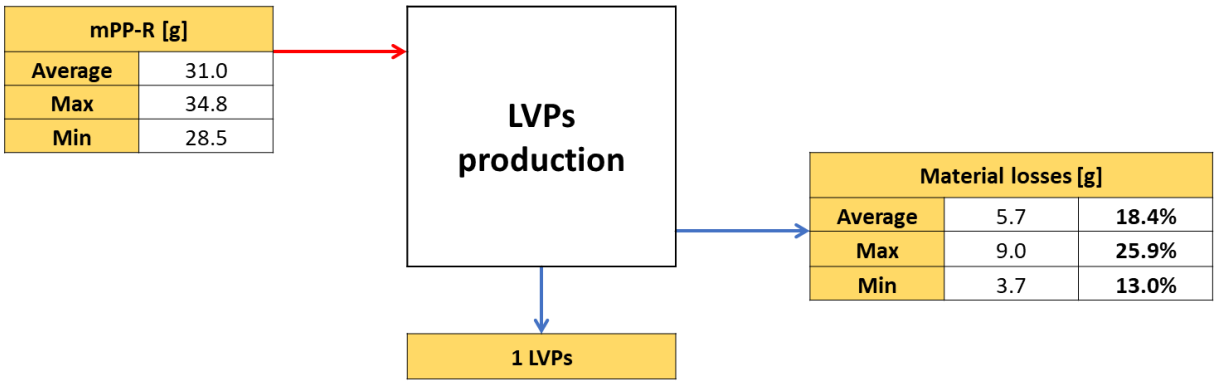

Figure 4. Mass balance of mPP-R in the LVPs production in September 2020, per unit of LVPs.

Table 2 shows the average inventory of materials associated with the production of one unit of LVPs in September 2020. The losses are treated in the following way:

- mPP-R waste is sent to a valorization facility, in which a mechanical recycling process is performed. The recycled mPP-R is later used to produce strings or parts of electrical components commonly made from polypropylene.
- Rubber waste is treated as undifferentiated waste and sent to the nearest landfill since it cannot be recycled.
- Wastewater from solution preparation is treated through a physical-chemical control before being discarded.
- Material losses of labels, information leaflets, and cardboard boxes are considered negligible.

Table 2. Inventory of inputs and outputs in the LVPs production in September 2020, per unit of LVPs.

	Unit	Amount
Input		
mPP-R granulate	g	27.0
mPP-R (bottle cap)	g	4.0
Rubber (bottle cap)	g	1.0
Bottle label	g	0.3
Cardboard box	g	16.2
Information leaflet	g	0.3
Sodium chloride	g	4.8
Water	L	0.8
Output - Final product (LVPs)		
Plastic packaging	g	31.0
Solution	L	0.5
Tertiary packaging	g	16.5
Losses		
mPP-R waste	g	5.7
Rubber waste	g	0.1
Sodium chloride	g	0.3
Wastewater	L	0.3

ii) Energy inventory

The energy inventory is built based on the electricity and natural gas bills of the pharmaceutical company in September 2020. The consumption of electricity and natural gas were allocated to the processes in the LVPs production in the following way:

- **Electricity:** It was obtained by measurements on the electrical panels and reviewed technical data (Table A2 in Appendix B). According to the production operators, the LVPs production line operated under normal operational conditions.
- **Natural gas:** It is associated with the industrial boiler that provides steam to the processes (e.g. sterilization of the LVPs). So, the consumption of steam provided for each process was used (Table 3A in Appendix B).

Table 3 presents the energy requirement in the LVPs production, this is further detailed in Table A4 in Appendix B. Energy consumption is divided between packaging production and solution preparation, but for packaging production is also divided in production and air conditioning and lighting.

Table 3. Energy requirements: inventory per unit of LVPs produced in September 2020.

LVPs production	Total	Packaging production				Solution preparation	
		Production		Air conditioning and lighting			
	[kWh]	[kWh]	%	[kWh]	%	[kWh]	%
Electricity	0.57	0.25	42.8%	0.20	34.5%	0.13	22.7%
Natural gas	0.72	0.71	99.0%			0.01	1.0%

3.3.2. Secondary data modeling

i) Production of mPP-R granulate

According to information from the pharmaceutical company, mPP-R granulate is mainly composed of polypropylene random copolymer (PP-R) and small amounts of plastic additives (up to 0.5 % by weight). PP-R is an ethylene/propylene copolymer produced by copolymerizing together propylene and small amounts of ethylene (usually 7% or lower), which is incorporated randomly in the polypropylene chain (Hisham A. Maddah, 2016). Plastic additives are chemical compounds that are added to polymers to provide better performance during shaping, functionality and ageing properties (Hahladakis et al., 2018).

The modeled composition of mPP-R granulate is presented in Table 4. Production data of mPP-R granulate was modeled with information available in literature and standards (complies with the European Pharmacopoeia (EDQM, 2013)), by lack and confidentiality of specific information related to the specific composition of mPP-R granulate (quantities and plastic additives). The production of polypropylene was modeled with data obtained from Ecoinvent database and the production of ethylene and plastic additives were modeled with data obtained from (ecoinvent, 2017). However, it was not possible to find data on all plastic additives listed in the European Pharmacopoeia (EDQM, 2013), so the composition had to be modeled only with the plastic additives listed below:

- **Plastic additive 09:** pentaerythrityl tetrakis [3-(3,5-di-tert-butyl-4-hydroxyphenyl) propionate]
- **Plastic additive 11:** octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl) propionate
- **Plastic additive 12:** tris(2,4-di-tert-butylphenyl) phosphite

Table 4. Modeled composition of mPP-R granulates.

Material	PP-R		Plastic additives		
	Polypropylene	Ethylene	Plastic additive 09	Plastic additive 11	Plastic additive 12
Composition [%]	95.5%	4.0%	0.17%	0.17%	0.16%

ii) Energy

The consumption of electricity and natural gas was modeled using specific literature data for Portugal, present below:

- **Electricity**: Based on Garcia et al., 2014 and Kabayo et al., 2019 on the consumption mix from 2012 to 2019 of medium voltage levels.
- **Natural gas:** Based on Safaei et al., 2017 and Safaei et al., 2015.

3.3.3. Transport

The transport inventory was built with primary data (type of transport, distances, location of origin, and transport loads). Table 5 presents the inventory data on the transport of input materials in the LVPs production, the type of transport was modeled with the processes available in the Ecoinvent database.

Table 5. Inventory data on the transport of materials.

Material	Type of transport	[km]	Location of origin
mPP-R granulate	Lorry >32t	2186	Italy (Ferrara)
Bottle cap	Lorry 16-32t	202	India (Gujarat)
	Transoceanic ship	10025	India (Hazira port)
	Lorry 16-32t	135	Leixões
Cardboard box	Lorry 16-32t	123	Leiria
Labels	Light vehicle	162	Vila Nova de Famalicão
Information leaflet	Lorry 3.5-7.5t	244	Loures
Sodium chloride	Lorry >32t	2931	Austria (Ebensee)

The transport of final product (LVPs) is performed to alternative hospitals locations in Portugal (Coimbra, Faro, Lisbon, Porto) and Spain (Catalonia, Galicia, Madrid, Seville). Therefore, as Table 6 shows, alternative distribution scenarios were considered: Average (Spain and

Portugal) corresponds to the average distance to all hospitals from the pharmaceutical company. The following scenarios correspond to the farthest hospital in Spain (Catalonia) and the closest hospital in Portugal (Coimbra) from the pharmaceutical company, respectively.

Table 6. Inventory data on the alternative distribution scenarios for the transport of LVPs.

Scenario	[km]	Location of hospitals
Average (Spain and Portugal)	412	(Coimbra, Faro, Lisbon, Porto, Catatonia, Galicia, Madrid, Seville)
Max distance to Spain	1048	Catalonia
Min distance in Portugal	51	Coimbra

The transport of final product (LVPs) is carried out by refrigerated transport with controlled atmosphere. Due to the lack of a specific process for this type of transport in the Ecoinvent database v.3.1, the transport of final product was modeled by adapting the transport model "lorry >32t with the following adaptations (Lévová, T. 2015):

- Increase of 20 [%] in diesel consumption per [t.km] compared to the transport model "lorry size class >32t".
- Consumption of 1E-05 [kg/t.km] of R134a refrigerant liquid, due to the refrigeration machine.

3.3.4. End-of-life

The reference scenario examined the end-of-life of plastic packaging based on existing national regulations for hospital waste. This packaging is currently classified as hazardous waste since it may be exposed to contamination during its use phase in hospitals (DGS, 2014). Therefore, in Portugal, they are sent to specialized incinerators for hazardous waste located in the "*Eco Parque do Relvão*" (APA).

The tertiary packaging is only used to contain the plastic packaging during the transport of LVPs, so there is no risk of contamination in hospitals. Therefore, it is classified as urban waste and sent to the nearest plant for its valorization. It is assumed that waste materials avoid the extraction of virgin raw materials. The recycled cardboard waste is used to produce linerboard and fluting medium (raw materials of a cardboard box) and the recycled wastepaper is used to

produce tissue paper. The allocation at the point of substitution is used to allocate the environmental impacts.

3.4. Alternative scenarios for plastic packaging waste

Alternative end-of-life scenarios for plastic packaging waste are based on the assumption that the plastic packaging is not exposed to contamination during its use phase in hospitals, so it is treated as urban waste that could be recycled or landfilled. This depends on whether there is a selective collection (for recycling) or whether it is classified as undifferentiated waste (for landfill).

Table 7 presents the average distance from hospitals in Portugal to the waste treatment facilities of each end-of-life scenario. For the transport of plastic packaging waste, it is used the process available in the Ecoinvent database v.3.1 for municipal waste collection service by 21 metric ton lorry.

Table 7. Average distances from hospitals in Portugal to the waste treatment facilities.

End-of-life	**Reference (Hazardous incineration) [km]**	**Municipal landfill [km]**	**Recycling [km]**
(Coimbra, Faro, Lisbon, Porto)	206	22	15

3.5. Future scenarios for packaging production

As mentioned above, the LVPs production line operated under normal operational conditions in September 2020, but internal processes in the packaging production are still in the optimization phase. Therefore, two consecutive future scenarios for packaging production are proposed with material efficiency improvements to reduce consumption of mPP-R granulate and material losses simultaneously, as well as the costs associated with mPP-R granulate.

Mass balances of the future scenarios for packaging production are shown in Figure 5. The future scenarios are based on the improvements below, which were defined based on the expectations of the pharmaceutical company.

i) Reduction of losses corresponding to around 21% of the losses in September 2020 (Figure 5a).

ii) Internal recycling of mPP-R waste to manufacture the hanger due to it is not in direct contact with the solution, so it does not have high material requirements. This is due to recycled mPP-R presents lesser quality than virgin mPP-R granulate, so it cannot be used to manufacture the bottle body.

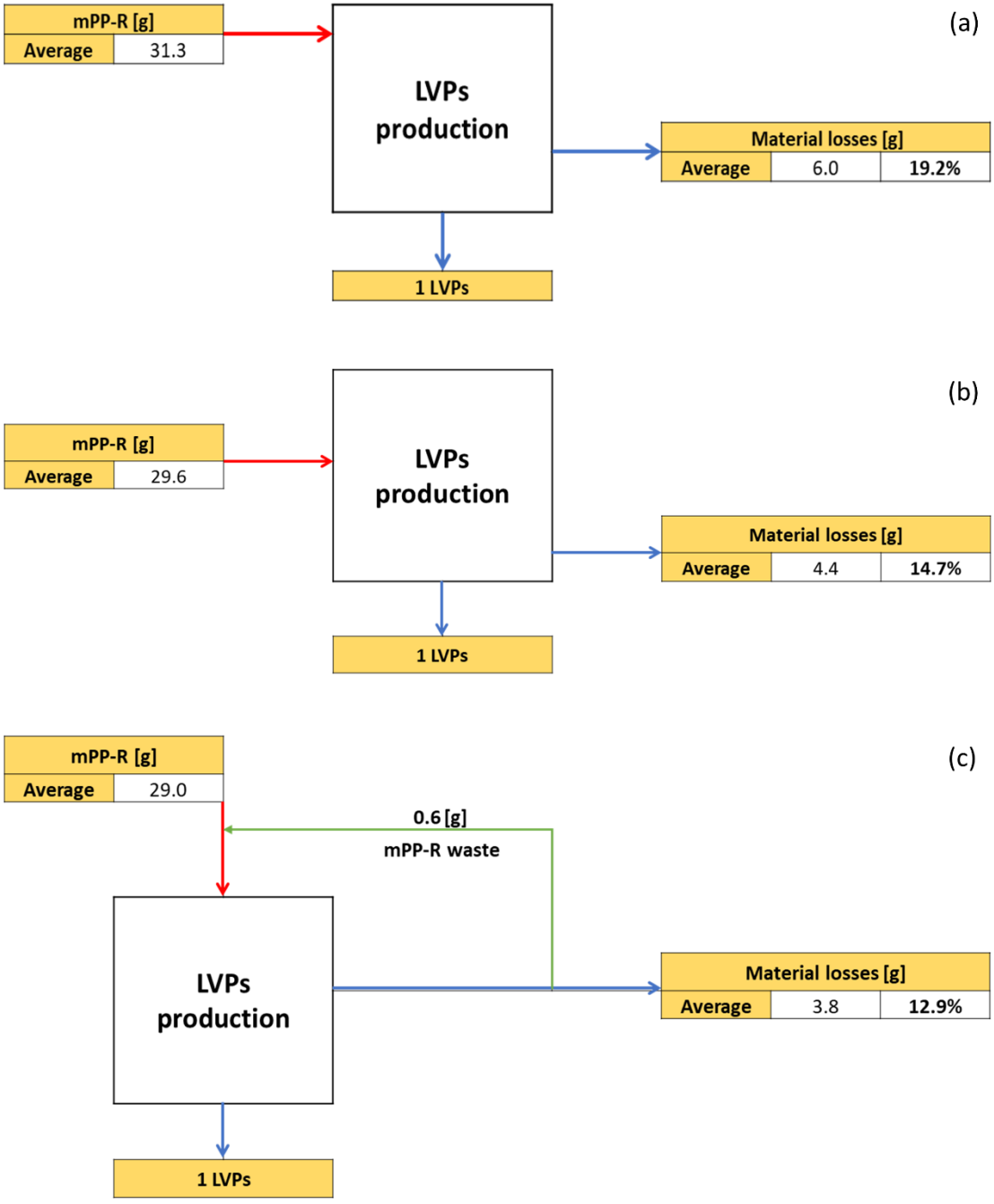

Figure 5. Mass balance of the future scenarios for packaging production, per unit of LVPs. (a) September 2020. (b) Future production. (c) Future production with internal recycling.

The first future scenario (Figure 5b: future production) considers only the first improvement. Comparing the figure 5b with the mass balance of mPP-R in September 2020 (Figure 4), it can

be observed that the material losses are between the variability, showing that it is possible to implement this improvement in the packaging production. The second future scenario (Figure 5c: future production with internal recycling) considers both improvements.

3.6. Environmental Impact Categories

Impact categories and methods selected are shown in Table 8. The selection has been based on recommendations from the Product Category Rules (PCR) for pharmaceutical products and processes (Siegert et al., 2019) and from Fazio et al., 2018.

Table 8. Selected impact categories and methods.

Impact category	Unit	LCIA method
Climate change	kg CO2 eq	Baseline model of 100 years of the IPCC (based on IPCC 2013)
Resource use (fossils)	MJ	CML Guinée et al. (2002) and van Oers et al. (2002).
Acidification	mol H+ eq	Accumulated Exceedance (Seppälä et al. 2006, Posch et al, 2008)
Freshwater eutrophication	kg P eq	EUTREND model (Struijs et al, 2009) as implemented in ReCiPe
Resource use (minerals and metals)	kg Sb eq	CML Guinée et al. (2002) and van Oers et al. (2002).
Ozone depletion	kg CFC-11eq	Steady-state ODPs as in (WMO, 1999)
Freshwater ecotoxicity	CTUe	USEtox 2.1. model (Rosenbaum et al, 2008)
Human toxicity cancer	CTUh	USEtox 2.1. model (Rosenbaum et al, 2008)
Human toxicity non-cancer	CTUh	USEtox 2.1. model (Rosenbaum et al, 2008)

4. Results and Discussion

The following chapter presents and discusses the results obtained in this study. First, in Section 4.1 the impacts associated to all life cycle stages (cradle-to-grave) are analyzed, followed by the results in each stage: LVPs production and waste management (September 2020) in Section 4.2, production and transport of materials in Section 4.3, transport of LVPs in Section 4.4 and end-of-life of waste materials collected from hospitals (reference scenario) in Section 4.5. Then, in Section 4.6 and Section 4.7 the analysis of the alternative scenarios for end-of-life and future scenarios for production are discussed, respectively. Finally, the main results are discussed in Section 4.8.

4.1. Life cycle impacts

The results obtained from the impact assessment for the 1 unit of LVP are shown in Figure 6 and Table 9. On the one hand, it can be highlighted that LVPs packaging production contributes more than 50 % to climate change, resource use (fossils), freshwater eutrophication and freshwater ecotoxicity due to the consumption of electricity and natural gas, and it also contributes more than 30% to the remaining categories. On the other hand, LVPs solution preparation contributes 15% and 17% to freshwater eutrophication and freshwater ecotoxicity, respectively, and less than 15% to the remaining categories. The lower contributions are due to the lower consumption of electricity and natural gas.

The following can also be noted from Figure 6 and Table 9: The production of materials contributes around 30% to resource use (fossils) and acidification due to mPP-R granulate, contributes 46% to resource use (minerals and metals) due to the cardboard box and bottle cap, and it also presents considerable contributions to climate change (16%) and human toxicity, non-cancer (20%). The transport of LVPs to hospitals requires refrigerated transport (with controlled atmosphere), which results in important contribution to ozone depletion (37%) in the distribution scenario “Average (Spain and Portugal)” (due to consumption of coolant R134a) and particularly for long transportation distances, contributing up to of 60% in the distribution scenario “Max (Catalonia, Spain)”. This scenario also contributes considerably more to resource use, minerals and metals (17%) and human toxicity non-cancer (18%). The end-of-life of LVPs from hospitals contributes 46% to human toxicity cancer due to the incineration of plastic packaging waste.

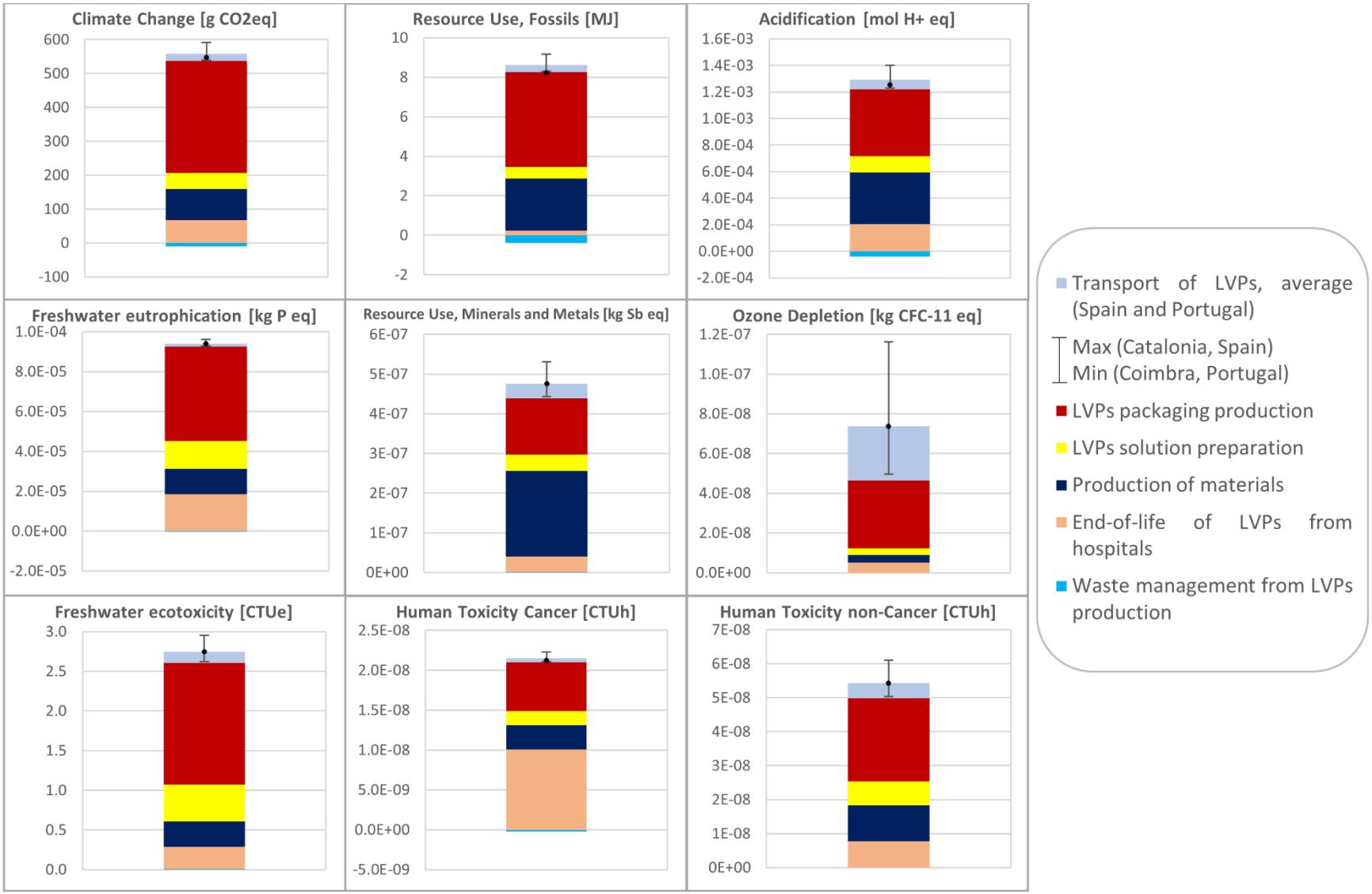

Figure 6. LCIA for the life cycle of 1 unit of LVPs.

Table 9. LCIA for the life cycle of 1 unit of LVPs.

Impact category	Unit	LVPs packaging production	LVPs solution preparation	Production of materials	Transport of LVPs, average	End-of-life of LVPs from hospitals	Waste management from production
Climate change	g CO2 eq	330.7	46.7	91.8	21.2	67.6	-10.3
Resource use, fossils	MJ	4.78	0.59	2.64	0.36	0.24	-0.39
Acidification	mol H+ eq	5.0E-04	1.2E-04	3.9E-04	7.2E-05	2.1E-04	-3.9E-05
Freshwater eutrophication	kg P eq	4.7E-05	1.4E-05	1.3E-05	1.4E-06	1.9E-05	-9.1E-09
Resource use, minerals and metals	kg Sb eq	1.4E-07	4.1E-08	2.2E-07	3.6E-08	3.9E-08	7.3E-10
Ozone depletion	kg CFC-11 eq	3.4E-08	3.2E-09	4.0E-09	2.7E-08	5.0E-09	7.3E-11
Freshwater ecotoxicity	CTUe	1.53	0.46	0.32	0.14	0.28	5.7E-03
Human toxicity cancer	CTUh	6.1E-09	1.8E-09	3.0E-09	5.1E-10	1.0E-08	-2.5E-10
Human toxicity non-cancer	CTUh	2.4E-08	6.9E-09	1.1E-08	4.4E-09	7.7E-09	6.1E-11

4.2. LVPs production and waste management

Figure 7 presents the contribution analysis associated to the LVPs production and waste management. It can be highlighted that the consumption of electricity in the LVPs packaging production contributes more than 65% to acidification, freshwater eutrophication, freshwater ecotoxicity, human toxicity cancer and human toxicity non-cancer due to the production, which contributes around 40% to these categories, as well as air conditioning and lighting with slightly inferior contributions than production (19% lower impacts) due to the lower consumption of electricity. The consumption of natural gas in the LVPs packaging production has large contributions on climate change (47%), resource use, fossils (54%) and ozone depletion (64%).

The following can also be observed from Figure 7: (i) LVPs solution preparation contributes around 20% to 6 (out of 9) impact categories, except for climate change, resource use (fossils) and ozone depletion. The consumption of electricity presents more than 90% of the impacts of the LVPs solution preparation in all categories, which can be seen in Table A5 in appendix C. (ii) Waste management presents minor environmental credits (less than 5%) on climate change, resource use (fossils), acidification, freshwater eutrophication and human toxicity cancer due to the valorization of mPP-R waste since it is avoided the production of virgin polypropylene, as shown in Table A6 in Appendix C. In contrast, there are minor contributions to the remaining impact categories (less than 1%) due to the recycling process of mPP-R waste and landfilling of rubber waste.

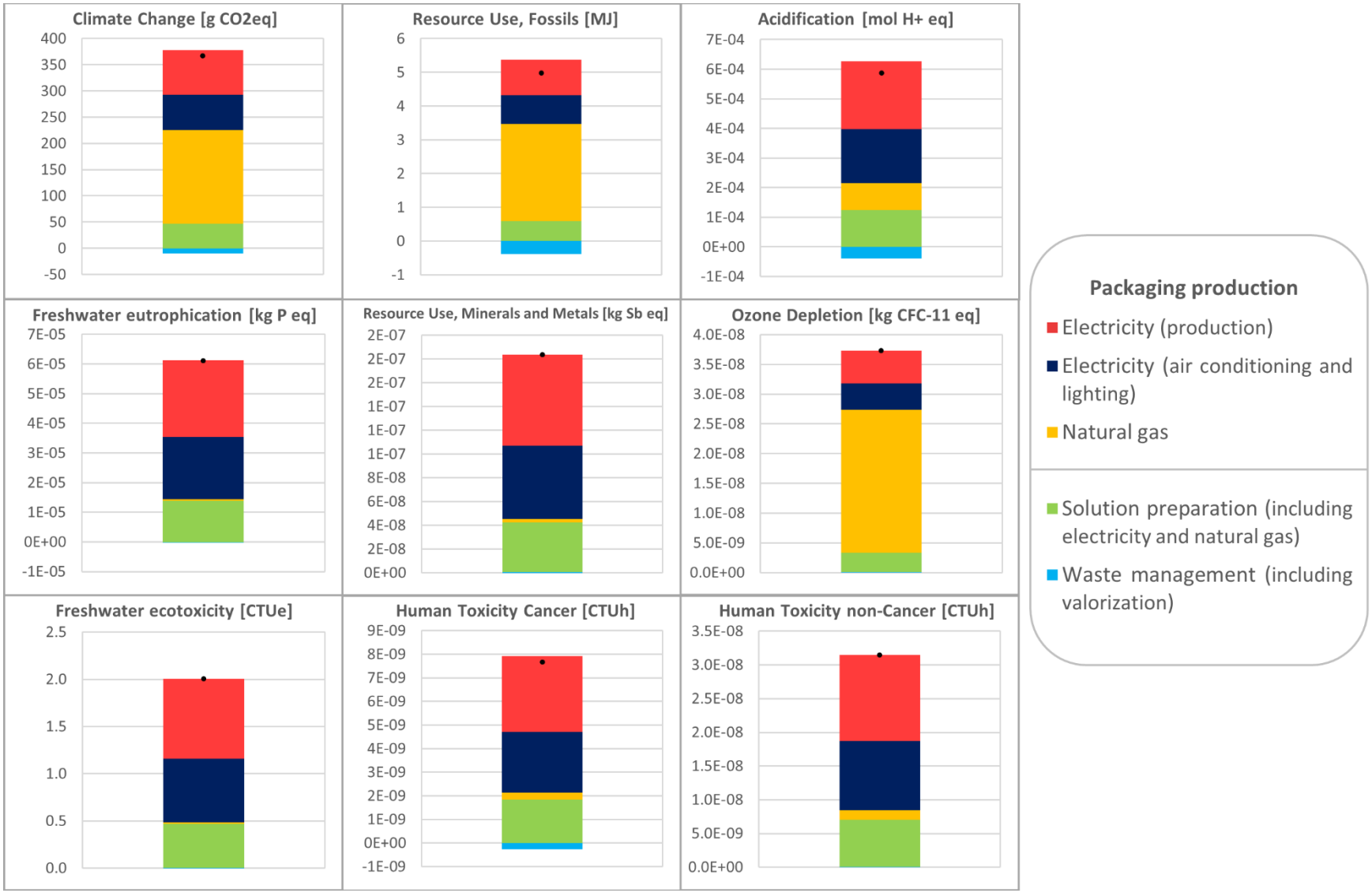

Figure 7. LCIA for manufacturing: LVPs production, waste management, per unit of LVPs.

4.3. Production of materials

Figure 8 illustrates the contribution analysis associated to the production of materials used in the LVPs production. It can be noted that mPP-R granulate contributes to the largest resource use, fossils (75%) and acidification (56%), as well as climate change (60%) and human toxicity, cancer (46%). In addition, the results of the production of mPP-R granulate, as shown in Table 10, indicate that polypropylene has the largest share of the impacts of the mPP-R granulate (more than 80%) in all categories, except for resource use (minerals and metals) and ozone depletion. This is due to the small share of ethylene and plastic additives in the modeled composition of mPP-R granulate.

Table 10. LCIA for the production of mPP-R granulate, per unit of LVPs.

Impact category	Unit	mPP-R granulate	Modeled composition			Transport
			Polypropylene	Ethylene	Plastic additives	
Climate change	g CO2 eq	59.3	51.8	1.9	0.9	4.76
Resource use, fossils	MJ	1.98	1.81	0.07	0.02	0.08
Acidification	mol H+ eq	2.2E-04	1.9E-04	5.0E-06	4.1E-06	1.7E-05
Eutrophication, freshwater	kg P eq	2.3E-06	1.7E-06	3.8E-09	2.2E-07	3.6E-07
Resource use, minerals and metals	kg Sb eq	1.5E-08	1.5E-09	2.9E-10	3.5E-09	9.4E-09
Ozone depletion	kg CFC-11 eq	1.0E-09	2.3E-11	1.2E-11	2.0E-11	9.4E-10
Ecotoxicity, freshwater	CTUe	7.7E-02	3.8E-02	8.6E-04	2.6E-03	3.5E-02
Human toxicity, cancer	CTUh	1.5E-09	1.3E-09	4.6E-11	1.5E-11	1.3E-10
Human toxicity, non-cancer	CTUh	2.1E-09	7.1E-10	1.0E-10	9.5E-11	1.1E-09

It can also be observed from Figure 8 that the cardboard box contributes 41% to resource use (minerals and metals) and more than 45% to freshwater eutrophication, ozone depletion, freshwater ecotoxicity and human toxicity non-cancer due to the amount of material required per unit of LVPs. The bottle cap contributes 38% to resource use (minerals and metals) due to polyisoprene rubber, as shown in Table A7 in Appendix C. Printed paper (information leaflet and labels) and sodium chloride presents minor contributions to all impact categories (less than 10%). These results also consider the contributions of the transport of each material, which are low compared to production.

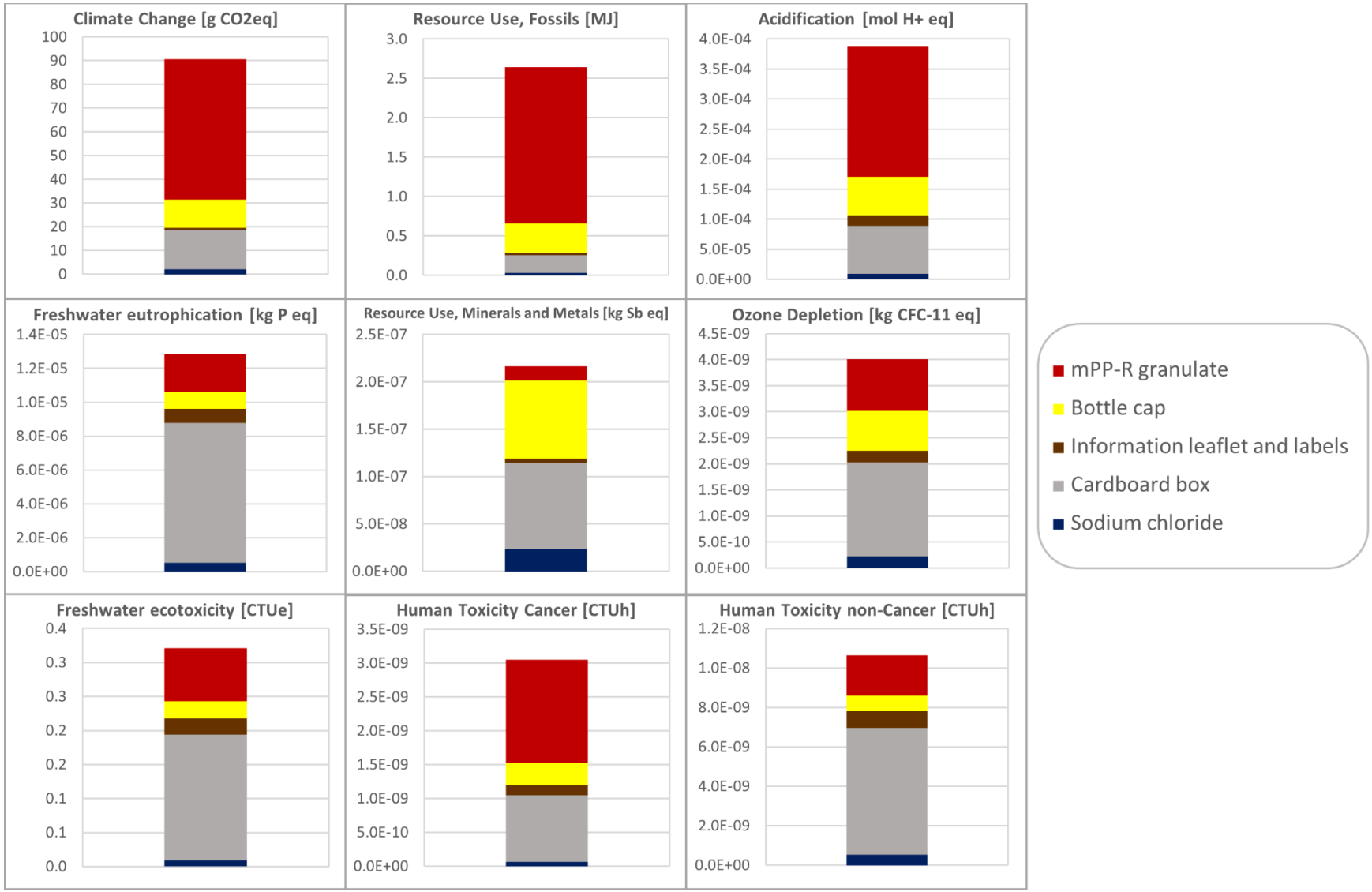

Figure 8. LCIA for the production of materials, per unit of LVPs.

4.4. Transport of LVPs to hospitals

The results of the distribution scenarios are shown in Table 11. It can be noted that "Max (Catalonia, Spain)" corresponds to an increase of 154% compared to the impacts of the average scenario due to a much greater distance. Conversely, "Min (Coimbra, Portugal)" corresponds to a decrease of 88% compared to the impacts of the average scenario. The large contribution of the transport of LVPs to ozone depletion is due to distance and coolant R134a, which contributes 85% to the impacts of the transport of LVPs in this category.

Table 11. LCIA results for the transport of 1 unit of LVPs.

Impact category	UNITS	Distribution scenario		
		Average (Spain and Portugal)	Max (Catalonia, Spain)	Min (Coimbra, Portugal)
Climate change	g CO2 eq	21.19	53.86	2.63
Resource use, fossils	MJ	0.36	0.91	0.04
Acidification	mol H+ eq	7.2E-05	1.8E-04	8.9E-06
Eutrophication, freshwater	CTUe	1.4E-01	3.5E-01	1.7E-02
Resource use, minerals and metals	kg Sb eq	3.6E-08	9.2E-08	4.5E-09
Ozone depletion	kg CFC-11 eq	2.7E-08	7.0E-08	3.4E-09
Ecotoxicity, freshwater	CTUe	0.14	0.35	0.02
Human toxicity, cancer	CTUh	5.1E-10	1.3E-09	6.3E-11
Human toxicity, non-cancer	CTUh	4.4E-09	1.1E-08	5.5E-10

4.5. End-of-life of waste materials collected from hospitals

Figure 9 presents the contribution analysis associated to the end-of-life of waste materials collected from hospitals. It can be observed that the incineration of plastic packaging waste contributes 99% to human toxicity cancer and more than 70% to the rest of impact categories, this may be due to the plastic packaging waste is treated as hazardous waste. In addition, the transport of plastic packaging waste presents a considerable contribution on resource use, fossils (28%), acidification (20%) and ozone depletion (22%).

It can also be observed from Figure 9 that the valorization of tertiary packaging waste presents large environmental credits on resource use, fossils (39%) and environmental credits more than 20% to freshwater eutrophication, ozone depletion, freshwater ecotoxicity and human toxicity non-cancer. This is due to the valorization of the cardboard waste (Table A8 in Appendix C), which avoids the production of linerboard and fluting medium (cardboard box) and tissue paper (wastepaper).

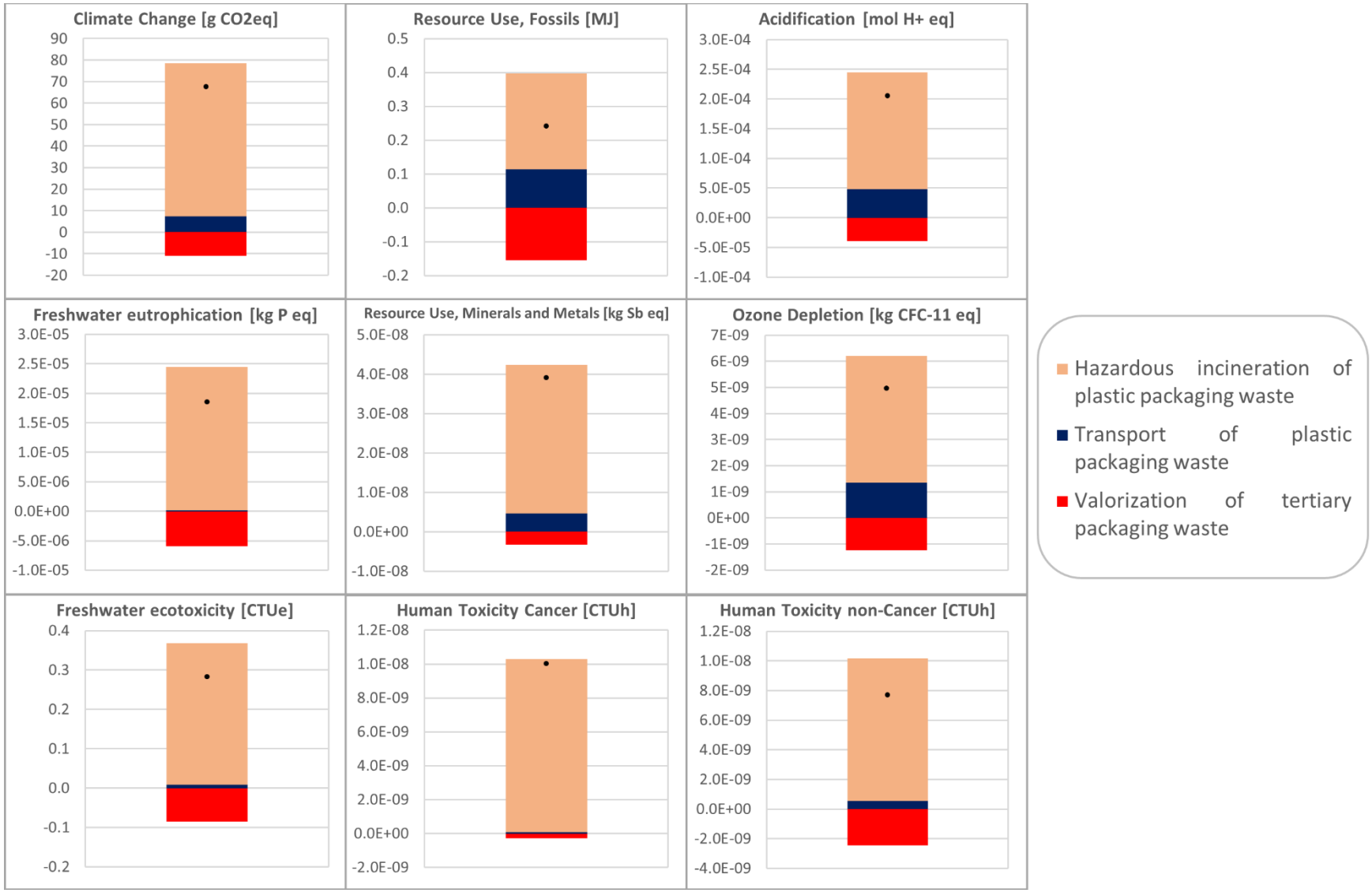

Figure 9. LCIA for the end-of-life stage: incineration of plastic packaging waste and valorization of tertiary packaging waste, per unit of LVPs.

4.6. Alternative end-of-life scenarios for plastic packaging waste

The results of the alternative end-of-life scenarios are depicted in Figure 10. It can be noted that recycling outperformed the reference and landfill scenario in all impact categories. Indeed, it had environmental credits in 7 (out of 9) impact categories, especially in climate change, resource use (fossils), acidification and resource use (mineral and metals), which are due to the valorization of plastic packaging waste since the production of the following materials are avoided: (i) virgin polypropylene (from mPP-R waste), (ii) rubber (from rubber waste) and (ii) tissue paper (from wastepaper). Moreover, the transport distance is 93% shorter than in the reference scenario.

It can also be observed from Figure 10 that landfill scenario outperformed the reference scenario in 7 (out of 9) impact categories since the municipal landfill treatment presented much lower impacts than hazardous incineration treatment and shorter transport distances. However, landfill scenario performed much worse than the reference scenario in freshwater ecotoxicity (703% higher impacts) and human toxicity non-cancer (293% higher impacts) due to the plastic packaging waste is treated as municipal solid waste.

Figure 10. LCIA for the alternative end-of-life scenarios for plastic packaging waste, per unit of LVPs.

4.7. Future scenarios for packaging production

The results of the future scenarios for packaging production are presented in Table 12. On the one hand, it can be noted that the future production and future production with internal recycling would represent a decrease in impacts of the production of mPP-R granulate of around 5% and 7%, respectively, in climate change, resource use (fossils), acidification and freshwater eutrophication due to less mPP-R granulate is consumed. On the other hand, there is a decrease in the environmental credits of the waste management from LVPs production due to less mPP-R waste is recycled (less polypropylene is avoided), this also represent a reduction in the impacts of the recycling process of mPP-R waste. In addition, the future scenarios for packaging production have a reduction in the total cost associated to mPP-R of up to 4% and 6%, respectively, as shown in the Table A9 in Appendix C.

Table 12. LCIA for the future scenarios for packaging production, per unit of LVPs.

Impact category	Units	Production of mPP-R granulate			Waste management from LVPs production		
		September 2020	Future production	Future production with internal recycling	September 2020	Future production	Future production with internal recycling
Climate change	g CO2 eq	59.3	56.5	55.2	-10.3	-7.9	-6.8
Resource use, fossils	MJ	1.98	1.88	1.84	-0.39	-0.30	-0.25
Acidification	mol H+ eq	2.2E-04	2.1E-04	2.0E-04	-3.9E-05	-3.0E-05	-2.6E-05
Eutrophication, freshwater	kg P eq	2.3E-06	2.2E-06	2.1E-06	-9.1E-09	-6.9E-09	-5.9E-09
Resource use, minerals and metals	kg Sb eq	1.5E-08	1.4E-08	1.4E-08	7.3E-10	5.6E-10	4.8E-10
Ozone depletion	kg CFC-11 eq	1.0E-09	9.8E-10	9.5E-10	7.3E-11	5.6E-11	4.8E-11
Ecotoxicity, freshwater	CTUe	7.7E-02	7.4E-02	7.3E-02	5.7E-03	5.0E-03	4.6E-03
Human toxicity, cancer	CTUh	1.5E-09	1.4E-09	1.4E-09	-2.5E-10	-1.9E-10	-1.6E-10
Human toxicity, non-cancer	CTUh	2.1E-09	2.0E-09	1.9E-09	6.1E-11	5.7E-11	5.5E-11

4.8. Discussion

The main results of this chapter are highlighted in this section. The results show that LVPs packaging production is an important contributor for all impact categories, especially for categories such as climate change, resource use (fossils), freshwater eutrophication and freshwater ecotoxicity (contributing more than 50% of the LC impacts), due to the consumption of electricity and natural gas. In contrast, LVPs solution preparation contributes considerably

less to all categories, with a 71% lower consumption of electricity than LVPs packaging production.

Results show that mPP-R granulate has the largest contributions to resource use, fossils (75%) and acidification (56%) (categories in which the production of materials contributes around 30% of the LC impacts), as well as climate change (60%) and human toxicity, cancer (46%). The cardboard box contributes 41% to resource use (minerals and metals) (category in which the production of materials contributes 46% of the LC impacts), as well as more than 45% to the remaining categories.

The transport of LVPs to hospitals requires refrigerated transport (with controlled atmosphere), which results in important ozone depletion, contributing 37% of LC impacts in the distribution scenario "Average (Spain and Portugal)" (due to consumption of coolant R134a) and particularly for long transportation distances, contributing up to of 60% of LC impacts in the distribution scenario "Max (Catalonia, Spain)".

The scenario analysis for the end-of-life of LVPs from hospitals shows that incineration of plastic packaging waste (reference scenario) has the largest contributions to human toxicity, cancer (99%) (category in which the end-of-life of LVPs from hospitals contributes 46% of the LC impacts), as well as more than 70% to the remaining categories due to the plastic packaging waste is treated as hazardous waste. Alternatives scenarios shown that recycling outperformed incineration and landfilling in all impact categories due to the production of virgin materials is avoided. Landfilling outperforms the incineration in 7 (out of 9) categories, except for freshwater ecotoxicity and human toxicity non-cancer due to the plastic packaging waste is treated as municipal solid waste.

The results of the future scenarios for packaging production suggest that "future production with internal recycling" presents a higher reduction in impacts and costs than "future production" due to less mPP-R material is consumed and less mPP-R waste is sent to the valorization facility. This in mainly due to the first improvement (reduction of material losses), which has the largest reduction potential in impacts and total cost.

5. Conclusions

This thesis presents the environmental life cycle assessment (LCA) of a new plastic packaging for 500 ml large volume parenterals (LVPs) manufactured by a pharmaceutical company in Portugal, aiming at identifying opportunities for environmental improvement, with the following specific objectives: (i) To analyze the environmental impacts and identify potential improvements for the manufacturing processes of the large volume parenterals (LVPs) at the pharmaceutical company; (ii) To analyze the environmental impacts of the production of materials and transport of final product for alternative hospital locations; (iii) To evaluate and compare different end-of-life options; (iv) To assess future production scenarios with reduction of losses and internal recycling of production losses

A life cycle (LC) model and inventory were implemented based on primary data collected at the pharmaceutical company. The results show that packaging production is important for all categories, especially for climate change, resource use (fossils), freshwater eutrophication and freshwater ecotoxicity (contributing more than 50% of the LC impacts), due to the consumption of electricity and natural gas in the pharmaceutical company. The mPP-R material and the cardboard box are the materials with the largest contributions, especially for resource use (fossils), acidification and resource use (minerals and metals). The transport of final product (LVPs) requires refrigerated transport (with controlled atmosphere), which results in important ozone depletion (due to consumption of coolant R134a), particularly for long transportation distances.

Two future scenarios for packaging production were assessed, considering: i) reduction of material losses; ii) reduction of material losses and reincorporation of internal waste of production. It can be noted that the second future scenario for packaging production presents a higher reduction in impacts and costs due to less mPP-R material is consumed and less mPP-R waste is sent to the valorization facility. However, the first improvement (reduction of material losses) presents a higher reduction potential in impacts and total cost than the second improvement (reincorporation of internal waste of production).

Alternatives scenarios for end-of-life assessed recycling or landfilling of plastic packaging. Results for the end-of-life scenarios show that recycling outperformed incineration of hazardous waste and landfilling in all impact categories, having environmental credits in 7 (out of 9) categories due to the production of virgin materials is avoided. Landfilling outperforms

the incineration of hazardous waste in 7 (out of 9) categories due to municipal landfill treatment and shorter distances from the pharmaceutical company.

With these findings, the following recommendations can be made: The reduction of material losses presents a higher reduction in impacts and total cost than the reincorporation of internal waste of production. Material improvements should also consider alternative options for the cardboard box with lower impacts. However, energy efficiency gains were not assessed, which could improve the environmental performance of LVPs in future scenarios, as shown in the results, the consumption of electricity and natural gas contribute considerably more to all impact categories, having a large impact reduction potential.

5.1. Limitations and future work

There were some limitations in the research presented in this thesis. The production processes analyzed in the pharmaceutical company are relatively new (production lines started in August of 2019), and they are still being improved when data collection was performed (September 2020). The consumption of electricity associated to air conditioning and lighting were allocated based on the volume of air-conditioned and illuminated area. In addition, it was necessary to handle the following data gaps: The composition of mPP-R granulate was modeled with information available in literature and standards; The material of the bottle cap heads (polyisoprene rubber) was approximated to synthetic rubber; The plastic packaging waste was considered as average hazardous waste in the treatment of hazardous incineration.

This thesis provides the following insights for future work that could be carried out in the pharmaceutical company and for future research:

- To update the life cycle model when production processes are fully optimized, using data for a longer time period.
- To assess different plastic packaging sizes (100, 200, 1000 ml), and other modes of distribution transport to international locations (air freight, transoceanic ship), and tertiary packaging in a sensitivity analysis.
- To consider the multiple functions of the plastic packaging to ensure the comparability with similar products available in the market with different type of packaging (e.g. solution bags) and materials.
- To compare the environmental performance of the new packaging for LVPs with the packaging previously manufactured by the pharmaceutical company.

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