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Environmental impact of the pharmaceutical packaging

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Executive Summary

1. Introduction

1.1 Background

The object of study of this project will be the pharmaceutical packaging, element that needs to be included in the distribution of any medicament. Nowadays, the global warming is a reality (Business Gateway, 2012) so that many companies are starting to introduce "environmentally friendly procedures" in their daily operations. This current also affects packaging, being normal to heard expressions like "green logistics" which focuses on sustainable material handling, waste management, packaging and transport (Rodrigue *et al*. 2009).

Pharmaceutical packaging has to convey information about the product, protect the product, and maintain the quality of the product through the entire distribution chain. But, from a pharma-perspective, packaging's main function is getting the product to the customer in a quality-based, protected manner (Hayes, 2010).

1.2 Problem Discussion

Packaging is characterized by trade-offs with other logistic activities. For instance, increase the protection that the package provides implies, from transportation point of view, decreases in the damage and theft in transit but also an increase in the packages weight and transport costs (Lambert *et al*.1998). Every decision related to the packaging has impact on some or other logistics activities hence a global vision for design is needed (Saghir. 2004).

Pharmaceutical packaging is characterized by three main aspects (Ferrón. 2012):

- Necessary and cheap: It is impossible to distribute pharmaceuticals without the protection that the packaging provides. In the other hand, the cost that the packaging represents is insignificant compared with others like active ingredients or the transport costs.
- Low percentage of the daily waste but very hazardous: Compared with the organic wastes that a standard family produces, the pharmaceutical packaging is insignificant. Anyway, the materials used are very difficult to recycle or process after their use.
- Very regulated element: every picture, design and material used, even each word of a leaflet, must fulfill the packaging regulations. The innovation possibilities are quite small in a very restrictive framework which try to protect at all cost the product.

The problem statement can be summarized as the necessity to conciliate these three main aspects that appear when designing the more environmentally friendly possible packaging. Due to this complexity, is possible that the perception of companies' performance could be away from the actual performance related to the environmental field.

1.3 Purpose and objective

The main purpose of this project is to explore the environmental performance related to packaging in the pharmaceutical industry. The thesis will try to determine if the industry is doing everything that is on its hand trying to reduce the packaging environmental impact and to compare their perception with the real environmental results. The main goal will be trying to determine the relation between the self environmental performance perceived by the companies and the real and objective environmental performance of the packaging exploring the existence of gaps. Other important objectives among others will be also: Determine what the most important aspects are when packaging designers create a pharmaceutical package, determine the importance of the environmental issues compared with others, determine the perception that the companies have about their own performance and try to find out what type of package is less/more environmentally harmful.

1.4 Delimitations

This project will take into account only four types of packages: blisters, bottles, sachets and inhalers. Also, only information related with the primary package will be used.

2. Method

2.1 Research method and tools

The main tool used in order to obtain companies' opinion about their own performance and about what is important when designing the packaging have been the packaging scorecard created by Olmats & Dominic (2003). The criteria to evaluate have been properly selected and they are the machinability, product protection, flow information, fill-rate, openability, patient adherence, product information, selling capability, safety, reduced use of resources , use of environmentally friendly materials and packaging cost. The scorecard has been distributed to 24 different collaborative companies – classified attending to their number of employees (small, medium and big) and to the type of products that they produce (generics, non generics and both types) – with a questionnaire that includes questions about materials used, procedures and more information than will be used to calculate the CO_2 emissions per dose of pharmaceutical. For these calculations, LCA Calculator software has been used together with data collected empirically by the author. In total, 64 pharmaceuticals have been used during this project. The way to establish contacts with the companies was via phone interviews, email, LinkedIn and using face-to-face interviews.

3. Frame of reference

Although the packaging have being designed traditionally to protect adequately the products from production centers to consumption points, this basic mission has been expanded in recent decades with the trade and logistic requirements. Therefore, simultaneously with the adoption of strategies of product differentiation through their packaging, companies must implement policies to reduce costs trying to maintain or improve their position in the markets where they operates. These costs are those associated with productive activities and logistics developed in the supply chain. Moreover, this vision must be seen in two ways: the direct way (from the production centers to the point of consumption) and the inverse way (the flux generated by waste product, once used, bound for treatment centers for reuse, recycling or recovery). In this context, authors like Johnsson (1997), Henriksson (1998), Klevas, (2005), Garcia and Prado (2008) or Bramklev (2009) associate three major functions with the packaging: the commercial, the forward logistics and reverse logistics. In recent years, elaborating on this variety of functions, a conceptualized integration between logistics and packaging has been accomplished with a particular emphasis on strategic and organizational implications (Bjärnemo, 2000, Hellström and Saghir, 2006, Garcia and Prado, 2008). The focus of Packaging Logistics is to integrate the design of the packaging from the earliest stages of product design.

The main regulatory framework in the pharmaceutical industry is established by the World Health Organization (WHO) in its "The International Pharmacopoeia" (WHO, 2011)([1]). The International Pharmacopoeia constitutes a collection of recommended procedures for analysis and specifications for the determination of pharmaceutical substances, excipients, and dosage forms that is intended to serve as source material for reference or adaptation by any WHO Member State wishing to establish pharmaceutical requirements. If it is true that all these documentation developed by international organizations – WHO, FDA, EMA – constitute the framework, are the national healthcare ministries and ministers who study, write and adopt the laws and regulations that will be applied in each country regarding pharmaceuticals and their packaging.

4. Analysis

The analysis tries to find out the perception that companies have related with different aspects related with the design of the pharma-packaging. Also, tries to determine the real performance regarding to the environmental aspects of that design. Finally, it attempts to compare both elements: the perceived and the real results. The most important results are provided below.

4.1 Made attending to the company size

The efforts given to reduce the environmental impact of packaging represent around the 20% of the designers attention, regardless of the company size. The self perception of the companies related with their environmental performance if lower than for the other types of criterion, with independency of the company size. Small companies show a lower CO_2 emissions per dose of pharmaceutical; in any case, there is just a slightly increment of the environmental performance when incrementing the weight of the environmental aspects. Finally, there is no improvement in the fill rate performance when the fill rate criterion rises.

4.2 Made attending to the type of products that the company produces

The importance of the environmental aspects is around 22%, regardless from the type of products that the company produces. The environmental aspects get always a lower perceived rate, but the difference with the others is pretty important in Generic and Non generic producers' case. Comparing the CO_2 emissions with the importance given to the environmental aspects, there is a high improvement in Non generics case: 30 mg CO_2/dose less for each 1% increase in the importance of the environmental aspects.

4.3 Additional results from the scorecard & empirical data

The most efficient presentation attending to the fill rate are inhalers and bottles made of aluminum. It is also remarkable the low efficiency of the sachets. In a typical box used for store 10 sachets can be stored 21 or even more pills using blister presentation. Finally, just note the difference between conventional blisters – made using a layer of aluminum and a layer of PVC – and blisters made using two layers of aluminum called Alu-Alu blisters. This last presentation is used only in exceptional cases when the medicament needs a really well protection against external agents, mainly moisture. Comparing presentations attending to their CO_2 emissions per dose sachets are the most harmful presentation with around a double impact than the other formats. The differences between bottles – glass, plastic or aluminum – are not significant. A big disparity between standard blisters and Alu-Alu blisters exists because the aluminum is much more harmful for the environmental than the PVC. Finally, in general terms, the conventional blister is the less harmful presentation option.

Comparing the weight given to the environmental aspects and the CO_2 emissions is possible to see a slight decrement when increasing the importance of those criteria – 4% reduction per 1% increment. The results that the comparison between the importance of the fill rate criterion and the real fill rate performance provides are also interesting: there are not changes in the result when increasing the importance of the fill rate.

4.4 Perceived environmental performance and real environmental performance

Calculating two factors – subjective performance factor and the global environmental score – that collect in one normalized figure companies' perception and the reality is possible to create a ranking that orders companies attending to their results. Using this ranking together with a matrix graphical representation is possible to confirm that the 56% of the industry has an incorrect perception about their performance. Also, is possible to characterize each area trying to find the most common company that appears there.

4.5 Statistical Analysis

The most important conclusions that can be extracted from the statistical analysis of the data are: with a 95% confidence level is possible to say that small companies have better environmental performance and with a 90% confidence level is possible to say that generic producers have worse environmental performance.

5. Main findings

After the analysis, the eight most important findings are:

- Three most important aspects when designing the packaging are: Machinability, product information and safety. Environmental aspects are not, therefore, among the most important.
- All the companies, regardless of size or type of products manufactured, give equal importance to environmental issues: around 22% of their efforts.
- The perceived environmental performance that companies have, regardless of their size or the type of products they produce, is lower than the perceived performance for others like human, economical or manufacturing aspects – 1.2X lower.
- Aluminum bottles and inhalers have the better fill rate performance. Conventional blisters and bottles made of glass and plastic have the same fill rate efficiency. Sachets and blisters made using two layers of aluminum are the worst option attending to this criterion.
- The most harmful presentations are aluminum blisters and sachets with a big difference: around a 4.8X more prejudicial than normal blisters.
- When the importance of the environmental aspects is increased during the designing process of the packaging, the mg of CO_2 per dose of pharmaceuticals is reduced slightly: 37.5 mg CO_2 reduced – about a 4% per 1% more importance given to those environmental aspects.
- In general terms, the fill rate performance has no changes when this aspect is more taken into account during the design process.
- The 56% of the industry have a misconception about their environmental performance. From this 56%, the 33% of them have an over perception about their performance and the remaining 67% have a less perception. The remaining 44% have a good perception about their discharge having around the 42% of them a high real and perceived performance compared with the remaining 58% that have a low real and perceived performance.

6. Discussion and conclusion

The environmental aspects are not a priority when designing the pharmaceutical packaging. Other aspects like machinability, safety or labelling have priority in this process. The industry needs more training in monitoring their environmental performance related to packaging: the 56% of the companies have an incorrect perception about their performance. Fortunately, 67% of those have it in a positive way: they think they are doing the things worse than what they are really doing and this can force them to improve their performance.

The regulatory framework is the most limiting element when introducing new environmentally friendly packages being the actual performance a secondary result that comes from the fulfillment process of those regulations. Finally, the environmental impact of the pharma-packaging is small compared with other daily emissions. For instance, the CO_2 emissions due to the packaging of the antibiotics consumed in Sweden during one year is less than a half of the emissions per passenger in a flight between Stockholm and Madrid.

Abstract

The pharmaceutical industry is influenced by many aspects and actors that make this industry one of the most complex ones. Packaging is probably the cheapest element that involves a pharmaceutical but it is also a necessary element. In a moment that global warming is topical, how important are the CO_2 emissions associated to the pharmaceutical packaging and how much attention the industry puts to reduce them will be studied along this project.

Evaluating objectively how harmful is the packaging and comparing results with the perception that companies have will provide the possibility to contrast and determine if the industry have a correct perception about their environmental performance. Two main tools will be used in order to make this comparison: on one hand, the packaging scorecard that determines what aspects are more important for the packaging designers and provides also information about how the companies see their own performance. On the other hand, the use of environmental software and data obtained empirically that enables to determine the real impact of the packaging. Considering each tool separately, some useful conclusion that complement the final comparison will be extracted.

Thereby, after calculations and analysis, it is possible to say that the 56% of the industry have a misperception about their performance, and the other 44% have a correct image about themselves. In addition, in general terms, the environmental aspect is placed in second level of importance having more relevance aspects like the machinability of the package or the security that it provides. Finally, interesting results have been extracted comparing companies attending to different criteria. For instance, it is possible to say that small companies produce pharmaceuticals with lower CO_2 emissions per dose of medicament, or that generic producers obtain a lower fill rate performance per package than non generic producers.

As conclusions, the environmental impact of the packaging is not a priority when designing it. There are many reasons that makes it like that: a tremendous restrictive legal framework, a little impact compared with other residues produced during the manufacturing of the pharmaceutical, a little production of scraps compared with other daily wastes, etc. It is a combination of trade-offs that makes packaging one of the most difficult elements to design between the involved ones in the supply chain.

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Abbreviations

CFCs	–	Chlorofluorocarbons
CSR	–	Corporate Social Responsibility
CTFE	–	Chlorotrifluoroethylenex
DPI	–	Dry Powder Inhaler
EMA	–	European Medicines Agency
FDA	–	Food and Drug Administration
G	–	Generics
G, NG	–	Generics & Non generics
GHG	–	Green house gas
GSK	–	GlaxoSmithKline
GWP	–	Global Warming Potential
HDPE	–	High density Polyethylene
HFAs	–	Hydrofluoroalkanes
LCA	–	Life Cycle Assessment
LDPE	–	Low Density Polyethylene
NG	–	Non generics
npMDI	–	Non-Pressurized Metered-dose inhaler
OPA	–	Oriented polyamide
OTC	–	Over the counter
PE	–	Polyethylene
PEN	–	Polyethylene Naphthalate
PET	–	Polyethylene Terephthalate
pMDI	–	Pressurized Metered-dose inhaler
PP	–	Polypropylene
PVC	–	Polyvinyl chloride
PVDC	–	Polyvinylidene chloride
RFID	–	Radio frequency identification
WHO	–	World Health Organization
WVTR	–	Water-vapor transmission rate

1. Introduction

Every pharmaceutical need to be correctly packaged and will be precisely that package the element studied in this thesis. A big number of elements need to be balanced during the design process of a package: aspects related with the machinability, with the protection of the product, with the customer, with the environmental impact… This project tries to be a description of all these interactions between factors that need to be kept in mind and will try to put efforts in analyze the environmental implications associated to the pharma-package.

Also, as main goal, an interesting comparison between how the industry and its constituent companies perceive their own environmental performance and the real performance reached by these same companies will be done, all inside the packaging frame.

This introductory chapter will try to give to the reader an insight and understanding regarding the thesis background, problem statement, objectives and delimitations.

1.1 Background

The efforts in every industry trying to reduce the environmental impact of their supply chains are a reality (Business Gateway, 2012). And all this efforts have the same purpose: combat the global warming, phenomenon whose existence nobody questions nowadays (Stonington, J, 2003). Today, is common to hear expressions like "green logistics" which consists in supply chain management practices and strategies that reduce the environmental and energy footprint of freight distribution. It focuses on material handling, waste management, packaging and transport (Rodrigue *et al.* 2009). In this way, Packaging, as a part of this supply chain, will be also affected by this new tendency.

Social and environmental issues are more important now than ever. For business, they represent some of the greatest opportunities to find new markets of profitable growth, more lasting and engaging sources of competitive advantage, and more effective ways to reduce cost and risk. Consumers no longer feel conflicted by the issues, but committed to supporting change (Fisk. 2010). Pay attention to environmental aspects is not only an ethical responsibility; it is also a business opportunity. In that way, reduce the environmental impact of the packaging, must be seen as an activity with two faces: an economic saving and a commitment with the society.

Recent reports coming out of Europe and the United States are all showing that the pharmaceutical industry, at large, is taking tremendous steps into "Going Green", so to speak. With the pharmaceutical industry facing looming expiring patents of some of their biggest blockbuster drugs, as well as the proper candidates to replace them, uncertainty looms in the pharmaceutical industry. Because of this economic incertitude in the pharmaceutical industry, many companies are looking for ways to completely shift their agenda to a greener agenda, to further cut costs, and win better publicity for their company (Smart Consulting Group, 2010). This environmental friendly tendency also affects to the pharmaceutical packaging: Today, there is tremendous opportunity within the manufacturing practices and processes for pharmaceutical packaging to become more sustainable. Sustainability is approachable from a holistic perspective as a way to determine how to have a positive impact throughout the supply chain, not just the raw materials or the way the product returns to the life cycle. Sustainability requires an approach that is focused on technical, environmental, and social practices (Lithgow. 2009).

Industry characteristics

Packaging is an important and essential element in pharmaceutical business. As Hayes (2010) – director of technical services in Packaging Machinery Manufacturers Institute – says, "Packaging has to convey information about the product, protect the product, and maintain the quality of the product through the entire distribution chain. But, from a pharmaceutical perspective, packaging's main function is getting the product to the customer in a quality-based, protected manner".

In recent times, pharmaceutical packaging has undergone a drastic amount of change. Sophisticated drug products, development of new medicaments diagnostics, stringent government requirements, large growing of the middle class, growth of organized retail and increase in number of prominent players with new emerging markets have increased the demand for pharma-packaging materials worldwide. Packaging design provides stability and shelf life to the drug and the delivery system, which becomes fundamental to the safety, convenience and compliance of drug use (Sunder. 2011).

Two decades ago, packaging was often an afterthought for many companies, viewed as merely the final step in manufacturing. But now, pharmaceutical makers are considering packaging earlier in development. They are looking to packaging and labeling as mediums to promote their products, increase patient compliance, and meet recent regulations (Swain. 1998). A common philosophy in pharmaceutical industry about the pharma-packaging can be synthesized using Cohen (1998) – director of packaging technology in Glaxo Wellcome (nowadays GlaxoSmithKline) – words: "The packaging component is a relatively small cost (of a prescription medicine), but it is focused on because it is a nondrug cost". For that reason, the attempts to decrease the use of the packaging will by the order of the day.

But, despite the attempts to reduce the packaging, how is evolving the global demand of packaging? Even with the pressure on pharmaceutical packagers to keep costs down, the demand for packaging is on the rise. The pharmaceutical packaging market grew 4.9% annually from 1993 to 1997, and has increased 7.9% each year between 1997 and 2003. The pharmaceutical packaging market has represented a market around $2.9 billion in 1997, $3.1 billion in 1998, and $4.6 billion in 2003 (Swain, E. 1998). According with GBI (Global Business Intelligence, 2011), the global pharmaceutical packaging market, worth $47.8 billion in 2010, is currently recording rapid expansion, with advances in manufacturing processes, technology innovation and integration. Growth is expected to be highest in emerging economies such as India and China, primarily due to increasing generics and contract manufacturing activities. Also, the global Pharmaceutical Packaging industry is forecast to grow at a compound annual growth rate of 7.3% in the next five years to reach a value of $78 billion in 2017. Other interesting prospect is that more than $142 billion worth of drugs going off-patent in the next five years, generic drug manufacturers will emerge as a major segment driving demand for pharmaceutical packaging. Pharmaceutical packaging industry is, therefore, immersed in a full growth phase.

Pharma-industry has strict packaging requirements and protocols because it deals with drugs that can help or harm people, so more is expected from the packaging machinery in terms of record keeping and the necessary processes to put a packaging machine in operation. If a little bit too much packaging is used in a product, more packaging in the waste stream will have to be recycled. Conversely, if not enough packaging is used to protect a product, the entire load (the

product and the associated packaging) ends up going through the waste stream (MacKinnon. 2010). Packaging selection, from the materials used to the thickness of the layers used, is game of balance.

Although pharma-packaging can sound as something simple, the industry is looking continuously for new methods, formulas and technologies. For instance, nanotechnology, the science of very small materials, is poised to have a big impact in pharma-packaging and will enable it to bring innovative and new generation packaging solutions to market. Increasing demand for medicaments delivery devices and blister packaging will also boost the growth of pharma packaging industry. The global market for nano-enabled packaging for blisters was $941 million in 2008 and is expected to grow to $2.10 billion by 2014 (Sunder. 2011).

It is necessary to say that effective and intelligent packaging has the potential to do so much more in addition to protecting and preserving items contained within, communicating marketing and informing the customers. As the packaging industry continues to develop increasingly sophisticated concepts, big pharmaceutical companies are starting to embrace innovations in this field to improve patient adherence to drug regimens. Patient adherence, also known as compliance, is the extent to which patients stick with medication they have been prescribed. For national healthcare systems, the problem of non-compliance costs lives and billions in unnecessary hospital treatment, while pharmaceutical companies lose revenue from lapsed prescriptions. In order to solve this type of problems, packaging companies have developed a system for transmitting electronic data of patients' self-medication which is rapidly advancing. In February 2011, Finnish packaging company Stora Enso unveiled the newest iteration of its adherence control packaging, Pharma DDSi Wireless. This technology is based on conductive ink on a carton board-based blister inlay, which is connected to a cellular module embedded in the package. The removal of pills is tracked and the information can be sent to an electronic database automatically via GSM or GPRS cellular networks (Lo. 2011). The most important aspect is that Stora Enso technology is just an example about how huge are the potential improvements in pharmaceutical packaging and how these advances can make customers and patients' lives easier.

1.2 Problem discussion

Although packaging is recognized as having a significant impact on the efficiency of logistical systems and activities such as manufacturing, distribution, storage and handling throughout the supply chain, many packaging dependent costs in the logistical system are frequently overlooked by packaging designers. Packaging specifications directly influence the time required for completing packaging operations which ultimately affects product lead time and due date performance to the customer (Saghir. 2004). Packaging is characterized by trade-offs with other logistic activities. For instance, increase the protection that the package provides implies, from transportation point of view, decreases in the damage and theft in transit but also an increase in the packages weight and transport costs. From warehousing point of view, this increase of protection implies increases in the cube utilization – stacking – but decreases in the cube utilization by increasing the size of the product dimensions (Lambert *et al*.1998). Every decision related to the packaging has impact on some or other logistics activities.

Keeping in mind all these trade-offs, and trying to synthesize and be concise, the pharmaceutical packaging is characterized by three main aspects (Ferrón. 2012):

- Necessary and cheap: It is impossible to distribute pharmaceuticals without the protection that the packaging provides. In the other hand, the cost that the packaging represents is insignificant compared with others like active ingredients or the transport costs – around a 2%.
- Low percentage of the daily waste but very hazardous: Compared with the organic wastes that a standard family produces, the pharmaceutical packaging is insignificant. Anyway, the materials used are very difficult to recycle or process after their use.
- Very regulated element: every picture, design and material used, even each word of a leaflet, must fulfill the packaging regulations. The innovation possibilities are quite small in a very restrictive framework which try to protect at all cost the product.

With this panorama, is pharmaceutical industry trying to reduce the environmental impact of the packaging? In Wear's – Sales director in Johnsen & Jorgensen – opinion, the pharmaceutical industry isn't doing enough, but there are various historic reasons for this and pharmaceutical industry is well aware that its products lag behind in the environmental stakes compared with other industries."In an industry that requires the most exacting health and safety standards, other design priorities, such as tamper-evidence, child-resistance or shelf-life will always take precedence. The nature of pharmaceutical products means that the majority of the containers used are disposable and only suitable for one use. Plastics dominate as the main type of material because of performance, durability and lightweight, but these are not easily recyclable. In addition, the bureaucracy that inhibits even simple changes to pharmaceutical packaging is also a major issue; any licensed drug or medicine that undergoes a change to its packaging container, closure or labelling, must be reregistered. This is often an expense and inconvenience that few manufacturers are prepared to bear" Wear (2010) says.

Probably, the reader ever experienced the feeling of realizing the existence of discrepancies between the reality and the self-perception related to different areas of our daily lives. This happens because the human cognitive process consists of four key elements: first there is the *reality*: what really happens out there and the confinement of our minds. Second, this *perception*: as noted or experience reality firsthand. Third are the *cognitive processes*: how is synthesized our perception of reality to create ideas and draw conclusions. And finally, there are the *conclusions*: they are our opinions resulting claims and beliefs as well as compression of the facts or data (Haskins. 2003). During this process, the problem arises when the bias between reality and our conclusions obtained through perception is too large. The same theory can be applied to any industry; in numerous occasions, on one side is company´s perception; on the other, operational reality about aspects like the brand image or the environmental impact of their products. This project will try to explore the existence of these gap related to the environmental impact of packaging.

The problem statement can be summarized as the necessity to conciliate these three main aspects – trade-offs between legal, economical and environmental aspects – that appear when designing the more environmentally friendly possible packaging. Due to this complexity, is possible that the perception of companies' performance could be away from the actual performance related to the environmental field.

1.3 Purpose and objectives

The main purpose of this project is to explore the environmental performance related to packaging in the pharmaceutical industry. Thus, the thesis will try to determine if the industry is

doing everything that is on its hand trying to reduce the packaging environmental impact – despite the low cost of this element and the regulatory framework – and to compare their perception with the real environmental results. Along this process, some objectives will try to be reached.

- The thesis will try to determine the relation between the self environmental performance perceived by the companies and the real and objective environmental performance of the packaging exploring the existence of gaps.

During the project, two main sources of information will be used: the packaging scorecard and data obtained empirically. Besides being necessary elements to reach the final objective, they will also provide interesting and useful information that will try to reach the following goals.

- Determine what the most important aspects are when packaging designers create a pharmaceutical package.
- Determine the importance of the environmental issues compared with others.
- Determine the perception that the companies, classified using different criteria, have about their own performance.
- Try to find out what presentation or type of package is less/more environmentally harmful.

Also, the comparison between the results obtained using these two tools will allow to establish comparisons looking for interesting relations.

- Is any relation between the given importance to the package fill rate and the real fill rate performance?
- Is any relation between the given priority to the environmental aspects of the package and the real impact of this package?

Finally, a statistical analysis will be made in order to determine, with different confidence levels, which type of companies are more or less environmentally friendly or if a relation between the put efforts and the obtained results exists.

1.4 Delimitations

Although during the contacts with the different pharmaceutical companies questions about four types of packages – blisters, sachets, inhalers and bottles – have been made, in order to compare the perceived environmental performance and the real performance obtained only standard blisters will be considered. This limitation comes from the difficulty to calculate normalized equivalent parameters that enable to compare results with independency of the type of package and because of the inexactitude of the data collected. The election of blisters for making that comparison is because for this type of presentation the availability of samples was higher and because it is the most common package nowadays.

The CO_2 emissions calculated for each pharmaceutical sample have been made considering the processing of the raw material and the transportation to the packaging/manufacturing center corresponding to the primary package. Emissions related with the secondary and tertiary package have not been considered.

The classification of the results has been made attending to two main criteria: the company size and the type of products that the company produces. Other possible distinctions can be made but are out of the boundaries of this thesis like distinguish the results attending to the manufacturing

country, or attending to the nature of the products produced by the companies: OTC – over-the-counter – or prescription medicaments.

The main reason that has ruled out these options is that the regulatory framework applicable to a certain package depends on the country where it will be sold and not on the manufacturing country. The correct study in that case will be an analysis comparing the regulations that are applied in each country. At this point, the author can advance that these differences are really small because all the national regulations are made using as base the World Health Organization – WHO – guidelines.

The collaborative companies in the project are of two types: global companies that sell and produce all over the world –in the sorting that will be explained later, they are the big and medium companies– and small companies that sell also around the world but they only produce in Spain –they will be the small companies. The reason of this limitation comes from the difficulties in the communication –often language difficulties– with little producers in other countries. The ignorance of behavior of small pharmaceutical outside Spain is one of the potential effects of this limitation.

2. Method

2.1 Research approach

The method used in this project consists in evaluate the environmental performance of the pharma-packaging in two different ways: from companies' perspective and objectively.
In order to obtain companies' self evaluation, the element used has been the Packaging Scorecard; this scorecard is based on research of functional criteria of packaging and the theories of 'balanced scorecard', a general management approach to evaluating organizational performance using different perspectives (Olsmats & Dominic, 2003). The main limitation of this tool is that if the researcher does not choose well the criteria to evaluate, the results do not provide relevant information. There is no a magic recipe when designing the scorecard, so each industry, even each company, needs a scorecard tailored to their necessities. Trying to solve this problem, a thorough analysis of the criteria that must be incorporated was made.

The scorecard was included in a bigger document called *Questionnaire* along this project. It has been sent to the companies via email or has been fulfilled establishing interviews with the respondents. The Questionnaire includes, a part from the scorecard, other questions related to the packaging procedures inside the companies: raw materials, distances and methods of transport of those materials, filling patterns of the different packaging units and so on. Some of the advantages and disadvantages of using a questionnaire are:

- Pros: Allows encompassing a bigger geographical area, to reach as many people as possible, demands lower time to reach the same number of people, facilitate the collection of information and do not need many explanations and great preparation for implementation, prevent the spread of information by focusing on forced-choice questions…
- Cons: No chance to help the respondent to answer, there are difficulties in monitoring and reviewing the information, lack of depth in the answers and no chance to go beyond the survey, takes a good time the choice of the universe and of the samples used… (Prado. 2006).

In order to correct these deficiencies, the questionnaire has been complemented arranging telephone interviews, tool and a technique extremely flexible, able to adapt to any condition, situation or person, as that enables to clarify questions, guide research and resolve the difficulties that the respondent may encounter (Cerda. 1991).

Trying to obtain an objective view of the packaging environmental performance, LCA Calculator software has been used. There are other softwares that provide similar results but the main reasons to use LCA have been: it is free, it is available online so it is not necessary to be installed in a certain computer, and finally, it is easy to use and to understand the results that it provides. Also, it has other minor disadvantages that will be exposed in other section below. This software need to be fed with numerical data related to the volume of materials used to manufacture the packaging. The way to obtain those weights has been an empirical measure method. More than sixty pharmaceutical packages have been weighed manually separating each component of the package: carton box, leaflet and the different layers or element that constitute the package. The main advantages of this tool are that it provides a greater control of the possible changes in the results of the study, since randomization blurs the action of confounding variables. Also, it provides the strongest evidence on which to base causal inferences and sometimes it may be the only possible design for a research question or hypothesis. Finally, they

can be easily replicated. On the other hand, used to be costly and require long time to do them properly. Also, too often, short run experiments result in invalid conclusions so that the sample needs to be sufficiently large for obtain conclusive results (Cayuela. 2011). In this thesis case, the weighing process took around twelve hours, and in order to obtain a large sample, a considerable number of packages were weighed.

The analysis of the data was made using, in first place, simple comparisons based on the same criterion. For instance, a simple barchart was used to compare the fill rate performance attending to the type of package. Other times ring-graphs were used, but always trying to use graphical tools that enable to obtain conclusions and find patterns easily because they make visible to the naked eye relationships between variables (García, J.M. *et al.* n.d). In order to compare the perceived environmental performance and the real results, the dot plot was the tool used because it is pretty useful when comparing sets or subgroups of data as is the case and also because it conserves the numerical information (Robbins. 2006).

Finally, at the end of the analysis section, a regression analysis is included trying to find relations between criteria. This analysis will be used to predict a measurement based on the knowledge of another with different confidence levels (Amstrong. 2012).

2.2 Process and tools used

2.2.1 Questionnaire

Scorecard

As has been explained before, this project tries to compare the perception of different pharmaceutical companies and the objective reality in different aspects related with the pharmaceutical packaging. The tool used to do a systematic evaluation was the Scorecard created by Olsmats and Dominic (2003).
First of all, the respondent needs to give weights to different criteria. These weights will be given attending to the importance to each criterion during the designing process of the packaging. Thus, the respondent gives a weight of 0 when the criterion is not important at all and a 100 when the criterion is extremely important, always from his/her point of view.

The respondent of the questionnaire also needs to evaluate his/her company's performance attending to different criteria using a scale between 0 and 4: 0 for "not applicable for the package", 1 for "not approved",2 for "approved",3 for "well approved" and 4 for "met excellently".
The criteria that the respondent needs to evaluate and give weight are showed in the example chart below – *Table 1*.

Table 1. Criteria studied in this project		
Criteria	**Score (0 – 4)**	**Weight (0 – 100)**
– Machinability	3	90
– Product protection	4	80
– Flow Information – barcodes…	2	70
– Fill-rate	3	50
– Other Value adding properties		
› Openability	2	60
› Compliance / Patient adherence	3	40
– Product information: Labelling, composition, leaflet…	4	100
– Selling capability: Marketing…	3	80
– Safety	4	70
– Reduced use of resources	2	60
– Use of environmentally friendly materials	2	50
– Packaging costs	3	30
Example of Scorecard evaluation and weight allocation section. Note that the scores and weights showed are just an example.		

A brief description of each criterion is exposed below.

- *Machinability:* refers to the ability of the packaging to be processed and manufactured effectively in the production line.
- *Product protection:* refers to the qualities of the package, its ability to protect the product in different environments from mechanical stress and to preserve its contents. Protection also means to prevent the product from reacting with the external environment.
- *Flow Information:* refers to the capability of the packaging for giving right information along the supply chain. For example, tracking information (identification, instructions, and destinations) as well as logistics-related information about the product (warnings, declaration of contents, barcode or RFID – Radio Frequency IDentification).
- *Fill-rate:* This criterion represents the effort to minimize the use of packaging for the same quantity of product. For instance: minimize the separation between pills in a blister or minimize the size of the box where sachets are contained or try to transport much as possible products in each pallet.
- *Other Value adding properties:*
  - *Openability:* ease of opening the packaging. Important among older patients and patients who need to consume large amount of medicaments each day.
  - *Compliance / Patient adherence:* Efforts to create methods or tools that help the patient to follow his medication program. For instance: Labels with the day of the week that can be adhered to a blister in order to remain if the patient has taken the medication that day or not.
- *Product information:* Labelling, composition, leaflet…: This criterion refers to all the legal requirements that the pharmaceutical need to fulfill in order to be sold: leaflet, composition, warnings and so on.
- *Selling capability:* Marketing…: Creative design of the packaging, printings, materials…Elements that help to sell the product.
- *Safety:* Elements (for instance, hard materials or difficult-to-open closures) that avoid the consumption of the products by children without the supervision of an adult.
- *Reduced use of resources:* Design the packaging in order to use the minimum quantity of material and parts.
- *Use of environmentally friendly materials:* The effort that the company puts on use materials with a low environmental impact.

- *Packaging costs:* Efforts that the company makes in order to reduce the final cost of the packaging.

These criteria will be clustered in 4 different groups in order to facilitate subsequent analysis.

Table 2. Classification of criteria

Group of Criteria	Criteria
Criteria related with human aspects	– Safety – Compliance / Patient Adherence – Openability
Criteria related with the environment aspects	– Use of environmentally friendly materials – Reduced use of resources – Fill-rate
Criteria related with the economics	– Packaging costs – Marketing – Machinability
Criteria related with product/manufacturing aspects	– Product protection – Flow information – Product information: Labelling…

This process of weight assignment for the different criteria has been asked to the respondent for two types of products: Over-the-counter (OTC) and prescriptions pharmaceuticals. In the evaluation of their own performance case, the score evaluation has been requested for four types of presentations: blisters, bottles, sachets and inhalers. For further information about these types of packages, the reader can refer to *Chapter 3:* Subsection *Types of pharmaceutical packaging.*

The possibility of include other criteria in order to be evaluated exists. One example could be the recyclability of the package. In this case, this criterion is not included because the possibility of recycle the pharma-package is really small: medicaments are chemical products and the combination of some of them during the recycling can provoke dangerous reactions or cross-contamination (Llano, 2012). Analyses like this one have been realized for each criterion in order to take the decision of including or discarding them.

Manufacture and Transport impact

Once the information about the company performance from its point of view is collected, it is time to ask for data that allows evaluating objectively their performance.
This project will be concentrated in the environmental impact of the packaging evaluated using a tool called LCA Calculator. This online service allows the user to calculate the environmental impact using as unit the kg of CO_2 emitted into the atmosphere during the manufacturing and transport process. How the program works is included in *Appendix 1 – LCA Calculator* at the end of the project but how the data necessary to fulfill the requirements of the software have been collected will be explained below. In order to validate the results provided *by LCA Calculator* a comparison between results has been made using other software called *openLCA* 1.2 (OpenLCA, 2012). Around ten comparisons have been made and attending the similarities between results, the author decided to continue working with *LCA Calculator*.

Some questions have been proposed to the respondent for each type of presentation. For instance, in blisters case, questions like what type of plastic is used to create the forming film or from where is transported the aluminum that is used to create the lidding layer have been asked. Questions about the secondary, tertiary and about the unit load have been made also but due to

the inaccuracy of the responses, this data has not been used. A copy of the questionnaire that has been used to obtain all this information is included in *Appendix 2 – Questionnaire*.

2.2.2 Contacting companies

Four main ways have been used in order to set up contacts and communication lines with the pharmaceutical companies.

- By email or web form: Around 150 emails and online web forms have been sent to more than 85 companies asking for collaboration with this project. The applications were sent mainly to the Swedish representatives and Spanish representatives of these companies. Also, some emails were sent to their respective heads of packaging placed normally in the headquarter facilities of the company. Finally, this method has not been very effective: almost all the Swedish representatives have replied the request but unfortunately, only a few of the companies have manufacturing or packaging processes in Sweden.
- LinkedIn social network: LinkedIn is a business-related social networking site. Here, is possible to find professionals from any industry. A Pro-User account was created in order to send private emails to pharmaceutical packaging professionals as designers and manufacturers. Around 50% of the respondents involved in this project, were contacted using this interesting service.
- By phone: In combination with the previous tool, definitely, this method has been the most successful and useful. People are more willing to collaborate when the interaction is face to face or by phone. Also, this system provides more flexibility and is easier to obtain accurate information. Further, it is faster than email.
- Face to face: This method was used only three times. The reason is that, as was said before, there are not manufacturing plants disposed to collaborate near to Lund, place where has been this project developed almost all its duration. By the way, during a travel to Spain, the visit to two manufacturing and packaging plants was possible and there, was possible to get the information directly from the respondents.

2.2.3 Primary and secondary packaging weighing process

Once the company has provide all the necessary data to use LCA Calculator software, the only thing missing are the weight of materials used. This is, for instance, the grams of plastic used in each blister, or the paper necessary to create a leaflet. When starting to think about how to get this information, the first idea was to ask directly to the company. Finally, it was discarded; probably, the respondent of the questionnaire will not have this information, or he/she would have to make a big effort to get it.

In order to solve this problem, a direct weighing process has been realized by the author of this project. For each company that has responded to the questionnaire, one product – blister, sachet, inhaler or bottle – has been weighed at least. These packages had been taken temporarily from a recycling collection box placed in a pharmacy in Spain. A total of 64 pharmaceuticals have been weighed; in the sample is possible to find antivirals, over-the-counters, antibiotics, cardiovascular drugs, drugs against the pain, gastric protection drugs, etc. In this way, a wide spectrum of pharmaceuticals has been taken into account along the study. The selection of the weighed products has been completely arbitrary and made attending to the availability of packages. This aspect gives more wide scope to this study enriching it and allowing the comparison between different types of presentations from the environmental point of view.

2.2.4 LCA Calculator

As has been mentioned before, the software used to calculate the environmental impact of the packaging was LCA Calculator available at http://www.lcacalculator.com/. LCA Calculator provides a simple way to assess the environmental impact of a product by calculating its energy input and carbon footprint from cradle to grave. The LCA Calculator is the perfect tool for designers or engineers working in the field of sustainable design, eco design and life cycle assessment. As has been said before, an example of calculation is shown for illustrative purpose is attached in *Appendix 1 – LCA Calculator*.

2.2.5 Collaborating companies

The success of this project would not have been possible without the help of pharmaceutical companies. This aspect was also the most risky; without companies' collaboration all the previous work would have been meaningless. Fortunately, after a large number of attempts and calls, has been possible to agglutinate the opinions, information and data from 24 different companies. They are based in different countries and different continents. Their productions plants are also placed in very different countries: from India to Italy via United States of America. Their number of employees, number of production plants, their budgets and sale levels are completely different, and this aspect gives even more value to this research since all companies in the industry have characteristics that can be closely approximated to the characteristics of any of the companies studied in this project.

Along this thesis will not be possible to give companies' names, their products, or the persons who have contributed helping with the questionnaire due to their privacy policy. Obviously this is not the best of situations but this problem will attempt to be compensated giving a complete characterization and description of the companies, always respecting the principle of industrial secret.

A summary table that collects the most important aspects about the collaborating companies is provided in table 3. That chart condenses all the information about the companies that have collaborated in this project.

- *Codename* refers to the name that will be used for a specific company along the project. It is just a convention.
- *Size* refers to the number of employees of the company. The differences are really huge as outlined below.
  - *Big:* This group agglutinates companies with a number of employees between 60000 and 112000.
  - *Medium:* Companies between 20000 and 50000 employees.
  - *Small:* Companies with a number of employees between 550 and 3000.
- *Nature of products* makes a distinction between companies that only produce OTC products, only Prescription products (P) or both of them. Most of them belong to the last group.
- *Type of products* makes a distinction between companies that produce generic medicaments (G) – a drug product that is comparable to brand/reference listed drug product in dosage form, strength, route of administration, quality and performance characteristics, and intended use –, companies that produce non generic drugs (NG) – brand pharmaceuticals in which, normally, the patent has not expired – or both of them.
- *Mainland* indicates where is the company registered and where is its headquarter.

Table 3. Collaborating companies classification attending to different criteria

Codename	Size	Nature of products	Type of products	Mainland
B1	Big	P & OTC	NG	USA
B2	Big	P & OTC	NG	Europe
B3	Big	P & OTC	NG	Europe
B4	Big	P & OTC	NG	USA
B5	Big	P & OTC	NG	Europe
B6	Big	P & OTC	G & NG	USA
B7	Big	P	NG	Europe
B8	Big	P & OTC	G & NG	Europe
M1	Medium	P & OTC	G & NG	Europe
M2	Medium	P & OTC	NG	Europe
M3	Medium	P & OTC	NG	Europe
M4	Medium	OTC	NG	Europe
M5	Medium	P & OTC	G	Europe
M6	Medium	P & OTC	NG	USA
M7	Medium	P	NG	Europe
S1	Small	P	NG	Europe
S2	Small	P & OTC	G	Europe
S3	Small	P & OTC	G & NG	Europe
S4	Small	P & OTC	NG	Europe
S5	Small	P & OTC	G & NG	Europe
S6	Small	P & OTC	G	Europe
S7	Small	P & OTC	NG	Europe
S8	Small	P & OTC	G	Europe
S9	Small	P & OTC	G & NG	Europe

2.2.6 Calculations and Analysis

After collecting all the data mentioned before, it was time to work with them. *Microsoft Excel* has been the most used application for compare and represent graphically the different figures that provide a better understand of the situations and allows the author to extract and get conclusions. In order to determine if significant differences exists between different companies attending to different criteria – size of the company or type of products they produce, for instance–, a statistical analysis program called *StatGraphics Centurion XV* has been used. All the result obtained using this software will be exposed in following sections.

2.2.7 Difficulties

Some difficulties and limitations have appeared during the collection information process and during the calculations are described below:

- The respondent does not have all the information requested: this problem have appeared frequently. This is due to the different nature of the data necessary to fulfill the questionnaire. In most cases, it has been solved giving some time to the respondent to find the information and establishing a second appointment. In other cases, the missing information was not obtained.

- The respondent is not the best person for the task to one hundred percent: occasionally, the contact in the company does not belong to the packaging design department. This is the case of the production or quality management employees that have contributed in this project. In almost all cases, the respondent's goodwill and effort have supplied this lack of knowledge.
- Inaccuracies in the information provided: Sometimes, the respondent only have inaccurate information. For instance, he/she knows that the forming film is made using plastic, but does not know exactly what type. Other common situation appears when asking for the origin of the raw material. The respondent usually knows the country from where it comes, but not the medium of transport used. Those are only a couple of common examples.
- LCA Calculator does not work fine with small numbers. It is designed for work with huge quantities of materials, conditions that does not satisfy the pharmaceutical packaging. The solution taken was to calculate everything using as base the production of one thousand units of product. This means one thousand cardboard boxes with their respective blisters inside, for instance.
- The classification of the companies attending to their number of employees is not probably the most equitable. The segments created do not embrace the same number of employees but it is the fairest trying to create groups with the same number of companies.

3. Frame of reference

This section tries to be a theoretical frame of reference that hosts the development of this master thesis. Some interesting theory about what is packaging logistics, the necessity of a holistic view along the supply chain, how can the environmental impact be measured and the differences between the perceived performance and the real performance will be exposed.
Also, a few commentaries about how the regulatory framework influences the packaging design and a useful overview of the types of packages studied in the project is included.

3.1 Packaging logistics

Although six main functions of packaging have been identified traditionally – containment, protection, apportionment, unitization, convenience and communication (Lockamy III, 1995) – this thesis will be focused on the environmental aspects and logistics. Thus, even though the packaging have being designed traditionally to protect adequately the products from production centers to consumption points, this basic mission has been expanded in recent decades with the trade and logistic requirements. Therefore, simultaneously with the adoption of strategies of product differentiation through their packaging, companies must implement policies to reduce costs trying to maintain or, hopefully, improve their position in the markets where they operates. These costs are those associated with productive activities and logistics developed in the supply chain. Moreover, this vision must be seen in two ways: the direct way (from the production centers to the point of consumption) and the inverse way (the flux generated by waste product, once used, bound for treatment centers for reuse, recycling or recovery). This last aspect, the result of increasing the awareness about the environmental aspects by the society (one of the pillars of the CSR – Corporate Social Responsability), has resulted in the development of specific legislation related to packaging area (Arca, J *et al.* 2011). In this context, authors like Johnsson (1997), Henriksson (1998), Klevas, (2005), Garcia and Prado (2008) or Bramklev (2009) associate three major functions with the packaging: the commercial, the forward logistics and reverse logistics. In recent years, elaborating on this variety of functions, a conceptualized integration between logistics and packaging has been accomplished with a particular emphasis on strategic and organizational implications (Bjärnemo, 2000, Hellström and Saghir, 2006, Garcia and Prado, 2008). The focus of Packaging Logistics is to integrate the design of the packaging from the earliest stages of product design. Continuing with this idea, and for a properly understanding of what is Packaging Logistics, it is very recommendable to resort to Saghir (2004) paper. In it, Saghir suggests the following definition of Packaging Logistics: "The process of planning, implementing and controlling the coordinated Packaging system of preparing goods for safe, secure, efficient and effective handling, transport, distribution, storage, retailing, consumption and recovery, reuse or disposal and related information combined with maximizing consumer value, sales and hence profit.". The key aspect is that Packaging Logistics should be considered as an integrated approach, where both systems of packaging and logistics interact, complement and adapt to each other. The total potential of improvement should be larger if an integrated approach was adopted.

If packaging is considered as merely a subsystem of logistics, it should be a part that indirectly mainly facilitates customer service. But packaging is closely related to the product itself and contributes to all of the 4P-s in the marketing mix – product, price, place and promotion. By its marketing capabilities and properties, packaging plays a decisive role in facilitating meeting consumers' needs and expectations. Packaging is not simply a marketing or distribution adjunct but pervades the total system view. The term logistical packaging has been used by academics

referring to a limited point of view, where it addresses packages that are customized for mainly logistical functions. Therefore the concept of Packaging Logistics, beside of focusing on the interface between the systems of Packaging and Logistics, recognizes the interdisciplinary nature of packaging and consider also, among other disciplines, its interfaces with marketing (Saghir, 2004).

3.2 Green logistics

Green Logistics is the integral transformation of logistics strategies, structures, processes and systems for companies and business networks serving to create environmentally rational logistics processes and an efficient use of resources. This new trend is based on making the best use of logistics resources and it promotes economic development by creating a circular economy, focusing on the use of raw materials, green storage, green transportation, processing and the recycling of wastes among others. These are the most important elements of green logistics. Combining with the behaviors of the public, business and government, they constitute the three reasons of the impulse of green logistics (Huchim, 2010).

Whether they call it eco-friendly, sustainable, biodegradable, or natural, companies are looking for ways to "go green" with their packaging (Atkinson, 2010). While helping the environment is one benefit of eco-friendly packaging, packing products using fewer and more sustainable materials reaps additional rewards: *Saving money* reducing excess packaging results in lighter and smaller shipments that cost less to transport; *maintaining business* switching to green materials can help meet or anticipate customer demands for eco-friendly suppliers and finally, *attracting consumers* because many shoppers will choose an environmentally friendly product over a conventional package. In Atkinson (2010) opinion, while eco-friendly packaging is a recent phenomenon, it is already a large and rapidly growing trend. Source reduction in packaging has been going on for decades as a way to reduce costs. Until recently, however, few companies were doing it to increase sustainability. Packaging specialists are also investigating new ways to recover materials showing interest in reducing the environmental impact of packaging under the framework established by the green logistics.

3.3 A holistic view through packaging

Each day, supply chains are more dynamic and uncertain, an interdependency of two-way relationships that increases risk and vulnerabilities for companies. In fact, obtaining a holistic view of supply chain has become a source of competitive advantage for high-performance businesses. Changes on nearly every front have combined to make modern supply chains much more complex and interconnected and so much more risky. These changes include global sourcing and production, information and communications technology, consumer expectations, pricing volatility and product availability, financial conditions and regulatory requirements. Developments in one area tend to affect other areas, whether positively or negatively. To understand and manage the risks in this new interconnected supply chain, companies need one thing above all: a holistic view across the enterprise supply chain. Therefore, packaging, as essential part of it, will be affected by this tendency. Even if they are considering supply chain risk, companies often look at it in silos, missing the across-the-chain view that would enable them to recognize similar risks that should be managed from a company-wide perspective. It is this holistic view that generates real value because it can help show how a decision taken in one function may affect the entire organization (Bowersox & Closs, 1996; Accenture, n.d).

Many companies are evolving new operating models in order to adjust to the risk interdependencies of the supply chain as they strive to achieve high performance. High-performance businesses are approaching supply chain risk in three ways:

- Assessing risk. To assess risk, some basic questions need to be asked; for example, what exactly is the supply chain? An inventory of key risks is always required, along with the effects and likelihood of each risk.
- Designing a framework to manage the supply chain. Once assessed, supply chain risks need to be managed via a framework that integrates all the key risk capabilities required.
- Implementing supply chain risk mitigation. Companies need a robust action plan funded with the appropriate resources to address the core of the risk issues and implement treatment—not just symptomatic relief (Accenture, n.d).

3.4 Carbon footprint

The purpose of this project is to explore the environmental performance of the pharmaceutical packaging. In order to be able to do comparisons between companies or between the self perceptions that companies have and the reality, the method used to quantify the environmental impact has been the carbon footprint. It has historically been defined as the total set of greenhouse gas – GHG – emissions caused by an organization, event, product or person (UK Carbon Trust, n.d). This environmental impact is measured by undertaking a GHG emissions inventory according to recognized international standards such as ISO 14064-1, PAS 2050 or GHG Protocol among others. The carbon footprint can be understood as a measure of the total amount of carbon dioxide (CO_2) and methane (CH_4) emissions of a defined population, product, system or activity, considering all relevant sources, sinks and storage within the spatial and temporal boundary of the population, system or activity of interest. It is calculated as carbon dioxide equivalent (CO_2e) using the relevant 100-year global warming potential – GWP100 (Wright, L.; Kemp, S., Williams, I. 2011). As has been said before, in this project, all the calculations related to the CO_2 emissions will be provided by specialized software.

Finally, one of the main objectives of this thesis is to evaluate the relation between the perceived environmental performance and the real discharge. The author of this thesis could not find any similar study applied to the environmental field but there are other similar studies applied to other topics. An example is Cerruti (2011) study about the sustainability leadership that compares the measured perception vs. the reality. Companies increasingly recognize that a proactive stance on sustainability is becoming a competitive necessity in attracting investors, employment talent and supply chain partners, as well as customers. Because of this, those responsible for creating and maintaining brand relevance need to pay close attention to their company's sustainability practices. Getting a handle on the opportunities for improvement in linking sustainability and brand strategy takes a clear understanding of the gap between what's actually happening and what the public believes is happening. On one side is perception and brand image; on the other, operational reality. In this project, a similar comparison will be made but attending to the perceived environmental image that companies have and, rather than the public perception, the actual performance measured objectively.

3.5 Influence of the regulatory framework

Understand the conduct of the pharmaceutical companies about the packaging is impossible without talking about the regulations that affect this element. In general terms, each decision that affects the packaging must meet and associated standard. This attitude is imposed first by the FDA – Food and Drug Administration – and the EMA – European Medicines Agency–, who

write and distribute guidelines to the different national healthcare system. These national organizations are the responsible to develop all the regulations and laws that affect the packaging in their own country and, therefore, all the prescription and OTC pharmaceuticals sold in that national territory.

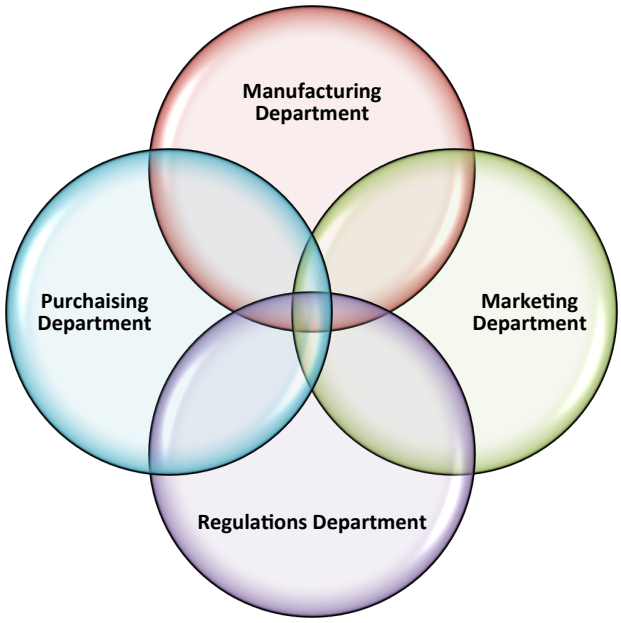
As has been said before, the main regulatory framework in the pharmaceutical industry is established by the World Health Organization (henceforth WHO) in its "The International Pharmacopoeia" (WHO, 2011)([I]). The International Pharmacopoeia constitutes a collection of recommended procedures for analysis and specifications for the determination of pharmaceutical substances, excipients, and dosage forms that is intended to serve as source material for reference or adaptation by any WHO Member State wishing to establish pharmaceutical requirements. The pharmacopoeia, or any part of it, shall have legal status, whenever a national or regional authority expressly introduces it into appropriate legislation. Apart from the Pharmacopoeia, WHO create Experts Committees that complement the information provided in the first document. Consequently, the WHO, in its 36th Expert Committee on specifications for Pharmaceutical Preparations, has a special chapter focused on the quality assurance in the pharmaceutical packaging area called "Guidelines on packaging for pharmaceutical products" which objective is aimed at ensuring that medicines arrive safely in the hands of the patients for whom they are prescribed (WHO, 2002)([II]). In this extensive document, recommendations about labelling, materials, child-resistant solutions, counterfeiting protection, etc. are provided.

If it is true that all these documentation developed by international organizations – WHO, FDA, EMA – constitute the framework, are the national healthcare ministries and ministers who study, write and adopt the laws and regulations that will be applied in each country regarding pharmaceuticals and their packaging. In order to illustrate how the packages design is an illustrative and generic example will be exposed.

Four main departments are involved in the designing process, with their own objectives and restrictions.

- Manufacturing department: The machinery involved in the packaging process is considerably expensive. These equipments are very standardized and each packaging line can produce, perhaps, two variants of a presentation. This department establishes things like the number of blisters per box, the size of the box, the materials that the machine can handle and so on. Their restrictions must be taken into account along the design process.
- Marketing department: Here is where packaging designers develop their artistic work. Their objective is to create pleasant designs for the packages trying to catch customers' attention and to persuade them. Their limitations come from the other three departments: regulations, limited budget, production constraints and so on.
- Records and regulations department: The packaging must fulfill the requirements of the country where the product is going to be commercialized. This department is in charge about things like the legibility of the leaflet, the wording and the images used in the package, the thickness and quality of the materials used in the package and so on. They give to the other departments the restrictions and boundaries that determine the limits where they can develop their abilities.
- Purchasing department: This department will try to reduce cost in order to get better margins for the company. Negotiate with suppliers, find new ones, reduce the waste, press the other departments to get better performance are some of their responsibilities.

Figure 1. Compromise between needs during the design process



Source: Ferrón, A. (2012)

The complexity of the process is huge with a lot of actors related trying to satisfy their objectives and working together to reach one same objective: a cheap, protective, legal and attractive package. But the process does not end when the product is launched. For instance, a change in the regulations can force the company to develop a new packaging design, or conversely, with the new regulation, the company is able to change their package creating a new one more effective and cheap.

As has been exposed, laws are thus a limiting element for companies' activities. The regulations that affect packaging are quite restrictive and their margin of movement is little. For this reason, all the packages that can be seen in a pharmacy are very similar: same dimensions, same number of pills per box, same materials, same leaflet format, etc. (Ferrón, 2012).

3.6 Types of pharmaceutical packaging

One of the reasons that can force the companies to reduce the packaging used in each product is the environmental impact that it causes. Obviously, not all the pharmaceuticals are presented using the same format: some of them are pills and are packaged using blisters; others are distributed in powder form and are transported inside sachets or bottles, etc. Not all these formats – also called presentations – have the same environmental impact. During this project, only four types of presentations, probably the most extended, are going to be taken into account: blisters, bottles, sachets and inhalers. Before further progress in the project, and for a better understanding, it will be good to present some information about these presentations.

3.6.1 Blisters

A blister is a term for several types of plastic packaging solutions used for small goods, food and pharmaceuticals. It is constituted basically by a cavity or pocket made from a moldable

layer – usually made using thermoformed plastic – and in the back it has and aluminum foal or plastic. The most important reason for introducing blister packaging technology in the pharmaceutical sector was to offer patients a clearly marked individual dose, enabling them to check whether they had taken the prescribed drugs on a given day. Moreover, the drugs that were not taken remained in the original package and were fully protected against adverse external conditions. The patient could handle the blister package more easily and could store it more conveniently than conventional packages – bottles, sachets and so on. Blisters are one of the most used pharmaceutical packages. Eighty-five percent of solid drugs in Europe are packed in blisters, compared with less than 20% of those in the United States. However, blister packaging is becoming more accepted in the United States as both manufacturers and consumers recognize its benefits. Advocates of blister packaging cite five aspects in which blister packaging is better than conventional packaging:

- Product integrity: Blister packaging helps retain product integrity because drugs that are prepackaged in blisters are shielded from adverse conditions. Furthermore, opportunities for product contamination are minimal, and each dose is identified by product name, lot number, and expiration date. Therefore, blister packaging ensures product integrity from the producer directly through distribution to the consumer.
- Product protection: Blister packaging protects pharmaceuticals in the home better than bottles do. For example, against moisture. Blister packaging keeps each tablet or capsule hermetically sealed in its own bubble. Medicaments that are not taken remain in the original package and are fully protected against external conditions. A blister protects a moisture sensitive tablet right up to administration.
- Tamper evidence: The dosage units are individually sealed in constructions of plastic, foil, and/or paper. The package must be designed so that one must tear the compartment to get at the product, and it must not be possible to separate the backing materials from the blister without leaving evidence. Once a bottle has been opened, whatever tamper-evident mechanism it had is gone.
- Possibility of accidental misuse: Blister packaging also can be made child resistant; most child-resistant blister packages contain a paper/film layer with a peelable adhesive. Companies also are experimenting with bitter coatings to deter children from putting packages in their mouths.

As Pilchik (2000) – The Techmark Group – explains, there are four basic components of pharmaceutical blister packages are the forming film, the lidding material, the heat-seal coating, and the printing ink. Forming films account for approximately 80–85% of the blister package, and lidding materials make up 15–20% of the total weight of the package.

- **Forming Film:** The forming film is the packaging component that receives the product in deep drawn pockets. One key to package success is selecting the right plastic film for the blisters in terms of its property type, grade, and thickness. Consideration must be given to the height and weight of the product, sharp or pointed edges of the final package, and the impact resistance, aging, migration, and cost of the film. The plastic also must be compatible with the product. There are several types of forming films:
  - **PVC**: PVC forming film is called rigid PVC because it is almost free of softening agents. Rigid PVC is a very clear, stiff material with a low WVTR (Water-vapor transmission rate). It exhibits excellent thermoformability; a high flexural strength; good chemical resistance; low permeability to oils, fats, and flavoring ingredients; easy tintability; and

low cost. These properties make rigid PVC the material of choice for blister packaging, and it essentially has 100% of the market for the plastic component. PVC films that are thermoformed have a thickness of about 254µm (micrometers). The main problem of PVC is that its combustion produces hydrochloride emissions and, under unfavorable conditions, highly toxic dioxins. Legislation in some European countries prohibits the incineration of PVC. This has created a bias toward the use of PP for blister packaging in Europe, where many pharmaceutical companies now stipulate that any new blister machines must be capable of handling both PVC and PP.

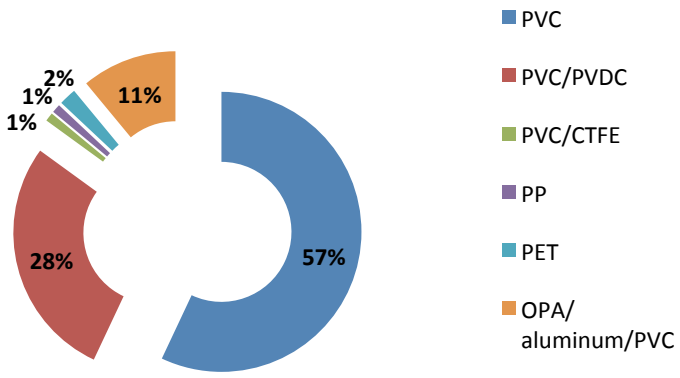
- **Polyvinylidene chloride (PVDC)–coated PVC:** Although its volume in pharmaceuticals packaging is small, PVDC plays a critical role in blister packaging as laminations or coatings on PVC. PVDC is the most common coating in blister packaging because it can reduce the gas and moisture permeability of PVC blister packages by a factor of 5–10. Coated PVC films have a thickness of 203-254 µm; the thickness of the PVDC coat amounts to 25-50 µm. The coating is applied on one side and usually faces the product and the lidding material.
- **PVC/chlorotrifluoroethylene (CTFE):** Films made from PVC and CTFE have the lowest water-vapor permeability of all films used for blister packaging. When compared with the water-vapor permeability of 254-µm PVC, the permeability of 203-µm PVC/19,3-µm CTFE is lower by a factor of 15. However, the environmental concerns regarding PVC also apply to PVC/CTFE films.
- **PP:** The water-vapor permeability of uncoated PP is lower than that of PVC and is comparable to that of PVDC-coated PVC. The thickness of PP films used in the thermoforming process ranges from 254 to 304 µm. Advantages of PP include easy recyclability, no release of toxins during incineration, and good moisture-barrier properties. PP is a possible replacement for PVC, especially in Europe. However, the use of PP has its drawbacks, for instance, the thermoforming. The temperatures required for thermoforming PP and for the subsequent cooling process must be controlled precisely. Other difficulties associated with the use of PP include its thermal instability, higher rigidity than PVC, and susceptibility to post-processing shrinkage. In addition, PP is difficult to run on a standard blister machine and cannot be processed as fast as PVC.
- **PET:** Can replace PVC but its relatively high water-vapor permeability compared with that of PVC will prevent its universal use. PVDC coated could have the same watervapor barrier effect as PVC, but this does not appear to be promising in view of the larger goal to replace chlorous plastics with PET.
- **Oriented polyamide (OPA) / aluminum/PVC or nylon / aluminum / PVC:** With a laminate structure consisting of 25µm OPA, 45µm aluminum, and 61µm PVC it is possible to eliminate water-vapor permeability almost entirely. Moreover, because of the large proportion of aluminum in the laminate, recycling this material has become feasible. Enormous efforts are being made to replace PVC with PP in such laminates to comply with environmental standards. Like other laminates containing aluminum, the OPA/aluminum/PVC laminate is cold-formed. Its cost per square meter can stand any critical comparison with PVDC-coated PVC. Cold-forming, however, requires more packaging material than thermoforming does to package the same number of the same size of tablets or capsules. This package is used in cases when it is extremely important to protect the product against moisture.

Table 4. Forming films comparison

Type	Thickness (µm)	WVTR (g/m²/day) 20ºC and 85% RH	Price compared with PVC
PVC	254	1.1	1
PVC/PVDC	254/30	0.17	2.1
PVC/CTFE	203/19	0.07	2.1
PP	304	0.20	1.3
PET	254	2.6	1.4
OPA/aluminum/PVC	25/45/60	≈0	2.9

Source: (Pilchik, R. 2000)

Figure 2. Materials world demand for blisters



Source: (Pasbrig. 2009)

- **Lidding material:** The lidding material provides the base or main structural component upon which the final blister package is built. It must be selected according to the size, shape, and weight of the product as well as the style of the package to be produced. Lidding materials range in caliper or thickness from 0.36 to 0.76 mm, but 0.46–0.61 mm is the most popular range. The surface of the lidding material must be compatible with the heat-seal coating process. Clay coatings are added to the lidding material to enhance printing. Heat-sealing and printability are both important considerations in blister packaging, and the lidding material must offer the best workable compromise. The lidding material must guarantee a WVTR that is at least as low as that of the forming films, and it must be suitable for the type of opening appropriate to the package. There are several types lidding materials:

  › **Hard aluminum:** It is the most widely used push-through lidding material in Europe. The foil usually has a thickness of 21 µm. There are endeavors, however, to reduce the thickness of this foil to 15 µm. The hardness of the aluminum facilitates push-through opening. Usually, only the print primer side features a printed design, but occasionally the side with the heat-sealing coating also can be printed. A double coat of heat-sealing coating (a heat-sealing primer and the actual heat-sealing coating) has become the standard for lidding materials. The heat-sealing primer ensures optimum adhesion of the heat-sealing coating to the aluminum foil.

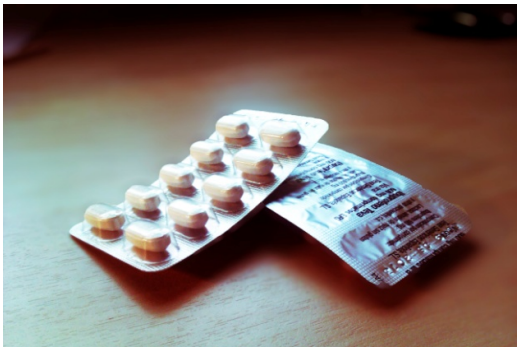
- **Soft aluminum (25 µm):** frequently is used for child-resistant push-through foils. With the exception of the type of aluminum used, the structure of this lidding material corresponds to that of hard aluminum (21 µm). The softness and thickness of this type of aluminum help prevent children from pushing tablets through it. This material also is supplied with a perforation along the sealed seams so that it cannot be peeled off the formed film in one piece.
- **Paper/aluminum:** In combinations of paper and aluminum, the weight of the paper amounts to 40–50 g/m^2. In Europe, the thickness of the aluminum typically is 28–48 µm, but in the United States it has a thickness of 15–25 µm. The reason for this difference lies in the fact that this lidding material is used in Europe for child-resistant push-through packages, so the aluminum foil must be relatively thin. In the United States, this type of material is used as a peel-off foil, so the foil must be relatively thick for effective peeling.
- **Paper/PET/aluminum:** Lidding material made of a paper/PET/aluminum laminate is often called peel off–push through foil. This kind of material is used predominately in the United States. The concept is to first peel off the paper/PET laminate from the aluminum and then to push the tablet through the aluminum.

Table 5. Comparison of lidding materials

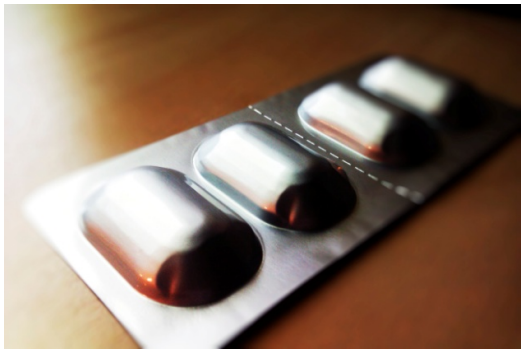
Type	Characteristics	Weight (g/m^2)	Price compared with 21 µm aluminum
21 µm Aluminum	hard, push through	60	1
21 µm Aluminum	hard, heat seal–coated, side-printed, push through	61	1.25
25 µm Aluminum	soft, child resistant	76	1.15
45 g/m^2 /25 µm paper/Aluminum	Peel off	121	1.55
45 g/m^2 (12 µm paper/PET/Aluminum	peel off or push through	142	2

Source: (Pilchik. 2000)

Figure 3. Most common blister presentations



Conventional Blister: PVC forming film + Aluminum Lid



Alu-Alu blister made with two layers of aluminum

Source: Taken by the author (2012)

- **Heat-seal coatings:** For blister packages, heat-seal coatings are perhaps the most critical component in the entire system. The appearance and physical integrity of the package depends upon the quality of the heat-seal coating. Heat-seal coatings provide a bond between

the plastic blister and the printed lidding material. These solvent- or water-based coatings can be applied to rolls or sheets of printed paperboard using roll coaters, gravure or flexographic methods, knives, silk-screening, or sprays. A successful heat-seal coating for blister packages must exhibit good gloss, clarity, abrasion resistance, and hot tack and must seal to various blister films. Hot tack is particularly important because the product usually is loaded into the blister and the lidding material heatsealed in place (face down) onto the blister. When the package is ejected from the heat-seal jig, the still-warm bond line must support its entire weight. A relatively low heat-seal temperature is desirable for rapid sealing and to prevent heat distortion of the blister film. Although heat-seal coatings used for blister packaging still are predominantly solvent-based vinyls (because of their superior gloss), water-based products are making some inroads. However, they must be evaluated carefully for hot-tack properties, gloss retention, adhesion to specific inks, and sealability to selected blister films. In addition, the heat-seal coating must precisely match the lidding material and the plastic material of the forming films. Precisely match means that with predetermined sealing parameters, a permanent sealing effect between the lidding material and the forming film must be guaranteed under any climatic conditions.

- **Printing inks:** They provide graphics and aesthetic appeal. They can be applied to the lidding material by letterpress, gravure, offset, flexographic, or silk-screen printing processes. Printing inks must resist heatsealing temperatures as high as 300ºC without showing any discoloration or tackiness (blocking). In addition, they must sufficiently resist abrasion, bending, and fading and must be safe for use with the intended product. Printing inks should not contain excessive amounts of hydrocarbon lubricants, greases, oils, or release agents.

3.6.2 Bottles

Bottles are really common packaging solutions for pharmaceuticals, especially in United States, not being so common in Europe where they are commonly used for over-the-counter products or for healthcare products like vitamin supplements. It's necessary to distinguish between three types of bottles: made of plastic, made of glass and made of aluminum.

Glass Bottles

Glass is widely used for pharmaceutical packaging for many reasons. Because it is transparent, pharmaceutical products can be easily visualized through the container itself. Despite its transparency, additives can be combined with the glass to facilitate light resistance. Glasses designed for pharmaceutical purposes are also very chemical resistant, so they do not interact with the medicament, and they are virtually impermeable to gaseous penetration. There are four types of glass used as pharmaceutical packaging materials according to the European Pharmacopoeia (2005):

- *Colourless glass* which is highly transparent in the visible spectrum.
- *Coloured glass* which is obtained by the addition of small amounts of metal oxides, chosen according to the desired spectral absorbance.
- *Neutral glass* which is a borosilicate glass containing significant amounts of boric oxide, aluminum oxide alkali and/or alkaline earth oxides. Due to its composition neutral glass has a high hydrolytic resistance and a high thermal shock resistance.
- *Soda-lime-silica glass* which is a silica glass containing alkali metal oxides, mainly sodium oxide and alkaline earth oxides, mainly calcium oxide. Due to its composition soda-lime-silica glass has only a moderate hydrolytic resistance.

Another important classification exists based on other parameter called hydrolytic stability. It is expressed by the resistance to the release of soluble mineral substances into water under the prescribed conditions of contact between the inner surface of the container or glass grains and water. The hydrolytic resistance is evaluated by titrating released alkali. According to their hydrolytic resistance, glass containers are classified as follows:

- Type I glass containers: neutral glass, with a high hydrolytic resistance due to the chemical composition of the glass itself. Type I glass containers are suitable for most preparations whether or not for parenteral use.
- Type II glass containers: usually of soda-lime-silica glass with a high hydrolytic resistance resulting from suitable treatment of the surface. Type II glass containers are suitable for most acidic and neutral, aqueous preparations whether or not for parenteral use.
- Type III glass containers: usually of soda-lime-silica glass with only moderate hydrolytic resistance. Type III glass containers are in general suitable for non-aqueous preparations for parenteral use, for powders for parenteral use (except for freeze-dried preparations) and for preparations not for parenteral use.
- Type NP: Untreated glass containers made of ordinary soda-lime glass. It is usually reserved for oral or topical medications.

The container chosen for a given preparation shall be such that the glass material does not release substances in quantities sufficient to affect the stability of the preparation or to present a risk of toxicity. In justified cases, it may be necessary to have detailed information on the glass composition, so that the potential hazards can be assessed. The inner surface of glass containers may be specially treated to improve hydrolytic resistance, to confer water-repellency, etc. The outer surface may also be treated, for example to reduce friction and to improve resistance to abrasion. The outer treatment is such that it does not contaminate the inner surface of the container.

Plastic Bottles

Plastic containers and closures for pharmaceutical use are made of materials in which may be included certain additives; these materials do not include in their composition any substance that can be extracted by the contents in such quantities as to alter the efficacy or the stability of the product or to present a risk of toxicity. For selection of a suitable plastic container, it is necessary to know the full manufacturing formula of the plastic, including all materials added during formation of the container so that the potential hazards can be assessed. The plastic container chosen for any particular preparation should be such that (European Pharmacopoeia. 2005):

- The ingredients of the preparation in contact with the plastic material are not significantly adsorbed on its surface and do not significantly migrate into or through the plastic.
- The plastic material does not release substances in quantities sufficient to affect the stability of the preparation or to present a risk of toxicity.

Most common materials used to produce plastic bottles are described below (Bormioli Rocco Packaging. nd):

- *Polyethylene (PE)* which is a thermoplastic polymer from the polyolefin family; it may have low density (LDPE) and be softer (molecular distribution with wider mesh) or have high density (HDPE) and be harder (molecular distribution with tighter mesh). PE is an excellent barrier against water and humidity, as well as resistant to shocks. It can be coloured with solid colours. It is used for the production of bottles destined for liquid and solid products.

- *Polypropylene (PP)* which is a thermoplastic polymer from the polyolefin family; it may be a copolymer or homopolymer. Depending on the kind of PP used, different physical characteristics may be obtained in the finished article with regard to softness, durability, transparency and more. PP is characterized by greater rigidity compared to PE; like PE, it is an excellent barrier to water and humidity, as well as shock resistant. It can be coloured with solid and transparent colours. Some types of PP can stand high sterilization temperatures, for example in autoclave at 121°C. IT is used for producing caps (Child Proof and Tamper Evident) and bottles.
- *Polyethylene Terephthalate (PET)* which is a thermoplastic polymer of the polyester family. PET is a highly transparent material and an excellent barrier against oxygen, carbon dioxide and gases as well as a good barrier against water and humidity; it has a high level of rigidity and mechanical resistance, and can be coloured with solid and transparent colours. It is used to produce bottles.
- *Polyethylene Naphthalate (PEN)* which is a polymer with excellent barrier properties against oxygen, humidity and UV rays, with greater resistance to hot filling and a better response to sterilization compared to the other plastic resins, as well as excellent physical and mechanical properties. It is used for producing bottles.

Aluminum bottles

Nowadays, it is common to see pharmaceuticals that are packaged using an aluminum bottle as primary package. In Europe, this presentation format is common for OTC pharmaceuticals that are produced in tablet format. These bottles are constructed using a 99.5% of aluminum and the exterior of the bottle can be printed in order to give to the package a better marketing performance. The lids of these bottles are almost always made using LDPE plastics.

Figure 4. Most common bottle presentations

Glass bottle Plastic bottle Aluminum bottle

Source: Pictures taken by the author

3.6.3 Sachets

A sachet refers to an envelope or bag for a granulate, while "granulate" refers to particles, granulate or spheronised particles. Sachets are very common inside the pharmaceutical packaging options. They are used for contain powder or other pharmaceuticals consumed by oral via. A lot of medicaments are sensitive to humidity, atmospheric air and/or light. A sachet for a pharmaceutical product should therefore preferably provide a barrier to humidity, atmospheric air and light. It is known that sachets tend to suffer from the drawback of

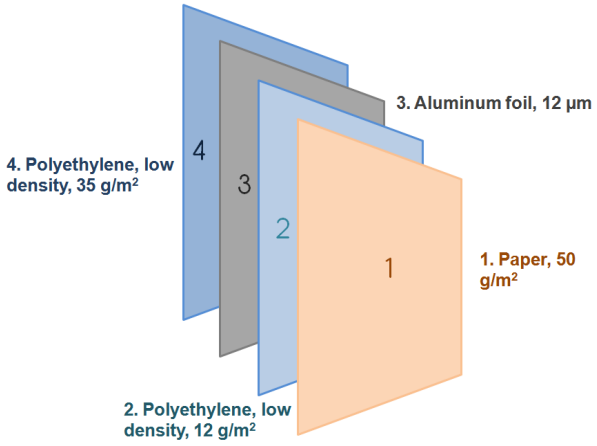
complicated manufacturing methods or high production costs. In order to being accepted by consumers, a sachet should preferably be easy to open without the use of any tool, as scissors. The filling process is also complicated: upon pouring granulate from a sachet preferably as little material as possible should be lost. An added problem is the static electricity that can appear during the filling process between certain granulate types and sachets. This is dependent of the type of granulate as well as the type of sachet. If static electricity is present, it tends to be difficult to pour granulate from the sachet. Finally, granulate in a sachet may be sensitive to degradation by light, humidity and/or air. This is also dependent of the type of sachet as well as the type of granulate. Preferably, a sachet should be easy to manufacture, easy to fill, easy to empty, and have an appealing look to improve patient compliance (Widestrom, C. 2007).
Different studies and researches recommend sachets made using different layers:

Table 6. Common constitution of a sachet

Layer number	Description	Possibilities	Recommendation
1	Paper (available for printing on)	Weight per unit area between 10-100 g/m^2	50 g/m^2
2	Bonding layer (preferably adhesive)	Weight per unit area between 6-20 g/m^2	12-15 g/m^2
3	Barrier layer	Thickness between 6-30 µm	12 µm
4	Sealing layer	Thickness between 15-50 µm Weight per unit area between 10-100 g/m^2	35 g/m^2

Source: (Widestrom, C. 2007)

Figure 5. Standard sachet constitution



Source: Made by the author

Figure 6. Example of sachet presentation

Source: Pictures taken by the author

3.6.4 Inhalers

Pharmaceutical Inhalers are common packaging presentations due to two main reasons: They provide a quick absorption into the blood stream and less medicine is needed for similar therapeutic results. The main problem of this system is that less than 20% of inhaled dosage reaches the lower respiratory system (University of Toronto, 2004). There are different types of inhalers and the most common are described below:

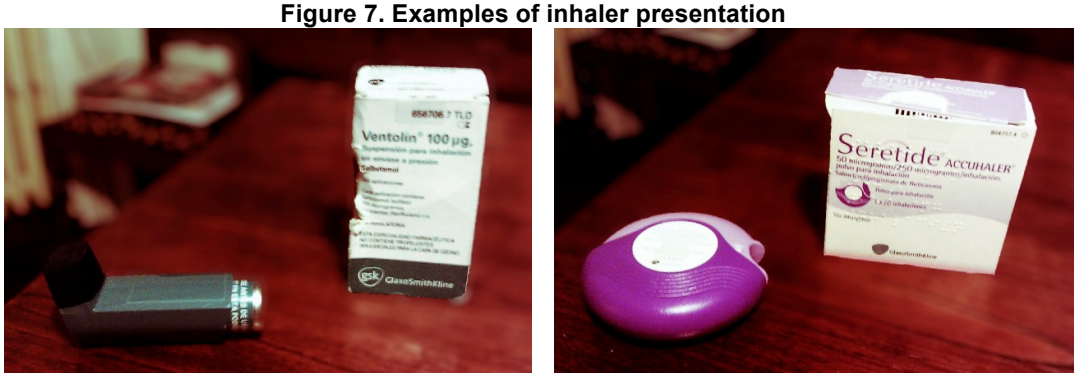
- Pressurized Metered-dose inhaler (pMDI): They are the most commonly used inhaler worldwide, and have been used since the mid 1950s. The aerosol is created when a valve is opened (usually by pressing down on the propellant canister), allowing liquid propellant to spray out of a canister, involving a complex process called cavitation. The drug is usually contained in small particles (usually a few millionths of a meter in diameter) suspended in the liquid propellant, but in some formulations the drug is dissolved in the propellant. In either case, the propellant evaporates rapidly as the aerosol leaves the device, resulting in small drug particles that are inhaled. Prior to the mid 1990s, pMDIs used various chlorofluorocarbons (CFCs) as their propellant, but with the elimination of CFCs in industry due to ozone depletion concerns, the propellants in new pMDIs typically use hydrofluoroalkanes (HFAs), which do not result in ozone depletion (Finlay. 2001).
- Non-Pressurized Metered-dose inhaler (npMDI): Also known as metered dose inhaler with a spacer, is an available option especially for children and infants who require inhalants. The spacer is a reservoir for the medication and is attached to the metered dose inhaler, which acts as a barrier prior to entering the mouth. When the canister is pressed, the medication travels into the spacer and the patient inhales the medication with the next breath. A face mask can also be attached to aid with administration (Rusell-DeLucas, C. n.d).
- Dry Powder Inhaler (DPI): A breath-activated inhaler which dispenses single, multi and pre-metered doses which have been accurately measured during manufacture. There are also device metered inhalers whereby a measured dose of medication to be released into a reservoir prior to actuation. With these devices deeper inhalation is required as there is no propellant gas to pump the delicate particles of medication into the lungs, but no coordination is required as with the pMDI. These breath-activated inhalers make the process a little more appealing to those who have coordination problems (Innovative Technology for Custom Machinery, 2011).
- Nebulizer: Nebulizers produce a mist of drug-containing water droplets for inhalation. They are usually classified into two types: electronic nebulizers and jet nebulizers. Jet nebulizers are more common due to their lower cost, and use a source of pressurized air to blast a

stream of air through a drug-containing water reservoir, producing droplets in a complex process involving a viscosity-induced surface instability that leads to nonlinear phenomena in which surface tension and droplet breakup on baffles play a role. In contrast, electronic nebulizers produce droplets by mechanical vibration of a plate or mesh. In either type of nebulizer, the drug is usually contained in solution in the water in the nebulizer and so the droplets being produced contain drug in solution (Finlay. 2001).

One of the most interesting aspects when analyzing inhalers is the propellant used in pMDI due to the problem with CFCs and the ozone layer. Following, most common propellants used are described:

- **CFC-114:** Chlorofluorocarbon compounds used basically as refrigerators and propellants in aerosols and inhalers. Due to the relation between the use of CFCs and the hole in the ozone layer, manufactures had to stop using CFCs that were replaced by HFC. Since December 31, 2008, inhalers that contain chlorofluorocarbon are not sold in the U.S (FDA, 2009).
- **HFC-134a, HFC-227ea:** Hydrofluorocarbon compounds are used in order to substitute CFCs. The use of these gases has created controversy. Numerous patients complain about the new HFC inhalers because the effect of the pharmaceutical is not the same compared with the CFC product.

Figure 7. Examples of inhaler presentation



Example of pMDI Example of npMDI

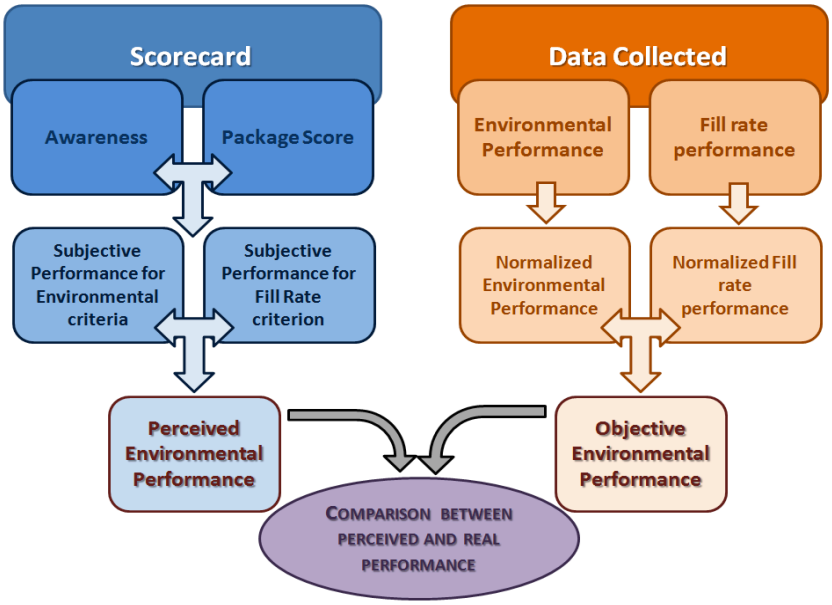
Source: Pictures taken by the author

4. Analysis

In this section, all the information both provided by the companies like personally collected will be analyzed trying to reach conclusions that give response to the questions presented in goals section. The final objective is to compare the perceived environmental performance of the companies and the real environmental performance. In order to be able to realize that comparison, some figures and parameters need to be calculated and analyzed before.

- The scorecard provides two types of information: the awareness related to the environmental impact and the self perception of the company attending to those environmental aspects. Both parameters will be combined creating a perceived performance that will be calculated for the environmental criteria – *reduced use of resources* and *use of environmentally friendly materials* – and for the *fill rate* criterion. The combination of both parameters determines the perceived environmental performance.
- The objective data collected give the opportunity to calculate the real performance of each company. Using LCA Calculator and calculating the fill rate efficiency, a good measure of the environmental performance will be created. The combination of both parameters determines the real-objective environmental performance.
- The combination of all this figures allows realizing the final comparison which will try to give response to the goals of the project.

Figure 8. Explanation of the methodology used in the analysis



Source: Made by the author

Summarizing, this analysis tries to find out the perception that companies have related with different aspects related with the design of the pharma-packaging. Also, tries to determine the real performance regarding to the environmental aspects of that design. Finally, it attempts to compare both elements: the perceived and the real results. The analysis will be made grouping

the results according to two criteria in particular: the size of the companies and the type of products they produce.

Trying to make this section as easy to read as possible, and as a guide, the following structure is going to be followed:

- Analysis made attending to the company size.
  - › Perception: importance of the different aspects and evaluation of them from company's point of view – results taken from the Scorecard.
  - › Real performance: emission per dose of pharmaceutical and fill rate efficiency – results obtained from LCA Calculator or measured empirically.
  - › Comparison: between the self perception and the real results – will be made for fill rate criterion and for the emissions of CO_2 due the packaging.
- Analysis made attending to the type of products that the company produces.
  - › Perception: importance of the different aspects and evaluation of them from company's point of view – results taken from the Scorecard.
  - › Real performance: emission per dose of pharmaceutical and fill rate efficiency – results obtained from LCA Calculator or measured empirically.
  - › Comparison: between the self perception and the real results – will be made for fill rate criterion and for the emissions of CO_2 due to the packaging.
- Other interesting results that answer questions proposed in goals section.
  - › Perception of the companies about OTC & Prescription pharmaceuticals
  - › Real environmental performance of different types of presentations.
- General comparisons trying to find trends or patterns.
  - › Comparison between the mg of CO_2 per dose of pharmaceutical vs. the weight of the environmental aspects given by companies.
  - › Comparison between doses of pharmaceuticals/liter of package vs. weight of fill rate criterion assigned by companies.
- Comparison between perceived and real environmental performance.
- Statistical Support.

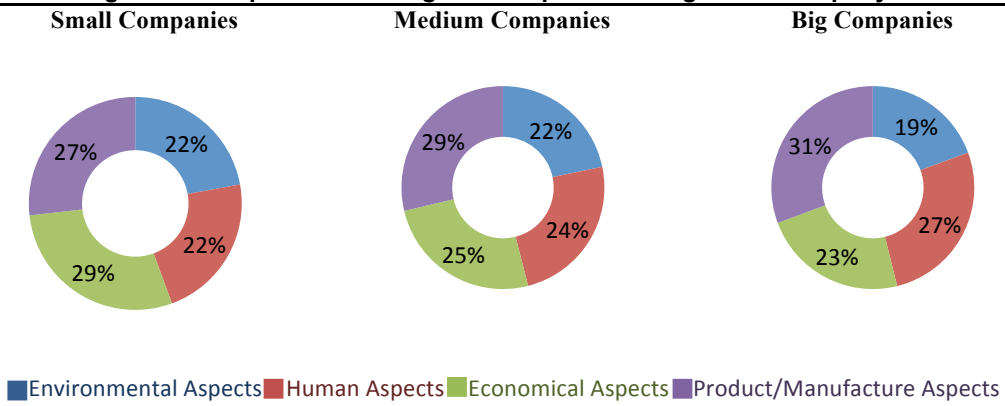
4.1 Attending to company size

Perception

In order to obtain a weighted score, each rate given by the companies for each criterion and presentation has been multiplied by the normalized weight for this concrete criterion. For further information about scorecard method, please read Olsmats and Dominic (2003) article.

Comparing the results (*figure A3.1* in *Appendix 3 – Additional information for the analysis*) between companies attending to their size, some things catch the eye. Small companies put more efforts in decrease the packaging cost. For them, the price of the final products is more important than for the medium and big ones. Offer a low price to the customers in case of OTC and to the public health systems in case of Prescription pharmaceuticals has a really big importance for these small companies; obtaining an agreement with public system for the prescription of one of their products can suppose an enormous difference for their economic welfare. Obviously, putting more effort in the economical aspects carry other consequences like decrease the importance of human or manufacture aspects.

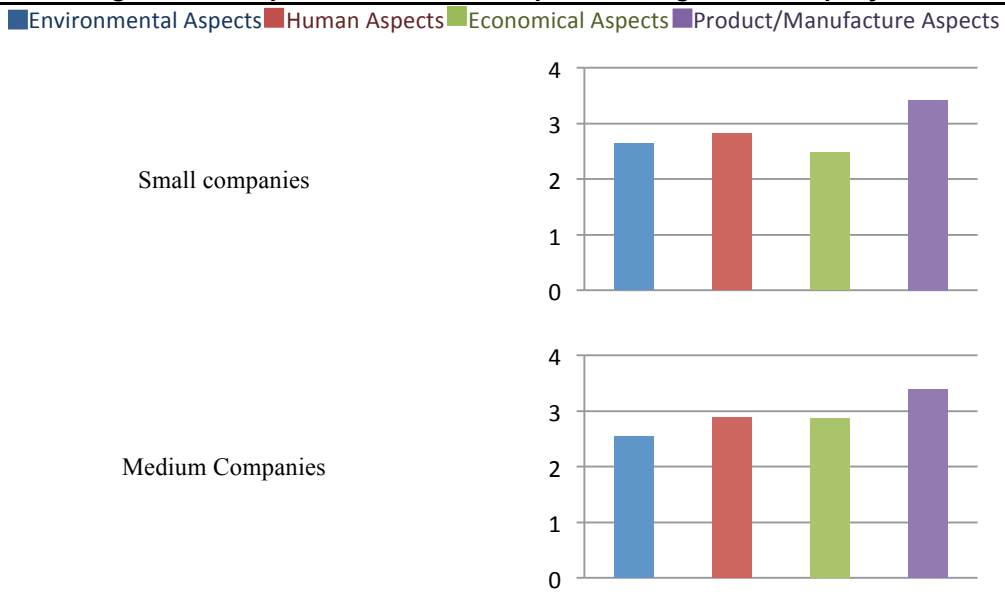
Figure 9. Comparison of Weights Groups according to the company Size

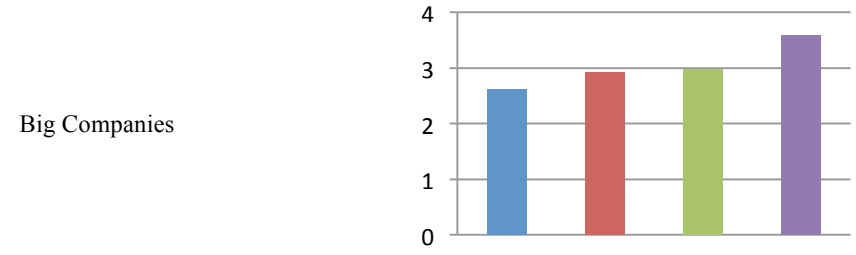


It is notorious the big importance that the big companies give to the patient compliance (10%) compared with the small and medium companies. This can happen because they have more resources and capital to make investments in this area. These results are almost exactly the same in OTC and Prescription medicines cases. *Figure 9* has an special relevance in this project purpose: independently of the size of the company, the importance given to the environmental aspects is almost the same (20%) which is a reasonable weight taking into account the trade-offs explained in problem discussion section.

Comparing the self -evaluation scores globally, the differences are not really high – around a 5% – between companies based on their size (*figure A3.2* in *Appendix 3*). Will be necessary to compare attending to score groups or according to each criterion to find significant differences.

Figure 10. Comparison of Score Groups according to the company Size



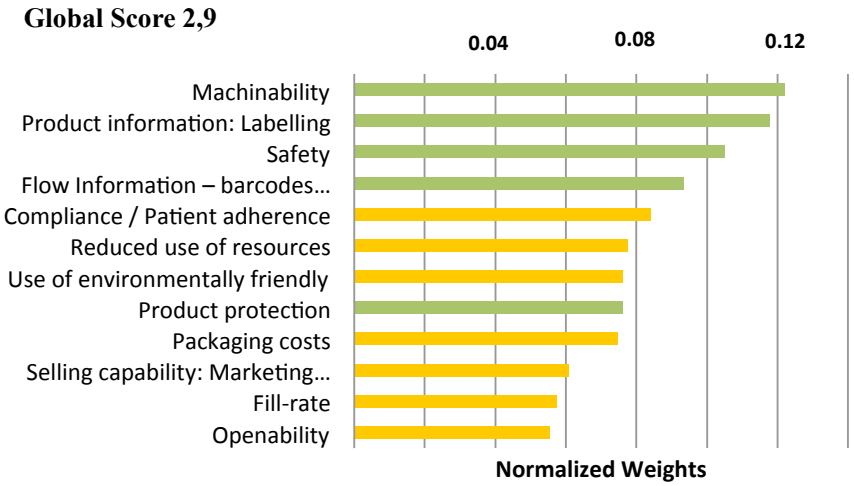


Companies, regardless of size, are not very satisfied about their environmental performance compared with others. Note that the combination of results, at this point, is the worst possible: environmental aspects have the lowest weight and are rated with the lowest score, compared with the others aspects of the design.

Other good way to observe and analyze the data provided by the scorecard consists in represent each criterion with a size proportional to its normalized weight combined with the score obtained. In that way, the longitude of each bar depends on the normalized weight obtained and the color is function of the score received – grey for scores between 0 and 1, red for scores between 1 and 2, orange for scores between 2 and 3 and finally, green for scores between 3 and 4. As a result of this, it is possible to create representations like the following ones.

Figure 11. Scorecard information for entire industry

Color legend: Scores [0 – 1] / [1.01 – 2] / [2.01 – 3] / [3.01 – 4]



The global score is obtained with the following formula:

$$Score = \sum_{each\ criteria} Weight \times Score$$

It reflects the industry's satisfaction with it overall performance evaluated between 0 and 4. Thus, pharmaceutical companies are reasonably satisfied with their packaging performance – 2,9 over 4. Also, it easy to see that the environmental criteria – use of environmentally friendly materials, reduced use of resources and fill-rate – are placed in the middle or in the bottom of the graph and coloured in yellow. This reflects the aspects mentioned before: intermediate or poor importance with intermediated assigned score.

Illustrative figures like the last one but made attending to the company size are available in *Appendix 3 – Figure A3.5*.

Real performance

The fill rate of the primary package has been calculated using the data collected empirically.

$$Fill\ rate = \frac{Number\ of\ pills\ per\ box\ (dose)}{Dimension\ of\ the\ box\ (cm^3)}$$

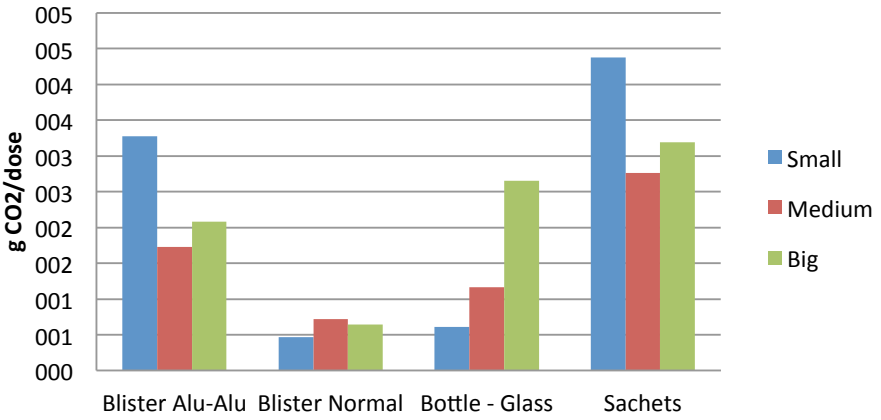
In order to work with more "friendly units", a base of one liter of volume has been established. This represents the number of pills that we could find in a primary package of one liter of capacity.

$$Fill\ rate = \frac{Number\ of\ pills\ per\ box\ (dose)}{Outter\ dimension\ of\ the\ box\ (cm^3)} \times \frac{1000\ cm^3}{1\ liter} = \frac{(doses)}{(Liter)}$$

The fill rate efficiency of the different presentations will be compared attending to the size of the company. Only have been compared those presentations which data are available related to products manufactured by companies from the three categories: small, medium and big companies (*Figure A3.6* in *Appendix 3*). In general terms, the performance of the small companies is higher than for the others. In their efforts to reduce costs, they include more pills in a shorter packaging box. In the other side are the big companies, who put less effort in increasing the fill rate.

Below is a comparison of different presentations based on the size of the company. Again, the comparisons have been made only when data for the three types of companies have been available and using the results provided by LCA Calculator software.

Figure 12. g CO_2/dose according to the company size and the presentation



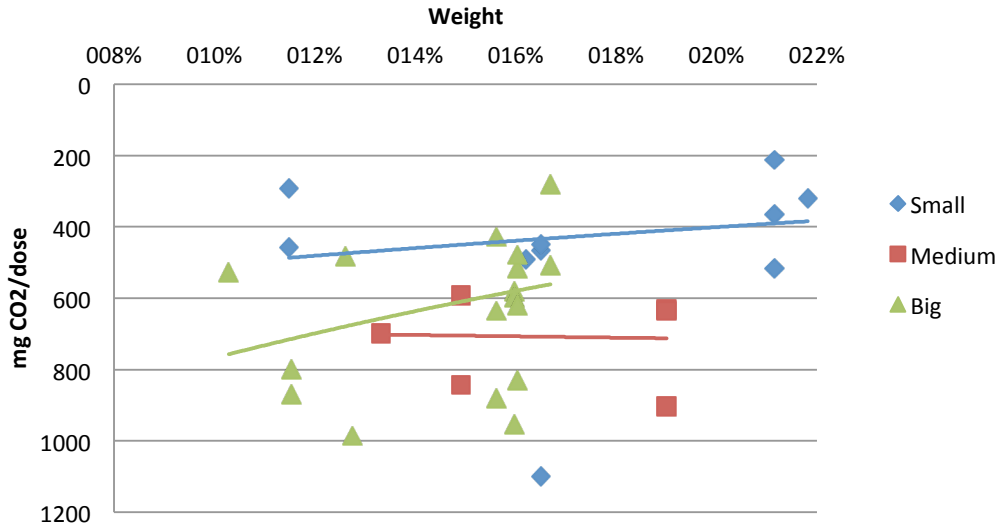
The emissions for a regular blister are the same for the three types of companies. It is due to all the industry uses the same processes and the same machines for create this type of package. Talking about sachets, small companies have a worse performance – 1.5X worse. The same happens in Alu-Alu blisters case. This presentation is more difficult to produce due to is not any layer made of a plastic material and to adhere the two metallic layers is necessary to add a third plastic element. The thinner the aluminum layers are, the harder is to make the union between

them. Big companies use more material when producing glass bottles – 5X worst than small companies.

Comparisons

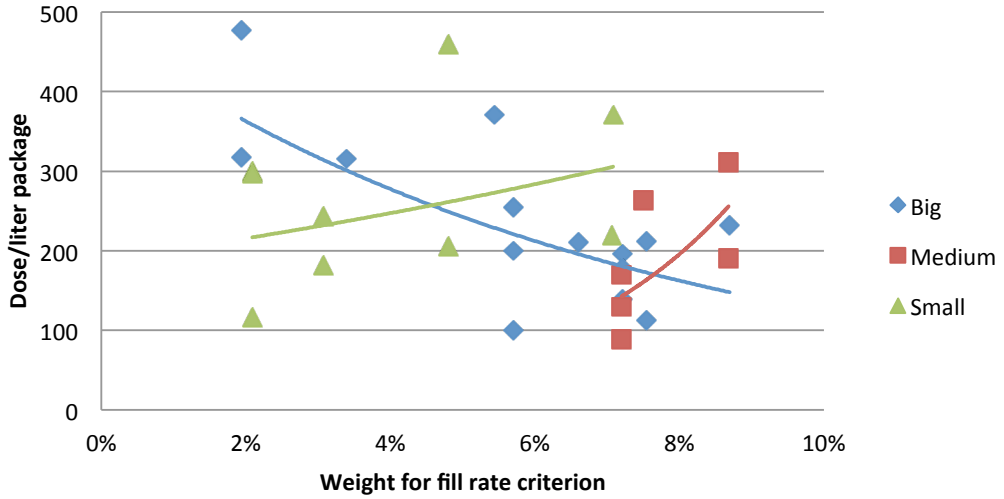
The comparison between the real performance and the perceived one will provide the most interesting results of this project. They attend only to standard blisters since for this presentation the data available are larger. Note that only the *reduced use of resources* and the *use of environmentally friendly materials* have been considered as environmental aspects. Fill rate criterion has not been taken into account because an independent analysis will be made. *Figure 13* represents the dotplot and the curve or regression of each type of companies attending to their size: the exponential lines represent therefore the average mg CO_2/dose of pharmaceutical for each weight given to the environmental aspects and for each type of companies.

Figure 13. Contrast attending company size for normal blisters



Small companies use to have a low environmental impact the evolution of the performance is logical: when the companies put more efforts to reduce the environmental impact, the results are better. Medium companies are in the opposite situation; the results are not improved when the importance of the environmental aspects grows. They obtain the worst result compared with others. For big companies, a little increment in the effort implies a considerable better result. Anyway, a priori, it appears that small companies are better in their environmental performance. The statistical analysis necessary to determine if the differences are significant and if a correlation between the size of the company and the level of impact exists will be done later.

Figure 14. Contrast attending the size of the company for normal blisters



In *figure 14* the weight of the fill rate criterion is compared with the fill rate performance. Big companies have a strange behavior. It is possible to see a strong tendency which consists in a decrease of the fill rate performance when the company gives more importance to it. Medium companies conduct is more reasonable: a higher importance to fill rate is translated into a higher performance. In any case, this type of companies used to put more efforts in improving this environmental aspect than the others. Small companies have a similar behavior than medium ones and their performance is intermediate between big and medium companies.

Summarizing, the importance of the packaging environmental impact is around 20%, regardless of the company size. The self perception of the companies related with their environmental performance if lower than for the other types of criterion, with independency of the company size. Small companies show a lower CO_2 emissions per dose of pharmaceutical; in any case, there is just a slightly increment of the environmental performance when incrementing the weight of the environmental aspects. Finally, there is no improvement in the fill rate performance when the fill rate criterion rises.

4.2 Attending to the type of products that the company produces

Perception

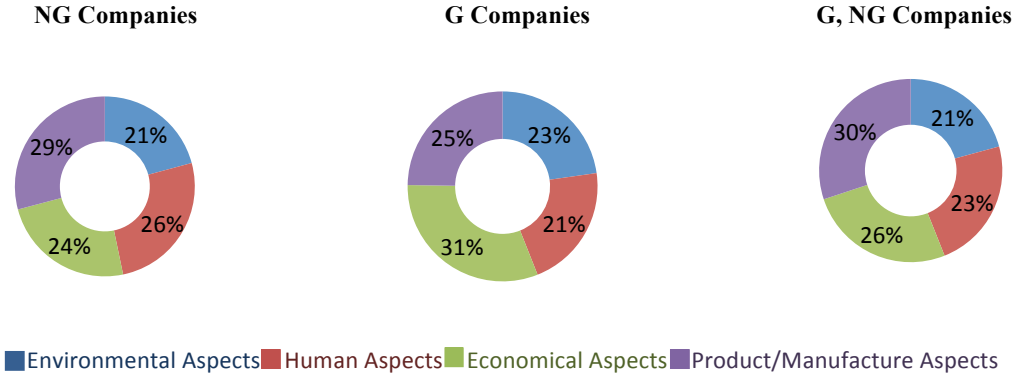
This section compares the results creating groups based to the type of products that the company produced: Non generic pharmaceuticals (NG), generic pharmaceuticals (G) or companies that produce both type of medicaments (G, NG).

Some indicative elements can be extracted from *figure A3.7* placed in *Appendix 3*. The importance that "G, NG" companies give to each criteria is really similar that the "NG" companies gives except for two criteria: Fill rate and openability. In this last cases, their conducts is closer to the "G" companies.

As in the case of small companies, "G" companies put more efforts in create cheap packages using a reduced amount of resources. In contrast, their attention to the product protection is lower compared with the other companies' groups. Again, as with small companies, for these companies, produce the pharmaceutical with a very competitive price is vital for their survival

due to the national health systems use to be their principal client. The similarity in the results can be because the combination between small company and generic manufacturer is quite common.

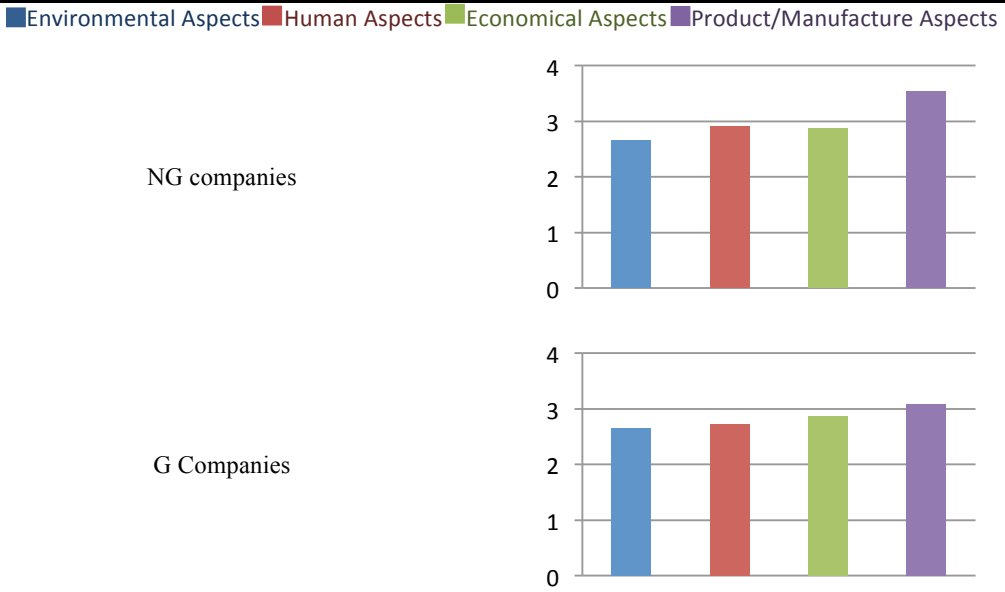
Figure 15. Comparison of Weights Groups according to the type of products the company produces

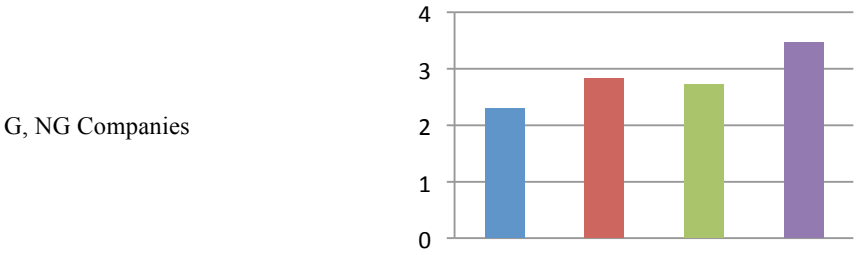


"NG" companies, in their interest in create packages friendlier from customers' point of view, give less importance to other aspects like the economical or environmental. The opposition situation appears in "G" companies' case. Again, the most remarkable point is that the importance given to the environmental impact is around 22% regardless the type of products that the company produces.

The differences in the evaluation process, as in the previous comparison based on the size of the company, are pretty small – less than a 6% (*Figure A3.8* in *Appendix 3*). Introducing the criteria group restriction, the results are much more interesting.

Figure 16. Comparison of Score Groups according to the company Size





A 22% of difference exists in the evaluation of environmental aspects compared with manufacturing aspects in the case of "NG" companies. Also, a difference around a 30% exists in "G, NG" companies when environmental aspects are compared with manufacturing aspects. In either case, manufacturing aspects always get the best rate compared with the others.

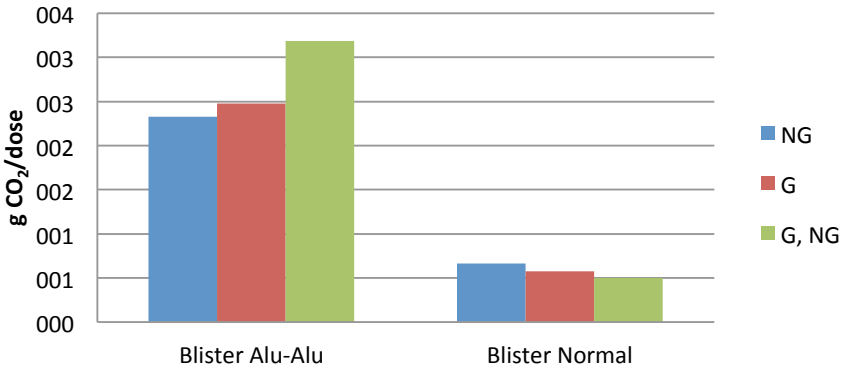
Comparing each criterion for each company group the results are as *figure A3.9* in *Appendix 3* shows. The evaluation that "G, NG" companies do themselves is almost the same that "NG" companies do. They bigger differences appear comparing with "G" companies. Their evaluations are always lower except for the use of resources and the packaging cost, aspects on which they think they are doing better.
Finally, the alternative representation of the scorecard results made attending to the classification used in this section is provided in *Appendix 3 – figure A3.10*.

Real performance

The fill rate efficiency of the different presentations has been compared attending to the type of products that the company produces. The performance of "G" companies and "G, NG" companies are almost the same. The result for standard blisters for "G, NG" companies looks atypical and come probably from anomalous samples. (*Figure A3.11* in *Appendix 3*).

Attending to the g of CO_2/dose of pharmaceutical, is possible to say that the emissions of the standard blisters are the same for the three types of companies and that "G, NG" Alu-Alu blisters are 1.4X more contaminants than "NG" or "G" ones.

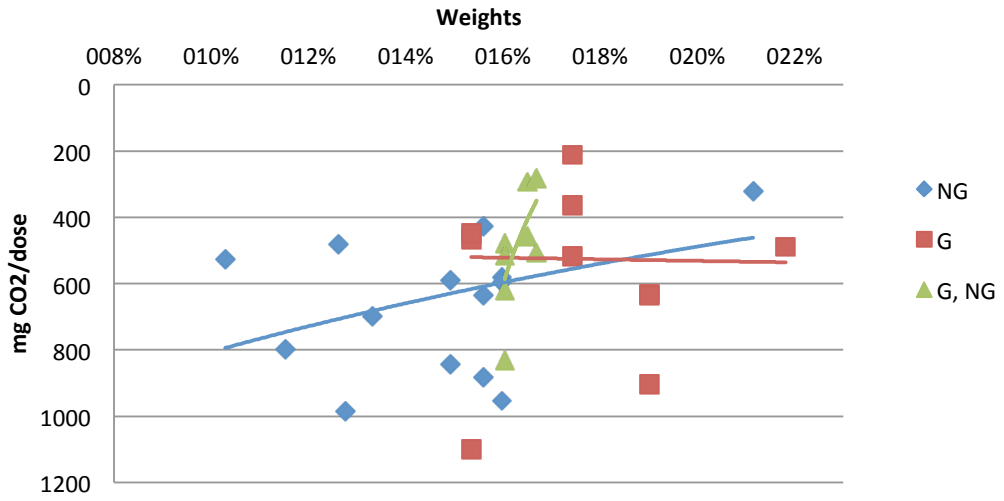
Figure 17. g CO_2/dose according to the type of products that the company produces and the presentation



Comparisons

As in companies' size case, the CO_2 emissions result and the importance given to it are going to be compared.

Figure 18. Contrast attending the type of products that the company produces for normal blisters



Thus, "G" companies put a lot of efforts in reduce the environmental impact but not always the expected result. For this companies, pay more attention to the environmental aspects does not imply a better performance. "NG" companies do not pay attention to the environmental aspect but sometimes, the results they get are fine. An increment in the efforts implies to obtain better results. "G, NG" companies put an intermediate amount of efforts and their results use to be positive.

Comparing the fill rate performance with the weight given to it, the results are surprising. In the three cases, the relation between the real performance and the efforts put by the companies is practically lineal: no matters the interest that the company put in improve the fill rate, the results are almost the same: "G, NG" companies are the most efficient and "G" companies the least efficient (*figure A3.12* in *Appendix 3*).

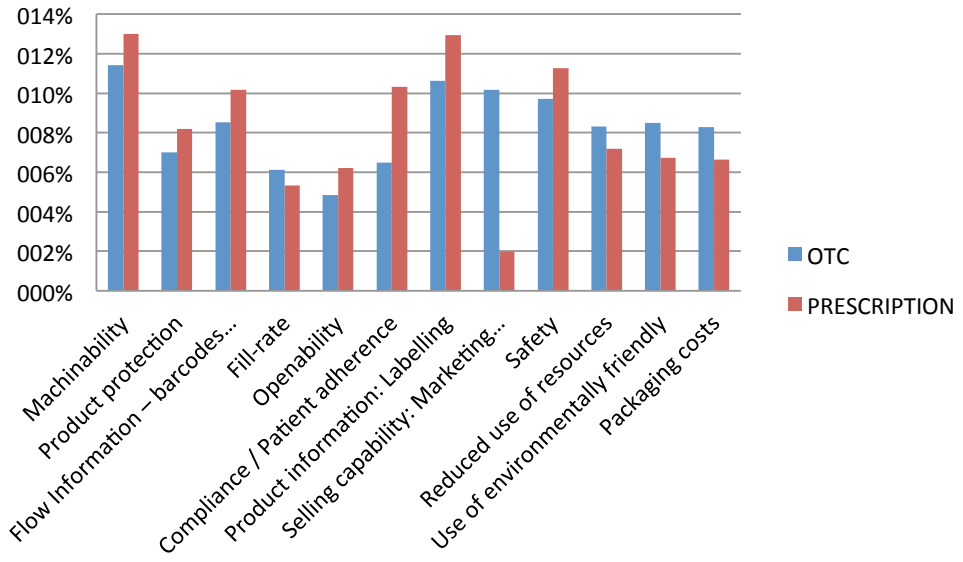
Summarizing, the importance of the environmental aspects is around 22%, regardless from the type of products that the company produces. The environmental aspects get always a lower perceived rate, but the difference with the others is pretty important in "G, NG" case. Comparing the CO_2 emissions with the importance given to the environmental aspects, there is a high improvement in "NG" case: 30 mg CO_2/dose less for each 1% increase in the importance of the environmental aspects. Again, as in companies' size case, there is no relation between the fill rate performance and the importance given to this aspect.

4.3 Additional results from the scorecard & empirical data

Extracted from the Scorecard

Additional information can be extracted from the scorecard. For instance, the weights and scores obtained comparing Over-the-counter products with prescription pharmaceuticals. The results provided in this subsections are independent from whether they are big or small companies or if they only produce generic pharmaceuticals or not. Thus, the *figure 19* only compares the weights given to each criterion for OTC and prescription products.

Figure 19. Weights for OTC & Prescription pharmaceuticals



Looking the data can be seen that ate three main criteria with the highest importance independently from the type of products: Machinability, product information and safety. The reasons are quite clear. It is not easy to change a packaging line because the machines involved in the automatic process of packaging are really expensive. For instance, a packer machine could be around 250000€ or 2254000 SEK (Lopez-Gonzalez, I. 2012). The packages need to be adapted to the available machines and for this reason all pharmaceutical packaging elements are really similar in dimensions and shapes. Also, the number of manufacturers of these automatic packaging robots is really small so the options are quite reduced. With this scene in mind, it is obvious that the machinability of the package/products stay in the top three. The pharmaceutical industry is hardly regulated; every product needs to be sold together with a leaflet where the active components are described among other things. It is mandatory, and for this reason, every company needs to put a big effort in doing it properly. Finally, the security of the package needs to be guaranteed; pharmaceuticals are dangerous products if ingested by accident by a child, for instance. The package need to be secure, strong and well closed to converse the medicine in optimal conditions until the moment of intake.

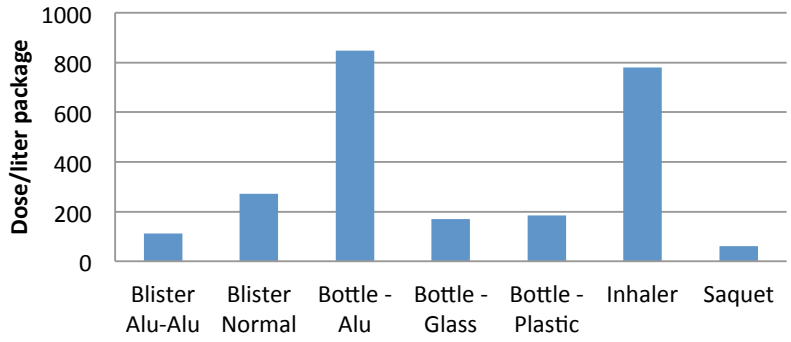
Also, some differences between OTC and Prescription medicaments can be explained easily. The efforts to improve the patient compliance are much higher in prescription pharmaceuticals case. It is due to the intake of this products use to be more crucial for the recovery of health by the patient. Companies are putting more efforts trying to create a system that helps people to follow their medicaments program. Other difference comes from the fact that it is not possible to sell prescription pharmaceuticals without prescription as its name indicates; due to this big difference, the patient has not the capacity to select what medicament needs to take. The doctors and medical professionals are responsible for determine what pharmaceutical needs to be taken by the patient. Marketing aspect related with the packaging like designs and graphics are not important in prescription cases but this is not like this when talking about OTC: companies need to persuade customers/patients using all the possible ways, including the packaging. In case of prescriptions medicaments, the labelling is even more important than in OTC case. This products are more strong and therefore, more dangerous. For this reason, the importance of the safety is higher too.

In general terms, there is no difference from companies' point of view analyzing their performance producing the packaging for OTC and for Prescription pharmaceuticals: Prescription medicaments are just a 2.5% better rated than OTC. For a graphic comparison, see *figure A3.13* in *Appendix 3*.

Extracted from the data collected empirically

It is interesting to compare the fill rate efficiency of the different types of presentations.

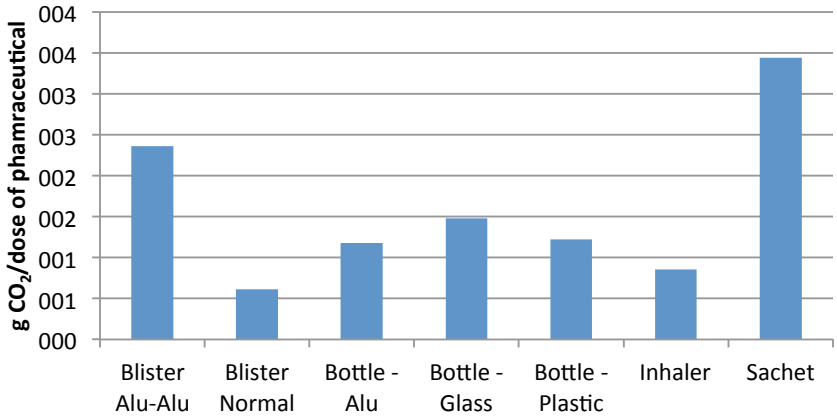
Figure 20. Doses per litter of primary packaging



The most efficient presentation attending to the fill rate are inhalers and bottles made of aluminum. In case of inhalers it is logical; the amount of active ingredient that needs to be inhaled in each shot is relatively small. Talking about bottles made of aluminum, the high fill rate is due to the shape of the product and the storage conditions needed. This presentation is used with OTC products made using tablet format; each pill is stored over the following without spaces creating a "tower" of pills that can be introduced in a tube made of aluminum. Obviously, products not very sensitive to the moisture can be packaged using this system. (Pictures of the different presentations are included in *Chapter 3*). Is remarkable the low efficiency of the sachets. In a typical box used for store 10 sachets can be stored 21 or even more pills using blister presentation. Finally, just note the difference between conventional blisters – made using a layer of aluminum and a layer of PVC – and blisters made using two layers of aluminum called Alu-Alu blisters. This last presentation is used only in exceptional cases when the medicament needs a really well protection against external agents, mainly moisture.

Now, comparing presentations attending to their CO_2 emissions per dose, some interesting conclusions can be extracted: Sachets are the most harmful presentation with around a double impact than the other formats. The differences between bottles – glass, plastic or aluminum – are not significant. A big disparity between standard blisters and Alu-Alu blisters exists because the aluminum is much more harmful for the environmental than the PVC. Finally, in general terms, the conventional blister is the less harmful presentation option. The use of packaging materials per dose is less than for other presentations: it is made using layers of aluminum and PVC with very small thickness.

Figure 21. g CO_2/dose of pharmaceutical attending to the presentation



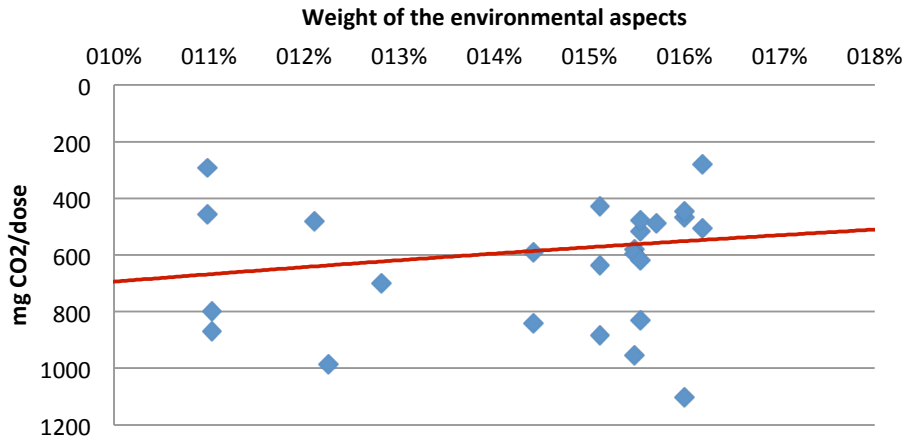
4.4 Overall comparisons

The objective of this section is to extract general conclusions that can be applied for the whole industry and that give response to the questions presented in goals section. Thus, distinctions between companies' sizes or between products produced are not going to be made along it.

Weight of the environmental aspects vs. real environmental performance

A slight tendency exits relating the environmental performance and the importance that the companies gives to the environmental aspects: more importance translates to better environmental results – 37.5 mg of CO_2/dose of pharmaceutical less for 1% increment in the weight of the environmental aspects.

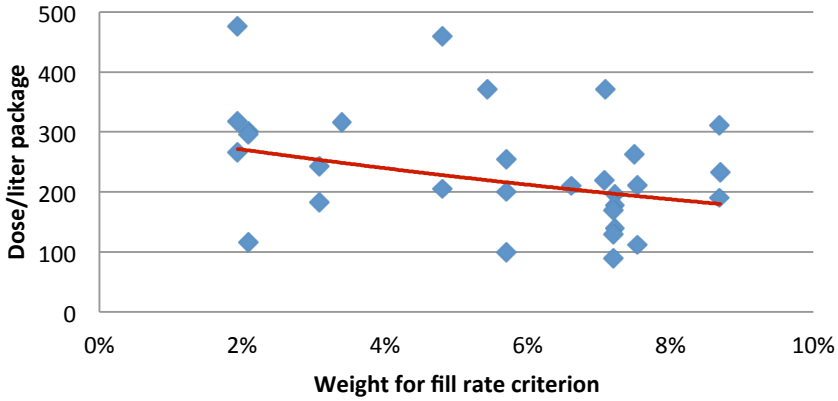
Figure 22. Comparison between the weight for environmental aspects the real performance



Weight of the fill rate criterion vs. real fill rate performance

Surprisingly enough, in general terms, if the fill rate criterion have more importance, the results are worst. This shows an inefficient performance of the industry because the results obtained are completely the opposite from what is expected: better performance when more efforts are put.

Figure 23. Comparison between the weight for the fill rate criterion and the real fill rate performance



4.5 Perceived environmental performance and real environmental performance

This comparison can be considered as the final goal of this thesis. To be able to carry it out, it is necessary to introduce a new parameter which tries to agglutinate the weight and the scores that the companies give to each criterion: the *Subjective Performance Factor*. It comes from the product between the weight that the company gives to the criterion and the rate between 0 and 4 that the company also gives to that criterion.

$$Subjective\ Performance\ Factor\ (SPF) = Weight\ of\ the\ criterion \times Rate\ for\ the\ criterion$$

Attending to the previous formula, the SPF has been calculated first for two of the three environmental aspects – *reduced use of resources* and the *use of environmentally friendly materials* – and then, for the *fill rate* criterion.

In order to compare the perceived environmental performance and the real environmental performance, some parameters need to be calculated:

- The perceived environmental performance related with the environmental aspects – *reduced use of resources* and the *use of environmentally friendly* materials – have been normalized: $normalized\ SPF\ Environmental\ aspeects = \frac{SPF\ environmental\ aspects}{\sum SPF\ environmental\ aspects}$

  $normalized\ SPF\ Fill\ rate = \frac{SPF\ fill\ rate}{\sum SPF\ fill\ rate}$
- The weighted average between the normalized perceived environmental performance related with the environmental and the normalized perceived environmental performance related to the fill rate criterion result in the SPF combined:

  $$SPF\ combined = \frac{normalized\ SPF\ Environmental\ aspeects + normalized\ SPF\ Fill\ rate}{2}$$
- The inverse of the mg CO_2/dose of pharmaceutical have been calculated and normalized: $mg\frac{CO_2}{dose}normalized = \frac{\frac{1}{mg\frac{CO_2}{dose}}}{\sum\frac{1}{mg\frac{CO_2}{dose}}}$. Using the inverses, the higher the $mg\frac{CO_2}{dose}normalized$, the better is the performance.

- The same process has been applied for the fill rate: $\frac{Dose}{liter\ package} normalized = \frac{\frac{Dose}{liter\ package}}{\sum \frac{Dose}{liter\ package}}$
- With this two results, a global score that reflects the real performance has been calculated: $Global\ Environmental\ Score = mg\frac{CO_2}{dose} normalized + \frac{Dose}{liter\ package} normalized$

The results obtained are provided below. Note that the anomalous results are marked in yellow and will not be taken into account for further analysis.

Table 7. Results for the comparison between perceived environmental performance and the real environmental performance

Company		Characteristics		Perceived environmental performance	Real performance
Codename	Size	Type of products 1	Type of products 2	SPF combined	Global Score
B1	Big	P, OTC	NG	0,052042248	0,038278788
B2	Big	P, OTC	NG	0,04359308	0,071952492
B3	Big	P, OTC	NG	0,046314015	0,048437874
B3	Big	P, OTC	NG	0,046314015	0,02713888
B3	Big	P, OTC	NG	0,046314015	0,053380333
B4	Big	P, OTC	NG	0,048510169	0,032628584
B4	Big	P, OTC	NG	0,048510169	0,045566559
B4	Big	P, OTC	NG	0,048510169	0,055727925
B5	Big	P, OTC	NG	0,047453955	0,04213468
B5	Big	P, OTC	NG	0,047453955	0,030015008
B6	Big	P, OTC	G, NG	0,037224455	0,064585261
B6	Big	P, OTC	G, NG	0,037224455	0,132666487
B7	Big	P	NG	0,040751996	0,054529487
B8	Big	P, OTC	G, NG	0,036942087	0,080940104
B8	Big	P, OTC	G, NG	0,036942087	0,059059076
B8	Big	P, OTC	G, NG	0,036942087	0,119353362
B8	Big	P, OTC	G, NG	0,036942087	0,047238279
M2	Medium	P,OTC	NG	0,039065069	0,050404141
M3	Medium	P, OTC	NG	0,061749774	0,04685435
M3	Medium	P, OTC	NG	0,061749774	0,051646735
M5	Medium	P, OTC	G	0,063323845	0,026891759
M5	Medium	P, OTC	G	0,063323845	0,038821097
M5	Medium	P, OTC	G	0,063323845	0,042793613
S2	Small	P, OTC	G	0,036342907	0,026628101
S2	Small	P, OTC	G	0,036342907	0,065589995
S2	Small	P, OTC	G	0,036342907	0,06664917
S3	Small	P, OTC	G, NG	0,034378815	0,056265177
S3	Small	P, OTC	G, NG	0,034378815	0,102450709
S6	Small	P, OTC	G	0,055807078	0,049767819
S6	Small	P, OTC	G	0,055807078	0,069133712
S6	Small	P, OTC	G	0,055807078	0,158471056
S7	Small	P, OTC	NG	0,076386662	0,08855468
S8	Small	P, OTC	G	0,05773647	0,055444711

The analysis of these data is going to be made using two systems: a ranking system and a matrix graph.

Ranking

This section analyzes where are the companies with the "best practices" results attending to the two parameters calculated. The expected result will be that the companies with better Perceived environmental performance will get the better real results and vice versa. An average of the results obtained for the products of each company have been used in order to create the ranking. In total, 16 different companies that produce blisters have been analyzed.

Table 8. Ranking of companies attending to the results obtained

Perceived environmental performance		Real performance
Ranking Number	Characteristics	Ranking Number
1st	**Small** company that produce **generics**	3th
2nd	**Medium** company that produces **generics**	15th
3th	**Medium** company that produces non **generics**	11th
4th	**Small** Company that produces **generics**	7th
5th	**Small** company that produces **generics**	2nd
6th	**Big** company that produces non **generics**	14th
7th	**Big** company that produces non **generics**	12th
8th	**Big** company that produces non **generics**	16th
9th	**Big** company that produces non **generics**	13th
10th	**Big** company that produces non **generics**	6th
11th	**Big** company that produces **non generics**	8th
12th	**Medium** company that produces **non generics**	10th
13th	**Big** company that produces **generics & non generics**	1st
14th	**Big** company that produces **generics & non generics**	5th
15th	**Small** company that produces **generics**	9th
16th	**Small** company that produces **generics & non generics**	4th

The expected result is that the position of each company based on both criteria was similar. This doesn't happen at all so a misperception in companies` environmental performance can be intuited. The use of the matrix representation will try to confirm this result.

Matrix

In this occasion, the perceived environmental performance and the real environmental performance are going to be compared creating a matrix where the axis will represent those parameters As a result of this, four areas can be distinguished.

- Area 1: In this area, the companies have a low perceived environmental performance but their real results are good compared with the other companies. Their awareness of the environmental issues is not adjusted properly.
- Area 4: In this area, companies also have a misconception about the awareness of the environmental issues. They have a high self perception about their environmental performance but the real results are bad compared with others.
- Area 3: Companies have a good perception about their own activities. They are conscious that they can do more for the environmental but due to different reasons; they are not doing enough to reduce the impact of the packaging.
- Area 2: this area is the antagonist of area 3. Companies placed in this region have a good awareness about their environmental capacities; they are doing better than the others and are aware about that.

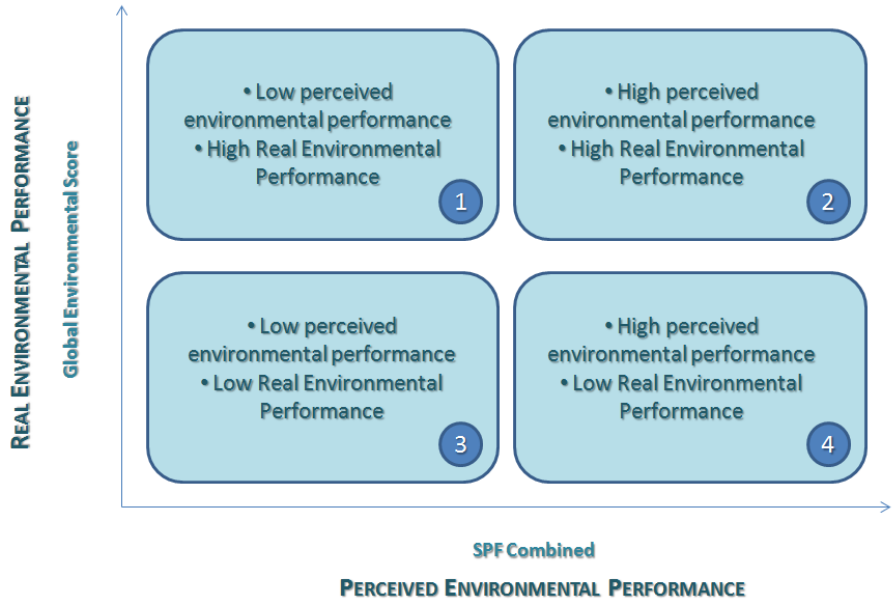
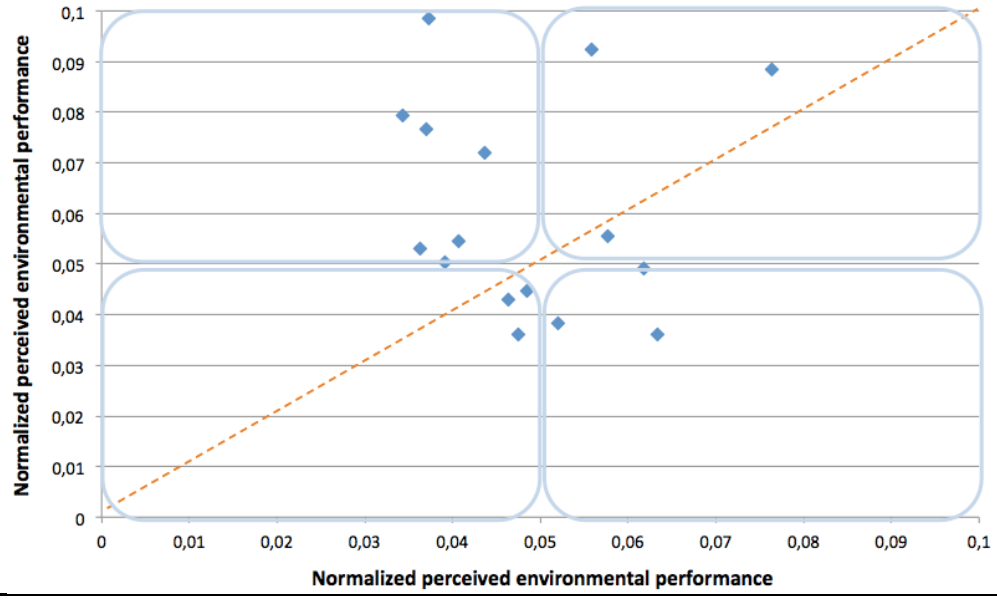


Figure 24. Results comparing the perceived performance and the real performance



Most populated area is number 1: the 31,5% of the industry have a high real environmental performance but low perceived one. Together with area 1, area 4 is also an incorrect perception area. In this second case, it harbors around the 18,75% of the companies. Areas 2 and 3 represent the optimal situation: a good relation between the perceived and the real environmental performance. The best of the possible situations represented by area 2 includes the 18,75% of the industry and finally, area 3 collects around the 25% of the results. Note that the axes are normalized so the expected result is that companies are placed around the bisectrix of the matrix; this means that for a perceived environmental performance of 0.05, the expected result is a real environmental performance of 0.05. In base of that, a 44% of the companies have a correct perceived environmental performance and a 56% have an incorrect perceived environmental performance.

Figure 25. Analysis of each area

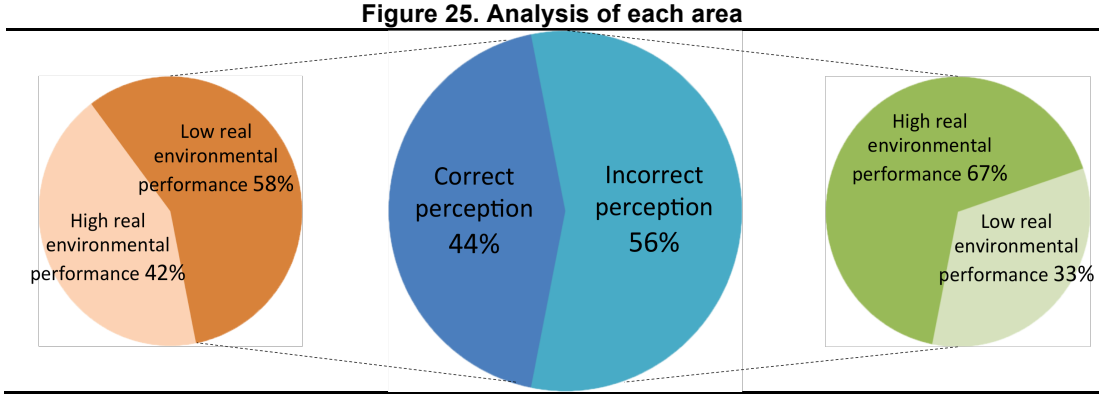
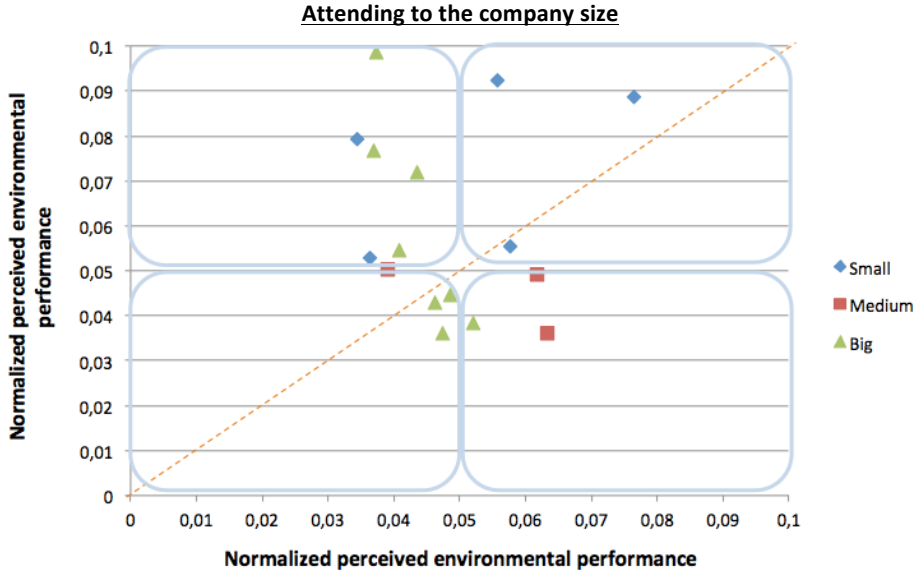


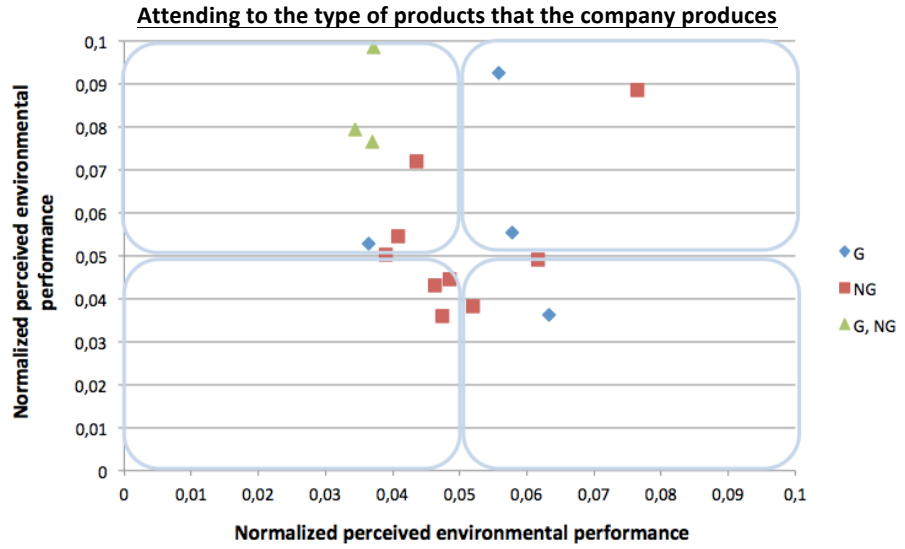
Table 9. Analysis of the data

Area	Percentage of the companies	Area	Percentage of the companies
Incorrect perception - Areas 1 and 4	56,25%	Area 1 - High real environmental performance	31,50%
		Area 4 - Low real environmental performance	18,75%
Correct perception - Area 2 and 3	43,75%	Area 2 - High real environmental performance	18,75%
		Area 3 - Low real environmental performance	25%

Below, a deep analysis of each area is going to be done. The objective is to characterize the companies that are placed in each region. In order to do that, a classification attending to the company size and attending to the type of the products that the company produces is going to be shown.

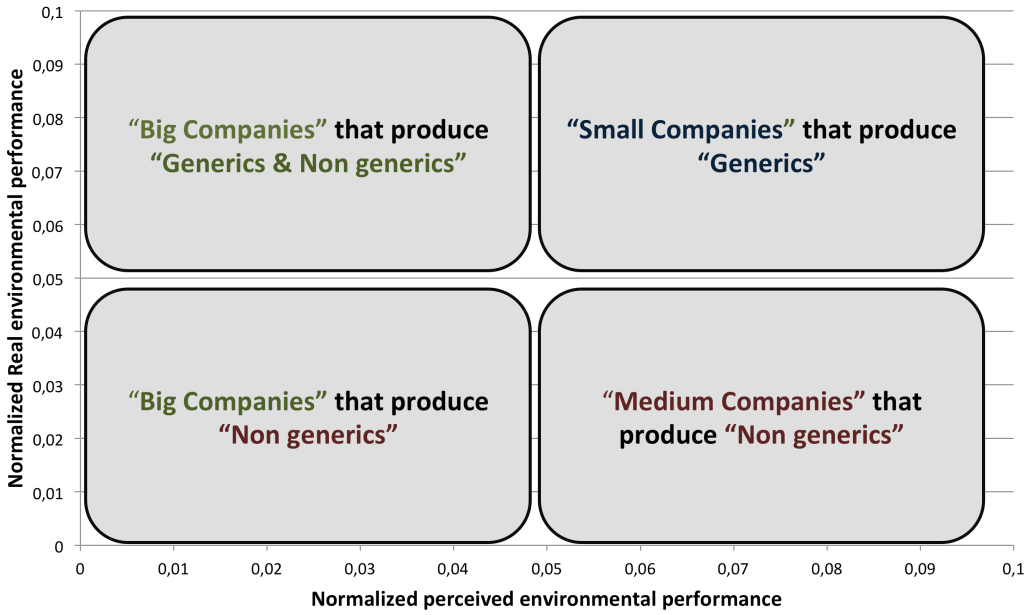
Figure 26. Analysis attending to different criteria





Attending to this, a characterization of the most common population that appears in each area can be done:

Figure 27. Characterization of each area



- Incorrect perception – Areas 1 and 4: It is possible to find medium and big companies that can produce every type of products.
  - › High real performance with low perceived performance – Area 1: This area is occupied mostly by big companies that produce generics and non generics.
  - › Low real performance with high perceived performance – Area 4: In this region, which is the most worrying one, is possible to find medium companies that produce non generics.

- Correct perception – Areas 2 and 3: The most common situation in this area is small and big companies that produces generics or non generics.

› Low real performance with low perceived performance – Area 3: This area is common for big companies that produce non generics.
› High real performance with high perceived performance – Area 2: Area occupied by small companies that produce generics.

4.6 Statistical Analysis

A deep statistical analysis has been realized trying to find relations between the results obtained objectively and criteria like the size of the company, the products they produce, their subjective performance, etc. The calculations are included in *Appendix 4: Statistical Analysis* so in this section only the more important results will be commented. As has been said before, the software used for that was *Statgraphics Centurion XV*. Note that this analysis only will be made for standard blisters presentations due to this is the most frequent format and the availability of figures is higher in this project.

Mg CO_2/dose of pharmaceutical attending to size, type and weight criterion

The statistical analysis reveals that only the *company size* criterion has relation with the emissions due to the packaging. Criteria like the *type of products* that the company produces or the importance that the company gives to environmental aspects has no statistical correlation. The main conclusions that can be extracted from this analysis is that it is possible to say, with a 90% confidence level, that small companies have less CO_2 emissions because of the packaging compared with medium and big ones.

Dose/liter of packaging attending to size, type and weight given to fill rate criterion

In this case, only the criterion "*type of products that the company produces*" has significant influence on the fill rate performance. The other criteria – the size of the company and the importance of the fill rate aspect – have no statistical influence. Thus, it is possible to confirm that, with a 95% confidence level, companies that produce only generics, have a lower fill rate performance compared with companies that produce non generic or both types of products.
An analysis based on the mg CO_2/dose of pharmaceutical & dose/liter of packaging attending to size, type and the SPF for those criteria has been done providing the same results that the previous ones.

Real environmental performance attending to size, type of products and perceived environmental performance

In this final case, only the criteria "size" and "type of products" have significant influence on the results. The fact that the perceived environmental performance has no influence in the real results obtained is remarkable. Thereby, it is possible to say with a 95% confidence level that small companies obtain a better real environmental performance. Also, with a 90% confidence level is possible to affirm that generic producers have a worst environmental performance.

5. Discussion

At this point of the project, some aspects are pretty clear: The pharmaceutical industry is not putting so much attention – or perhaps, not enough – to the environmental impact of the packaging. For them are other aspects more important, like the machinability or the safety of the product. At least, half of the industry has a low perceived environmental performance that reflects the real situation. The little influence that bigger efforts have on the final environmental performance has been confirmed; this means that the efforts are not being applied in the correct areas or in the correct ways. Finally, the 56% percent of the industry have a misperception about their own environmental performance. At least, only the 33% of them have a high perceived environmental performance and a low real one.

With this panorama, it is clear that the environmental impact of the packaging is in the second level of importance for the industry; there are many reasons that can explain this situation.

The first, and more important, is the legal framework that regulates the pharmaceutical industry. As has been explained in Chapters 1 and 3, the law tries to preserve the integrity and security of the pharmaceutical over other aspects requiring the use of determined materials, thickness and processes. The possibilities of reduction in the material use or the use of alternative and more environmental friendly materials is sometimes impossible due to the necessity of fulfill this legal requirements. Even when the package has been approved, companies try to reduce or delete certain parts of the package, but this process implies that the new version of the package need to be again approved by the authorities and need to fulfill those mentioned minimum requirements. Thus, the environmental impact is a secondary priority forced by the legal framework.

Other important aspect is the cost of the packaging. Companies need to spend hundreds of Euros – or Swedish crowns – to create safe packages using the less quantity of materials trying to create cheapest possible solutions. The package is seen as an extra cost, beside it is completely necessary. Make investment that allows the company to create packages less harmful with the environment and, at the same time, can pass the regulations, is sometimes seen as a waste of money and time. This efforts use to be seen as something more interesting if they are applied to R&D or to other business sections.

Fortunately, and finally, say that although is not an excuse, the pharmaceutical packaging does not represent one of the bigger wastes that modern and occidental society generates. For instance, the chemicals used to produce the pharmaceuticals, are much more hazardous for the environmental that any materials used in the package. To illustrate this topic, some easy calculations have been made and are showed below. Also, an equivalence chart is provided trying to convert the kg of CO_2 in something more visual and easy to understand.

Table 10. Equivalences between CO_2 emissions and daily activities emissions

Quantity of CO_2	Equivalence	
80 grams of CO_2	Making 1 cup of tea	
160 grams of CO_2	Making 2 cups of tea	
1.60 kg of CO_2	Making 16 cups of tea	
16 kg of CO_2	26 days watching TV	
160 kg of CO_2	Drive a small car 1240 km	
1600 kg of CO_2	You need to plant 2 trees	
16 tons of CO_2	Would fill 3 Olympic swimming pools	

Source: LCA Calculator

In base of this data, ingest any pharmaceutical in any presentation format implies a CO_2 emission due to the package less than make a cup of tea. Even to take a complete antibiotic treatment of 10 days (2 doses per day) presented in Alu-Alu blister represents less than the half emissions of preparing a cup of tea. But the figures change slightly when we think about the global consumption of pharmaceuticals. Just for giving an example, according to OECD Health data, in 2011, the consumption of antibiotics in Sweden was 15.8 daily doses (only one dose per day treatment) per 1000 people and per year. For a Swedish population around 9.4 million, this suppose a global year consumption of antibiotics around 148520 doses per year of antibiotics. Assuming that all this pharmaceuticals are presented in a standard blister, the global CO_2 emissions due to the antibiotics packaging in Sweden per year rises to 81 kg of CO_2. This is equivalent to drive a small car 620 km. In the case of Spain, the same calculation gives an emission around 500 kg of CO_2. This is a trip in a small car of 3875 km.

Finally, take now into account not only the antibiotics and add also the antidiabetics, antidepressants and anticholesterols. Assume the best of the possible scenarios: the presentation used is standard blister. For Sweden case, the emissions would be around 1985 kg of CO_2. In Spanish case, the figure rise to 9800 kg of CO_2 due to the pharmaceutical packaging of antidiabetics, antidepressants, anticholesterols and antibiotics. This is equivalent to fill 1.6 Olympic swimming pools. As the reader can see, the CO_2 emissions due to the pharmaceutical packaging are not very high if we compare it with other quotidian figures: the kg of CO_2 emitted during a flight between Stockholm and Madrid is around 190 kg CO_2 per seat (Jardine, C. 2009), more than the double of the emissions due to the antibiotics packaging in Sweden in a year. In case of Spanish antibiotics, their CO_2 emissions due to the packaging are less than three seats in that flight between Sweden and Spain.

6. Conclusion

6.1 Main findings

This section attempts to collect the main important findings that can be extracted from this thesis and also give response to the objectives established at the beginning of thereof.
The results obtained are going to be grouped attending to the source that has allowed the obtaining of them: scorecard, empirical data, comparisons, perceived environmental performance & real environmental performance and statistical analysis.

Scorecard

- Three most important aspects when designing the packaging are: Machinability – the aptitude of the packaging for being processed –, product information – leaflet and labelling indicating what product is inside the package – and safety – the protective capacity of the package trying to avoid interactions between the pharmaceutical and the external atmosphere. Environmental aspects are not, therefore, among the most important.
- All the companies, regardless of size or type of products manufactured, give equal importance to environmental issues: around 22% of their efforts.
- The perceived environmental performance that companies have, regardless of their size or the type of products they produce, is lower than the perceived performance for others like human, economical or manufacturing aspects – 1.2X lower.
- The perceived general performance is higher for big companies than for medium and small ones. Also, it is higher for non generics producers compared with generic producers and for producers of both types of medicaments.

Data collected empirically

- Aluminum bottles and inhalers have the better fill rate performance. Conventional blisters and bottles made of glass and plastic have the same fill rate efficiency. Sachets and blisters made using two layers of aluminum are the worst option attending to this criterion.
- It is not surprising that the most harmful presentations are aluminum blisters and sachets with a big difference: around a 4.8X more prejudicial than normal blisters. These presentations provide the better protection at the expense of use aluminum, which is environmentally harmful as has been explained before.

Overall Comparisons

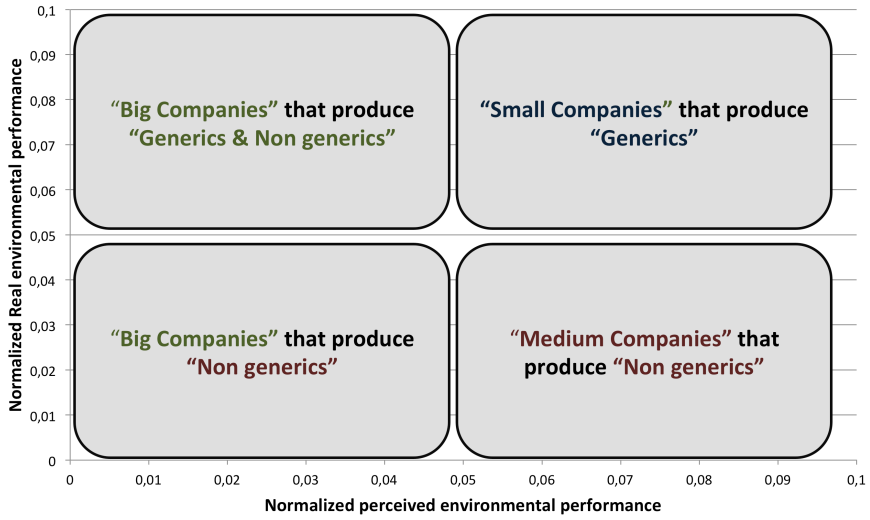
- When the importance of the environmental aspects is increased during the designing process of the packaging, the mg of CO_2 per dose of pharmaceuticals is reduced slightly: 37.5 mg CO_2 reduced – about a 4% per 1% more importance given to those environmental aspects.
- In general terms, the fill rate performance has no changes when this aspect is more taken into account during the design process. Even the fill rate performance decreases when companies increment their efforts to improve it, which is highly surprising and alerts about an anomalous behavior.

Perceived environmental performance and real environmental performance

- The 56% of the industry have a misconception about their environmental performance. From this 56%, the 33% of them have an over perception about their performance and the remaining 67% have a less perception.

- The remaining 44% have a good perception about their discharge having around the 42% of them a high real and perceived performance compared with the remaining 58% that have a low real and perceived performance.
- The characterization of the companies that appear in each area is shown below:

Figure 26. Characterization of each area



Statistical analysis

- The statistical analysis of the data provides the capacity to ensure, with different confidence levels, the tendencies observed previously on the data. Below are some of the main conclusions extracted and their respective confidence levels.
  - With a 90% confidence level, small companies are less pollutant than medium and big ones.
  - With a 95% confidence level, generic producers have a lower fill rate performance.
  - Considering together the fill rate criteria and the CO_2 emissions – global environmental performance – due to the packaging, it's possible to say:
    - With a 95% confidence level, small companies obtain a better real environmental performance**.**
    - With a 90% confidence level is possible to affirm that generic producers have a worst environmental performance.

6.2 Theoretical implications

The difference between the reality and companies' self-perception is worrying on the 56% of the cases. Fortunately, all those companies that have a misperception in a negative way: this means that they think they are doing things worst that what they are really doing which is the best of the possible alternative because the opposite case –perceive that you are doing better than what the reality reflects– eliminates the necessity of improvement.

In the other 44% of the cases, companies have a correct perception about their own performance. Despite the efforts to reduce the packaging impact are not very high, at least, the industry in general terms is aware of this situation, which makes the panorama less worrisome.

This result reflects the importance of having a holistic view when designing the pharmaceutical packaging (Wever, 2009). Also, it reflects how trade-offs in packaging decisions can affect the

environmental impact of packaging and how, because of the need to prioritize, the environmental aspects are relegated to a second layer (Kamarthi *et al.* 2003).
Note also how useful is the packaging scorecard. From author´s point of view, if the criteria are well selected, this tool, despite its limitations, provides excellent information about companies' internal point of view and the results are pretty well adjusted to the real situation. The differences between the packaging scorecard results and the measured fill rates might be related to bad perception of the reality. This reflects that the scorecard might need clear guidelines for filling it out or need to be complemented with other measures.

6.3 Practical implications

Pharmaceutical industry needs to introduce or to improve its environmental monitoring systems related with the packaging. Almost a third of companies have an incorrect view of the situation, which reflects that the mechanisms established are not working correctly. Probably, an improvement on existing systems or introducing new methods more suitable to the needs of each company can reverse this situation. In few words, some companies need more training in this area.
Also, this thesis reflects the low importance that pharmaceutical packaging designers are putting trying to reduce the environmental impact. The main reason, in author's opinions, is that industry works according to the regulations satisfying the requirements and looking for cheap packages; the result in environmental words is just a secondary result. Thus, if the authorities are looking for less pollutant packages, will be necessary to change the national laws that are applicable for the pharma-packaging. Also, the future seems little promising for the environment: new tendencies and technologies are making possible to introduce, with reasonable prices, intelligent packages that will help the patients to follow their prescription programs but, on the other hand, this packages include higher wastes and are more difficult to recycle due to the materials they include.

6.4 Possible Future Research

Some ideas about possible continuations or additions to this project are going to be suggested, based most of them on the possibilities that the scorecard provides.

As the reader can notice, the scorecard provide the company's subjective point of view about different areas and criteria: environmental, human, economical and productive aspects. But only the information related with the environmental aspects has been used during this project. Thus, a lot of possible research can be done using the other three types of data. Below, some examples and possible comparison, like the one made in this project, are suggested:

- Compare the efforts that the company made to create packages easier to use and what the customer or patient perceive. Using a survey is possible to determine the customer satisfaction attending to different criteria: compliance, openability, child-resistance…
- Compare the efforts to create packages that protect properly the pharmaceutical with the real protection provided. This last one can be measured with detector that determines how much time the package protects against the moisture, for instance, in a determined atmosphere. Other more sophisticated indicators can be used to analyze this performance.
- Compare the level of sales with the investment dedicated to marketing.
- Compare the level of discarded packages with the investment in quality systems.
- Try to find out if the best-in-class companies and those with a correct and high perception about themselves have specific tools for monitoring their environmental performance.

- Explore the regulatory differences that affect to the pharma-packaging basing on different countries.

The possibilities are enormous and from here, the author encourages anyone who wants to continue with this interesting work.

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Appendixes

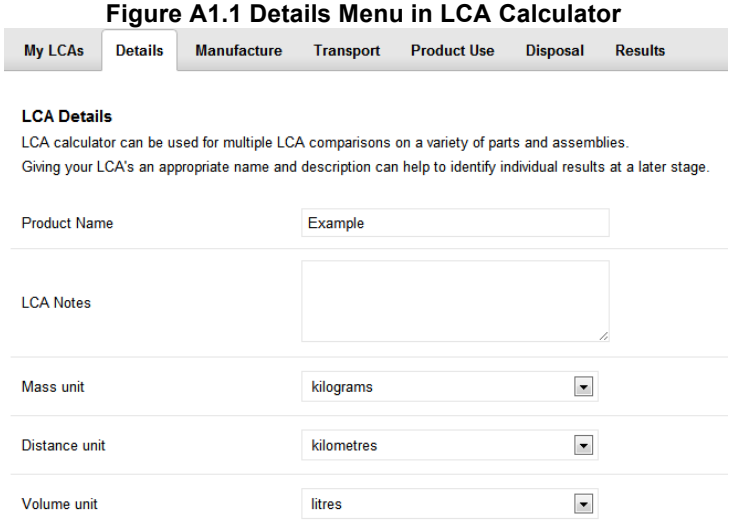
Appendix 1 – LCA Calculator

This appendix explains the most important possibilities that LCA Calculator offers. Remind that the software is available online with just creating a free account at www.lcacalculator.com.

Details

In this first flange is necessary to give a name to the file, select the mass unit , distance unit and volume unit.

Figure A1.1 Details Menu in LCA Calculator

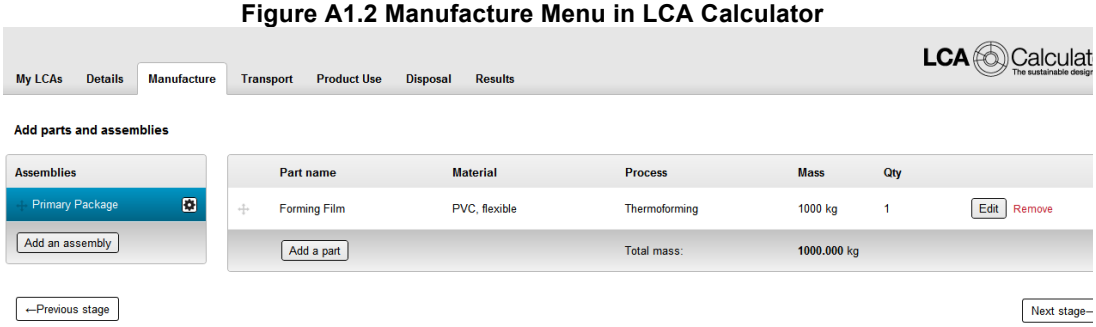


Source: LCA Calculator Software

Manufacture

In manufacture section is necessary to create different assemblies. In this case, two have been created: one for the primary package – blister, sachet, inhaler or bottle – and other for the secondary package which is commonly a cardboard box together with the leaflet. It is also necessary to determine the manufacturing region – Africa, Asia, Europe, North America and so on. Inside each assembly, parts must be created. For each part, is necessary to select the material, the manufacturing process, the mass and the number of units. An example for a blister is shown below.

Figure A1.2 Manufacture Menu in LCA Calculator

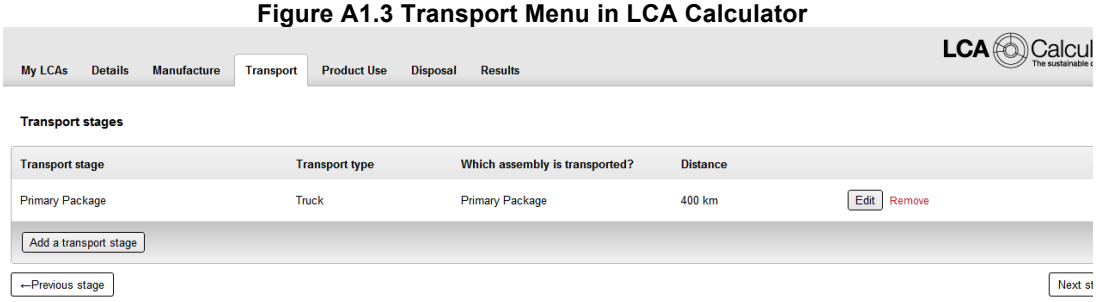


Source: LCA Calculator Software

Transport

In transport section, is necessary to select which part is transported, what transport type is used and what distance it is transported.

Figure A1.3 Transport Menu in LCA Calculator

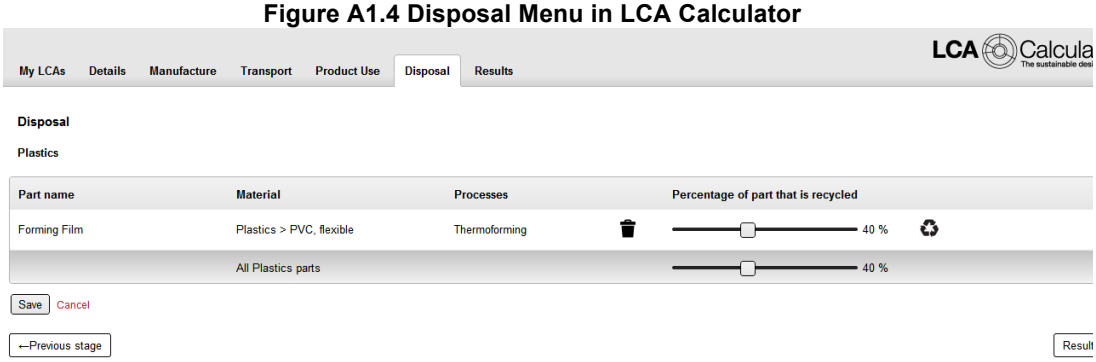


Source: LCA Calculator Software

Disposal

In this section, is necessary to determine what percentage of the each part is recycled.

Figure A1.4 Disposal Menu in LCA Calculator



Source: LCA Calculator Software

Results

Finally, LCA Calculator provides us an overview with the result than can be downloaded in PDF format.

Figure A1.5 Example of the results provided by LCA Calculator

Appendix 2 – Questionnaire

Following is included an exact copy of the questionnaire that has been sent to the companies or used as pattern in order to do the interviews telephonically.

QUESTIONNAIRE

Information about the respondent:

Name: Email:

Company:

Department:

Experience:

→ 1. DESIGNING PROCESS

This section tries to map what aspects are more important, from the packaging designer point of view, when creating a new pharmaceutical packaging. Please, evaluate the importance of each aspect between 0 % (low weight) and 100% (high weight) for each type of product: Over-the-counter or prescription pharmaceuticals. An appendix with support information is at the end of this document.

› **Over-the-counter products (if the company produces)**

Note: Please, don´t give the same weight to all the aspects. Think, from your point of view, what is more importance from a pharmaceutical packaging perspective.

Criteria	Weight (0 – 100)	Comments
– **Machinability**	Choose an element	
– **Product protection**	Choose an element	
– **Flow Information – barcodes…**	Choose an element	
– **Fill-rate**	Choose an element	
– **Other Value adding properties**	Choose an element	
› **Openability**	Choose an element	
› **Compliance / Patient adherence**	Choose an element	
– **Product information: Labelling, composition, leaflet…**	Choose an element	
– **Selling capability: Marketing…**	Choose an element	
– **Safety**	Choose an element	
– **Reduced use of resources**	Choose an element	
– **Minimized use of hazardous substances**	Choose an element	
– **Packaging costs**	Choose an element	

› **Prescription medicament/drug (if the company produces)**

Note: Please, don´t give the same weight to all the aspects. Think, from your point of view, what is more importance from a pharmaceutical packaging perspective. Use the comments column if it is necessary.

Criteria	Weight (0 – 100)	Comments
– **Machinability**	Choose an element	
– **Product protection**	Choose an element	
– **Flow Information – barcodes…**	Choose an element	
– **Fill-rate**	Choose an element	
– **Other Value adding properties**	Choose an element	

› **Openability**	Choose an element
› **Compliance / Patient adherence**	Choose an element
– **Product information: Labelling, composition, leaflet…**	Choose an element
– **Selling capability: Marketing…**	Choose an element
– **Safety**	Choose an element
– **Reduced use of resources**	Choose an element
– **Minimized use of hazardous substances**	Choose an element
– **Packaging costs**	Choose an element

→2. EVALUATION SECTION

The objective of this section is to evaluate the packaging performance of each criterion from the company point of view. In order to do that, the respondent will have to give a score between 0 and 4 to each aspect. Please, evaluate this criterion for these four types of packaging: blisters, bottles, inhalers and sachets.

Type of packaging	Criteria	Score
Blisters	– Machinability	Choose an element
	– Product protection	Choose an element
	– Flow Information – barcodes…	Choose an element
	– Fill-rate	Choose an element
	– Other Value adding properties	
	› Openability	Choose an element
	› Compliance / Patient adherence	Choose an element
	– Product information: Labelling, composition, leaflet…	Choose an element
	– Selling capability: Marketing…	Choose an element
	– Safety	Choose an element
	– Reduced use of resources	Choose an element
	– Minimized use of hazardous substances	Choose an element
	– Packaging costs	Choose an element
Bottles	– Machinability	Choose an element
	– Product protection	Choose an element
	– Flow Information – barcodes…	Choose an element
	– Fill-rate	Choose an element
	– Other Value adding properties	
	› Openability	Choose an element
	› Compliance / Patient adherence	Choose an element
	– Product information: Labelling, composition, leaflet…	Choose an element
	– Selling capability: Marketing…	Choose an element
	– Safety	Choose an element
	– Reduced use of resources	Choose an element
	– Minimized use of hazardous substances	Choose an element
	– Packaging costs	Choose an element
Sachets	– Machinability	Choose an element
	– Product protection	Choose an element
	– Flow Information – barcodes…	Choose an element
	– Fill-rate	Choose an element

	– Other Value adding properties	
	› Openability	Choose an element
	› Compliance / Patient adherence	Choose an element
	– Product information: Labelling, composition, leaflet…	Choose an element
	– Selling capability: Marketing…	Choose an element
	– Safety	Choose an element
	– Reduced use of resources	Choose an element
	– Minimized use of hazardous substances	Choose an element
	– Packaging costs	Choose an element
Inhalers	– Machinability	Choose an element
	– Product protection	Choose an element
	– Flow Information – barcodes…	Choose an element
	– Fill-rate	Choose an element
	– Other Value adding properties	
	› Openability	Choose an element
	› Compliance / Patient adherence	Choose an element
	– Product information: Labelling, composition, leaflet…	Choose an element
	– Selling capability: Marketing…	Choose an element
	– Safety	Choose an element
	– Reduced use of resources	Choose an element
	– Minimized use of hazardous substances	Choose an element
	– Packaging costs	Choose an element

→ 3. MANUFACTURE & TRANSPORT IMPACT

This section tries to evaluate the environmental impact of the pharmaceutical packaging distinguishing between different types of packaging: blisters, bottles, sachets and inhalers.

› 3.1 BLISTERS

Most representative product in the company with this presentation from your point of view:

Note: If you don't want to provide one, indicate briefly how the primary packaging of the product is.

Most representative size of this product (20 pills, 30 pills….):

Answer the following question in basis of the product indicated above.

– Primary Packaging (in contact with the product)
  - ***Forming film***

Material used: Elija un elemento. Comments if it is necessary:

This packaging element is produced in *country* and it is transported to *countries.*

Example: It is produced in Poland & Romania and transported to (Portugal, Spain, Italy) and (Sweden, Norway) respectively

This packaging element is transported using Elija un elemento. (select the most representative)

  - ***Lidding Material***

Material used: Elija un elemento. Comments if it is necessary:

This packaging element is produced in *country* and it is transported to *countries.*

This packaging element is transported using Elija un elemento. (select the most representative)

- Secondary Packaging (if it exists) – carton box for instance

Material used: Elija un elemento. Comments if it is necessary:

This packaging element is produced in *country* and it is transported to *countries.*

This packaging element is transported using Elija un elemento. (select the most representative)

Leaflet material

- Tertiary Packaging (if it exists) – shipping box

Material used: Elija un elemento. Comments if it is necessary:

This packaging element is produced in *country* and it is transported to *countries*

This packaging element is transported using Elija un elemento. (select the most representative)

Number of Secondary packages in each Tertiary package:

For instance: 10 carton boxes inside 1 shipping box

- Load unit (if it exists) – pallet

Type of pallet Elija un elemento. Comments if it is necessary:

Material used: Elija un elemento. Comments if it is necessary:

This packaging element is produced in *country* and it is transported to *countries*

This packaging element is transported using Elija un elemento. (select the most representative)

Protective layer: Elija un elemento. Comments if it is necessary:

Number of Tertiary packages in each Load Unit:

For instance: 64 shipping boxes over 1 pallet.

3.2 BOTTLES

Most representative product in the company with this presentation from your point of view:
Note: If you don't want to provide one, indicate briefly how the primary packaging of the product is.

Most representative size of this product (50ml, 150 ml….):

Answer the following question in basis of the product indicated above.

- Primary packaging (in contact with the product)
  - ***Bottle***

Material used: Elija un elemento. Comments if it is necessary:

This packaging element is produced in *country* and it is transported to *countries.*

This packaging element is transported using Elija un elemento. (select the most representative)

- ***Desiccant***

If desiccant is used, indicate type: .

- Secondary Packaging (if it exists) – carton box for instance

Material used: Elija un elemento.

This packaging element is produced in *country* and it is transported to *countries.*

This packaging element is transported using Elija un elemento. (select the most representative)

Leaflet material

- Secondary Packaging (if it exists) – carton box for instance

Material used: Elija un elemento. Comments if it is necessary:

This packaging element is produced in *country* and it is transported to *countries.*

This packaging element is transported using Elija un elemento. (select the most representative)

Leaflet material

- Tertiary Packaging (if it exists) – shipping box

Material used: Elija un elemento. Comments if it is necessary:

This packaging element is produced in *country* and it is transported to *countries*

This packaging element is transported using Elija un elemento. (select the most representative)

Number of Secondary packages in each Tertiary package:

For instance: 10 carton boxes inside 1 shipping box

- Load unit (if it exists) – pallet

Type of pallet Elija un elemento. Comments if it is necessary:

Material used: Elija un elemento. Comments if it is necessary:

This packaging element is produced in *country* and it is transported to *countries*

This packaging element is transported using Elija un elemento. (select the most representative)

Protective layer: Elija un elemento. Comments if it is necessary:

Number of Tertiary packages in each Load Unit:

For instance: 64 shipping boxes over 1 pallet.

3.3 INHALERS

Most representative product in the company with this presentation from your point of view:
Note: If you don't want to provide one, indicate briefly how the primary packaging of the product is.

Most representative size of this product (50ml, 150 ml….):

Answer the following question in basis of the product indicated above.

- Primary packaging (in contact with the product)
  - *Bottle*

Material used: Elija un elemento. Comments if it is necessary:

This packaging element is produced in *country* and it is transported to *countries.*

This packaging element is transported using Elija un elemento. (select the most representative)

  - *Propellant*

If propellant is used, indicate type:. Elija un elemento.

- Secondary Packaging (if it exists) – carton box for instance

Material used: Elija un elemento. Comments if it is necessary:

This packaging element is produced in *country* and it is transported to *countries.*

This packaging element is transported using Elija un elemento. (select the most representative)

Leaflet material

- Tertiary Packaging (if it exists) – shipping box

Material used: Elija un elemento. Comments if it is necessary:

This packaging element is produced in *country* and it is transported to *countries*

This packaging element is transported using Elija un elemento. (select the most representative)

Number of Secondary packages in each Tertiary package:

For instance: 10 carton boxes inside 1 shipping box

- Load unit (if it exists) – pallet

Type of pallet Elija un elemento. Comments if it is necessary:

Material used: Elija un elemento. Comments if it is necessary:

This packaging element is produced in *country* and it is transported to *countries*

This packaging element is transported using Elija un elemento. (Select the most representative)

Protective layer: Elija un elemento. Comments if it is necessary:

Number of Tertiary packages in each Load Unit:

For instance: 64 shipping boxes over 1 pallet.

› 3.4 SACHETS

Most representative product in the company with this presentation from your point of view:
Note: If you don't want to provide one, indicate briefly how the primary packaging of the product is.

Most representative size of this product (10 sachets, 20 sachets….):

Answer the following question in basis of the product indicated above.

- Primary packaging (in contact with the product)
  - *Sachet*

Composition of the sachet:

Example: 4 layers: Paper, Polyethylene, aluminum foil, Polyethylene

This packaging element is produced in *country* and it is transported to *countries.*

This packaging element is transported using Elija un elemento. (select the most representative)

- Secondary Packaging (if it exists) – carton box for instance

Material used: Elija un elemento. Comments if it is necessary:

This packaging element is produced in *country* and it is transported to *countries.*

This packaging element is transported using Elija un elemento. (select the most representative)

Leaflet material

- Tertiary Packaging (if it exists) – shipping box

Material used: Elija un elemento. Comments if it is necessary:

This packaging element is produced in *country* and it is transported to *countries*

This packaging element is transported using Elija un elemento. (select the most representative)

Number of Secondary packages in each Tertiary package:

For instance: 10 carton boxes inside 1 shipping box

- Load unit (if it exists) – pallet

Type of pallet Elija un elemento. Comments if it is necessary:

Material used: Elija un elemento. Comments if it is necessary:

This packaging element is produced in *country* and it is transported to *countries*

This packaging element is transported using Elija un elemento. (select the most representative)

Protective layer: Elija un elemento. Comments if it is necessary:

Number of Tertiary packages in each Load Unit:

For instance: 64 shipping boxes over 1 pallet.

→ 4. FINAL QUESTIONS

Some open questions are collected in this section. The objective is to have a better understanding of the procedures in the company. Please, feel free to answer whatever you consider appropriated.

- How significant can be the impact due to changing some aspects of the packaging (for instance, the number of pills per blister)?

- What drive the company to change the packaging?

- What initiatives have the company nowadays in order to create environmentally friendly packages?

- What is the theoretical yield (number of packages finished correctly) of a blister/bottle/sachet/inhaler packaging line?

  Blister line: Bottle line: Sachets line:

  Inhaler line:

→5. APPENDIX - SUPPORT INFORMATION

5.1 Designing process information

Machinability: refers to the ability of packaging material to be processed effectively in the production line. This category focused on the filling operation.

Product protection: refers to the qualities of the package, its ability to protect the product in different environments from mechanical stress and to preserve its contents. Protection also means to prevent the product from reacting with the external environment.

Flow Information: refers to the capability of the packaging give right information in the supply chain. For example, tracking information (identification, instructions, and destinations) as well as logistics-related information about the product (warnings, declaration of contents, barcode or RFID).

Fill-rate: Try to minimize the use of packaging for the same quantity of product. For instance: minimize the separation between pills in a blister or minimize the size of the box where sachets are contained. Try to transport much as possible products in each pallet.

Other Value adding properties: refers to other functions than the basic requirements on the package

> *Openability:* ease of opening the packaging. Important among older patients and patients who need to consume large amount of drugs each day.
>
> *Compliance / Patient adherence:* Create methods or tools that help the patient to follow his medication program. For instance: Labels with the day of the week that can be adhered to a blister in order to remain if the patient has taken the medication that day or not.

Product information: Labelling, composition, leaflet…: mainly to inform and promote the product. Information is mainly for consumer to select the right product, instruction about how to handle, nutrition chart and other information about warnings, recipes and declaration of contents. The aim is to identify and sell the product

Selling capability: Marketing…: Creative design of the packaging, printings and so on. Elements that help to sell the product.

Safety: Elements (for instance, hard materials or difficult-to-open closures) that avoid the consume of the products by children without the supervision of an adult.

Reduced use of resources: Design the packaging in order to use the minimum quantity of material.

Minimized use of hazardous substances: If it is necessary to use hazardous substances or materials, the effort in reducing the quantity. For instance, the use of CFCs in inhalers.

Packaging costs: How important is to create a packaging with low manufacturing costs.

Appendix 3 – Additional information for the Analysis

This appendix tries to collect useful information for a better understanding of the analysis. It includes numerous figures in order to make *Chapter 3 – Analysis* easier to read.

Attending to company size

Perception

Figure A3.1 Weights attending to company size

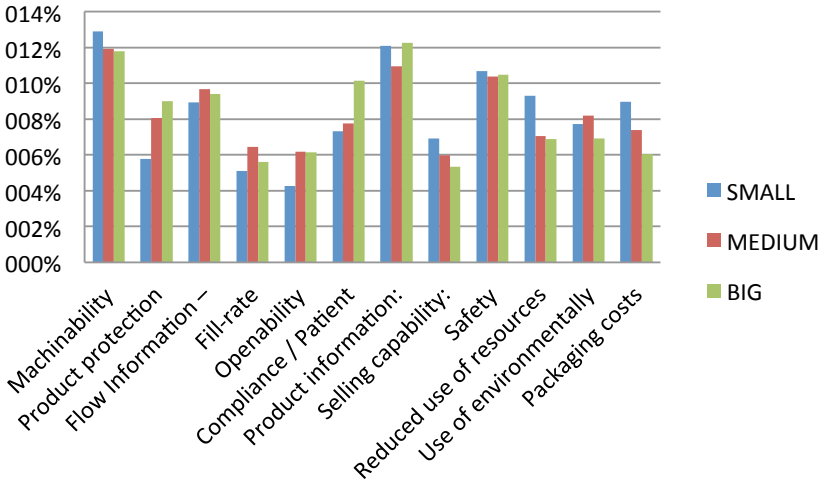


Figure A3.2 Score acording to Company Size

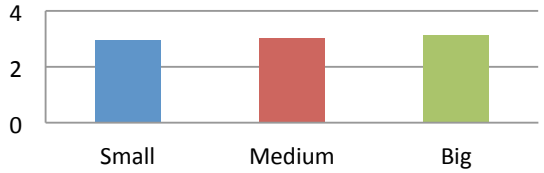


Figure A3.3 Scores for each criteria attending to Company Size

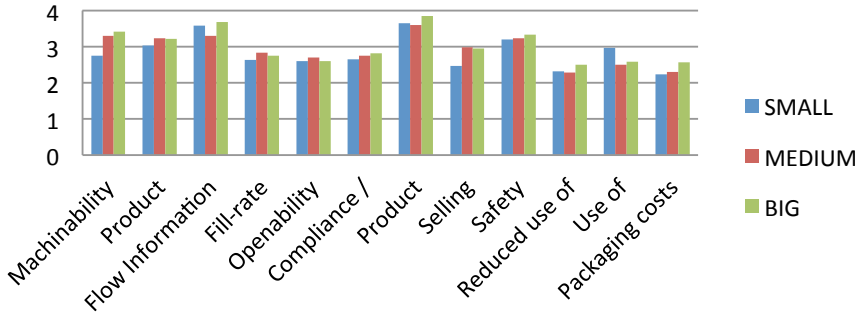


Figure A3.3 compares each criterion evaluation for each company size. It is interesting to see that companies, regardless of size, are really satisfied about their performance when talking about manufacturing aspects. This is due to the systems involved in this activities are really well-known, are really standardized and are really adjusted in order to get the better production

rate. Also, is striking the evaluation of the human aspects by small companies: they know that they are not doing the best in order to do the life easier to their customers and patients.
The self perception of big and medium companies about their performance is almost the same but when talking about small companies, three points are remarkable: they have a low self evaluation about the machinability process and about their selling capability. Probability, this is due to they do not have the same production rate and the chain is not as tight as in the case of larger companies. Their marketing performance is also lower probability because of for them is more difficult to achieve a satisfactory market share in a very competitive market as pharmaceutical is. Finally, they have a higher perception about the low environmental impact of the materials they are using. When comparing the self-performance evaluation attending to other criteria like the type of presentation, it is easy to see that are slight differences – around a 10%. Bottles use to have more problems during the mechanization and filling operation. Due to this aspect, mainly, the global score is lower (*figure A3.4*).

Figure A3.4 Comparison according to the presentation

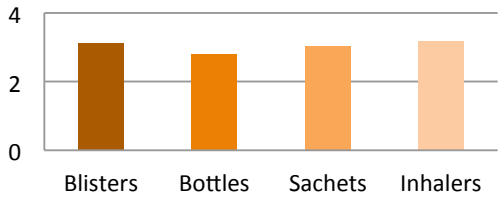
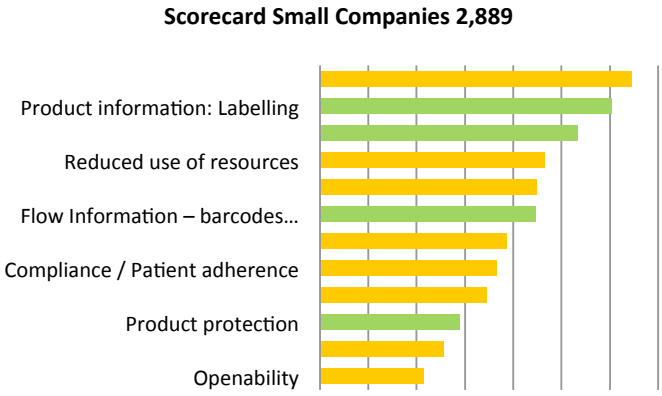
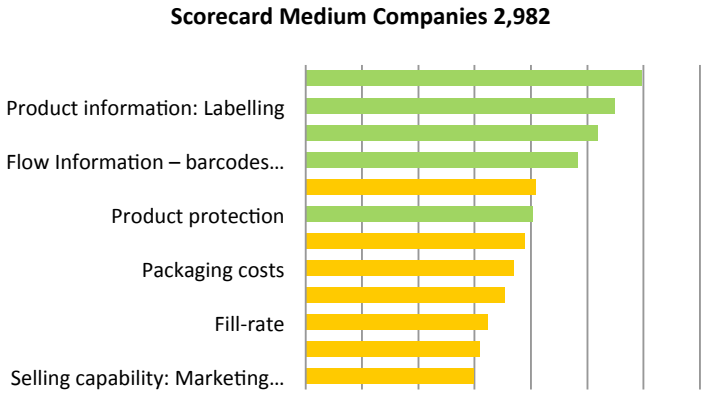
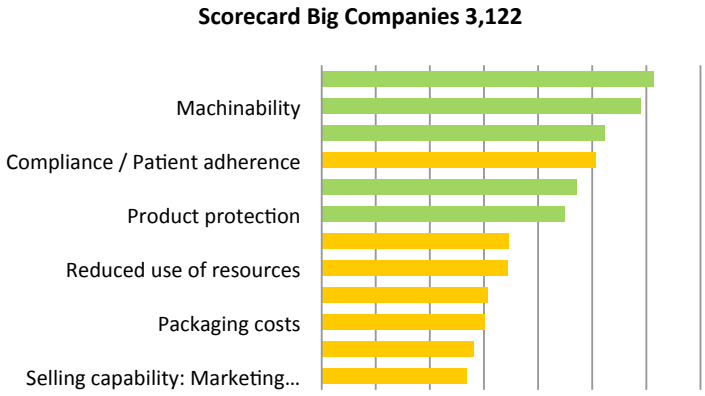


Figure A3.5 Scorecard information comparison attending to company size
Color legend: Scores [0 – 1] / [1.01 – 2] / [2.01 – 3] / [3.01 – 4]

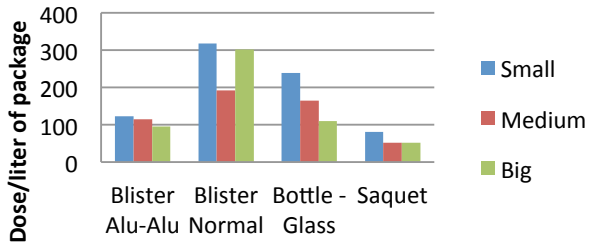






Real performance

Figure A3.6 Dose/liter of primary package attending to company size and presentation



Attending to the type of products that the company produces

Perception

Figure A3.7 Weights attending to the type of products the company produces

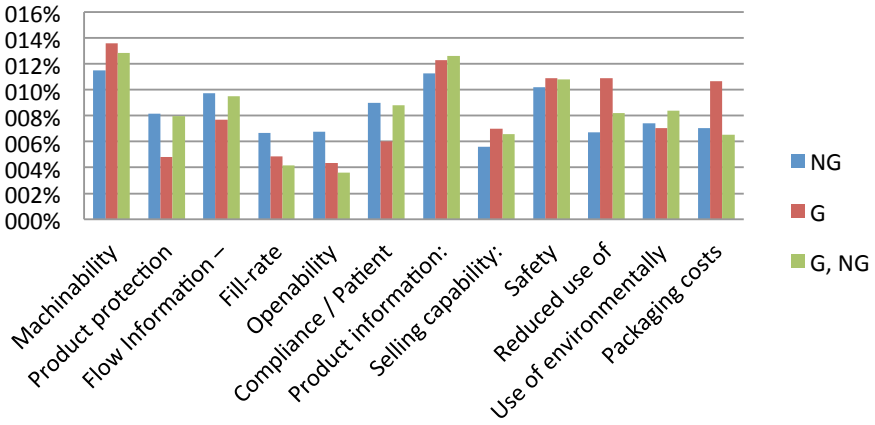


Figure A3.8 Score acording to the type of products that the company produces

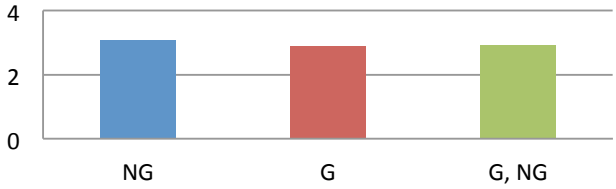


Figure A3.9 Scores for each criteria attending to the type of products that the company produces

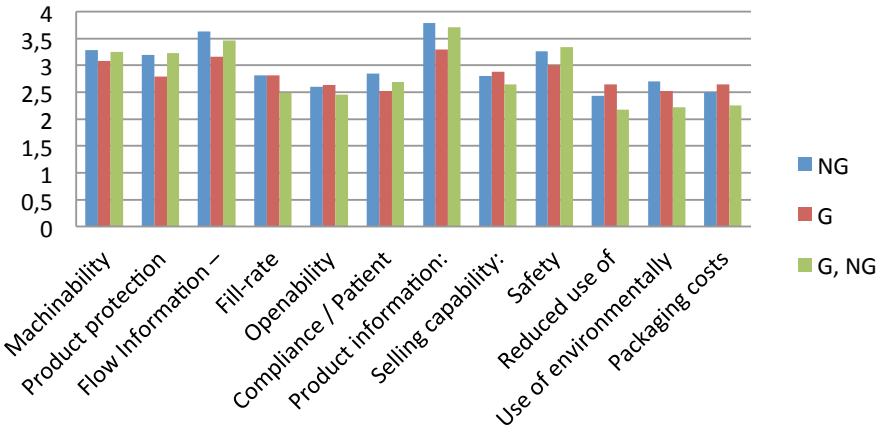
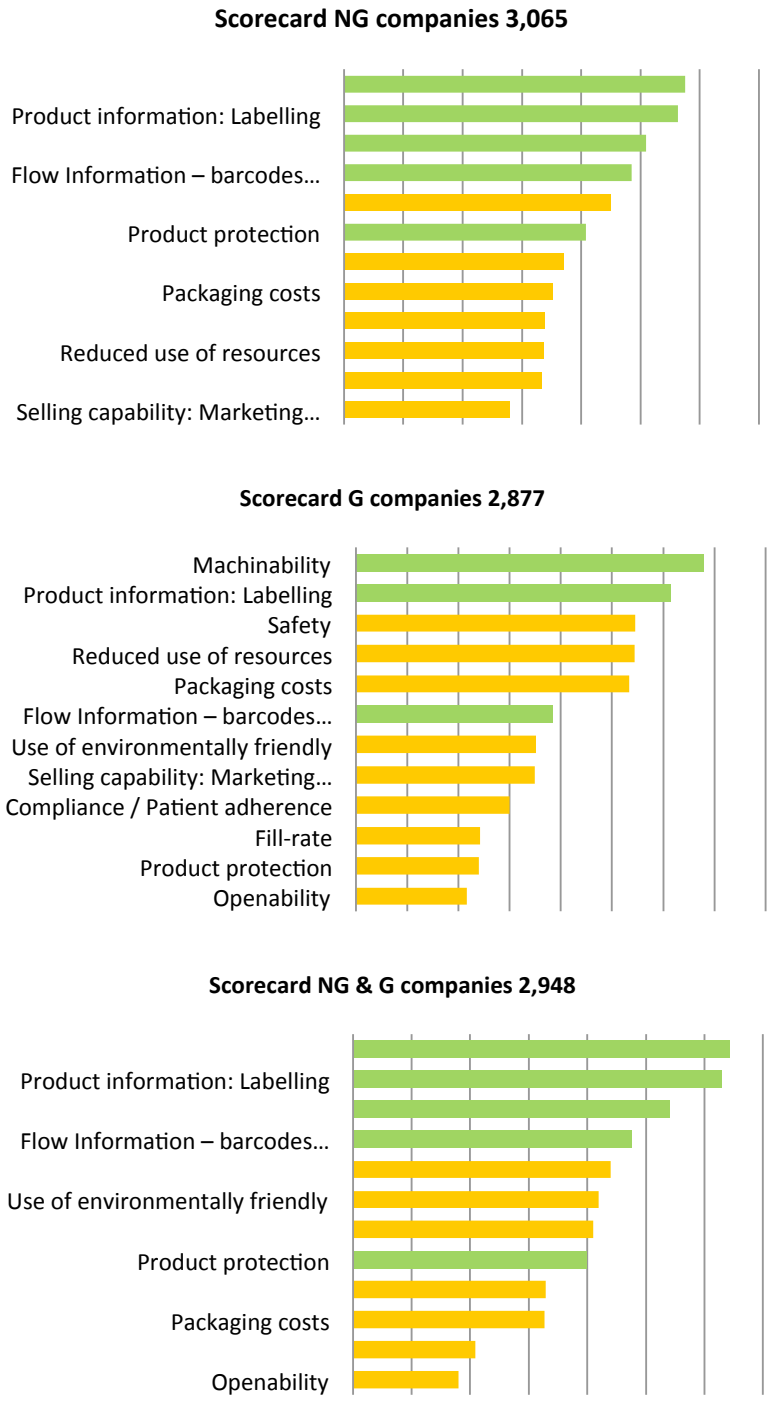


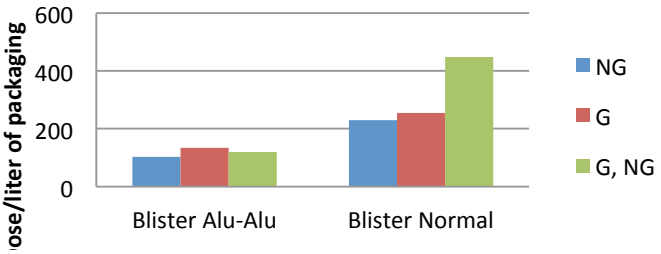
Figure A3.10 Scorecard information comparison attending to the type of products that the company produces

Color legend: Scores [0 – 1] / [1.01 – 2] / [2.01 – 3] / [3.01 – 4]



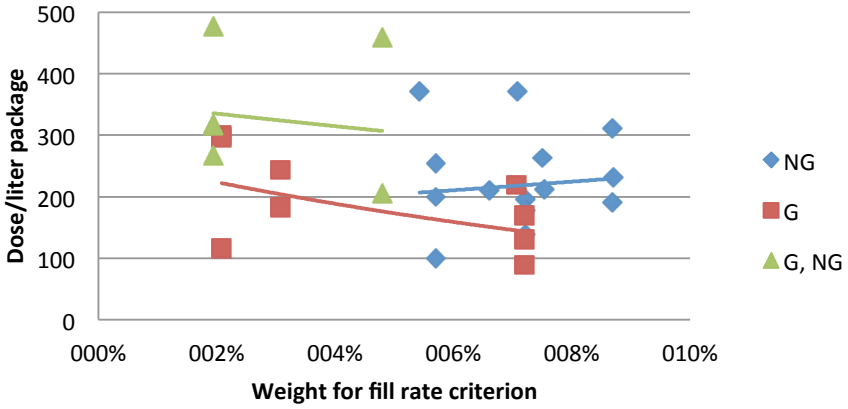
Real performance

Figure A3.11 Dose/liter of primary package attending to the type of products that the company produces and presentation



Comparison

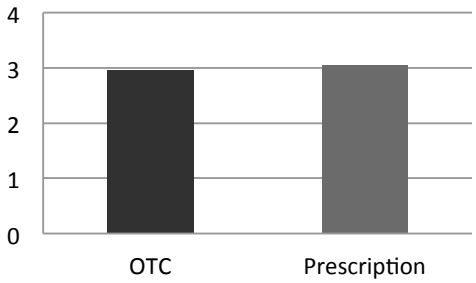
Figure A3.12. Contrast attending the type of products that the company produces for normal blisters



Additional interesting results

Extracted from the Scorecard

Figure A3.13 Comparison according to the type of product



Appendix 4 – Statistical Analysis

The statistical analysis has been divided in three parts: Descriptive analysis of the data, construction of the model, and contrasts. In order to not create a very big appendix, only the contrasts are included below. By the way, the assumptions of normality, homoscedasticity and independence ware checked all studied cases.

Company size, type of products, importance of the environmental aspects and CO_2 emissions study

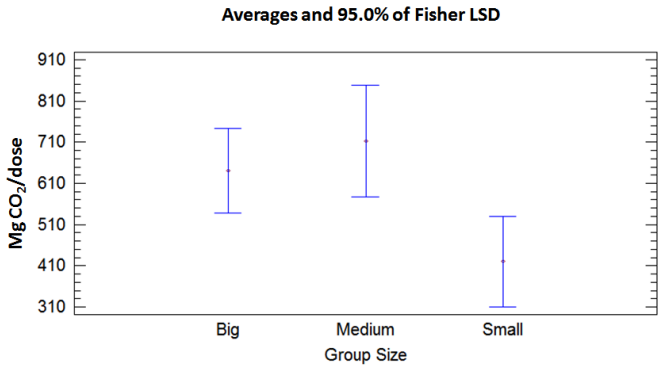
Contrasts

In this section, ANOVA contrasts are going to be explained.

Analysis of Variance for mg of CO_2/dose of pharmaceutical					
Source	**Sum of squares**	**Df**	**Mean Square**	**Reason-F**	**P-value**
Principal Effects					
A:Group Size	288569,	2	144284,	3,58	0,0431
B:Group Type	215348,	2	107674,	2,67	0,0891
C:Weight	142062,	3	47353,8	1,17	0,3397
RESIDUES	1,00893E6	25	40357,2		
TOTAL (FIXED)	1,57489E6	32			

Since the P-value for Group size factor is lower than 0.05, this factor has statistically significant effect on mg ofCO_2/dose with a 95% confidence level. The other criteria – the type of products that the company produces or the weight they give to the environmental aspects– have no significant effect on the emissions. Note that there is no interaction between the factors in this model: no interaction between group size, group type and weights. Let´s confirm these results with the *multiple contrast range* and with the *graphic of averages.*

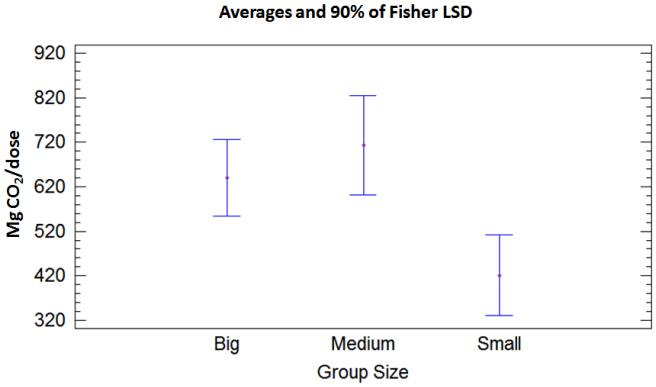
Multiple Range Test for mg CO_2/dose by Group Size Method: 95,0 percentage LSD				
Group Size	***Cases***	***Average LS***	***Sigma LS***	***Homogeneous groups***
Small	10	420,941	75,3638	X
Big	17	640,723	70,9978	XX
Medium	6	712,993	92,8227	X
Contrast	***Sig.***	***Difference***	***+/- Limits***	
Big - Medium		-72,2692	255,604	
Big - Small		219,782	235,912	
Medium - Small	*	292,051	240,518	
* indicates a significant difference.				



If we go a step further and reduce the confidence level to a 90%, there are differences between large and medium companies over small ones, which would be the least polluting.

Multiple Range Test for mg CO_2/dose by Group Size Method: 95,0 percentage LSD				
Group Size	*Cases*	*Average LS*	*Sigma LS*	*Homogeneous groups*
Small	10	420,941	75,3638	X
Big	17	640,723	70,9978	X
Medium	6	712,993	92,8227	X
Contrast	*Sig.*	*Difference*	*+/- Limits*	
Big - Medium		-72,2692	211,993	
Big - Small	*	219,782	195,661	
Medium - Small	*	292,051	199,481	

* indicates a significant difference.



Company size, type of products, importance of fill rate aspect and fill rate performance study

Contrasts

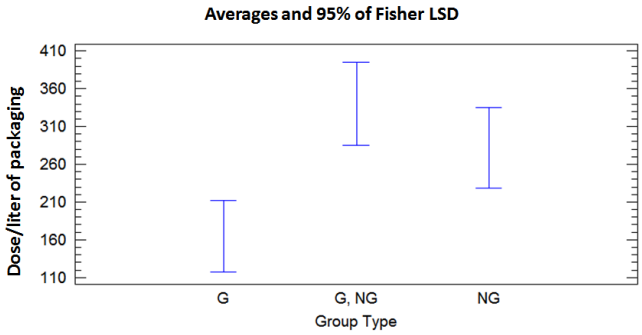
ANOVA contrasts are going to be explained below.

Analysis of Variance for mg of dose/liter of packaging					
Source	**Sum of squares**	**Df**	**Mean Square**	**Reason-F**	**P-value**
Principal Effects					
A:Group Size	27492,4	2	13746,2	2,02	0,1561
B:Group Type	78334,7	2	39167,4	5,74	**0,0095**
C:Weight for Fill rate	13601,4	2	6800,68	1,00	0,3843
RESIDUES	156849,	23	6819,51		
TOTAL (FIXED)	280301,	29			

Since the P-value for Group Type is lower than 0.05, this factor has statistically significant effect on dose/liter of packaging with a 95% confidence level. The other criteria – the size of the company and the weight they give to the fill rates– have no significant effect on the fill rate performance. Note that there is no interaction between the factors in this model: no interaction between group size, group type and weight for the fill rate. Let´s confirm these results with the *multiple contrast range* and with the *graphic of averages.*

Multiple Range Test for dose/liter of packaging Method: 95,0 percentage LSD				
Group Size	*Cases*	*Average LS*	*Sigma LS*	*Homogeneous groups*
G	9	164,904	32,2708	X
NG	15	282,162	36,4688	X
G, NG	6	339,995	37,6103	X
Contrast	*Sig.*	*Difference*	*+/- Limits*	
G - G, NG	*	-175,092	108,603	
G - NG	*	-117,259	108,519	
G, NG - NG		57,8329	106,896	

* indicates a significant difference.



Company size, type of products, subjective performance factor and environmental impact study

In this section, the same study is going to be done introducing the subjective performance factor. The method will be the same and some of the previous calculations will be useful for this case.

Contrasts

In this section, the contrasts made using ANOVA table are explained.

Analysis of Variance for mg of CO_2/dose of pharmaceutical					
Source	**Sum of squares**	**Df**	**Mean Square**	**Reason-F**	**P-value**
Principal Effects					
A:Group Size	7797,81	2	3898,91	0,54	0,5920
B:Group Type	79048,4	2	39524,2	5,44	**0,0120**
C: SPF	10710,2	3	3570,05	0,49	0,6917
RESIDUES	159740,	22	7260,91		
TOTAL (FIXED)	280301,	29			

Since the P-value for Group type factor is lower than 0.05, this factor has statistically significant effect on fill rate performance with a 95% confidence level. The other criteria – the size of the company and the SPF for the fill rate criterion– have no significant effect on the fill rate performance. Note that there is no interaction between the factors in this model: no interaction between group size, group type and SPF. These results are the same as the obtained in a previous section. With this study we can conclude that there is no correlation between the SPF factor that the company obtains for fill rate criterion and the real performance about fill rate.

Company size, type of products, global perceived environmental performance and real environmental performance

Contrasts

In this section, ANOVA contrasts are going to be explained.

Analysis of Variance for Real Environmental Performance					
Source	**Sum of squares**	**Df**	**Mean Square**	**Reason-F**	**P-value**
Principal Effects					
A:SPF Global	0,0000894419	2	0,0000447209	0,20	0,8208
B:Size	0,00213604	2	0,00106802	4,76	**0,0187**
C:Type	0,00169762	2	0,000848811	3,78	**0,0380**
RESIDUES	0,00516327	23	0,00022449		
TOTAL (FIXED)	0,0094472	29			

Since the P-value for Group size factor is lower than 0.05, this factor has statistically significant effect on Real environmental performance a 95% confidence level. The type of products that the company produces also has influence on the real environmental performance with a 95%

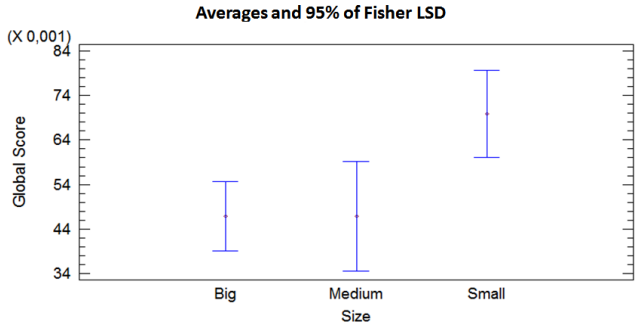
confidence level. Note that there is no interaction between the factors in this model: no interaction between group size, group type and weights. Let´s confirm these results with the *multiple contrast range* and with the *graphic of averages.*

Multiple Range Test for Real Environmental Performance
Method: 95,0 percentage LSD

Group Size	*Cases*	*Average LS*	*Sigma LS*	*Homogeneous groups*
Medium	6	0,0468331	0,0084016	X
Big	15	0,0468814	0,0053135	X
Small	9	0,0698668	0,0066543	X

Contrast	*Sig.*	*Difference*	*+/- Limits*
Big - Medium		0,00004827	0,0225547
Big - Small	*	-0,0229854	0,02009
Medium - Small	*	-0,0230337	0,0182246

* indicates a significant difference.



Multiple Range Test for Real Environmental Performance
Method: 90,0 percentage LSD

Group Size	*Cases*	*Average LS*	*Sigma LS*	*Homogeneous groups*
G	9	0,0391156	0,006149	X
NG	15	0,0565811	0,005004	X
G, NG	6	0,0678845	0,009406	X

Contrast	*Sig.*	*Difference*	*+/- Limits*
G - G, NG	*	-0,0287689	0,0190371
G - NG	*	-0,0174655	0,0151308
G, NG - NG		0,0113034	0,018316

* indicates a significant difference.