Evaluation of Alternative Packaging for Solid Oral Dosage Forms

An assessment from Elanco's perspective

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Elanco

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Abstract

Aluminum blisters are a widely used packaging type in the pharmaceutical industry, including Elanco Animal Health Inc., a major player in the animal health business. Excellent barrier properties and convenience of usage to the consumers make it an ideal solution. Unfortunately, due to lack of innovation since its invention in the 1960s, there have been certain shortcomings in it use; like lack in consumer centricity, lack of environmental friendliness, difficulty of opening, etc. This project aims to overcome these shortcomings by assessing 22 different alternatives. A packaging scorecard was used to assess the alternatives against the following attributes: product protection, consumer acceptance, marketing, environmental impact, regulatory, investment and material costs, technical feasibility, and novelty.

These aspects were assessed by expert interviews from experts at Elanco Animal Health and throughout the pharmaceutical industry. It includes experts from tooling companies, foil suppliers and contract manufacturers. A consumer study and a benchmark study were conducted to better define the intended area of innovation. The alternative solutions vary from minor improvements in the visual appearance of the blister to flexible, multi-dose systems. From the 22 assessed alternatives, 10 have been scored higher than or equal to the current aluminum blisters. Overall, a flexible, single-dose solution seemed to be the most promising alternative because it combines the functional aspects of blisters while mitigating its disadvantages, like ease of opening and environmental friendliness.

Keywords: pharmaceutical packaging, blister packaging, animal health industry, alternative solution, packaging innovation;

Executive summary

The animal health industry is a highly competitive and innovation-driven market that has undergone many changes in recent years. In 2016, around 9.9 billion US dollars were spent on animal health pharmaceutical products (Animal Health Institute, 2020; Donovan & Pham, 2018; Helmstetter, 2018). One of the main players in the animal health business is Elanco Animal Health Inc., a global animal health company with headquarters in Greenfield, Indiana (USA), is one of the main players in the animal health business with a product range that covers companion animals (dog, cats), farm animals (cow, pig, chicken) and aquatic animals (fish). Elanco, like other animal health companies, is under constant pressure to innovate, hence this project in assessing innovative packaging of animal health products. The packages currently in use at Elanco include bottles, dispenser systems, tubes, syringes, vials, bags, flexible intermediate bulk containers (FIBC) and blisters.

This project intended to innovate in the companion animal product packaging space, specifically, the aluminum blisters currently used at Elanco Animal Health were challenged and compared to alternatives. Elanco's experience with the aluminum blister has highlighted many advantages to this type of packaging: excellent product protection and good consumer acceptance. However, even as the blister appears well suited to Elanco's purposes, there are disadvantages to its use, such as difficulties for elderly or disabled customers, child resistance and environmental concerns. This project aims to overcome these shortcomings by assessing 22 possible solutions for the improvement of blister packaging and its alternatives. Ten of the alternatives are attempts to improve the current blister, while the others change the packaging system completely.

The alternatives have been found in a mixture of already existing ideas from the packaging development team, ideas that were inspired by the benchmarking process, ideas that have come from different stakeholders and the consumer behavior study. These alternatives have been selected from three sources: novel ideas already in the minds of Elanco's packaging team, the results of the benchmarking study that was carried out to identify innovations in pharmaceutical packaging, and a consumer behavior study.

The alternatives were assessed using a packaging scorecard with the following attributes: product protection, consumer acceptance, marketing, environmental impact, regulatory, investment and material costs, technical feasibility, and novelty.

The aspects were assessed during expert interviews from experts within Elanco and throughout the industry. It includes experts from tooling companies, foil suppliers and contract manufacturers. From Elanco, experts from regulatory, marketing, procurement, and research and development were consulted. A consumer study and a benchmark study were conducted to better define the intended area of innovation. The benchmark study indicated that blisters and bottles are the main packaging systems used in the animal and human health industry for tablets. The consumer study showed rising concerns in environmental impact, convenience, and ease of opening.

The alternative solutions vary from minor improvements in the visual appearance of the blister to flexible, multi-dose systems. Of the 22 assessed alternatives (see Figure 1), ten have scored higher than or equal to the current aluminum blisters. Overall, the flexible, single-dose solution (Solution 7) seemed to be the most promising alternative. This alternative enjoys the functional aspects of blisters while decreasing its lack in convenience and environmental impact. In addition, the solution shows potential further improvements in environmental friendliness.

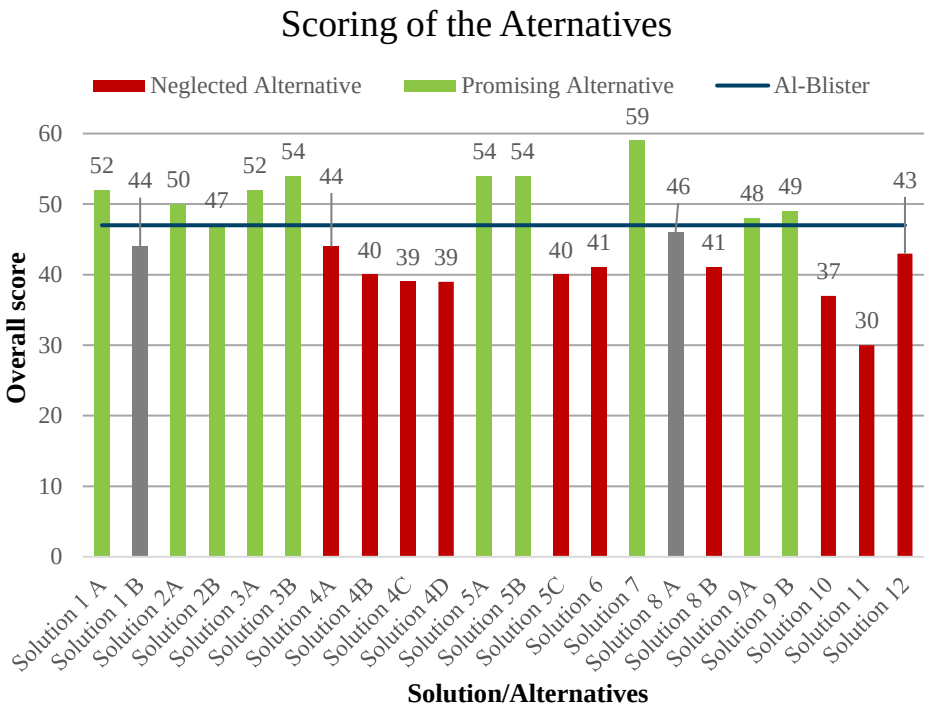

Figure 1: Overall scoring of the alternative packaging alternatives

Solutions, which improved upon the currently used blister, also appeared promising. A trend was noticed in which alternatives that achieved greater environmental friendliness often lacked in sufficient product protection to be able to replace the current blister packaging. No significant relation between the scores of a particular aspect and the overall score were found.

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A big thank you goes to Elanco Animal Health which has been hosting me during my internship and which made this master thesis possible. It was an amazing stay in Basel. Since day one, I felt welcome in the R&D department of Elanco. In particular, the global packaging team under Elke Wagner supported me during my stay at Elanco.

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A big thank you goes to my FIPDes family, FIPDes cohort 8. Before joining FIPDes, I did not know that you can get to know 22 people so fast and so easy. Together we lived in three different countries, we have suffered from RER B in Paris, have managed to find housing in Dublin and finally have enjoyed our Swedish Fika in Lund. All of my classmates have made my time during these two years enjoyable!

At this point, I would also like to take the chance to thank my family, which has supported me throughout my whole studies.

Basel, May 2020

Lukas Luggin

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List of Acronyms and Abbreviations

Table 1: List of acronyms and abbreviations

Abbreviation	Explanation	Abbreviation	Explanation
ACE	Animal Care Expansion Product Development	PA	Polyamide
API	Active Pharmaceutical compound	PE	Polyethylene
CA	Companion animal	PET	Polyethylene terephthalate
CMC	Chemistry, manufacturing, and controls	PMDA	Pharmaceuticals and medical devices agency
COC	Cyclic olefin copolymer	POM	Polyoxymethylene
CR	Child resistance	PP	Polypropylene
CVM	Centre for veterinarian medicine from FDA	PS	Polystyrol
EMA	European medicines agency	PVC	Polyvinyl chloride
FA	Food / farm animal	SOD	Solid oral dosage form
FDA	Food and drug administration	USP	Unique selling point
OTC	Over the counter	WHO	World health organization

1 Introduction

The animal health sector is a highly competitive and innovation-driven market, which has undergone many changes in the recent years. Generally, animal health is divided into companion/family animals and farm/livestock animals. Of the 9.9 billion US dollars spent on animal health pharmaceutical products in 2016, nearly 60% was spent in the companion animal sector (Donovan & Pham, 2018). In the farm animals sector, farmers are primarily concerned with antibiotic resistance and new methods to detected and prevent diseases (Animal Health Institute, 2020; Helmstetter, 2018). The companion animal (CA) industry, by contrast, is focused on improved quality of animals life because companion animals are increasingly viewed as a family member. New demands of the customers on behalf of their companion animals drive changes in the animal health industry.

These new needs require a broad innovation approach, therefore the animal health industry is investing up to 8.5% of its sales into research and development projects (Animal Health Institute, 2020; Donovan & Pham, 2018; Helmstetter, 2018). Elanco, likewise, experiences the demand for more innovation, hence this project in innovative packaging of animal health projects.

1.1 Elanco Animal Health Inc.

Elanco is a global animal health company with headquarters in Greenfield (USA) and is ranked among companies such as Zoetis Animal Health, Bohringer Ingelheim Animal Health, Merck Animal Health and Bayer Animal Health as one of the largest animal health companies in the world (Statista, 2019). Elanco specializes in pharmaceuticals and feed additives for animals. Their product range covers companion animals (dog, cats) to farm animals (cow, pig, chicken) to aquatic animals (fish). Elanco's corporate vision states: food and companionship enriching life. This vision drives the 7,000 employees in more than 40 countries (Elanco, 2019; Meier, 2020).

Elanco was founded in 1954 and was part of Eli Lilly and Company until September 2019. Throughout its history, Elanco acquired various companies to broaden its product portfolio and gain a strategic position. One such acquisition was Steallmune One in 2010 and Novartis Animal Health in 2015. The acquisition of Bayer Animal Health Business is planned for 2019/2020 (Elanco, 2019; Meier, 2020).

Elanco's product portfolio ranges from tablets, chewable tablets, vaccines, in-feeds etc. (Elanco, 2019; Meier, 2020). Elanco's target customers are pet owners, veterinarians and farmers (Elanco, 2015).

Today the company operates in over 90 countries, with regional hubs in Basel, Shanghai, and Sydney (Elanco, 2015; Meier, 2020). Depending on the local need, administrative offices, manufacturing and research and development sites are found throughout the world (see Figure 2).

Figure 2: Elanco sites along the globe (Elanco, 2019)

One of Elanco's research and development departments is located in Basel, Switzerland. The packaging world of Elanco varies from bottles, dispenser systems, tubes, syringes, and vials to bags, flexible intermediate bulk containers (FIBC) and blisters. This project focuses on innovations for aluminum blisters.

The company has a strong focus on innovation, despite the fact that they are working in a highly regulated industry with very complex development processes (Meier, 2020).

1.2 Research Problem & Question

This project intends to innovate in the companion animal product packaging space, specifically; the aluminum blisters currently used at Elanco Animal Health will be challenged and compared to alternatives. Elanco's experience with the aluminum blister has highlighted many advantages to this type of packaging: good product protection and good consumer acceptance. And while the blister appears perfect for Elanco's applications, there are disadvantages to its use: difficulties for elderly or disabled customers, child resistance, and environmental concerns. As it stands, blister packaging has been used in the pharmaceutical industry since the 1960s without major changes.

Despite the advantages of using blisters, the need for continued innovation, and the found challenges for aluminum blisters led to the following research question:

How can the current aluminum blister packaging be improved and what are the alternatives?

Evaluation of the different solutions according to the Elanco's needs.

This lack in consumer centricity and innovation has not only been identified by Elanco but also by academia. According to academia, the pharma industry lacks in consumer centricity. Lack in consumer centricity revolves in lack in compliance and represents problems for the consumer. This lack in consumer centricity can be overcome by having a consumer-centric packaging approach. Here in special packaging designs targeted to the use of the drug are important (Carli Lorenzini, Mostaghel, & Hellström, 2018; Stegemann, Ternik, Onder, Khan, & van Riet-Nales, 2016). A common problem for the pharmaceutical packaging is the ease if opening and the environmental friendliness of pharmaceutical packaging solutions.

Improvements in packaging are not limited to improvements in consumer centricity and environment but improvements can be done in various areas of packaging. The purpose of packaging is not only protection but packaging is also responsible for brand recognition and often acts as a silent salesman at the point of sale (Hellström & Olsson, 2017).

In this thesis, important aspects of pharmaceutical packaging are going to be highlighted (see chapter 2). To create a sustainable packaging alternative and to avoid a unilateral improvement the alternatives have been evaluated from a holistic viewpoint. In special consumer insights and a benchmark study have been important to do so.

1.3 Limitations & Focus

The thesis is limited to find alternatives for the aluminum blisters for solid oral dosage forms for companion animals. This limitation has been made, in order to focus more on a specific problem. It was found that in special for the end consumer blister packaging brings negative attributes. Pharmaceuticals for the B2B sector are often more adapted to their use. So for example for the medicine applications exists, which are delivered with the packaging.

The aluminum blister was used as focus of this study because it is widely used in Elanco Animal Health. In addition it has also a much higher environmental influence, compared to the thermoformed blisters (for more information see chapter 2.2).

In the study no specific tablet was taken into account in order to keep a broad range open and also because the selected solution has to fit a wide range of tablets. Compared to other industries the product amounts in the animal health industry are quite small and it was not limited to one specific tablet. In the animal health area tablets are often linked to the companion animal size, which decreases the amount of tablets with the same packaging sizes again.

The thesis will not provide a detailed design brief or detailed marketing information, but is oriented towards a technical approach, taking costs, environmental concerns and consumer aspects into account, without analyzing them in detail. This aspects are highly linked to business cases and cannot be analyzed in detail in this first evaluation.

2 Theoretical Background

In pharmaceutical packaging, the packaging system consists of three levels: primary, secondary and tertiary packaging. In the example of tablets packed in blisters, the secondary packaging is typically a folding box, grouped into a corrugated cardboard box (Pålsson, 2018; Robertson, 2016). In the pharmaceutical industry, the primary packaging is often the major protection layer (Dean, Evans, & Hall, 2000).

As in the food industry, the major functions of packaging are protection, containment, apportionment, unitization, communication and convenience (Pålsson, 2018; Robertson, 1990). Compared to the packaging in food or other industries the pharma packaging has to meet some additional requirements (see chapter 2.1) and is placed in the special framework of the drug development process. The drug development process is cost and time intensive. It includes the selection of the pharmaceutical active substance (API), the drug and packaging development as well as the post-launch development. In the following chapter, some of these specialties will be highlighted to show their influence on the packaging development.

2.1 Requirements for Pharmaceutical Packaging

The requirements upon pharmaceutical packaging include certain properties and the passing of specialized tests. These are highly dependent on the nature of the drug itself and the properties of the intended package. The pharmaceutical packaging must protect the drug from the environment and contaminants during its shelf life. Additionally, the interaction between the packaging and the drug must be minimized

while still matching the consumer's expectations. Consumer expectations range from elegant designs to convenient and safe ways of using the packaging. At the same time, the packaging has to be cheap and easy to handle in the manufacturing process (Chen, 2016; Dean et al., 2000). In the following chapter, the main requirements are elaborated upon further.

2.1.1 Product Protection

In the pharmaceutical industry, the main purpose of the packaging is the protection of the drug. The solid oral dosage (OSD) is protected from possible degradation factors such as oxygen, moisture and, in some cases, from light (Chen, 2016; Expert 14, 2020). The packaging further confers protection against biological contamination and physical damages.

It is important to consider the interaction of the OSD with the packaging material: migration of the drug product must be limited in all directions. In the pharmaceutical packaging area the stability of the product over a defined time is important. (Expert 11 & Expert 12, 2020; World Health Organisation, 2002).

2.1.2 Convenience

Packaging convenience describes the manner in which the package improves the product experience. Included in the scope of convenient pharmaceutical packaging are attributes like ease of opening, apportionment and good transportability. In the farm animal industry, convenience also describes that the product is easily administered to the animal and it is safe to use (Ahmed, 2002; Drašković, 2010; HCPC, 2015; Pålsson, 2018). Especially in over the counter products (OTC) products, lack in convenience of the packaging often results in a different buying decision for the next time.

2.1.3 **Compliance**

Compliance, also referred to as adherence, describes the tendency of patients to follow prescription orders from the doctor. Lack in compliance is not only a problem in the animal health but also in the human health industry. Noncompliance with a drug plans can cause serious problems, such as non-effective treatment and development of treatment resistances. Around 30 to 50% of patients do not take their medicine in a manner compliant with the prescription. In animal health care, this number is even higher. Easy application systems for drugs leads to higher compliance in the animal health sector (Abood, 2007; Ahmed, 2002; Expert 4, 2020; Expert 7, 2020; Horne, Weinman, Barber, Elliott, & Morgan, 2005; Veterinary Practice, 2013; World Health Organisation, 2002).

2.1.4 **Legal Perspective**

In order to ensure the quality of products, monitor side effects and prevent consumers from harm, the pharmaceutical industry is highly regulated with legislations imposed not only on the finished drug product, but also on the research methods and manufacturing practices. (Dean et al., 2000; European Commission, 2020; Expert 5, 2020). Regulations differ throughout the globe and, as such, it is hard to be aligned with all of them. In the pharmaceutical industry, three nations comprise a majority of the world's market: USA, Europe and Japan (see Figure 3). As other countries have harmonized their regulations through the International Conference on Harmonization (Dean et al., 2000; Expert 6, 2020), the regulatory requirements for these three countries (Europe – EMA, USA – CVM and Japan – PMDA) have become the primary regulatory focus.

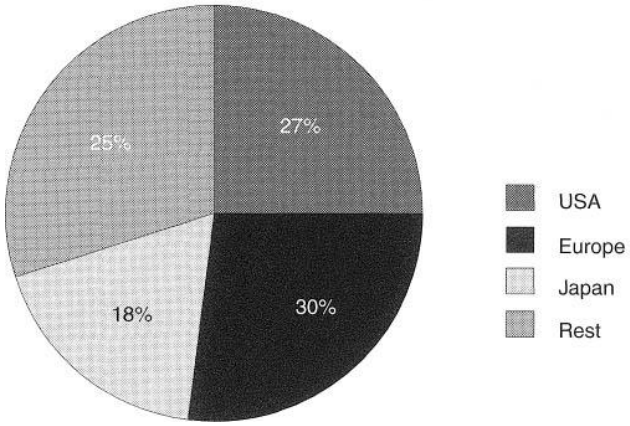

Figure 3: Major pharmaceutical markets (Human and Veterinary)

In Europe, the legislation and applications regarding pharmaceuticals have been overseeing by the European Medicines Agency (EMA), while, in the USA, the Food and Drug Administration (FDA) is responsible for all regulations regarding food and drugs (EMA, 2020a; FDA, 2020c; PMDA, 2020), including veterinary drugs with the it subdivision CVM (Center for veterinarian medicine).

The authorization of new drugs from the laboratory to the product in the market is taken in several steps. In Europe, there are different paths pharmaceutical products can follow to become authorized. One of these ways is trough EMA, which involves several lab studies and information on stability, effectiveness, bioavailability, and toxicology of the new product (EMA, 2018, EMA, 2020d). Even the manufacturers and suppliers of the different components and their specifications are submitted to the authorities for review and approval.

Products in the pharma industry must be approved along with the packaging, which demonstrates the critical role played by the packaging. Future changes in the packaging require the authorization of the relevant authorities. Depending on the change that has been made after the launch, various post-approval processes must be used (EMA, 2020b, EMA, 2020c). The authorization and post approval process

of medications is regulated in the European Union with EU Regulation (EC) No 726/2004 from 31 March 2004 and with EU Commission Regulation No 1234/2008 from 24 November 2008. (European Commission, 2008; European Parliament, 2004). In the USA, the Code of Federal Regulations Title 21 in chapter 514.8 regulates post modifications and the application of products in the animal health industry (FDA, 2020b).

In the European Union, post-approval changes are categorized as minor changes (variations of Type IA or Type IB) or major changes (variations of Type II). The USA divides the post-approval chemistry, manufacturing, and controls (CMC) changes into minor, moderate and major changes. Depending on the type of variation, the dossier for the variation changes as well as the time until it is approved and can be implemented (European Commission, 2013; FDA, 2007).

2.1.5 **Child Resistance/ Elderly-friendliness**

Depending on the toxicity of the drug product, child resistance is a legal requirement for pharmaceutical packaging. The requirement of child resistance depends mainly on the toxicity of the API and the concentration in the drug. If child resistance is required, then the elderly-friendliness of the packaging must also be tested (FDA, 2020a).

Child resistance means that the packaging is difficult to open for children under five years of age. The child resistant packaging is intended to prevent children from getting fast and easy access to harmful or toxic drugs (F02 Committee, 2018). Child resistance requirements are defined by both European and American Standards. In the European Union, child resistance is regulated in DIN EN ISO 8317:2016-05 for re-closable containers and in DIN EN ISO 862:2016-09 for non-reclosable containers. These standards define the maximum number of children that should be able to open the packaging in a defined time. The child resistance test is carried out

following strict procedures. Child resistant variants have to be tested in combination with the final packaging because used material and size influence the openability (Code of Federal Regulations, Deutsches Institut für Normung, 2016a, 2016b, 2016c; F02 Committee, 2018).

The elderly friendliness of packaging solutions is tested in the same study. Elderly friendliness is has become increasingly important in the last year, but it has not been taken into account as a priority in the design of pharmaceutical packaging (Carli Lorenzini, 2018; Code of Federal Regulations; F02 Committee, 2018).

2.2 Blister Packaging

All of these before mentioned requirements must be meet by blister packaging, which is the target object in this project. Blister packaging is widely used as the primary packaging for medical applications. In Europe, approximately 80% of solid medicaments are packed in blister packaging. According to the World Health Organization (WHO), blisters can be defined as:

"a multi-dose container consisting of two layers, of which one is shaped to contain the individual doses. (World Health Organisation, 2002, p. 124)"

As described in the definition, blisters are made out of two different foils: the forming foil and the lidding foil. During the packaging process, cavities are formed with the forming foil and the lidding foil closes the cavity (see Figure 4). The cavities are made by thermoforming or cold-forming.

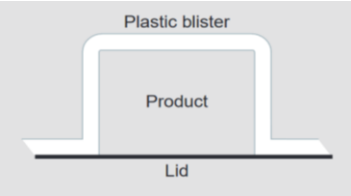

Figure 4: Blister packaging (Pilchik, 2000a)

Thermoforming films are made without aluminum and are based on materials like PVC. For Al/Al blisters, cold-forming technology is used. The cavity design is influenced by the used materialproperties, such as stiffness, tensile strength and the maximal elongation (Dean et al., 2000; Pilchik, 2000a; Robertson, 2016).

The composition of the basic blister foil is shown in Figure 5. Material properties of the blister's components are responsible for the water vapor, gas and light transmission rates. (Amarji et al., 2018; Pilchik, 2000a; Pilchik, 2000b).

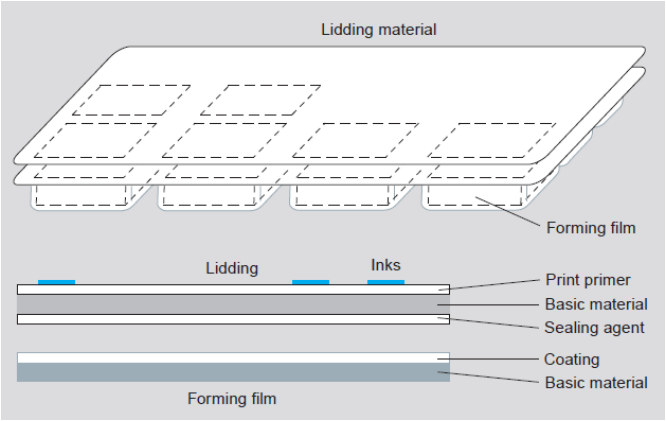

Figure 5: Basic composition of the forming and lidding foil of blister packaging (Pilchik, 2000a)

For a typical lidding foil (see Figure 6), compositions of cellulose primers, aluminum layers and heat-sealed lacquer (based on PVC) are possible. The composition of the forming foil (see Figure 7) is often more complex than the lidding foil. A typical forming foil is composed of oriented PA, polyurethane (primer), PVC and various adhesives (Expert 8, 2020; Expert 9, 2020).

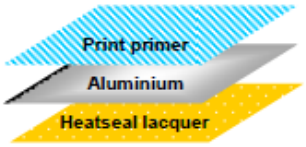

Figure 6: Composition of a typical lidding foil (Wagner, 2020)

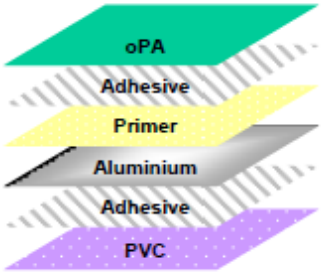

Figure 7: Composition of a typical forming foil (Wagner, 2020)

2.2.1 **Blistering Process**

The packaging process is the last step in the manufacturing process of an oral solid dose drug. The blister packaging process depends on the tablet dimensions, shape, properties, and packaging material. As well as on the blistering line. This section is focusing on the Al/Al blister cold-forming packaging process.

An overview of the process is shown in Figure 8. The packaging process starts with the unwinding step, in which the foil is unwound from the rolls. Cavities are then formed into the forming foil by cold-forming or thermoforming. During cold-forming the aluminum foil is formed without a preheating step by using stamps and pressure. This step is indicated as B in Figure 8. Due to the low forming capabilities of aluminum foils, the cavities are bigger than the cavities with thermoforming films. This leads to bigger blister cards compared to thermoforming blisters. In the next step, the tablet is placed in the cavity (Pilchik, 2000a; Pilchik, 2000b; Prodieco, 2020; Romaco, 2020a; Schlindwein & Gibson, 2018; Uhlmann, 2020).

The tablets are fed into the cavities by using different technologies such as vibration or with brushes. After the loading of the cavities, the lidding foil is sealed on top. During the sealing step, variable data can be embossed on the lidding foil, such as expiration date and batch number. This step is followed by the die cutting-step in which the blisters are separated from each other (Pilchik, 2000a; Pilchik, 2000b; Prodieco, 2020; Romaco, 2020a; Schlindwein & Gibson, 2018; Uhlmann, 2020).

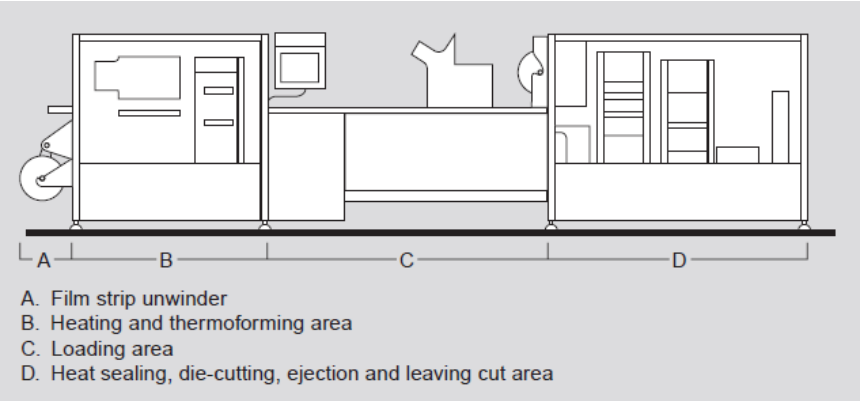

Figure 8: Blister packaging line (Pilchik, 2000b)

The finished blister is then transferred to the cartoning step in which blisters are gathered and packed with a leaflet into the secondary folding box. This step is followed by packing the folding boxes into a group package, which typically is a shipping box. The shipper is then palletized and is ready for shipment.

2.2.2 **Evaluation of Blister Packaging**

Blister provide, due to their aluminum layer, a high level of protection against light, moisture and air. Blister packaging is already widely used and therefore well accepted by the consumer, particularly due to its convenience. The single unit packaging enables accurate and convenient handling, since individual blisters can

be separated from each other, especially if a perforation has been manufactured into the foil layers in the blister. This enables accurate apportionments, which can be conveniently be carried around. The single packaging is further advantageous in that it reduces the probability of accidental misuse of the drug compared to multi-dose packaging solutions, specifically those misuses involving dosage errors, although some easy-to-open blisters have been reported as not ideal in this regard (Pilchik, 2000a).

A challenge facing blisters is that child resistant blister packaging solutions are not elderly friendly. The older generation often has problems opening child resistant solutions without an opening aid, such as scissors. This challenge will get more attention in the next years as the society continues to age (MJS Packaging, 2014; Swain, 2000)

A disadvantage of aluminum blisters is their environmental impact. A study from Raju, Sarkar, Sharma, Singh, and Singla (2016) showed that an aluminum blister has a 70% bigger global warming potential compared to PVC blisters. Some trends have shown that environmental friendliness of pharmaceutical packaging will increase in importance in the future (Llano, 2012; Quelch, 2019; Raju et al., 2016).

3 Methodology

This thesis marks the first step of a larger project, which has the goal to find a suitable alternative to the current Al/Al blister packaging. A *parallel design approach*, according to Nielsen and Faber (1996), will be followed, in which several different solutions are developed separately and evaluated according to different aspects (Nielsen & Faber, 1996).

The advantage of the *parallel design* approach compared to an *iterative design* is that several alternatives can be evaluated simultaneously and so decrease the number of iterative cycles. On the other hand, the *iterative design process* is more resource-efficient compared to the *parallel design approach*. (Brown & Katz, 2009; McGrew, 2016; Nielsen, 1993; Nielsen & Faber, 1996).

In the following chapter, various methodologies are described and used to explore how the current blister packaging can be improved and what alternatives can replace blisters. This chapter includes the methods conferred a better understanding of what the underlying problem and in what context the innovation is taking place.

3.1 Solution Finding Process

These solutions were selected from an assortment of already existing ideas from the packaging development team, ideas that were inspired by the benchmarking study that have come from different stakeholders and the consumer behavior study. These ideas have then been assessed and evaluated according to chapter 3.5.

3.2 Benchmarking Methodology

Benchmarking is a method, which is widely used in all industries. During benchmarking, a product, service or business strategy is compared with others; possibly including other parts of the same company, competitors or organizations working in the same area of interests or with similar products. In benchmarking, best practice examples are explored and then challenged with the own product/service (Anand & Kodali, 2008; Stapenhurst, 2009).

In this study, benchmarking was used to explore the definition of the business standard and the current state of innovations in the pharmaceutical area. It provides an overview of the aspects in which competitors are innovating, which alternative packaging can be found in the market, and an initial inspiration for new innovations.

In this study, a qualitative benchmarking of competitors from the animal health industry as well as a qualitative, functional benchmarking in the human health industry was used. Product screening in other industries, such as the human pharmaceutical industry, is described as functional benchmarking. In the human health industry the primary packaging has the same function as in the animal industry (Ahmed & Zairi, 1999; Anand & Kodali, 2008). The primary packaging of oral dosage drugs was analyzed.

The method selected in which to benchmark was public domain benchmarking, wherein publicly available information are used. This information was accessed mainly on the webpages of the companies of interest, as well as some core products that have been purchased for direct comparison (Stapenhurst, 2009).

3.2.1 **Animal Health Industry**

In order to constrain benchmarking in the animal health area, only the oral dosage drugs for companion animals from the five biggest companies were included. The five leading companies in the animal health business (see Figure 9) were identified and ranked by their revenue in 2018 (Statista, 2019).

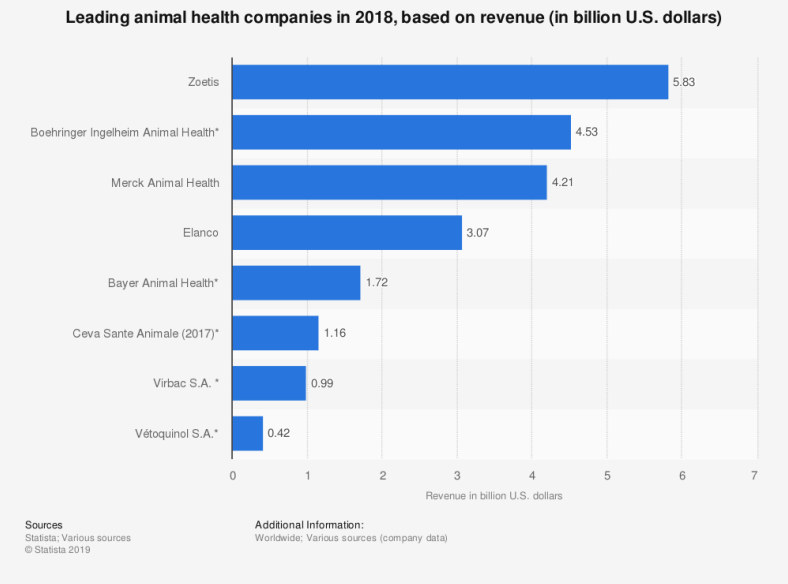

Figure 9: Leading animal health companies in 2018, based on their revenue (Statista, 2019)

3.2.2 **Human Pharma Industry**

Benchmarking in the human pharmaceuticals has been done on the primary packaging of oral dosage products for consumers and professionals. The benchmarking in the human pharmaceutical industry was limited to best-practice examples from leading companies (see Figure 10) based on their revenue (Reuters, 2019). Due to the time limit of the project, a non-systematic approach was taken to

screen the products from the human pharmaceutical industry. In total, three companies, Roche Holding AG, Pfizer, and Bayer AG, have been screened for best practice examples.

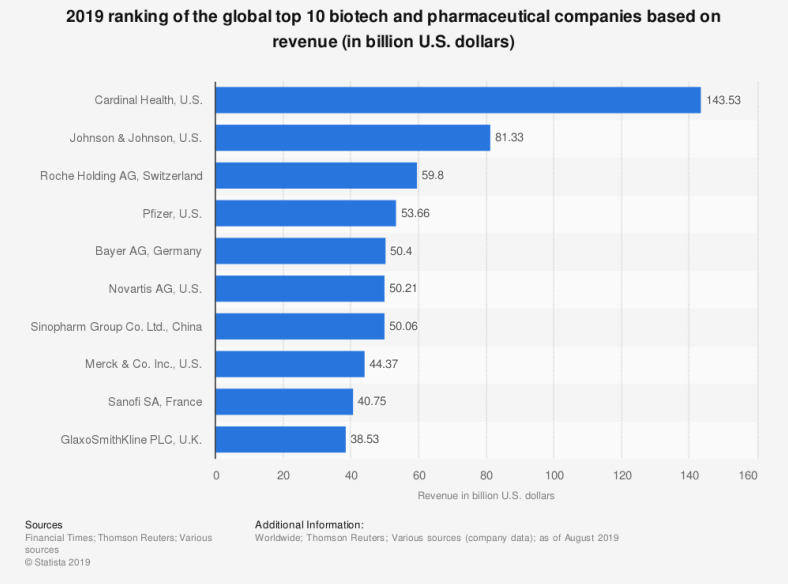

Figure 10: Leading biotech and pharmaceutical companies, based on their revenue (Reuters, 2019)

3.3 Consumer Insight Methodology

Consumer insights are important to get a better understanding of the customer favorites, preferences and how the customer is handling the products. Consumer behavior studies help to tailor future packaging solutions directly to the target consumers. In addition, it helps to define the target consumer (Schiffman, Kanuk, & Hansen, 2012). In order to better analyze the consumer behavior for this project, data was gathered by the following methods.

3.3.1 **Marketing Study**

A marketing study on US Consumer Segmentation in 2018 was carried out by an international marketing company[1]. The aim of the study was to understand the attitudes, behaviors and needs of pet owners and was carried out in 2018. The study was carried out in a defined target market and was about a specific product range[2]. Due to confidentiality reasons, the marketing study and deep details are not included in the appendix of this thesis (Elanco, 2018).

3.3.2 **Consumer Behavior Interview**

A consumer survey was carried out via in-depth interviews with users of OSD (human and animal). In total seven Elanco employees were interviewed, none of them had any interaction with packaging or drug development. The interviewees held jobs mostly in administrative departments of the company. It can be assumed that they just have a consumer view on the packaging.

In-depth interviews were held with a questionnaire as a guideline. The questionnaire can be found in Appendix A. The majority of the questions are open-ended and allowed the interviewee to elaborate further and to answer with their personal experiences. To get a better understanding some answers were followed by follow-up questions.

[1] The name of the marketing company is not mentioned, because the information is considered confidential.

[2] Due to confidentiality reasons, the interviewed market and purpose is not mentioned.

Figure 11: Blister packaging that was shown during the interview

During the discussions, a blister package without branding was shown (see Figure 11) to the interviewee to explain what blister packaging looks like. The advantage of in-depth interviews is that the gathered information is more reliable compared to other forms of consumer insights, like an online survey. A strength in this interview type is that open-ended questions are used, on which the consumer can further elaborate the answers by himself (Hellström & Olsson, 2017; Schiffman et al., 2012).

In addition, the interviewer received a better perception of how the consumer uses the blister packaging and what the in-use thoughts of customers are. The interview evaluation was based on a simplified version of the qualitative content analysis from Mayring (2015). This method allows an objective and qualitative analysis in which the participants' answers were categorized according to different topics. And thus the important feedback is determined (Mayring, 2015). In the approach, the interviews were summarized and categorized according to different topics.

3.4 Expert Interviews

The expert interview in this study was used as an information source. The expert interview is a method to get a fundamental understanding of different areas. Expert interviews are critically analyzed and based on theoretical background information (Bogner, Littig, & Menz, 2002). It is important for the interviewer to have knowledge in the area of interest to avoid a paternalism effect, in which the

interviewer is led to some conclusion (Kaiser, 2014). For the interview, discursive-argumentative interviewing is used to have an open discussion and reliable insights. The expert interview is used on a qualitative basis to get information (Bogner et al., 2002, 2009).

An expert interview is lead by guidance questions. These guidance questions for the different expert interviews can be found in Appendix A (Bogner et al., 2002, 2009; Kaiser, 2014). By having some guidance questions and goal information, the expert interview is kept in a discussion. A common way to evaluate and gather the information is based on the qualitative content analysis according to Mayring (Mayring, 2015). In this thesis, a simplified approach (see Figure 12) according to Bogner et al. (2009) is used to understand and evaluate the information from the expert interviews (Bogner et al., 2002, 2009; Kaiser, 2014).

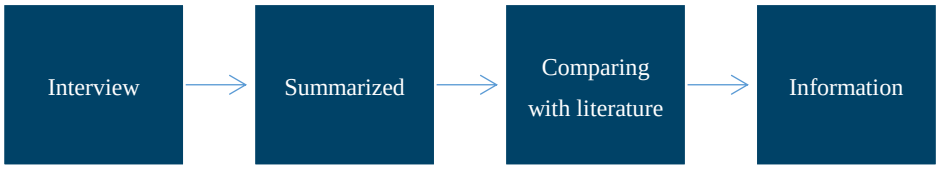

Figure 12: Simplified evaluation of expert interview used in this project – based on Bogner et al. (2009)

First, the interview was summarized and categorized. Second, it was compared to current literature. The results are found throughout the thesis.

The experts were interviewed via Skype calls or face to face. The expert interviews took place at Elanco and were held in English or in German. Due to COVID-19 concerns, no visits of machines, factories and offices were included.

Expert interviews in different expertise areas are hold to get a holistic view on the packaging development and the areas, which interacts with pharmaceutical packaging. The expertise areas varies from tablet development, tablet stability, foil suppliers to consumer behavior experts. Different departments within Elanco, such as legal, marketing and research & development, have been interviewed to understand the problem of aluminum blisters, as well as the requirements on packaging from an Elanco point of view. Table 23 in the appendices (see appendices A.1) shows a summary of the Elanco internal experts.

Table 24 (see appendices A.2) shows the external experts, which have been interviewed. The external experts come from tooling companies, suppliers, contract manufacturers (CMOs) and research institutes. Experts were selected to get a deeper understanding of the selected alternatives and to understand them from different viewpoints. So for example the contract manufacturer have been selected to understand how the alternatives perform on the packaging line.

The tables (Table 23 & Table 24) details the interviewed area of the expert interviews and their area of competences within the companies. Additionally, it describes where guidance questions for the interviews are found. Due to confidentiality reasons, the different companies and the name of the experts are masked.

In order to get objective and reliable data from the expert interviews, the information from the interviews was compared against each other and against current literature. By using this approach, as much the personal opinion of the experts and their own preferences as possible was eliminated, which is one of the main disadvantages of using expert interviews (Bogner et al., 2009; Kaiser, 2014).

3.5 Methodology of the Assessment

Blister alternatives were assessed for product protection, consumer acceptance, marketing aspects, environmental impact, regulatory aspects, material and investment cost, technical feasibility and novelty. The list of assessments was selected based on requirements in the pharmaceutical area and brand requirements.

The different aspects have then been scored from 1 to 3 according to their importance for an improved version of blister packaging. Here, a 1 represents aspects which are considered as additional requirements or extra requirements. A score of 2 represents aspects which are important for Elanco. Requirements, which can be considered as basic needs and are essential are scored with a 3.

Each alternative packaging solution was further evaluated and rated for each aforementioned aspect on a scale from 1 to 4. A 1 indicates that the alternative do not meet the requirements of the particular aspect, while a 4 indicates that the aspect's specific needs are well met. A more detailed description is found in the following subchapters. The evaluation was done on a discussion basis with Elke Wagner (Head of the Global R&D Packaging Development), Max Rehpenning (Packaging engineer at Elanco) and Lukas Luggin (Master Student Packaging Development).

The evaluation method is based on the scorecard method of Henrik Pålsson in packaging logistics. This method was used to identify the most promising solution. An overall score is calculated by using the weighted sum of the aspects to compare the alternatives. (Pålsson, 2018).

In the following subchapters, the methodology for gathering information according to the different aspects is described. In the evaluation, it is assumed that a continuous supply of materials and the supply of tooling is not an obstacle.

3.5.1 **Product Protection**

Product protection is one of the most important aspects on a pharmaceutical package and is an essential attribute for new packaging solutions. Poor product protection can lead to degradation of the oral solid dosage form. This can lead to less effective drugs and unwanted side effects (EDQM, 2020). Elanco will make no compromises in packaging integrity, water vapor transmission rate, air transmission rate and exposure to light into account. In an evaluation of the alternative, new packages are ranked for protection effectiveness against the following scale: low product protection (1); potential lower product protection (2); product protection compared to blisters (3); increased product protection (4).

Product protection was assessed by taking the specifications of the products and packaging materials into account. This knowledge is then compared with the help of expert interviews from the Research and Development department at Elanco (Methodology - see section 3.4).

3.5.2 **Regulatory**

As described in chapter 2.1.4, the pharmaceutical packaging area is highly regulated and packaging solutions must be registered with the governing agencies. Therefore, regulatory aspects are an essential attribute for new packaging alternatives. Small changes in the packaging can make large differences in the regulatory process. Therefore, the packaging solutions in this thesis were evaluated according to how easy it could be registered and how much its implementation varys from the standard registering process. The registration process for each solution was ranked against the following scale: complicated or impossible registration (1); standard registration process with large hurdles (2); standard registration process with small hurdles (3); standard registration process (4). It was assumed that the implementation of the solution is done as part of a new product registration.

The regulatory aspects of the blister alternatives were assessed with the help of expert interviews (Methodology - see section 3.4) with the regulatory affairs department within Elanco. This information was cross-controlled by taking the current regulations and standards in the United States of America and Europe into account.

3.5.3 **User-friendliness**

Elanco perceives user friendliness to be an important feature. The consumer of the product is mainly the pet owner, but can also be a veterinarian. Each consumer type has different expectations from a package, so here, the end consumer is assumed to be the pet owner. The aspects that have been considered for evaluation are ease of opening, packaging size, transportability, and apportionment. It should be noted that some aspects mentioned in the consumer survey are addressed here as well. The user friendliness for each solution was ranked against the following scale: not meeting (1), partially not meeting (2), partially meeting (3) and meeting the user friendliness requirements (4).

The user friendliness and therefore the consumer acceptance and usability of the alternatives were analyzed by the consumer insights (Methodology - see section 3.3), which were gathered at the beginning of the study and by analyzing the alternatives with experts from the marketing department (Methodology - see section 3.4).

3.5.4 **Marketing**

Marketing aspects of new packaging solutions are important specifically brand recognition, storytelling and consumer perceptions (such as environmental friendliness, premium product appearance, etc.). The packaging solutions in this thesis were ranked for marketability against the following scale: not meeting (1), partially not meeting (2), partially meeting (3) and meeting the marketing requirements (4).

The alternatives were assessed according to marketing requirements by expert interviews (Methodology - see section 3.4) with the marketing department within Elanco.

3.5.5 **Investment and Material Costs**

The cost of a new alternative is a crucial factor as the cost of the final product is one of the main driving factors in the industry. The assessment of a solution's cost covers tooling, new packaging lines, line speed, material costs and minimum order quantities. The cost of each new solutions is ranked against the following scale: high costs (1), medium costs (2), cost comparable to blisters (3) and low costs.

The investment and the material costs were analyzed by expert interviews (Methodology - see section 3.4) and quotations from contract manufacturer organizations (CMOs) and machine and material vendors.

3.5.6 **Technical Feasibility**

Technically feasibility within the Elanco network is important because it determines the ease with which the solution can be implemented, not only in the sense of whether it is feasible but also how complex the implementation will be. In the implementation of every new product, the packaging line must adapt and, therefore, the complexity of this adaptation has been evaluated. The availability within the existing Elanco network is also considered. The implementation complexity of each solution is ranked against the following scale: low complexity (4), medium complexity (3), and high complexity (2). A fourth rating, non-feasible (1), has been reserved for solutions that require extensive machine or packaging line changes.

The technical feasibility of the suggested alternatives were analyzed by expert interviews (Methodology - see section 3.4) with experts within Elanco and manufacturer organizations (CMOs), machine and material vendors.

3.5.7 **Environmental Impact**

Environmental friendliness is considered a secondary requirement. More about environmentally aspects of the solutions can be found in chapter 8.4. The environmental impact of a solution was evaluated for the amount of material per drug and the type of material (mono- or multi-material) used. The type of material was determined to be of more importance than material weight per drug. The environmental impact is ranked against the following scale: multi-layered material with high weight per tablet (1), mono-material with high weight per tablet (2), multi-layered material with low weight per tablet (3) and mono-material with low weight per tablet (4).

The environmental impact of the different packaging solutions was evaluated by considering the material amount and material composition. This was examined by expert interviews from the various supply companies (Methodology - see section 3.4).

3.5.8 **Novelty**

The novelty of a solution is considered a secondary requirement. It is rated according to the widely presence of the solution in the pharma area (1), the presence in animal pharma area (2), the presence only in the human pharma area (3) and the non-existence in the pharma area (4).

The novelty of the alternatives was evaluated through benchmarking (Methodology - see section 3.1) and by discussion with the packaging development team.

4 Benchmarking

A benchmarking study was implemented to gain broader understanding of tablet packages that are currently in commercial use. Observations made during the study can be found in Appendix D (Benchmarking on animal health products – Appendix D.1 and benchmarking on human health products – Appendix D.2). The ideas from benchmarking has been used to develop the alternatives from chapter 6.

4.1 Animal Health Products

Benchmarking orally administered animal health products produced 43 products for further investigation. The distribution of primary packaging types is presented in Figure 13. Blisters were the most widely used primary package (24 examples out of 43) followed by bottles (13 out of 43). A deeper evaluation of the different packaging types will be laid out in the following chapter.

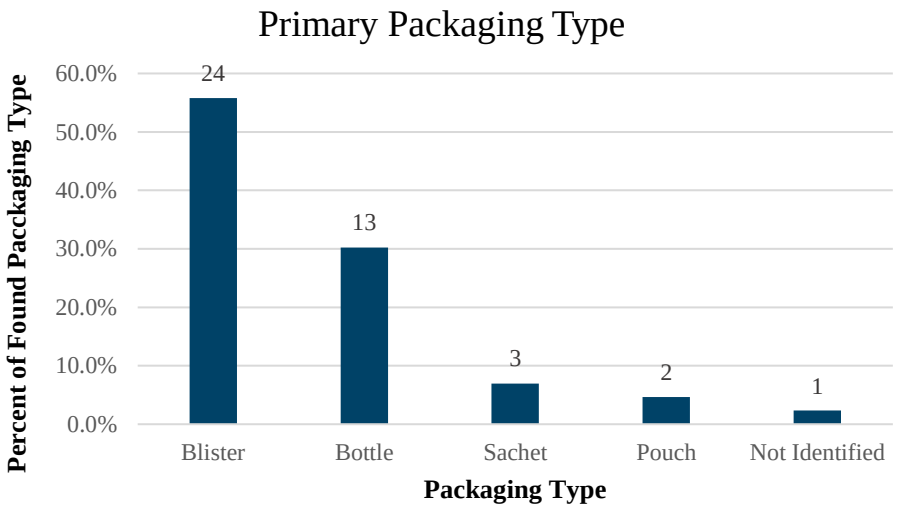

Figure 13: Types of Primary Packaging Found in Animal Health Product Benchmarking Study

4.1.1 **Blister Packaging**

Blister packages were the most common packaging type found, accounting for over half of the products evaluated. The 24 evaluated products in blisters varied in construction material, size, shape and color. Blisters were manufactured from either plastic or aluminum. Due to the production process of plastic blisters, they often have more defined shapes than aluminum blisters. The sizes varied, also, from large (see Figure 14) to small (see Figure 15) cavities. Finally, the colors (of plastic blisters) varied from white to transparent (see Figure 16). Some blisters, like Drontal (Bayer Animal Health - see Figure 16), have additional decorative details embossed onto the packaging: in this case, a dog bone embossment.

Figure 14: Trocoxil from Zoetis (Tsokanos SA, 2020)

Figure 15: Palladia from Zoetis (Sprzedajemy.pl, 2020)

The product Palladia (Zoetis Animal Health), shown in Figure 15, is sold in perforated, single-dose blisters with a child-resistant opening feature. Child resistance is achieved with *Peel & Push* technology, in which a layer of PET paper laminate is peeled off of the blister, allowing the drug product to be pushed through the remaining aluminum layer (Constantia, 2020).

Figure 16: Drontal from Bayer (Santa Cruz, 2020)

Figure 17: Drontal XL from Bayer (Prado Mermoz, 2020)

4.1.2 **Bottle**

Out of the 43 products evaluated in the animal health benchmarking study, 13 products were found packaged in bottles of various forms or styles. One distinguisighing attribute seen in some bottled products, like Baytril (Bayer Animal Health - Figure 18), was the use of colored lids, while others had white lids and were only identifiable by their label. It was further found that manufacturers are using the same type of bottle for a range of API concentrations, leaving only the label to distinguish differences. A generalisation over the whole product portfolio was not found.

Figure 18: Baytril from Bayer in different API concentrations (Bayer, 2020c)

4.1.3 **Other Primary Packaging Forms**

In addition to blisters and bottles, products were also found sold in pouches (see Figure 19) and sachets (see Figure 20). The product Alenza (Bayer Animal Health - Figure 19) has a re-sealable zip lock.

Figure 19: Alenza from Bayer (Bayer, 2020c)

Figure 20: Synulox from Zoetis (Pet Drugs Online, 2020)

4.2 Human Health Products

Benchmarking in the human health industry identified a number of different blister forms. The color of the blister often varied widely between products. For example Aspirin (Bayer - see Figure 21) has the brand color has been incorporated into the blister material itself, while Viagra (Pfizer – see Figure 22) has incorporated not only the tablet color into the blister material, but also the shape of tablet as a design element in the card.

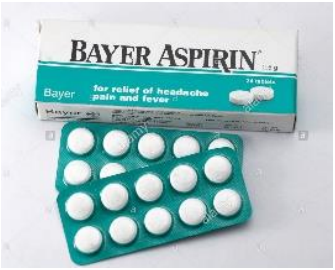

Figure 21: Aspirin from Bayer

Figure 22: Viagra from Pfizer

Other unique blister designs were found, like LO/OVRAL (Pfizer - see Figure 23). Other primary packaging forms such as bottles, tubes/vials (see Figure 24), strip packs (see Figure 25) and sachets (see Figure 26) were found.

Figure 23: LO/OVRAL from Pfizer

Figure 24: Aleve from Bayer

Figure 25: Aspirin from Bayer

Figure 26: Aspirin from Bayer

5 Consumer insights

A panel of seven consumers were interviewed to obtain a deeper understanding of the value of packaging at the consumer level. A larger study group was not possible due to time constraints. All panelists were Elanco employees who are of European descent and are currently living in Europe. Interviews for the customer insight study were conducted from 25.02.2020 to 28.03.2020. A summary of consumer interviews can be found in Appendix B (see chapter B.2). As is summarized graphically in Figure 27, the panelists are primarily using pharmaceutical packaging for themselves and their children, and only two of the seven (see Figure 28) are companion animal owners. Observations made in this study assume that customer preferences regarding pharmaceutical packaging are not dependent on the intended patient, i.e. companion animal products versus human health products. Therefore, panelists without companion animals were included in the study (Ahmed, 2002).

Figure 27: Panelists' primary uses of pharmaceutical packaging

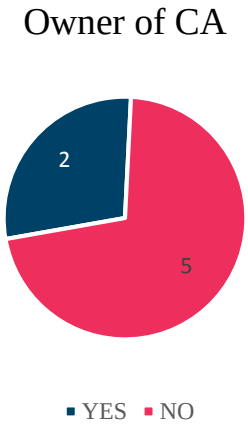

Figure 28: Ownership of companion animals among panelists

5.1 Consumer Aspects of Pharmaceutical Packaging

From the consumer insights (see Figure 29), it is evident that ease of opening, product protection, and convenience are the main aspects when they consider the requirements for medical packaging. Convenience, as it relates specifically to packaging, means that the packaging simplifies the use of the product (Pålsson, 2018). Consumer aspects includes for example product usage, secure take away, and hygienic aspects as well reminders on the packaging and to ability to see the amount of product remaining in the package. Ease of opening can also be considered aspect of convenience, but in the consumer study it was measured separately because of it is importance to the consumer.

These aspects have also been found in the consumer behavior study from Vaanholt et al. (2018), which showed that medical packaging should be easy to open and that convenience plays an important role. For instance, consumers prefer reminder packaging (Vaanholt et al., 2018).

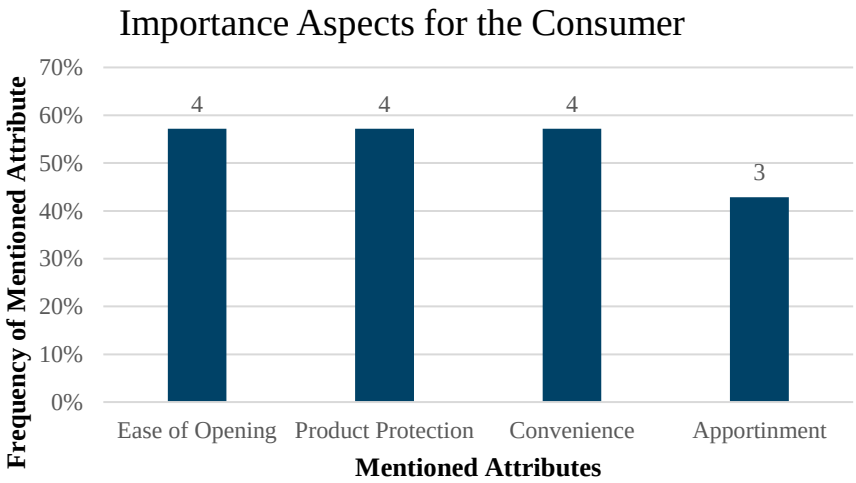

Figure 29: Importance aspects of pharmaceutical packaging features for the consumer

Directly related to ease of opening are the topics of child-resistant and elderly-friendly packaging. While child resistant packaging was viewed by panelists as an important feature, it was not a primary concern. Elderly-friendliness, by comparison, has been called for in researchers such as Carli Lorenzini (2018). Some panelists in the interview also shared they have had to open pharmaceutical packages for elderly relatives that could either not open themselves or had difficulty reading the indicated dosage (Carli Lorenzini & Hellström, 2017; Notenboom et al., 2014). Additionally, injuries commonly occur during open when tools, such as scissors or knives, are used, so it is important that the elderly can open the packages (Davis, 2015). This is particularly relevant to packaging development groups as the group of elderly consumers increase (Elanco, 2018).

5.2 Consumer Acceptance of Blisters

Consumers are generally satisfied (see Figure 30) with the use of blister packaging because they are convenient and protect the drug from outside influences. In the figure below, a consumer rating of five represents high satisfaction/importance and zero represents low satisfaction/importance. Blisters rated especially high for usability with the advantages of a single-dose specifically being mentioned. The consumers also mentioned unfavorable aspects of blisters, such as environmental impact and the volume efficiency. Some interviewees have even broken the medicament during the opening.

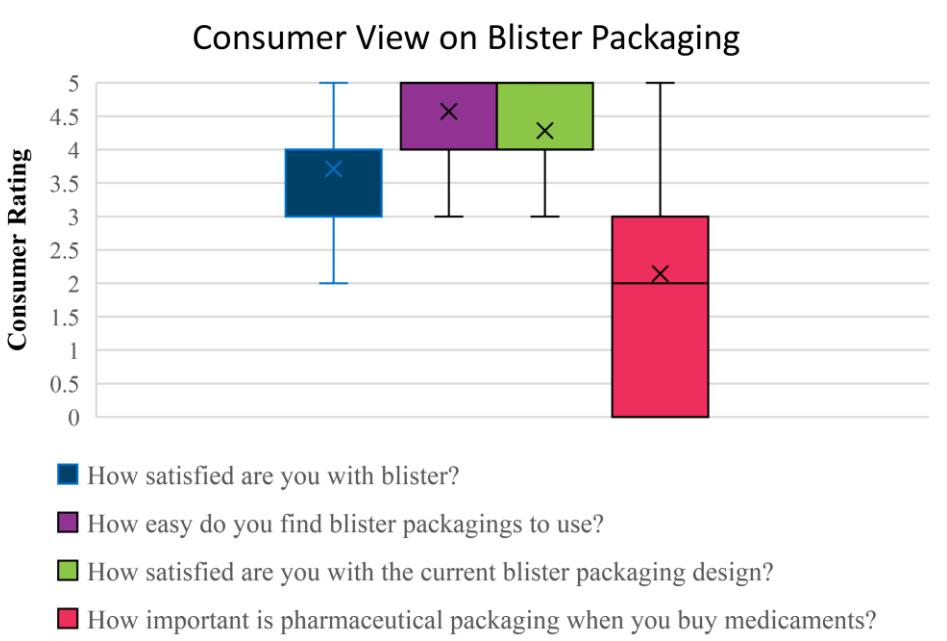

Figure 30: Blister-specific consumer insights

5.3 Important Aspects for Improved Packaging Systems

The consumer interviews showed that consumers prefer packaging which is easier to open and which is more environmentally friendly. Additionally, the consumer highlighted the importance of convenient features, such as perforations to separate the tablets from each other. It is important for the consumer that doses (single or multiple doses per package) are aligned with the recommended dosage for the tablet. The consumer would like to see reminder packages as well as application features for multi-dose packaging.

Overall, the consumer study showed that the packaging form is not a major concern for consumers (see Figure 30) and the interviewees are not seeing it as a unique selling point (UPS). Nerveless, it is important that the packaging meets consumer needs and is minimizing post-purchase cognitive dissonance (Hellström & Olsson, 2017; Schiffman et al., 2012).

The consumer insight highlighted different aspects which are taken in to account in the evaluation and development of the further analysis.

6 Description of Alternatives

In the following chapter, the different alternatives to the blister are described and analyzed further. An overview of the different alternatives can be found in Appendix C (see Table 25).

6.1 Solution 1 – Embossing of Blisters

Embossing means in this case that different shapes, symbols and / or information are pressed in the blister. Flexible dates such as expiration date and batch number are already labeled on the blister card either by printing or by embossing. By embossing, the imprinted figure rises out of the blister (see Figure 31). It is possible to emboss the Elanco logo, different pictograms or day indications.

Figure 31: Embossing examples: Embossing of text, embossed can and embossing of logo (Alibaba, 2020; Kozak, 2019; Yoon & Lee, 2009)

This technique already exists in the animal and the human health industry. Depending on the embossing design, embossing can increase brand visibility, consumer usability and marketing opportunities of the product.

Depending on the position of the embossment, it can be differentiated between embossing A and embossing B. The technical feasibility and product protection of the solution varies with the positioning of the embossment.

Generally, the embossing is done with a stamp or implemented in the sealing roller. The stamp is made of POM. Embossing is easier to implement when flexible materials, such as films for thermoforming, are used. Films for thermoforming have the advantage that they are easier to form and, thus, more accurate graphics can be embossed. Embossing of variable dates is normally done on the sealing tool (Expert E2, 2020).

6.1.1 **Solution 1A – Embossing A**

Embossing A is easily implemented in the current production lines. Embossing A would be implemented with the embossing of variable data at or after the sealing step, depending on the line setup. Embossing in a second step is preferable because it is easier to change the embossing elements.

The smallest possible size of the embossment depends on the filigree and complexity of the design. Embossing requires a space of 3-4 mm to the next disturbance of the sealing, such as corners, perforations and cavities. The 3-4 mm space is required to assure complete sealing and good product protection. If embossing is done within that range, the sealing is disturbed.

The free space for embossing is, therefore, limited and in order to accommodate the embossment, an increase in the size of the blister card is often needed. This increases material costs and can change the cartoning process. The stability of the blister card is impacted as well (Expert E1, 2020; Expert E18, 2020; Expert E2, 2020). Depending on the design, the embossment will be done by the sealing roller. A sealing roller with special embossing details costs around 8000 to 10000€ according to ET1 (Expert E1, 2020).

6.1.2 **Solution 1B – Embossing B**

Compared to embossing A, embossing B is technically more challenging and must be implemented at the forming step. Here the embossing must be done with stamps. The implementation of solution 1B leads to high risks of holes and ruptures in the blister foil. Raptures and holes cannot be accepted in the blister to maintain product protection. To prevent such an event, additional inspection of the forming foil is needed which, in turn, requires changes on the blister-forming machine. The solution requires larger cavities and, therefore, bigger tablets to be more feasible. The development of the stamps is associated with the design costs of around 2000 – 3000€ according to ET2. The company approximates the stamp costs with 200€. Due to the high wear and tear of the stamps, additional costs of 5000 to 10000€ are approximated in the implementation of a full packaging line, running the whole year (Expert E1, 2020; Expert E18, 2020; Expert E2, 2020).

6.2 Solution 2 – Blister Shape

This alternative is already widely used in human pharmaceutical blister packaging. In this case, the blister is formed in different shapes. Possible designs can vary from simple shapes, where only the corners are modified to total reshaping of the blister with changes of the cavity position. Many aspects vary widely to the degree of shaping. Small changes (see chapter 6.2.1) and big changes (see chapter 6.2.2) are evaluated separately (Expert E1, 2020; Expert E2, 2020).

6.2.1 **Solution 2A – Blister Shape A**

Blister shape A describes small changes in the outer shape of the blister card. Small changes of the blister card can be rounding the edges or shaping the blister into specific shapes.

The shaping of the blister card is done at the die-cutting step after the blister is made. Normally, the blister card is cut out as a rectangular from the net. In this alternative, the rectangular die is replaced with another shape.

This shape is, in a technical sense, easily feasible and has no major influence on the stability and in the cartoning process compared to blister shape B. The positioning of the cavity is not changed in this solution. The major costs come from the investment cost in a new die shape and, possibly, larger foil consumption (Expert E1, 2020; Expert E2, 2020). Different designs with this solution are already found in the human pharmaceutical area.

6.2.2 **Solution 2B – Blister Shape B**

In blister shape B, the positioning of the cavity can also be changed. In this case, the cavities are part of the blister design and help to make the design visible.

The solution requires an adaptation of the feeding and die-cutting process. The adaption of the feeding process leads to major technical challenges and to higher implementation costs. These challenges include the fact that feeding is not simultaneous and that the cavities are not in a line. Similar to blister shape A, this alternative requires a special die-shape. The shape of the blister card will not be similar to the current rectangular shape and must be implemented at the current die-cutting step. Handling of the net after the die cutting step is not problematic and does not require a suction unit.

In order to produce blisters cards in this way, the entire packaging line must be adapted to the designed blister. It requires a change in the gathering technology after the die-cutting. While, normally, the blisters are transported via screws to the cartooning apparatus, shaped blisters are either gathered manually or by robots (Expert E1, 2020; Expert E18, 2020; Expert E2, 2020)

The robot uses pick-and-place technology with cameras. The cameras help the robot to rotate the blister into the correct orientation. Robots enable greater flexibility in the machine as well, because the tooling solution is not adapted to one specific blister shape (Expert E1, 2020; Expert E18, 2020; Expert E2, 2020).

6.3 Solution 3 – Colored Blister

In the process of manufacturing colored blisters, Al/Al blisters are colored with different techniques. Various ways of coloring are possible, from coloring in a way that different symbols and text appear to having the whole blister in the same color. The coloring can represent the Elanco blue and so increase the branding or enhance the handling of different blisters, for example, each color represents a specific animal. The blister is easier to recognize as Elanco blister if it is colored in Elanco blue (Expert 3, 2020; Expert 4, 2020).

Solution 3A (see chapter 6.3.1) and solution 3B (see chapter 6.3.1) differ in their coloring technology. The two coloring methods differ in technical feasibility and in how they would be implemented. In this description, both solutions are applied on the current aluminum blister and only on those surfaces, which are not in contact with the drug.

6.3.1 **Solution 3A – Colored Blister A**

In this alternative, the lidding foil and /or the forming foil is colored. The coloring can increase brand recognition and enable easier recognition for the consumer.

According to Company ES7, the lidding foil is colored by a colored varnish (see over-lacquer in Figure 33). The color in the varnish is a food-grade dye. The implementation is connected with minimum ordering quantity and price increasing (Expert E13, 2020).

For the forming foil (see Figure 32), the primer or the adhesive is colored. The coloring of the primer increases the costs of the forming foil. A minimum purchase quantity applies. After forming, no color changes can be seen at the areas where the material is stretched (Expert E13, 2020; Expert E9, 2020).

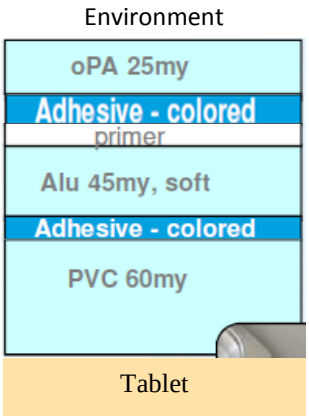

Figure 32: Coloring of the forming foil (Expert E9, 2020)

6.3.2 **Solution 3B – Colored Blister B**

Solution 3B enables to color the whole blister or to color in different designs. Coloring method 1, coloring method 2, and coloring method 3 are used to color the lidding and the forming foil. The coloring method is chosen according to the ordered foil amount. Depending on the method, different amounts of various colors can be used in the design. Method 1 and method 2 must be used for ordering amounts greater than a certain amount[3] with a selection of only 8 to 9 different colors to be used (Expert E13, 2020; Expert E9, 2020).

Method 1 is a roll-to-roll technique, which results in high quality coloring. Here the coloring pattern is engraved as a cavity in the cylinder. The cylinder is placed in a ink bath, from whence it applies the ink to the substrate (Gonzalez-Macia & Killard, 2017; Szentgyörgyvölgyi, 2016).

Method 2 is a relief coloring method. Here the ink is applied by a rubber roll to the substrate. The ink is raised above the non-coloring areas of the rubber roll and thus applies the ink to surface of the substrate (Gonzalez-Macia & Killard, 2017; Izdebska, 2016).

The third method is expensive in industrial prints, but can be done for small volumes. Colors used for coloring method 3 are temperature resistant up to 250°C. Only 30% of the blister surface is colored to prevent migration issues (Braun & Echsel, 2020; Expert E13, 2020).

The lacquer layer at the top of the foil protects the colored blister B and gives it a shiny look. The color of the aluminum foil is always visible and is a factor to consider in the final appearance of solution 3B, though, with the use of white

[3] Exact amount is not mentioned due to confidentiality reasons.

lacquers this effect can be decreased. Coloring on both sides of the lidding foil (see Figure 33) can be done and is often partnered with a transparent forming foil. (Expert E13, 2020; Expert E9, 2020). For colored blister B, no minimum purchase amount is required. Depending on the coloring method, equipment costs apply.

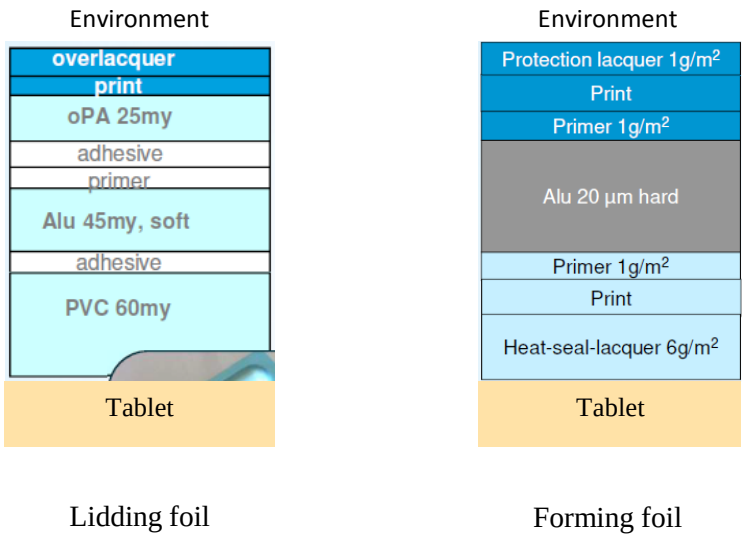

Figure 33: Schematically illustration of the composition foil composition with printing (Expert E9, 2020)

6.4 Solution 4 – Active Solution

The four previously described solution vary in the technologies implanted in their construction and yet rely on the same principles for their effective protection of the enclosed product. Active packaging material, by contrast, include specialized material in the packaging itself to extend the shelf life of the drug product or to make it otherwise more favorable to the consumer. Active solution A and Active solution

B contain integrated scavengers for oxygen, moisture and/or odor (active solution C). One application of this class of package is active solution D with its own unique method of protecting products from oxidation.

The goal of this solution is to prevent the degradation of the active substance contained in the blister packaging. The degradation process can be initiated by light, moisture, or oxygen (Dean et al., 2000; Expert 14, 2020; Schlindwein & Gibson, 2018).

6.4.1 Solution 4A – Active Solution A

Solution 4A is integrated within the lidding or the forming foil. This active solution is composed of a carrier and the active substance. The carrier, in like manner, is composed of a major substance (PP, PE...) and a minor substance. To this substrate the active substance is added. The major substance of the carrier forms an extra layer in the packaging. The minor layer forms pores in the carrier where the active component is seated (see Figure 34), which, in turn, is responsible for the reduction of moisture and/or oxygen in the cavities (Expert E4, 2020).

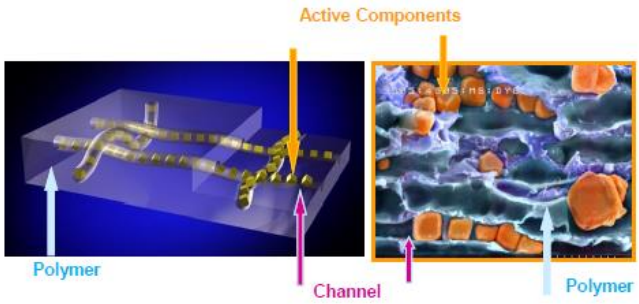

Figure 34: Active layer composition (Expert E4, 2020)

This approach allows the package designer to control the internal environment to predefined conditions. Alternatively, the package is effective until its active substance is saturated; for example, an oxygen scavenger binds as much oxygen as it can hold.

Oxygen and moisture absorption can be implemented separately or together. High barrier foils are more favorable to use in this solution, because, if low barrier foils are used, then the scavenger is saturated faster and the positive effect of the scavenger is lost (Capen et al., 2012; Expert 11 & Expert 12, 2020; Expert 14, 2020).

The application of active solution A complicates the handling processes in manufacturing. The foil must be used within certain time[4] because they are activated when exposed to moisture and oxygen. If the blister production line is stopped for a short period[5], then the unwound material must be disposed. The shelf life of the foil, after it has been manufactured and before it is used, is shortened compared to classic blister foils (Expert E9, 2020).

6.4.2 **Solution 4B – Active Solution B**

The active solution B operates on the same principle described in solution 4A (see chapter 6.4.1). This solution is implemented punctual on the lidding foil. The active solution B is attached to the lidding foil by heat-staking before the lidding foil is applied over the blister cavities. This process avoids extra costs in adhesives and additional steps. Investment in the addition of the heat-staking device on a current blister line is required to implement active solution B.

[4] Exact timing is not mentioned due to confidentiality reasons.

[5] Exact timing is not mentioned due to confidentiality reasons.

Because the scavenger makes direct contact with the drug product, there is a risk or migration of the API into the active pad. Certain materials have already shown migration of API into the packaging material(Expert 15, 2020).

The cost per cavity depends highly on the size and complexity: absorbed material or materials, absorbing to a certain level or to the maximum, material used as major component, etc. The cost[6] for oxygen absorbance are higher than for moisture absorbance (Expert E4, 2020). The solution is, at the moment, available at Company EC1 on thermoforming blisters where the production line speed is slightly decreased compared to thermoformed blisters without active solution 4B. The decrease in line speed[7] is due to the heat-staking step (Expert E18, 2020).

6.4.3 **Solution 4C – Active Solution C**

This solution is implemented as active solution A (see chapter 6.4.1) or as active solution B (see chapter 6.4.2) and absorbs chemicals that cause an unpleasant odor while opening.

The odor is caused by flavors added to the drug product formulation, which makes the drug appealing to companion animals (Expert 3, 2020; Expert 4, 2020). With the implementation of odor control, the volatile components in the headspace are absorbed and the intensity of the odor is decreased. The intensity that the odor reaches in the headspace is dependent on the specific volatile components involved (Liu & Little, 2012).

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[6] Exact cost range is masked due to confidentiality reasons.

[7] Exact line speed is not mentioned due to confidentiality reasons.

The odor in drugs is often based on a combination of different compounds and cannot be related to a certain component. The complex odor source[8] makes the development of the absorbent challenging (Expert 11 & Expert 12, 2020).

The active odor-absorbing substance must be developed individually for every specific odor. The co-development with Company ES1 for the odor absorbent is time- and cost-intensive. The application costs, depending on the odor complexity, are comparable to the oxygen absorber costs of active solution B[9]. This solution is favorable for drugs with intensive odors. In the future, the technology of odor release over time will be available and can be implemented if regulatory bodies allow (Expert E4, 2020).

6.4.4 **Solution 4D – Active Solution D**

Active solution D aims to replace oxygen by other gases, such as nitrogen and carbon dioxide. The process takes place in the sealing tool, shortly before they are sealed with the lidding foil. In a first step, the oxygen will be evacuated to achieve negative pressure. The oxygen can be evacuated until 0.3% oxygen remains. The cavity is then flushed with another gas, like nitrogen or carbon dioxide. Evacuation until 0.3 % remaining oxygen reduces the line speed because the evacuation takes longer. Evacuation without influence on the line speed can be done until remaining oxygen reaches 1%. The evacuation of the oxygen is the time-consuming step of solution 4D.

[8] Not mentioned due to confidentiality issues.

[9] Exact costs are not mentioned due to confidentiality reasons.

Machine manufactured by Company ET3 can be implemented in the production lines in order to include active solution D in the process (Expert E3, 2020). The application of active solution 4D is already widely used in the food packaging industry and is not used in the oral solid drug industry.

6.5 Solution 5 – Rigid, Multi-dose Bottle

The idea behind rigid multi-dose bottles is to replace the blister with a bottle. Bottes are already widely used and are not considered to be new technology anymore. Bottles are more widely accepted in the USA then in Europe. The bottle is preferred in the USA for historical and consumer behavioral reasons (Pilchik, 2000a; Pilchik, 2000b).

Bottles are made in different ways. Two of the most common ways are blow molding (referred as method 1) and injection molding (referred as method 2). Depending on the needed technology, a combination of these different technologies is used (Dean et al., 2000). Bottle A is made by method 1 and bottle B and C are made by method 2 and are discussed in detail below.

6.5.1 **Solution 5A – Rigid, Multi-dose Bottle A**

This bottle types describes a rigid, multi-dose bottle made by blow molding. The focus of this idea is to have a unique bottle shape, such as can be seen Figure 35. An increase in marketing and consumer behavior attributes has been observed for customized rigid, multi-dose bottles (Expert 3, 2020; Expert 4, 2020).

Rigid, multi-dose bottle A is made by method 1. In method 1 it can be differentiated between injection blow molding and extrusion blow molding.

Injection blow molding is divided in two steps: In the first step, the parison is made by injection molding and in the second stage, the parison is blown to the final bottle shape in a mold. The result is the finished bottle. Molding according to this method is used to produce soft drink bottles by companies such as Coca-Cola[10].

In the extraction molding, an extruded tube is clamed in a mold. The tube is then blown up to the mold shape and the bottle is formed. A co-extrusion with two materials is possible (Dean et al., 2000).

To increase the environmental friendliness of bottles, a molding with recycled plastic and virgin plastic is possible, but this requires higher investment. The two molding according to method 1 vary in the packaging material which is used to make the bottle. Materials like PP, HDPE and PC are preferred for injection blow molding, while PP and PC are not preferred for extrusion blow molding (Dean et al., 2000).

Figure 35:Example of a shaped bottle (Expert E5, 2020)

[10] Coca Cola is a soft drink company with seat in Atlanta (USA). The Coca-Cola company is known for brands like Coca-Cola, Fanta etc. Coca-Cola is considered as one of the most valuable brands worldwide (The Coca-Cola Company 2020).

The development of a customized bottle typically takes around 12 weeks plus time for mold production and qualification. When the new mold is designed, embossing can be added for additional price (Expert E5, 2020). The prices vary highly with the type of technology used in the bottle production. The investment costs for injection blow molding are higher than for extrusion blow molding. This higher investment costs can be compensated by lower piece production costs[11]. The lower production price per piece is related to the higher production speed (Expert E5, 2020). Generally, the prices are highly connected to the number of cavities in the mold.

Child resistance features are easy to implement in this solution and several options already exist as child resistant cap systems (see Figure 36), such as push & turn or press & turn (Expert E5, 2020). To assure child resistance the solution has to be retested with the specific bottle.

Figure 36: Different child resistant solutions for rigid multi-dose bottles - press & turn and push & turn solutions (Expert E5, 2020)

[11] Investment and piece costs are not mentioned because of confidentiality reasons.

6.5.2 **Solution 5B – Rigid, Multi-dose Bottle B**

This bottle type describes a bottle made by method 2. This solution is a standardized system that exits in different sizes. The bottles are made from PE or PP (Expert E11 & Expert E12, 2020).

In the molding method 2, the hot plastic material is transported under pressure into a cold mold and is held there until hardened. During injection molding, the temperature of the material and the mold are critical parameters. With molding method 2, various simple bottle shapes can be made (Dean et al., 2000).

At Company ES6, a molded bottle is standardized and delivered in form of a cylinder (see Figure 37). By sticking to the standardized sizes and form, costs are decreased. The bottle can be made in all colors. For the colored bottles, a minimum order quantity applies[12], which depends on the bottle size. In order to have company specific colors, a master batch[13] must be purchased. The bottle supplier is producing first prototypes to check the color before the serial production with colored bottles starts (Expert E11 & Expert E12, 2020).

Embossing with logos and engravings in the bottle or the lid are possible to improve user compliance and marketing aspects. Embossments are made with blind plates in the mold. For the blind plates an investment costs depending on the design applies. A separate plate must be made for each cavity in the mold (Expert 3, 2020; Expert 4, 2020; Expert E11 & Expert E12, 2020).

[12] Exact amounts cannot be revealed due to confidentiality reasons.

[13] Exact quantity of the master batch are not mentioned due to confidentiality reasons

A company specific shape of the bottle is feasible with this molding technique. The investment costs[14] depends on the degree of the complexity, the development process and tooling costs. The development time depends on the design (Expert E11 & Expert E12, 2020).

Application of moisture and oxygen absorbents in the lid are possible for lids with a certain diameter. The moisture absorber will be applied in form of a puck, placed in a special compartment in the lid (see Figure 37).The desiccant puck is made of silica gel and has a shelf life of two years. It is made from a food grade material and is activated after certain hours of placing in the lid. Minimum order quantities for lids are applying. As described in chapter 6.1, this can increase the shelf life and the in-use stability significantly (Expert E11 & Expert E12, 2020). The application of absorbent material can be implemented also in the bottle material (Expert E4, 2020).

Figure 37: Bottle with absorbance puck (Expert E11 & Expert E12, 2020)

All described options are able to be produced with bioplastic made from sugar cane, but this means a price increase.

[14] Costs are not approximated because of confidentiality reasons.

6.5.3 **Solution 5C – Rigid, Multi-dose Bottle with Application Feature**

Here the bottle has an added application feature. The adding application feature adds a high value to the consumer usability. The dispenser is made by molding method 2 of different materials. Different polymers are used in order to decrease the friction between the moving parts. The dispenser has to be adapted to the tablet size to ensure that one tablet is dispensed at the time.

The tablet size limits the ability of implementation of the feature. For big tablets, it is not possible to use the dispenser because it must increase in size, in tandem with the tablet, to a maximum size. The dispenser is developed for tablets ranging from a certain diameter[15]. Tablet shape and thickness also impact the technical feasibility of the solution. With complex tablet shapes, the complexity of dispenser development increases. Small, round tablets are preferred for use with dispensers, along with tablets with low moisture content.

The application can include moisture and oxygen pads to increase product protection. The development time of the dispenser system is typically one year long and associated with high development costs. The solution can be made with bioplastic made from sugar cane.

[15] Ranging diameter is not made public due to confidentiality reasons.

6.6 Solution 6 – Effervescent Tubes

In this solution, the tablets are packed in tubes similar to the classical vitamin effervescent tablet (see Figure 38). The main body is made by molding method 2 (for description of injection molding, see chapter 6.5.2). The lid often contains silica gel or molecular sieves, which are used as oxygen and moisture scavengers. The tubes have a certain diameter[16]. After production, the tube can be printed with up to eight colors in offset HD technology. Different surface technologies, such as roughen and embossment, can be used (Sanner, 2020).

While tablets in a bottle are poured in and are free to roll about, tablets in a tube are stacked on top of each other. This is achieved by a flat feeding process in the tube packing line. In the process, tablets are stacked and then put in to the tube. Certain tablet dimensions in diameter and height are required for stacked packing[17]. The tablet requires a flat surface, like those on the effervescent tablets. This package is not feasible with tablets that don't have the correct size and shape (Expert E1, 2020; Romaco, 2020b).

Figure 38: Example of Tube packaging for Vitamin C (Turbosquid, 2020)

[16] Diameter is not mentioned due to confidentiality reasons.

[17] Minimal requirements on the tablet properties are not mentioned due to confidentiality reasons.

6.7 Solution 7 – Flexible, Single-dose Solution A

Solution 7 is similar to the current blister packaging. The flexible, single-dose solution was developed before blister packaging and was widely used in the past. This solution, like blisters, is a unit dosage form, which has increased consumer convenience aspects (Dean et al., 2000).

While a blister package is preformed by stamps, the tablet itself creates the cavity in this solution. The solution can be carried out with similar protective layers found in blister packaging. The used foils are composed of multi layered materials[18] are used (Expert E6 & Expert E7, 2020).

Technically, a flexible, single-dose solution A production line is similar to a blister packaging line. The packaging lines have a feeding station, a sealing step and a die-cutting step. The foils are unwound from the rolls and brought to the feeding and sealing step. A notable difference to blister production is that the feeding and sealing steps are done in a vertical orientation. As described in the following picture (see Figure 39), the tablet is placed in a pocket formed by the two foils. The pocket is formed around the tablet and, after closing, it is sealed directly in this pocket. The pockets are of similar volume to the cavities in blisters. The sealing tool must be adapted to the tablet size. Sealing roll costs[19] depends on the cavity shape and the width of the sealing roll.

[18] Composition of the foil is not mentioned due to confidentiality.

[19] Approximation is not given due to confidentiality.

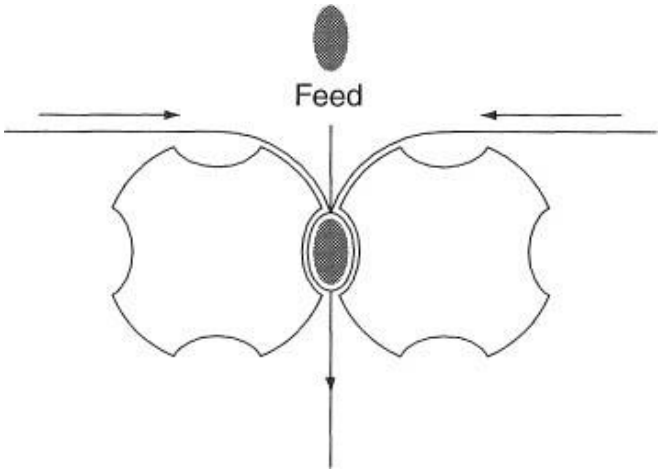

Figure 39: Schematic of packing process of flexible single-dose solution A (Dean et al., 2000)

Longitudinal and transverse division follows the sealing process. Similar to blisters at this step, perforations are made mechanically or with lasers And are followed by embossing and printing of variable data. At the last step, different shapes are cut out. The cost[20] of the packaging line is depending on the complexity of the tablet and forms.

Solution 7, once cut, are picked by a robot and forwarded to the cartoning step. Depending on the shape of the solution, the cartoning equipment must be adapted to the current production needs (Droulers & Roullet, 2005; Expert E1, 2020). The line speed[21] is higher compared to blister packaging.

The feasibility of solutions 7 depends on the tablet properties. Tablet hardness must exceed a minimum. The geometrical shape further limits the feasibility of the

[20] No approximation due to confidentiality.

[21] Not mentioned due to confidentiality.

solution (Droulers & Roullet, 2005; Expert E1, 2020; Vassia, 2020). A common problem with this machines is the formation of wrinkles during sealing, which lead to tunnels or pores through the seal. These wrinkles cause losses in product protection and must be monitored. The tendency to wrinkle varies from foil to foil and must be carefully evaluated in every case (Droulers & Roullet, 2005; Expert E18, 2020).

Flexible, single-dose solution A enhance consumer handling by offering three possible opening mechanisms: tearing apart, pushing through and push-peel. Tearing apart and push through are made with perforations in the foil. These perforations are made in the foil prior to use in manufacturing. The perforation is done in the top layer of the foil in order to maintain product protection while still offering an easy to open feature. The perforation can be mechanically made with spikes or with lasers (Expert E1, 2020; Expert E13, 2020; Expert E6 & Expert E7, 2020). The laser perforations can be made in various patterns to achieve opening at different force levels. Laser technology has the advantage that it is more accurate and makes cutting in all different directions possible (Expert E13, 2020), while mechanical perforations are done only in machine direction (Expert E6 & Expert E7, 2020).

With the help of different laser patterns or through perforations in different directions, child resistant opening features can be achieved (Expert E13, 2020; Expert E6 & Expert E7, 2020). Child resistant packaging concepts already exist but must be developed further. In order to develop a company-specific laser pattern, a minimum order is required with an anticipated development time of several weeks[22] (Expert E13, 2020).

[22] Development time and costs are masked due to confidentiality.

6.8 Solution 8 – Flexible, Multi-dose Solution

In this flexible, multi-dose solution, the same amount of tablets are packed as in the blister packaging. The solution is re-closable and can be equipped with a child resistant, re-closable seal (see chapter 6.8.1). The solution can be released as a flow back or as a three sealing bag. The re-closeability (see Figure 40) is achieved by the application of a zip lock (Expert E14, 2020; Expert E9, 2020).

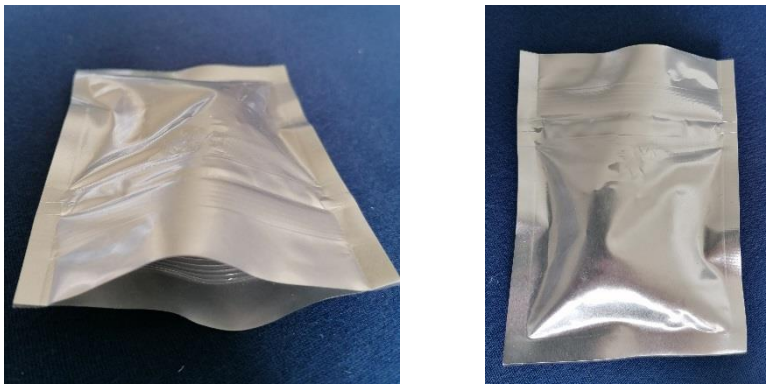

Figure 40: Example of a flexible, multi-dose solution (Expert E14, 2020)

The three-sealing bag can be made in two different ways: either by sealing two foils together (one foil forms the front and one the back), or the same foil is folded to make the back and front (Dean et al., 2000; Expert E18, 2020; Expert E9, 2020). The three sealing bag is used by Company ES8 and can be produced in different sizes[23].

[23] Minimal sizes are not mentioned due to confidentiality.

During the flow pack production, the foil is sealed so that it forms a tube which is then further sealed to separate a package from the adjacent packages or bulk foil. This technology allows a fast filling process (Dean et al., 2000; PouchWorth, 2020).

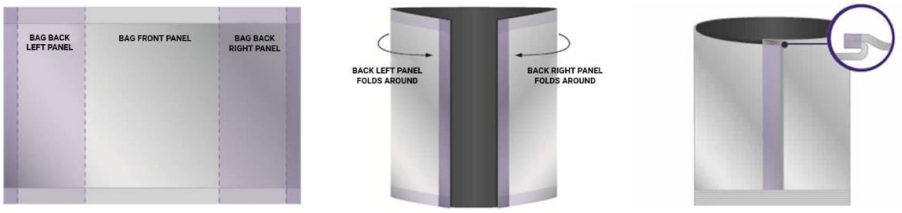

Figure 41: Schematic of the creation of flow packs (PouchWorth, 2020)

In production, multi-dose packages are delivered pre-formed to the CMO, where it is filled with tablets and sealed.

The foil for the solution 8 can be composed of aluminum, PET and PE. Depending on the composition of the foil and the material thickness, different barrier qualities can be achieved. It is also possible to apply moisture absorbent material in the flexible, multi-dose solution, which leads to a reduction of the moisture therein (Expert E9, 2020).

6.8.1 Solution 8B – Child resistant flexible, Multi-dose solution

The solution is made in the same way as described above, but is fitted with a child resistant reclosing system. The child resistance is achieved by equipping it with either method 1 or method 2. Different systems for both closing systems exists. Company ES8 and Company ES10 implement method 1. The child resistance in both variations is achieved by pressing stop locks to open it (Expert E14, 2020). The other possibility of a re-closable bag is the application of method 2. The child resistant method 2 is made by Company ES5 or Company ES11.

Solution 8B can be made as a flow bag or a three-seal bag (see chapter 6.8) with minimum dimensions width and height[24]. Smaller pouches cannot be implemented with method 2, because it is difficult, from a technological perspective, and is hard to open. Company ES8 has larger minimum sizes[25] for use of the method 2 of solution 8B (Expert E14, 2020; Expert E16, 2020; Expert E17, 2020; Expert E9, 2020; Expert E9 & Expert E10, 2020).

In method 2, child resistance is achieved by the implementation of a hidden opening mechanism. Effectiveness of child resistance for this type depends on the material used and the size of the solution.

6.9 Solution 9 – Flexible, Single-dose Solution

In flexible, single-dose solutions, the tablets are packed individually into a flexible unit, such as a solution 9A (see chapter 6.9.1), or solution 9B (see chapter 6.9.2). In both cases, the tablet will be packed as a single-dose. Both solutions can be made from an aluminum foil, PE and PET layers. In addition, layers of paper can be added to increase the stiffness. All material combinations are possible provided that they are sealable (Expert E13, 2020; Expert E9, 2020).

The opening mechanism of both solutions is made child resistant by applying fold and tear options as well as by using different perforation techniques. The perforation is applied by mechanical perforation or lasers. Mechanical perforation works only in the machine directions. Lasers are able to make perforation patterns in every

[24] Minimal width and height of solution 8B with opening method 2 is considered as confidential.

[25] Minimum size of the solution 8B offered by Company ES8 is a confidential information.

corner and are more accurate. Perforations are made in the outer PET layer in order to weaken the foil on a specific point and thereby guide the opening feature. The strength needed to open the foil can be adjusted by alternating the laser pattern (Expert E13, 2020; Expert E9, 2020). Child resistant solution already exist on the market.

6.9.1 Solution 9A – Flexible, Single-dose Solution B

The flexible, single-dose solution is formed as a three- or four-sealed solution. The sachet line can be operated as a horizontal or vertical machine. In this solution, the sachet is first formed by sealing three sides of the sachet. Then the solution is filled and sealed. Generally, solution 9A has more space for artwork on the front than solution 9B because of their larger surface (Bühler, 2020; Expert E18, 2020; Omag, 2020; Robertson, 2016).

6.9.2 Solution 9B – Flexible, Single-dose Solution C

In the production of solution 9B, foil is unwound and formed into a tube by sealing the ends together. In this tube of packaging foil, the tablets are placed. After placing each tablet, the bottom/top of the package is sealed. This technology is 25% faster than blister machines and is widely used for granules in the food and pharmaceutical areas. Typically a flexible, single-dose solution C packaging is 4 times taller than width (Bühler, 2020; Expert E18, 2020; Omag, 2020; Robertson, 2016).

6.10 Solution 10 – Rigid, Multi-dose Can A

The solution 10 exists in different sizes and heights. The rigid, multi-dose can is produced by seaming or molding, depending on the height of the can. The tin can comes with child resistant lid or with a Klipp-Klapp® lid (see Figure 42), though both lack in product protection (Expert E15, 2020).

The child resistant variation of solution 10 must be equipped with another protective layer inside, because the opening mechanism is not airtight. To avoid this, the thread is attached to a molded PVC tub, such that the can contains a PVC compartment linked to the thread. The mold can be sealed with a plastic film so that product protection lasts until the first opening. Child resistance of the opening mechanism is certified, but only for large diameters (Expert E15, 2020).

The Klipp-Klapp® solution has a gasket in the lid to achieve air and water tightness. The implementation of the gasket is done by hand and require high amounts of machinery to automate the process. A lacquer will be applied in the inside to assure no interaction with the tin can (Dean et al., 2000; Expert E15, 2020)

Figure 42: Examples for tin can solution: Child Resistant tin can and Klipp-Klapp® tin can (Expert E15, 2020)

The lid can be customized by printing on it. The printing is done by digital or offset printing. This printing method is done on the top and bottom surface. Full printing (including the sides) is done by off-set printing. Individual printing designs for offset printing are associated with a minimum ordering quantity[26] (Expert E15, 2020, Expert E15, 2020).

The can solution can be filled on bottle packing lines, but due to the special design, the lid must be put on manually. The price[27] of the can depends on the size, but it is high compared to other alternatives (Expert E15, 2020; Expert E18, 2020).

6.11 Solution 11 – Rigid, Multi-dose Can B

This solution is a small aluminum rigid, multi-dose can (see Figure 43). It has a good barrier against gas, moisture, aroma and light. The solution 10 is made of aluminum and sealed with aluminum foil. They require a minimum diameter[28]. The solution is associated with high prices. In addition, a high investment for the design, tooling and stacker must be made[29].

[26] Minimal order quantities are kept confidential.

[27] Price approximations are considered as confidential information.

[28] Considered as confidential information.

[29] Investment costs are confidential information.

Figure 43: Example packaging for Medican solution

6.12 Solution 12 – Semi Flexible Solution

Company ES4, a design company, developed this semi-flexible solution. It approaches elderly-friendliness and is easy to open. The semi flexible solution can be implemented as a blister style, a multi-dose bottle, or as a single-dose unit. The multi-dose solution can be reclosed, but loses its protection against oxygen and moisture (Expert E8, 2020).

Solution 12 is designed such that the container opens along a predetermined breaking point. That point is defined by having a special mixture of co-polymers of various stretchability and unique design features. The design assures that the tablets are kept in place during opening and allows opening with one hand (Expert E8, 2020)

The semi flexible solution is made from PET as the main material, along with other polymers. It is possible to produce the solution from PS, PP or COC. The product is made by thermoforming. Aluminum is not used to produce the solutions because it is not sufficiently flexible. In order to achieve the predefined break point, a high polymer flexibility is needed. Company ES4 has partnered with Company ET3 as a tooling company and Company ES5 as a foil supplier.

The manufacturing process is similar to the process of thermoforming blisters in that after thermoforming, the tablets are fed in a similar way as in blisters into the cavities. The forming foil is then sealed with a lidding foil.

This process requires investment in a completely new packaging line (Expert E8, 2020). The development for a customized solution takes several weeks after the design briefing and another several weeks to get the first samples[30]. The design costs depend on the degree of modification from an existing core design. Costs for the adaption of the standard solution design to an Elanco specific design are applied. In addition, royalties per unit sold must be paid[31].

[30] The time line for the development and the prototyping face cannot be mentioned due to confidentiality issues.

[31] The costs for the development of the solutions and the height of the royalties are masked in order to keep align with the confidentiality.

7 Assessment

In the following chapter, the different alternatives have been assessed according to product protection, regulatory, user-friendliness, marketing, costs, technical feasibility, environmental impact and novelty. The assessment was done according to the methods elaborated in chapter 3.5, which are summarized in the following table (see Table 2).

Table 2: Summary of the assessment methodology

Aspect	Importance	Rating	
		Score	Description
Product protection	3	1	Low product protection
		2	Potential lower product protection
		3	Product protection compared to blisters
		4	Increased product protection compared to blister
Regulatory	3	1	Complicated or impossible product registration
		2	Standard registration process with large hurdles
		3	Standard registration process with small hurdles
		4	Standard process
User Friendliness	2	1	Not meeting user friendliness requirements
		2	Partially not meeting user friendliness requirements
		3	Partially meeting user friendliness requirements
		4	Meeting user friendliness requirements

Marketing	2	1	Not meeting marketing requirements
		2	Partially not meeting marketing requirements
		3	Partially meeting marketing requirements
		4	Meeting the marketing requirements
Costs	2	1	High cost
		2	Medium cost
		3	Costs comparable to blisters
		4	Low costs
Technical feasibility	2	1	Non-technical feasible
		2	High complexity changes and technical feasible
		3	Medium complexity changes and technical feasible
		4	Low complexity changes and technical feasible
Environmental impact	1	1	Multi-layered material with high weight per tablet
		2	Mono material with high weight per tablet
		3	Multi-layered material with low weight per tablet
		4	Mono material with low weight per tablet
Novelty	1	1	Widely used in animal pharma
		2	Presence in animal pharma
		3	Presence in human pharma
		4	Non-presence in the pharma area

7.1 Alternatives

In the following chapter, the alternatives are assessed and compared with the current aluminum blister (see assessment chapter 7.1.1).

7.1.1 **Aluminum Blister**

As discussed in chapter 2.2.2, blister is ranked highly in user friendliness, product protection and registration ease. Blister packaging is widely used and brings no unique marketing opportunities and is considered non-novel (Expert 3, 2020; Expert 4, 2020). In terms of costs and technical feasibility, the aluminum blister again ranks highly because the material and the forming methods are industry standard (Expert E18, 2020). The main disadvantage can be found in its environmental impact.

The aspects mentioned above and in the different parts of the project, specifically in chapter 2.2.2, lead to the following evaluation (see Table 3) of the blister packaging.

Table 3: Summary rating – aluminum blister

Attribute	Rating	Attribute	Rating
Product protection	3	Technical feasibility	4
User friendliness	3	Costs	3
Marketing	2	Environmental impacts	1
Regulatory	4	Novelty	1

7.1.2 **Solution 1 – Embossing of Blisters**

Embossing of blisters results in increased user friendliness and marketing. Depending on the design, embossing can increase brand visibility, consumer usability and the marketing opportunities of the product. Features, which allow a fast recognition of the product increase consumer usability and compliance because they can be distinguished easily from other products. In addition, the texture and firmness of packaging are often used to influence consumers' purchasing and consumption behavior. Studies have been shown that the packaging texture influences product perception (d'Astous & Kamau, 2010; Racat & Capelli, 2020; Velasco & Spence, 2019). In the pharmaceutical industry, this can be effective for both the veterinarian and the lay consumer. The product is easy to distinguish from the competitors' products.

The solution is easily implemented from a regulatory perspective, especially if benefits, such as fast recognition, are highlighted. Embossed pictograms must be taken from official approved sources in order to achieve an easy registration. Legal authorities such as EMA provide approved pictograms, which should be used on pharmaceutical packaging (Expert 5, 2020; Expert 6, 2020). There is a small risk that the artwork appears too advertising. Embossing B has a higher risk of being rejected by the authorities because it can lead to foil damage. The solution can even be implemented in the currently used blister packaging. This would require a CMC change from the CVM. In Europe, it would be a change according to B.II.a.1: change or addition of imprints, embossing or other markings including replacement, or addition of inks used for product marking. Changes of this type are easier to implement, especially if the change results in better usability by the consumer (European Commission, 2013; Expert 5, 2020; Expert 6, 2020).

In environmental friendliness and costs the solution is comparable with blister packaging, with some additional costs in tooling and increased foil usage. The investments are not heavy, but the running costs are higher and require more monitoring (Expert E1, 2020).

The aspects mentioned above and in chapter 6.1 are summarized in according to the fulfillment of the different aspects. The results for embossing of blisters are summarized in Table 4.

Table 4: Summary rating – Solution 1

Solution 1A - Embossing A			
Attribute	**Rating**	**Attribute**	**Rating**
Product protection	3	Technical feasibility	4
User friendliness	4	Costs	2
Marketing	4	Environmental impact	1
Regulatory	4	Novelty	2
Solution 1B - Embossing B			
Attribute	**Rating**	**Attribute**	**Rating**
Product protection	2	Technical feasibility	3
User friendliness	4	Costs	2
Marketing	4	Environmental impact	1
Regulatory	3	Novelty	2

7.1.3 **Solution 2 – Blister Shape**

Both blister shape variations are ranked highly for product protection. The protection is similar to the current aluminum blister, as long as the sealing areas are respected in the design.

Unique blister shapes create better consumer bonding and brand recognition. Some companies, like Coca Cola[32], have a unique bottle shape that carries their values and branding. A unique blister shape helps to establish Elanco as a brand faster (Expert 1, 2020; Lindstrom, 2005; Velasco & Spence, 2019). Studies have shown that the shape of the packaging directly impacts how the product is rated by the consumer (Becker, van Rompay, Schifferstein, & Galetzka, 2011). The unique shape of the blister also helps the veterinarian to distinguish quickly between products for different animals, if the blister has an animal specific shape. From a marketing perspective, shaped blisters might be seen as less environmentally friendly. Nevertheless, the overall attractiveness of the blister is increased. Blister shapes of type B are preferred for marketing strategies that rely on storytelling (Expert 3, 2020; Expert 4, 2020).

From a regulatory point of view, the change is easy to implement in new products as well as to add to existing products. According to EU Regulations, the change falls under B.II.e.4: Change in shape or dimensions of the container or closure (immediate packaging). CVM considers it as a CMC change. The change in the blister design is considerable, but it is easily approved by the authorities. Blister shapes of type A are easier to approved then changes of type B. Shapes from type B are more novel and have the risk to attract children.

[32] Coca Cola is a soft drink company with seat in Atlanta (USA) and is known for the Coca-Cola branded glas bottle (The Coca-Cola Company (2020)

Attractiveness to children is seen negatively by the authorities, because it increases the possibility of children playing with toxic substances (European Commission, 2013; Expert 5, 2020; Expert 6, 2020).

The implementation of shaped blisters requires investments for new die shapes and, depending on the design, line adjustments. In some cases, more material is used, which increases the material costs slightly. For an environmental analysis, this alternative is equivalent to the standard blister (Expert E1, 2020; Expert E18, 2020).

The aspects mentioned above and in chapter 6.2 are summarized in the rating according to the fulfillment of the different aspects. The results for blister shape solutions are summarized in Table 5.

Table 5: Summary rating – Solution 2

Solution 2A - Blister shape A			
Attribute	**Rating**	**Attribute**	**Rating**
Product protection	3	Technical feasibility	3
User friendliness	4	Costs	3
Marketing	3	Environmental impact	1
Regulatory	4	Novelty	2
Solution 2B - Blister shape B			
Attribute	**Rating**	**Attribute**	**Rating**
Product protection	3	Technical feasibility	2
User friendliness	4	Costs	2
Marketing	4	Environmental impact	1
Regulatory	3	Novelty	4

7.1.4 **Solution 3 – Colored Blister**

Colored blisters are, in some aspects, comparable to the current blister packaging. The product protection rating of the blister will not be changed through addition of a color (Expert E13, 2020; Expert E9, 2020).

The risk coming from migration is decreased by the usage of non-toxic, food grade inks. Using Elanco blue in the blister increases brand awareness and is an opportunity for Elanco to strengthen the company-consumer bond. Studies done with Nivea[33] products have shown that product preference is related to their color branding. (Expert 1, 2020; Expert 3, 2020; Expert 4, 2020; Velasco & Spence, 2019).

Coloring of pharmaceutical packaging reduces medication errors and confusion by using different colors for different animal sizes or species. The color of the blister can, for example, be linked to the dog size. In this way, veterinarians do not have to look at the descriptions to distinguish between different dog sizes. Handling for the consumer is easier because they can already distinguish the product from the color. This can also lead to higher product compliance because it is easier to see. A colored package influences the in-use behavior of customers (Droulers & Roullet, 2005; Souza, Silva, Lopes, Diniz, & Ferreira, 2019; Velasco & Spence, 2019).

Overall, the design and color must be chosen carefully, considering that all designs deliver messages in the physiological, the associational and the cultural environment in which they are received and must match the consumer expectations to have a

[33] Nivea is a brand of Beiersdorf Global AG (Germany). The personal care brand produces mainly creams. The brand is famous for the classic Nivea cream, which is sold in a blue tin can (Beiersdorf (2020).

positive post purchasing experience. Here, cultural differences must be understood as well (Velasco & Spence, 2019).

From a regulatory point of view, the change is easily implemented with new products. A post-approval is possible. The change requires a major CMC change from the CVM and, in Europe, a change according to B.II.a.1: Change or addition of imprints, embossing or other markings including replacement, or addition of inks used for product marking. The regulations regarding necessary information, readability and allowed pictograms on pharmaceutical packaging remain applicable to colored blisters. Extensive advertising design is not allowed on pharmaceutical products (European Commission, 2013; Expert 5, 2020; Expert 6, 2020).

The implementation of the colored blister solution does not affect the machinability of the foils (Expert E18, 2020).

Differences between solution 3A and 3B are found only in their costs. The costs for solution 3B are slightly higher, but the minimum order quantities are much smaller than for solution 3A. By implementation of colored blister A for different products this disadvantage can be avoided (Expert 17, 2020; Expert 18, 2020).

The environmental impact is dependent on the origin and composition of the coloring (EuPIA, 2013). The implementation of colored blister alternatives were not found in the animal health competitor product screening, but is widely used in the human health industry (see chapter 4.2).

The aspects mentioned above and in Chapter 6.3 are summarized according to the fulfillment of the different aspects. The results for colored blister solutions are summarized in Table 5.

Table 6: Summary rating – Solution 3

Solution 3A – Colored blister A			
Attribute	**Rating**	**Attribute**	**Rating**
Product protection	3	Technical feasibility	4
User friendliness	4	Costs	2
Marketing	4	Environmental impact	1
Regulatory	4	Novelty	2
Solution 3B – Colored blister B			
Attribute	**Rating**	**Attribute**	**Rating**
Product protection	3	Technical feasibility	4
User friendliness	4	Costs	3
Marketing	4	Environmental impact	1
Regulatory	4	Novelty	2

7.1.5 Solution 4 – Active Solution

The degradation process of and API can be initiated by light, moisture, or oxygen (Dean et al., 2000; Expert 14, 2020; Schlindwein & Gibson, 2018). This solution attempts to extend shelf life by oxygen and moisture control. Increased shelf lives are favorable to the veterinarian because they can store products longer. From a marketing perspective, increased shelf lives confer a competitive advantage (Expert 3, 2020; Expert 4, 2020). The increased shelf life adds flexibility in terms of logistics and shipment to the point of sale (Expert 15, 2020).

Active solutions enable a change from aluminum blister to thermoforming blisters with similar barrier properties (Expert E18, 2020), but, in this project, an implementation in aluminum blister are assumed. Therefore, the environmental friendliness of the solution is limited (see chapter 7.1.1).

Overall, all active solutions results in higher investment and material costs than blister packaging. From a regulatory point of view, all active solutions require increased regulatory oversight because they increase the interaction between drug and packaging. However, similar solutions are already found in food and medical device packaging. No active solutions are used for oral dosage form packaging in the animal and the human health industry.

7.1.5.1 Solution 4A – Active Solution A

An active film confers a longer shelf life; a highly favorable attribute from the supply chain's and consumer's point of view. Presently, Elanco's goal is to achieve certain shelf life for all products[34], while extending the shelf life has an additional marketing effect for a veterinarians (Expert 1, 2020; Expert 2, 2020).

Research has shown that in 2007 approximately 1020 tons of medical products in the animal and human health industry were disposed. One of the main reasons for the disposal of unused drugs was that they were expired (Ekedahl, 2006; Persson, Sabelström, & Gunnarsson, 2009). By prolonging the shelf life, the amount of disposed drugs can be decreased. Unused drugs are hazardous to the environment, specifically if they are not disposed of in the correct way (Boxall, 2004; Paut Kusturica, Tomas, & Sabo, 2017). While active solution A can have a positive effect on the environment, all active solutions are assumed here to be implemented in

[34] The targeted shelf life is not mentioned due to confidentiality reasons.

aluminum blisters and, as such, another layer of material has been added to the solution. So the solution is comparable with blisters from an environmental point.

The supply chain, after manufacturing, is more flexible because the shelf life is increased and more time can be spent during shipment. This flexibility come with constraints in the supply chain from the supplier of the blister material to the manufacturing site of the drug product. The film itself has a decreased shelf life of and is more complicated to handle at the manufacturing site, since, during usage on the line, the time is limited until the film becomes activated (Expert E18, 2020; Expert E4, 2020; Expert E9, 2020).

The solution can be implemented without any investment in machines. Added costs are coming from the active material (Expert E4, 2020; Expert E9, 2020).

The CVM and the European Pharmacopeia have already approved films with active layers, though not in blisters for tablets. This would be a novel application of active layers, despite the films already being used in other pharmaceutical packages (Expert E4, 2020; Expert E9, 2020).

The aspects mentioned above and in chapter 6.4.1 are summarized by their fulfillment of the different aspects. The results for active solution A are summarized in Table 7.

Table 7: Summary rating – Solution 4A

Attribute	Rating	Attribute	Rating
Product protection	4	Technical feasibility	2
User friendliness	3	Costs	1
Marketing	2	Environmental impact	1
Regulatory	4	Novelty	3

7.1.5.2 Solution 4B – Active Solution B

The consumer impact of active solution B is comparable to active solution A with the added advantage that the consumer is more aware of the implementation of an active solution, resulting in increased consumer confidence and awareness of the new technology.(Expert 4, 2020). There is a possibility, though that the consumer thinks that the solution is part of the medication (Expert 3, 2020).

From a procurement point of view, this solution is preferred because less active material is used. This result in lower material costs compared to the active solution A. In addition, the flexibility is increased (Expert 18, 2020; Expert E4, 2020). From an environmental perspective, the solution is slightly better because less active material is used.

The aspects mentioned above in chapter 6.4.2 are summarized by their fulfillment of the different aspects. The results for solution 4B are summarized in Table 8.

Table 8: Summary rating – Solution 4B

Attribute	Rating	Attribute	Rating
Product protection	4	Technical feasibility	2
User friendliness	3	Costs	1
Marketing	3	Environmental impact	1
Regulatory	2	Novelty	3

7.1.5.3 Solution 4C – Active Solution C

Active odor packaging does not affect product shelf life in blister packaging, but rather increases the consumer preference by removing substances in the blister headspace. The smell is thus reduced for the consumer while remaining strong enough to be attractive to the companion animal (Expert 11 & Expert 12, 2020; Expert 3, 2020; Expert 4, 2020).

Due to the complexity of flavors in tablets, the development of an odor scavenger is cost intensive and difficult to develop. As soon as the flavor changes, new scavengers must be developed and tested according to the sufficiently odor reduction for the consumer while remaining attractive to the animal. The implementation per cavity can be estimated to fall in the range of oxygen absorbance scavengers (Expert E4, 2020). This is a big disadvantage in terms of costs.

The aspects mentioned above in chapter 6.4.3 are summarized ranked for fulfillment of the different requirements. The results for active solution C are summarized in Table 9.

Table 9: Summary rating – Active solution C

Attribute	Rating	Attribute	Rating
Product protection	3	Technical feasibility	2
User friendliness	4	Costs	1
Marketing	4	Environmental impact	1
Regulatory	1	Novelty	4

7.1.5.4 Solution 4D – Active Solution D

The solution is preferred for oxygen sensitive tablets, with benefits particularly for flavors, odors and colors, which are often sensitive to oxygen (Church & Parsons, 1995; Coles & Kirwan, 2011). The solution is easily implemented because it is already a standard method in the food industry and with equipment from Company ET3 it is easy add to production lines. The technically challenging part is to develop the proper gas mixture and the added complexity of having gas as part of the production process. Company ET3 is the only supplier of this solution in the pharmaceutical area and is not equipping machines made by competitors with their own technology (Expert E3, 2020).

Solution 4D is not implemented yet in OSDs. This, along with the fact the gas is in direct contact with the drug, presents challenges to the registration process (Expert 6, 2020).

The aspects mentioned above and in chapter 6.4.4 are summarized according to their fulfillment of the different aspects. The results for active solution D are summarized in Table 10.

Table 10: Summary rating – Solution 4D

Attribute	Rating	Attribute	Rating
Product protection	4	Technical feasibility	3
User friendliness	3	Costs	1
Marketing	1	Environmental impact	1
Regulatory	2	Novelty	4

7.1.6 **Solution 5 – Rigid, Multi-dose Bottle**

Because bottles expose their contents to the environment when opened, they do not provide as good product protection as the blister. Contaminants can enter the bottle, as well as moisture and oxygen when they are opened. The moisture and oxygen barrier is lower of bottles compared to aluminum blisters. Therefore, products in bottles must be less sensitive against the degradation then products in blister. Depending on the number of tablets in the bottle, the in-use stability may need to be increased.

During the consumer behavior study (see chapter 5), it was seen that consumers in Europe prefer single-dose units because they see them as more hygienic and because of the convenience of being able to carry individually packaged doses . On the other hand, bottles are preferred in cases when a dose must be taken every day (Expert 3, 2020; Expert 4, 2020; Smith, W., 2018).

Bottles have a tremendous marketing opportunity with many opportunities for branding. As such, an Elanco specific branding is possible. An Elanco shaped bottle increases brand recognition, especially in cases, like over the counter goods, where brand marketing is of greater importance (Expert 3, 2020; Expert 4, 2020; Velasco & Spence, 2019).

The regulator implementation of a bottle is easy, as long as it is implemented with a new product. Bottles are already widely used, but requirements for multi-dose solutions such as in-use stability and dust formation have to be met (Expert 5, 2020; Expert 6, 2020).

Company EC1 has already a filling line for bottles where all types of round-necked bottles are packaged. A feasibility check with the finished bottle form and size is necessary. Extraordinary shapes, like triangular bottles, are not possible to fill on the Company EC1 packaging line. Capping is done manually at this contract manufacturer, but in the future, it can be automated.

From an environmental point of view, bottle solutions are highly favorable because the material per tablet is decreased compared to blisters. In addition, bottles are often made with mono materials and are easier to recycle (Singh, Sharma, & Malviya, 2013).

The costs vary highly between the different technologies, but overall the costs are comparable with blisters. The difference in bottle production method of Solution 5A and Solution 5B does not lead to difference in the rating (see Table 11).

Bottle in special forms and colors are used in the human pharma industry, but not in the animal pharma industry. More unique bottle features require technologies with varying costs, particularly for unique shapes and colors, since, though used in the human pharmaceutical industry, they are not used in the animal pharmaceutical industry. Broadly, however, they are comparable to blisters.

The aspects mentioned above and in chapter 6.5 are summarized according to their fulfillment of the different aspects. The results for rigid, multi-dose bottle A & B solutions are summarized in Table 11.

Table 11: Summary rating – Solution 5

Solution 5A - Rigid, multi-dose bottle A			
Attribute	**Rating**	**Attribute**	**Rating**
Product protection	3	Technical feasibility	4
User friendliness	2	Costs	3
Marketing	4	Environmental impact	4
Regulatory	4	Novelty	3

Solution 5B - Rigid, multi-dose bottle B			
Attribute	**Rating**	**Attribute**	**Rating**
Product protection	3	Technical feasibility	4
User friendliness	2	Costs	3
Marketing	4	Environmental impact	4
Regulatory	4	Novelty	3

7.1.6.1 Solution 5C – Rigid, Multi-dose Bottle with Application Feature

The bottle with application feature has lower product protection because the bottle is never totally closed. Product protection is decreased because the application feature is not tight and there is uncontrolled oxygen/moisture migration.

With the application feature, some of the major negative effects of multi-dose packages are negated. The consumer, is able to take the tablets out in a single unit without getting in contact with the rest of the drugs in the bottle (Smith, W., 2018). During the consumer survey customers indicated that an application features would be a plus. As such, the application feature adds benefits for both consumer usability and marketing opportunity (Expert 3, 2020; Expert 4, 2020). From a regulatory aspect, it is similar to the bottle solution, but due to the lack in product protection, there is a risk that the registration is failing.

In cost and environmental friendliness, the solution ranks poorly because the feature is cost intensive in development and production. The application of solution 5C adds unnecessary material and use multiple polymers.

The aspects mentioned above and in chapter 6.5.3 are summarized according to the fulfillment of the different aspects. The results for bottles with application feature are summarized in Table 12.

Table 12: Summary rating – Solution 5C

Attribute	Rating	Attribute	Rating
Product protection	1	Technical feasibility	3
User friendliness	4	Costs	1
Marketing	4	Environmental impact	1
Regulatory	3	Novelty	3

7.1.7 Solution 6 – Effervescent Tubes

While the tube confers good product protection, it is not equal to blister packaging. Due to ease to opening and the ability to get the tablets one by one, the product is user friendly, but bulky and takes a lot of space.

From a marketing perspective, the solution does not fulfilling marketing requirements because this type of packaging is already highly associated with effervescent tablets. The packaging solution does not match the consumer expectations and can lead to misunderstanding of the product usage (Expert 3, 2020; Expert 4, 2020; Gilal, Zhang, & Gilal, 2018).

In regulatory and environmental friendly aspect, the tube solution is comparable with bottles (Expert 5, 2020).

Though the tube is already found in the human health industry (see Chapter 4.2) and can therefore not be considered as totally new, it still has a high potential in the animal health industry.

The aspects mentioned above and in chapter 6.6 are summarized according to the fulfillment of the different aspects. The results for effervescent tubes are summarized in Table 13.

Table 13: Summary rating – effervescent tubes

Attribute	Rating	Attribute	Rating
Product protection	2	Technical feasibility	2
User friendliness	2	Costs	3
Marketing	1	Environmental impact	4
Regulatory	4	Novelty	3

7.1.8 **Solution 7 – Flexible, Single-dose Solution A**

Solution 7 has similar product protection properties and consumer friendliness properties with blister packaging. Like blisters, they are single-dose packages and are easy to carry around, easy to open, and are lighter. Depending on the tablet height, the flexible, single-dose solution A can be larger than a blister, which is unfavorable to the consumer. The push-through technology implemented in solution 7 allows an easier opening for elderly people. (Expert E1, 2020; Expert E6 & Expert E7, 2020) The flexible nature of the material gives them an environmentally friendly appearance, as noted in the consumer behavior interviews (see chapter 5).

Marketing sees the solution as fresh because good protection can be achieved with less material. The flexibility and ease of blister shaping create a unique selling point. They have increased printing possibilities and appear to be a more modern style of blister (Expert 3, 2020; Expert 4, 2020).

The flexible, single-dose solution A is easily implemented when they are coupled with the registration of a new tablet.

Also if the solution is larger than a blister for a similar-size tablet, it can be still seem environmentally friendly because less material per tablet is used. In addition,

recyclable foils with around 90% mono-material have been developed, but these materials fall short of Elanco's product protection standards.

The solution is occasionally used in the human health industry, but no example for such solutions is found currently in the animal health market (see Chapter 4).

The aspects mentioned above and in chapter 6.7 are summarized according to the fulfillment of the different aspects. The results for flexible, single-dose solution A are summarized in Table 14.

Table 14: Summary rating – Solution 7

Attribute	Rating	Attribute	Rating
Product protection	3	Technical feasibility	4
User friendliness	4	Costs	4
Marketing	4	Environmental impact	3
Regulatory	4	Novelty	3

7.1.9 Solution 8 – Flexible, Multi-dose Solution

The closing system in this solution does not form a complete seal, so product protection is considered lower than blister packaging. It does not protect the tablet from mechanical damage (Expert E14, 2020).

The child resistant version of the closure (solution 8A) is difficult to open at these smaller sizes and there is limited opportunity for storytelling. From a usability perspective, the solution is comparable to multi-dose solutions, such as bottles (Expert 3, 2020; Expert 4, 2020). This solution is easy to register if all necessary tests, like dust formation, are successfully evaluated (Expert 5, 2020; Expert 6, 2020).

The implementation of multi-dose solution 8 is technically feasible but, it is requires high investments because the existing contract manufacturer does not have filling lines for this solution. Furthermore, the production of the child resistant version is challenging from a technological point of view (Expert 17, 2020; Expert E9, 2020). The material is made of multilayered aluminum foil, but the amount of packaging material per dose is minimized (Expert E9, 2020).

The aspects mentioned above and in chapter 6.8 are summarized according to the fulfillment of the different aspects. The results for solutions 8 are summarized in Table 15.

Table 15: Summary rating – Solution 8

Solution 8A - Flexible, multi-dose solution A			
Attribute	**Rating**	**Attribute**	**Rating**
Product protection	2	Technical feasibility	3
User friendliness	2	Costs	3
Marketing	3	Environmental impact	4
Regulatory	4	Novelty	2
Solution 8B – CR flexible, multi-dose solution B			
Attribute	**Rating**	**Attribute**	**Rating**
Product protection	2	Technical feasibility	2
User friendliness	1	Costs	2
Marketing	3	Environmental impact	4
Regulatory	4	Novelty	3

7.1.10 **Solution 9 – Flexible, Single-dose Solution B & C**

This single-dose solutions are made of aluminum foil and their barrier properties are comparable to blisters. The product is easy for the consumer to use and can be easily carried around. From a marketing perspective, solution 9A have some negative images associated by the consumer (Expert 4, 2020).

Solution 9A are perceived by consumers to resemble candy packaging. In the same way, solution 9B can resemble packages of sugar or granules rather than tablets. Both flexible single-dose packages are easily implemented from a regulatory point of view because similar products already exists on the market. The technical feasibility is rated higher for solution 9B because CMOs that have already implemented the equipment were evaluated already(Expert 8, 2020; Expert E18, 2020).

From a material costs perspective, solution 9A and solution 9B approximately equal in cost. Solution 9B are packed faster because more lines can be packed simultaneously. The line speed comes with slightly higher investment costs because the solution is usually not adapted to tablets and are more used for granules. The solution is easy to implement from a regulatory point of view because it is a single-dose solution with a good barrier protection (Expert 5, 2020; Expert 6, 2020).

As described in chapter 3.2.1, solution 9A is already found on the animal health market.

The aspects mentioned above and in chapter 6.9 are summarized according to the fulfillment of the different aspects. The results for the single-dose solutions are summarized in Table 16.

Table 16: Summary rating – Solution 9

Solution 9A - Flexible, single-dose solution B			
Attribute	**Rating**	**Attribute**	**Rating**
Product protection	3	Technical feasibility	3
User friendliness	3	Costs	3
Marketing	2	Environmental impact	3
Regulatory	4	Novelty	2
Solution 9B - Flexible, single-dose solution C			
Attribute	**Rating**	**Attribute**	**Rating**
Product protection	3	Technical feasibility	2
User friendliness	3	Costs	4
Marketing	2	Environmental impact	3
Regulatory	4	Novelty	3

7.1.11 Solution 10 – Rigid, Multi-dose Can A

Rigid, multi-dose can A has, compared to blisters, poor product protection, although it is user friendly and easy to market. From a regulatory point of view, this solution is an unconventional solution for tablets and therefore harder to register. Solution 10 is also common as candy packaging, which adds to the risk for misuse (Expert 5, 2020). Compared to other solutions, the rigid, multi-dose can A is much more expensive and investment in new technologies for automated packing would be required. Conversely, this solution is highly favorable from an environmental point of view because it is made of mono-materials. The solution has not been implemented in the pharmaceutical packaging industry for tablets.

The aspects mentioned above and in Chapter 6.10 are summarized according to the fulfillment of the different aspects. The results for solution 10 are summarized in Table 17.

Table 17: Summary rating – Solution 10

Attribute	Rating	Attribute	Rating
Product protection	2	Technical feasibility	3
User friendliness	2	Costs	1
Marketing	3	Environmental impact	3
Regulatory	2	Novelty	4

7.1.12 Solution 11 – Rigid, Multi-dose Can B

The solution 11 has good barrier properties, but the small diameter leads to a huge headspace, which in turn compromises the product protection. From a consumer and marketing perspective, the solution is large and already affiliated with coffee, milk and Nespresso® capsule[35]. Generally, it is easy to register this solution, but the headspace is too large. The solution requires a lot of unnecessary material per tablet and is cost-intensive, both in the investment of new lines and in the production packaged products. Similar solutions are already found for effervescent tablets in the animal health industry (see Figure 44).

[35] Nespresso® is a company focused on coffee machines and coffee capsules. Nespresso® belongs to the Nestlé Group. Nespresso® is widely known for their coffee capsules (Nespresso (2020).

Figure 44: Effydral (ApoAnimal, 2020)

The aspects mentioned above and aspects mentioned in Chapter 6.11 are summarized according to the fulfillment of the different aspects. The results for the solution 11 are summarized in Table 18.

Table 18: Summary rating – Solution 11

Attribute	Rating	Attribute	Rating
Product protection	2	Technical feasibility	2
User friendliness	1	Costs	1
Marketing	2	Environmental impact	1
Regulatory	3	Novelty	2

7.1.13 **Solution 12 – Semi Flexible Solution**

The semi flexible solution has similar product protection properties as bottles because they are made of similar materials . No material with higher barrier properties, such as aluminum, can be used. The multi-dose solution can be reclosed, but it loses protection against oxygen and moisture.

The solution approaches an elderly-friendly and easy to open solution. Ease of opening stems from large opening features that enable one-handed opening, as well as improved handling for people with physical disabilities. The solution is designed from a consumer-centric mindset. Opportunities for storytelling and improved handling would generate marketable qualities (Cernic, Kogawa, & Salgado, 2018; Expert 3, 2020).

From a regulatory point of view, the solution cannot be changed during a regular yearly inspection but would require a total resubmission of the product with all necessary studies (i.e. stability) and documentation (see Chapter 2.1.4).Presently, a new tablet in this solution could be implemented, but there would be risks. Losing moisture and oxygen protection after the first opening is a risk for all multi-dose solutions, the solution 12 notwithstanding (EMA, 2020c; European Commission, 2008; Expert 5, 2020).

From a cost perspective, the solution is not acceptable because Company ES4 requires designing costs and royalties for the use of their product. In addition, investments in new machinery would have be made. The solution is slightly better than blister from an environmental perspective it mainly uses mono materials, which can be recycled (Expert 17, 2020; Expert E8, 2020).

The solution is used already in the food and fast consumer goods industry for sauces or powders in the kitchen. The packaging is used as well for dressings and baby food powders.

The aspects mentioned above and in Chapter 6.12 are summarized according to the fulfillment of the different aspects. The results for the Solution 12 are summarized in Table 19.

Table 19: Summary rating – Solution 12

Attribute	Rating	Attribute	Rating
Product protection	2	Technical feasibility	2
User friendliness	4	Costs	1
Marketing	4	Environmental impact	2
Regulatory	3	Novelty	4

7.2 Summary of the Assessment

In Table 20, the assessments (E) of the new packaging solutions are compared with the current blister packaging. An overall score was calculated by using a weighted sum. All requirements are weighted according their importance (I). All solutions that do not fulfil one of the aspects (score = 1) are considered unsuitable. Secondary requirements, such as environmental impact and novelty, are excluded from this rule.

Alternatives marked orange don't fulfil at least one aspects, while those marked gray have a lower overall score than the current blisters, but have been fulfilling all aspects to a certain extend. Solutions marked green are considered better than or similar to the current blister. These solutions are the most promising. In total, 10 out of 22 solutions are promising. Solution 7 was identified as the most promising solution and is marked in dark green in the following Table.

Table 20: Summarizing of the assessment – part 1

Solutions	Product Protection		Regulatory		User Friendliness		Marketing		Costs		Tech. feasibility		Environ-ment		Novelty		Score
	I	E	I	E	I	E	I	E	I	E	I	E	I	E	I	E	
Al Blister	3	3	3	4	2	3	2	2	2	3	2	4	1	1	1	1	47
Solution 1A	3	3	3	4	2	4	2	4	2	2	2	4	1	1	1	2	52
Solution 1B	3	2	3	3	2	4	2	4	2	2	2	3	1	1	1	2	44
Solution 2A	3	3	3	4	2	4	2	3	2	3	2	3	1	1	1	2	50
Solution 2B	3	3	3	3	2	4	2	4	2	2	2	2	1	1	1	4	47
Solution 3A	3	3	3	4	2	4	2	4	2	2	2	4	1	1	1	2	52
Solution 3B	3	3	3	4	2	4	2	4	2	3	2	4	1	1	1	2	54

Table 21: Summarizing of the assessment – part 2

Solutions	Product Protection		Regulatory		User Friendliness		Marketing		Costs		Tech. feasibility		Environ-ment		Novelty		Score
	I	E	I	E	I	E	I	E	I	E	I	E	I	E	I	E	
Solution 4A	3	4	3	4	2	3	2	2	2	1	2	2	1	1	1	3	44
Solution 4B	3	4	3	2	2	3	2	3	2	1	2	2	1	1	1	3	40
Solution 4C	3	3	3	1	2	4	2	4	2	1	2	2	1	1	1	4	39
Solution 4D	3	4	3	2	2	3	2	1	2	1	2	3	1	1	1	4	39
Solution 5A	3	3	3	4	2	2	2	4	2	3	2	4	1	4	1	3	54
Solution 5B	3	3	3	4	2	2	2	4	2	3	2	4	1	4	1	3	54
Solution 5C	3	1	3	3	2	4	2	4	2	1	2	3	1	1	1	3	40
Solution 6	3	2	3	4	2	2	2	1	2	3	2	2	1	4	1	3	41

Table 22: Summarizing of the assessment – part 3

Solutions	Product Protection		Regulatory		User Friendliness		Marketing		Costs		Tech. feasibility		Environ-ment		Novelty		Score
	I	E	I	E	I	E	I	E	I	E	I	E	I	E	I	E	
Solution 7	3	3	3	4	2	4	2	4	2	4	2	4	1	3	1	3	59
Solution 8A	3	2	3	4	2	2	2	3	2	3	2	3	1	4	1	2	46
Solution 8B	3	2	3	4	2	1	2	3	2	2	2	2	1	4	1	3	41
Solution 9A	3	3	3	4	2	3	2	2	2	3	2	3	1	2	1	3	48
Solution 9B	3	3	3	4	2	3	2	2	2	4	2	2	1	3	1	3	49
Solution 10	3	2	3	2	2	2	2	3	2	1	2	3	1	3	1	4	37
Solution 11	3	2	3	3	2	1	2	2	2	1	2	2	1	1	1	2	30
Solution 12	3	2	3	3	2	4	2	4	2	1	2	2	1	2	1	4	43

The final score of the alternatives is visualized in the following graph (see Figure 45). The combination of different improvement features leads to the increased overall score of an alternative. For example, attributes that aimed to improve the current aluminum blister can be implemented in the blister alternatives as well.

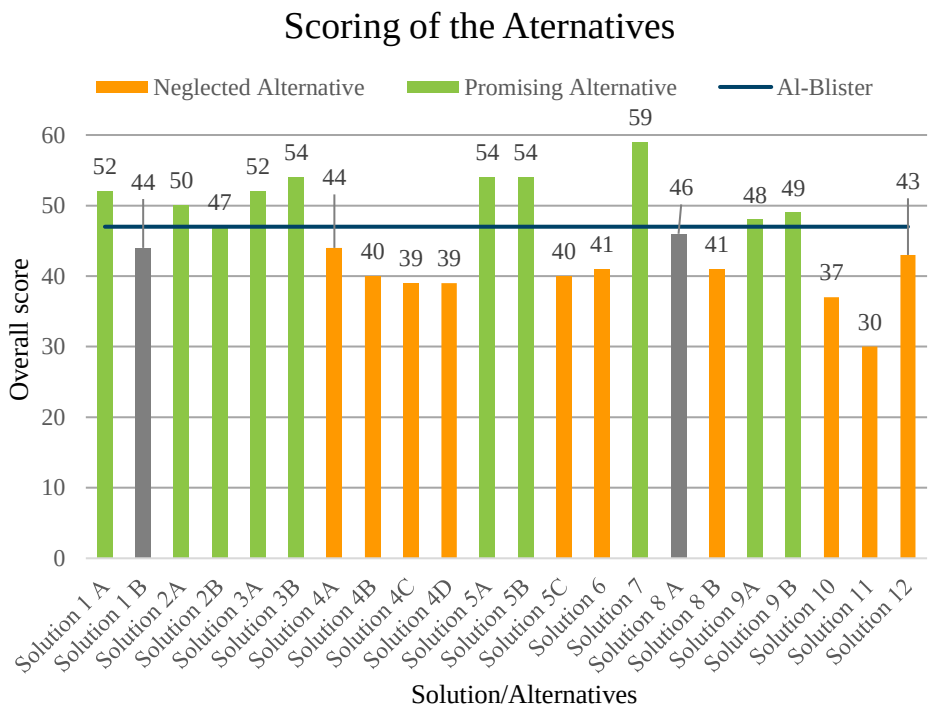

Figure 45: Scoring alternatives

Ten of the 22 alternatives were modifications to the current aluminum blister (solution 1 to 4). These alternatives seemed to have more potential than completely replacing the blister. They retain the advantages of the blister while improving its visual appeal. Only the active blisters solutions did not follow this trend and scored worse than the blister due to the technical difficulties they cause, rendering them suitable only to special cases.

Colored blister (see Figure 46) solutions achieved a particularly high score. Such solutions are more favorable to implement for Elanco due to time and investment.

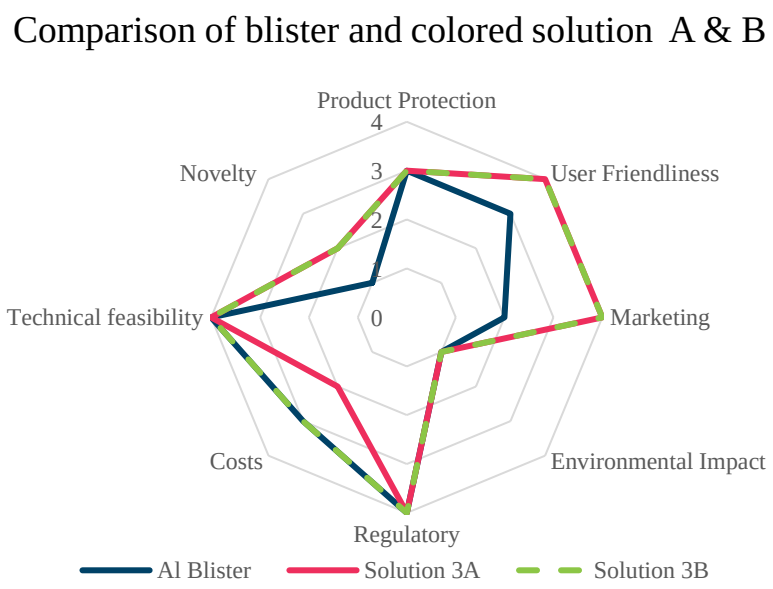

Figure 46: Direct comparison of colored blisters with the current blister

Alternative multi-dose solutions generally had low scores. The consumer insight study has confirmed that single–dose units are preferred. For multi-dose systems, it is generally more challenging to provide sufficient product protection and user friendliness, although the bottle is widely accepted and used.

Bottles and flexible single-dose units, such as solution 7, solution 9A and solution 9B are scored higher than the current blister. The assessment found that the manufacturing process of the rigid, multi-dose bottle did not affect its score in this evaluation. Similarly, there was no major difference in score between flexible, single-dose solution B and C. Surprisingly, the flexible, single-dose solution A is scored much higher than the other flexible, single-dose unit alternatives.

Flexible, single-dose solution A packaging are the most promising solution compared to all other alternatives. They bring improvements in user friendliness, marketing, environmental friendliness, costs and novelty (see Figure 47). Solution 7 is scored higher than blisters in the most important aspects and, in Environmental impacts, solution 7 is scored high again due to the decreased material used per dose. The environmental impact of the solution can be further decreased with the application of mono-materials and the elimination of the aluminum.

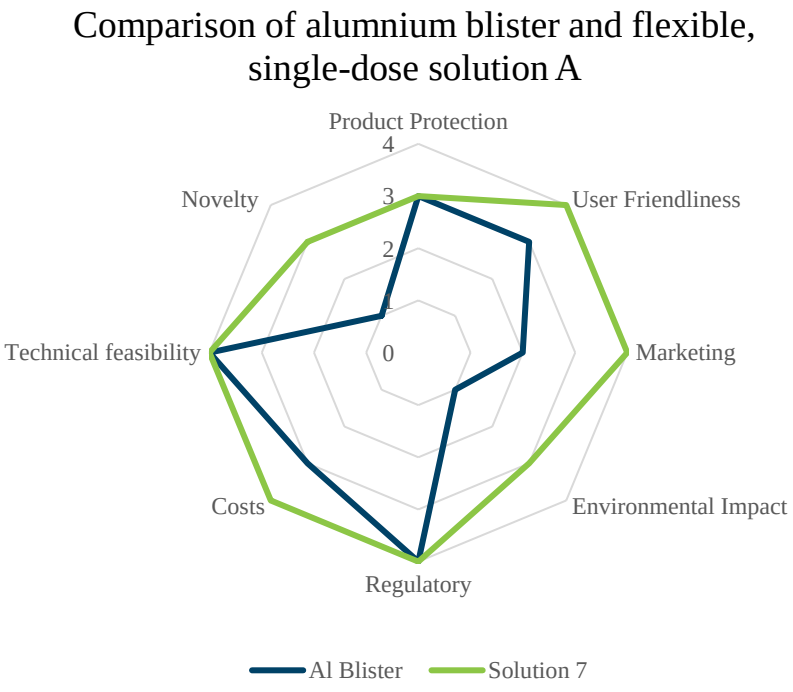

Figure 47: Direct comparison of Solution 7 with blister

During this analysis, it was determined that user-friendliness and cost are the driving aspects in the overall score of a particular packaging solution.

8 Discussion

In this chapter the area of innovation, relations between the assessed aspects and limitations of the assessment is discussed further. The chapter contains also a comment on environmental impact of packaging.

8.1 Area of Innovation

At the beginning of this thesis, it was assumed that improvement of blister packaging can only be done with new materials and improved opening technologies. During discussions with experts and further elaboration, it was encountered that improvement possibilities of blisters are various. Current blister packaging can be improved by increasing brand recognition, consumer attributes and by increasing product protection, which leads to increased shelf life. It was encountered that consumers are not caring about the primary packaging of pharmaceutical products, but it was found that small improvements are able to improve the consumer centricity of the blister.

During the elaboration of the topic it was recognized, that innovation and development in the pharmaceutical packaging area are limited. The main limitations comes from regulatory, product protection and costs. Product development processes in the pharma industry a time and cost intensive and has to be funded by the high margin of products on the market. The decrease of the product margins due to higher packaging costs is therefore often neglected.

8.2 Relations Between the Assessed Aspects

As a rule, the novelty of a technology and the ease of passing it through a regulatory body stand opposed to each other: entirely new solutions require an extensive process in order to achieve approval for use. While this has held true in some cases, overall, in regards to packaging, there has been no significant relationship found, possibly because the actual changes in package are functionally small. The same rule of inverse relationships was theorized for cost/technical feasibility and product protection/environmental friendliness. This evaluation has found no significant relationship in any of these cases, though, in the case of product protection, this is an ineffective assumption because packaging solutions that were environmentally friendly but did not confer adequate product protection were not evaluated in this assessment.

8.3 Limits and Comments of the Assessment

In this chapter, the limits of these assessments are discussed as well as where the failure sources in the assessment are.

8.3.1 **Specificity of the Alternatives**

Some alternatives present a broad range of shapes and appearances for the final product and, depending on the specific selections, the evaluation might return slightly different results. For example, the technical feasibility of different blister shapes is depending on the design. Rounding of the corners is easily implemented while shaping the blister like a specific form is much more challenging. Depending on the degree in special the technical feasibility, regulatory and costs are changing.

Another example is the bottle. If the Elanco-specific bottle consists of a special shape, it is easy and cheap to implement, but if it were to be a triangle, for example, then the solution is nearly impossible to realize technically. As such, changes in the technical complexity of the package will affect the cost and the regulatory pathway.

8.3.2 **Regional Differences**

Regional differences in regulatory, consumer behavior and marketing exists. Although the trend of globalization and harmonization will see these regional discrepancies decrease, they still exist and remain relevant today (Hanf & Winter, 2017; Usunier, 2001). This project attempted to maintain an international perspective where possible but was primarily focused on Europe and the USA. The effect of environmentally friendly packages is also highly dependent on where the product is sourced and where it is disposed (Barik, 2019; Prakash, Siddharth, & Gunasekar, 2019). To elaborate further on this project a defined target group /target market should be defined.

8.3.3 **Costs**

Due to the early nature of the project, it is difficult to estimate costs. Costs must be are based on a concrete and defined business case. To elaborate upon this thesis, a detailed cost analysis of any selected alternatives is recommended.

8.3.4 Diversity of Solutions

The previously describe alternatives are best suited to different applications as they are designed with different uses in mind. Therefore, without specific business cases, they are difficult to compare, especially in regards to ranking user friendliness, cost and technical feasibility.

Some features were hard to compare because the solutions were fundamentally different, such as ease of opening of a multi-dose package compared to a single-dose package. In particular, there can be no ranking of the re-closability of single-dose package.

8.3.5 Objectiveness of Experts

The external experts are not totally objective in their evaluations and answers because they have a personal interested in the implementation of their technology. Internal experts at Elanco, likewise, are not completely objective because they have their personal preference and have often made efforts to broaden their opinions.

8.3.6 Limited of Consumer Research

Due to the limited amount of research available on the influence of packaging features on consumer behavior in pharmaceutical area, research from food packaging or other fast consumables is widely used to assess packaging solutions.

8.4 Comment on Environmental Impact

Environmental friendliness is a rising trend in the pharmaceutical industry and has been seen as important to the consumer (see chapter 5). During the search for alternatives, environmentally friendly solutions were often found, but their level of product protection was lower than current packaging systems used at Elanco and would have a negative impact on stability.

Elanco, has not yet a global environmental strategy for packaging. Elanco must decide to focus their strategy on either recyclability of materials, material reduction, bio-based material or biodegradable materials. Also a combination of the different strategies is possible.

In the use of alternative materials (see Figure 48), it has to be distinguished between new bio based polymer materials, which are fully or partially made from biomass and biodegradable materials, which can be degraded in industrialized composting plants (Hellström & Olsson, 2017; Plastics New Zealand, 2020; Reddy, Vivekanandhan, Misra, Bhatia, & Mohanty, 2013).

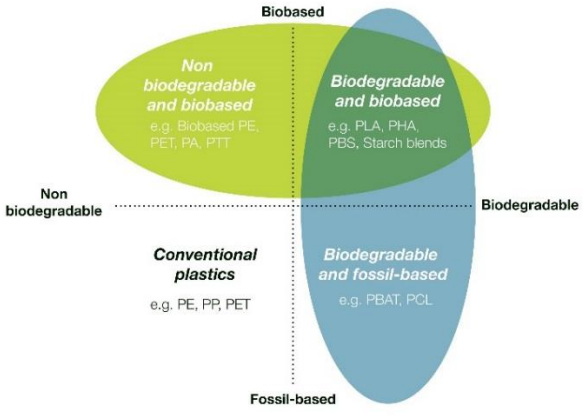

Figure 48: Overview of biodegradable and biobased materials (Plastics New Zealand, 2020)

In this project, environmentally friendly has been defined as the use of mono-materials and material reduction. The European Union has identified material reduction as a major step towards a zero waste society. This measurements have been seen as the most effective on a global scale, without taking local circumstances into account. Taking the resource of the material into account was not possible, due to the high level of the analysis and due to the different material supplier for a global player in the animal health sector (Hellström & Olsson, 2017; Taufik, Reinders, Molenveld, & Onwezen, 2020; Verghese, Lewis, & Fitzpatrick, 2012; Zero Waste Europe, 2020).

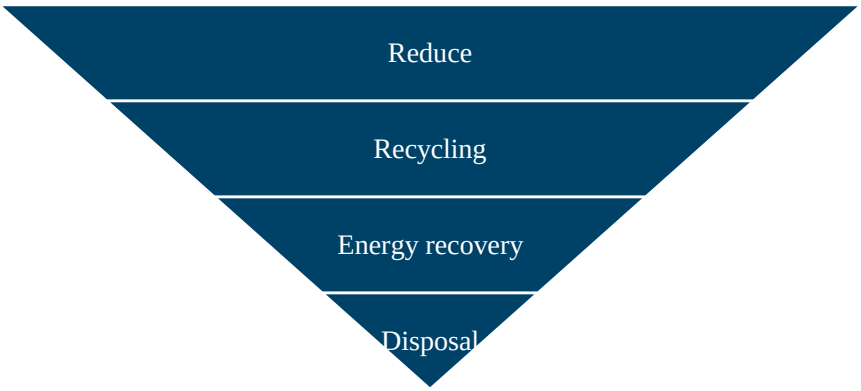

Figure 49: Zero waste hierarchy according to the EU (Zero Waste Europe, 2020)

9 Conclusion & Recommendation

This assessment of alternative packaging solutions has highlighted the difficulties for packaging innovators in the pharmaceutical industry and the need therein for them to succeed in their innovations. It is essential to differentiate from the competitor. An improved package can improve the performance of a product and gain, therefore, a larger market share (Ahmed, 2002).

The assessment of the alternatives shows that flexible single-dose solutions, colored blisters and branded bottles have a high potential to replace aluminum blister packaging in the future. The most promising packaging solution should be evaluated further with specific business cases. Prototyping and a consumer insight study will be necessary to narrow the wide field of options. In future, a parallel design approach will be used to further develop a packaging alternative for the aluminum blister. Some attributes or solutions can be combined and implemented in various alternatives.

Although some solutions present technical challenges that limit their immediate use. They still warrant consideration, since some special application may be interesting in the future. Others solutions may not be relevant for all OSDs, but may be applicable to specific products with special requirements. A reevaluation is necessary considering each product.

In this thesis, many different topics have been mentioned that deserve more research and development from academia, but Elanco should make efforts to engage in this research as well. In general, the influence of packaging attributes on consumer behavior in a pharmaceutical background is poorly studied. Studies on the effect of unused drug products and the marketing is necessary.

Consumer behavior in medicine represents a large area in which academia has not initiated research, possibly due to such studies being kept confidential by the pharmaceutical companies that conduct them.

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Appendix A Expert Interview

A.1 Expert Interviews – Elanco

The following table (see Table 23) gives an overview, with which experts in Elanco have been interviewed. The table details where each expert's guidance questions can be found and what area of development they represent.

Table 23: Elanco internal expert Interviews in the different expert areas

Expert area	Expert	Company	Date	Guidance question
Consumer behavior	Expert 1	Elanco	24-02	A.1.1.1
	Expert 2	Elanco	26-02	A.1.1.2
Marketing	Expert 3	Elanco	17-02	A.1.1.3
	Expert 4	Elanco	04-03	A.1.1.4
Regulatory	Expert 5	Elanco	26-02	A.1.1.5
	Expert 6	Elanco	18-02	A.1.1.6

ACE	Expert 7	Elanco	07-04	A.1.1.7
Research and Development	Expert 8	Elanco	22-02.	A.1.1.8
	Expert 9	Elanco	24-02	A.1.1.9
	Expert 10	Elanco	29-02	A.1.1.10
	Expert 11	Elanco	29-01	A.1.1.11
	Expert 12	Elanco		
	Expert 13	Elanco	29-01	A.1.1.12
	Expert 14	Elanco	28-01	A.1.1.13
	Expert 15	Elanco	14-04	A.1.1.14
	Expert 16	Elanco	28-02	A.1.1.15
Procurement	Expert 17	Elanco	24-03	A.1.1.16
	Expert 18	Elanco	16-03	A.1.1.17

A.1.1 Guidance Questions

In the following chapter, the guidance questions for the external interviews have been listed.

A.1.1.1 Expert 1 – Interview from 24-02-2020

- Who is the target group of Elanco?
- What is the Elanco consumer thinks about blister Packaging?
- How is the consumer purchasing the Elanco products?
- What is a typical Elanco consumer look like?
- What packaging features is the consumer looking for?

A.1.1.2 Expert 2 – Interview from 24-02-2020

- What are common consumer complaints from a packaging side?
- What is the opinion of B2B consumers on Elanco packaging?
- What is the opinion of veterinarians on the blister packaging?

A.1.1.3 Expert 3 – Interview from 17-02-2020

- What is the role of marketing in the pharmaceutical industry?
- What is the most important information regarding marketing in the pharmaceutical area?
- How is marketing in the pharma industry differentiating from marketing in the other sectors?
- What do you think about the alternatives from a marketing perspective?

A.1.1.4 Expert 4 – Interview from 04-03-2020

- What are the most important features for the consumer?
- What is a no go for consumers in the B2B but also to the end consumer?
- What do you think about the alternatives from a marketing perspective?

A.1.1.5 Expert 5 – Interview from 26-02-2020

- How is the packaging in the pharmacy regulated?
- What are the differences between regulation from the EU and CVM?
- What do you think from a regulatory point of view of the different alternatives?
- How do single-dose and multi-dose solutions differ?

A.1.1.6 Expert 6 – Interview from 18-02-2020

- What information are necessary to but on the primary packaging in the pharmacy?
- How changes in the packaging are communicated to the authorities?
- What are the most important regulations to keep in mind at primary packaging?
- What do you think from a regulatory point of view of the different alternatives?

A.1.1.7 Expert 7 – Interview from 07-04-2020

- What is ACE and what are you doing?
- Why is the department separated from R&D?
- How do you choose the projects that you are working on in ACE?
- How is ACE organized?

A.1.1.8 Expert 8 – Interview from 22-02-2020

- What is the project about?
- What is the reason behind the projects?
- What should be my part of the project?
- How is the R&D department in Elanco organized?

A.1.1.9 Expert 9 – Interview from 24-02-2020

- What are the current solutions that you have been looking into?
- Why have you chosen this solution?
- With which supplier are you already in contact?
- Where did you find these solutions?

A.1.1.10 Expert 10 – Interview from 29-02-2020

- What are the most common failures of products within Elanco?
- How are you supporting other departments by the experimental design?
- What kinds of tests have been done in Elanco?

A.1.1.11 Expert 11& Expert 12 – Interview from 29-01-2020

- How product formulation does influence packaging development?
- What are the current trends in product development?
- What steps are done at product development?
- What are the common indices of failure in the tablet industry?
- What should a pharma packaging have for you from a formulation point of view?
- What are the current problems you encounter with the aluminum blister?

A.1.1.12 Expert 13 – Interview from 29-01-2020

- What is the analytic department doing within Elanco?
- What are the difficulties in the development of analytical techniques?
- What are the important aspects you have encountered that should be kept in mind at the development of new packaging systems?

A.1.1.13 Expert 14 – Interview from 28-01-2020

- How is the stability of the drugs tested in Elanco?
- In which climate zones are stability tests carried out?
- What are the risks of the degradation of tablets?
- What are the indices of failure at tablets?
- How satisfied are you with aluminum blisters from a stability point of view?

A.1.1.14 Expert 15 – Interview from 14-04-2020

- What perspectives have to be taken into account regarding quality?
- How does quality differ in the pharma industry from other industries?
- What problems have you already encountered regarding packaging?
- What are the reasons for complaints from the consumer regarding packaging?

A.1.1.15 Expert 16 – Interview from 28-02-2020

- How is open innovation handled in Elanco?
- Where are the innovation project coming from?
- How could packaging innovation be handled in the future?

A.1.1.16 Expert 17– Interview from 24-03-2020

- Where does our suppliers seat?
- What are the requirements for Elanco supplier?
- Which solution are from a procurement view most feasible?

A.1.1.17 Expert 18 – Interview from 16-03-2020

- How do you choose Elanco current suppliers?
- What have been procurement issues in the past?
- What business cases have you already evaluated regarding primary packaging?

A.2 Expert Interviews – External

The following table (see Table 24) gives an overview, with which external experts an interview was hold. The table details where in the appendices each expert's guidance questions can be found and what area of development they represent.

Table 24: External expert interviews in different expert areas

Expert area	Expert	Company	Date	Guidance question
Tooling company	Expert E1	Company ET1	12-03	A.2.1.1
	Expert E2	Company ET2	12-02	A.2.1.2
	Expert E3	Company ET3	18-03	A.2.1.3
Supplier	Expert E4	Company ES1	19-03	A.2.1.4
	Expert E5	Company ES2	02-04	A.2.1.5
	Expert E6	Company ES3	20-03	A.2.1.6
	Expert E7			
	Expert E8	Company ES4	01-04	A.2.1.7
	Expert E9	Company ES5	18-03	A.2.1.8

	Expert E9	Company ES5	24-03	A.2.1.9
	Expert E10			
	Expert E11	Company ES6	11-03	A.2.1.10
	Expert E12			
	Expert E13	Company ES7	06-03	A.2.1.11
	Expert E14	Company ES8	17-03	A.2.1.12
	Expert E15	Company ES9	25-02	A.2.1.13
	Expert E16	Company ES10	27-03	A.2.1.14
	Expert E17	Company ES11	16-04	A.2.1.15
CMOs	Expert E18	Company EC1	06-03	A.2.1.16

A.2.1 Guidance Question

In the following chapter, the guidance questions for the external interviews have been listed.

In the following chapter, the guidance questions for the external interviews have been listed.

A.2.1.1 Expert E1 – Interview from 12-03-2020

- How is possible to implement the alternatives which are related to changes in tooling?
- What are the particularities for solution 7?
- How does embossing influence the blister line?
- How does die-cutting influence the blister line?

A.2.1.2 Expert E2 – Interview from 12-02-2020

- How is possible to implement the alternatives which are related to changes in tooling?
- How does embossing influence the blister line?
- Is there any difference from a technical point of view where the embossment is placed?
- How does die-cutting influence the blister line?

A.2.1.3 Expert E3 – Interview from 18-03-2020

- At what step can modified atmosphere packaging be applied?
- How does the application of MAP influences the packaging speed?
- Is MAP already applied in blister packaging lines?
- How can the current blister packaging lines be modified for MAP?

A.2.1.4 Expert E4 – Interview from 19-03-2020

- What kind of scavengers exists?
- What is the working principle for the scavenger?
- How can scavengers be applied?
- What is the shelf life of scavengers?
- Does scavenger influence the maschinability?

A.2.1.5 Expert E5 – Interview from 02-04-2020

- Is it possible to have a Elanco specific bottle?
- What are the design costs and how long would it go?
- What techniques could be used to make bottles and how are they differing?

A.2.1.6 Expert E6 & Expert E7 – Interview from 20-03-2020

- What materials are you using for solution 7?
- How can solution 7 be applied for child resistance?
- What are the limits for flexible, single-dose packaging solution A?

A.2.1.7 Expert E8 – Interview from 01-04-2020

- What is your company about?
- What differs in your solutions from the rest?
- How can be child resistance be applied at the solution?

A.2.1.8 Expert E9 – Interview from 18-03-2020

- What different blister foils do you have?
- How can blister foils be modified?
- Does colored blister foil have an impact?
- What other alternatives could you supply?

A.2.1.9 Expert E9 & Expert E10 – Interview from 24-03-2020

- What kind of flexible materials do you supply?
- How can this solution be made in a child resistant way?
- What are your solutions for single usage flexible packaging?

A.2.1.10 Expert E11 & Expert E12 – Interview from 11-03-2020

- What sizes can the bottle be supplied?
- How is the bottle made?
- How is can be scavengers applied?
- How does the dispenser system work?

A.2.1.11 Expert E13 – Interview from 06-03-2020

- How can the blister foil be colored?
- What coloring methods exist?
- Does coloring influences the packaging line?
- What are the newest development in child resistance of blisters?

A.2.1.12 Expert E14 – Interview from 17-03-2020

- What are the minimal sizes of re-closable pouches?
- What kind of re-closing system are you using?
- How can the pouch be made child resistant?

A.2.1.13 Expert E15 – Interview from 25-02-2020

- How is the tin can be made?
- How can a first opening experience be assured?
- How can the barrier properties be assured?

A.2.1.14 Expert E16 – Interview from 27-03-2020

- What kind of child resistant closing solutions are you offering?
- What is the difficulties in child resistant opening features?
- Was it already examined in the past? Which sizes?

A.2.1.15 Expert E17 – Interview from 16-03-2020

- How can the solution be implemented?
- What kind of bags are you producing?
- What is the minimal size?

A.2.1.16 Expert E18 – Interview from 06-03-2020

- How does the different alternatives behave in the packing line?

Appendix B Consumer Survey

B.1 Consumer Survey - Question

Age: _____ Sex: _____ Date: _____

What is your nationality? _____ Where do you live? _____

How often do you use medicaments in a week? _____

When was the last time that you opened a pharmaceutical packaging? _____

For whom do you use them the most?

Myself	
Partner	
Children	
Parents or elderly people	
Companion animal	
Farm Animal	
Others	

What kind of primary packaging do you see when you use pharmaceuticals?

Glass bottles	
Plastic bottles	
Blister	
Tubes	
Sachets	
Others	

Do you have any companion animals? _____

How often do you give your CA drugs in a year? _____

Showing blister packaging at this moment

What is the most important thing for you when you think at pharmaceutical packaging?

_____

How satisfied are you with Blister packaging? On a scale from 1 to 5. _____

How easy do you find this kind of packaging to use? On a scale from 1 to 5. _____

How satisfied are you with the current blister packaging Design? On a scale from 1 to 5. _____

How important is a the packaging for you when you buy medicaments? On a scale from 1 to 5. _____

Is an improved version of the packaging a unique selling point for you?_____

If yes, would you spent more money for it? _____

What kind of problem do you see the most with this kind of packaging systems?

_____

_____

_____

What borders you the most when you are using blister packaging?

_____

_____

_____

What do you like at blister packaging of packaging system?

_____

_____

_____

Can you give an example for a **good** packaging in the food or in the pharmaceutical area?

_____

_____

_____

Can you give an example of a **bad** packaging? For example one where you got angry. Why?

_____

_____

_____

B.2 Consumer survey - Answers

The age of the interviewees varies from the mid-twenties to mid-fifties. The interviewees are European citizens and are mainly living in Switzerland (except one). The interviews have been hold between the 25th February 2020 and the 28th March. The interviewee are using medicaments daily (28.6%), once per week (14.2%), once per month (28.6%) or occasionally (28.6%). At the point of the interview, all panelists have been using pharmaceutical products within a week. All panelists are familiar with blisters. Amon blisters the also use plastic bottles, tubes and glass bottles.

In the following chapter, the different answers of each panelists are summarized.

B.2.1 Panelist 1

The panelist has two cats and it is 54 years old. The panelist, originally from Germany, currently lives in Switzerland and uses medicine every day for herself. The panelist is most familiar with Blisters, specifically one that is transparent.

For the panelist, a good package which is easier to open that the competitor's would be a USP. The panelist is primarily interested in packaging which is easy to empty and which enables a good usage. The main negative point in packaging that the panelist has experienced is that they are hard to open.

The hard to open feature is also the main disadvantages found in the blister packaging. The panelist has already had one experience where she was not able to open the blister and needed a scissor. The panelist complained about the huge space that blister packaging takes compared to other solutions. On the contrary, the panelists acknowledge the good barrier properties of the aluminum blister packaging solution.

B.2.2 Panelist 2

The panelist comes from Switzerland and she is 42 years old. The panelist is using medicaments on a daily basis and has last experienced them a day ago. The panelist is using them for herself and uses mostly blisters. A Pharmaceutical cream, packaged in a tube, is also used.. The panelist has no companion animals.

The most important features for her are that the packaging is safe and that the drug products are individually packaged. In addition, an elderly-friendly opening mechanism is important because the panelist remembers that her grandmother has had problems to open the packaging on her own medications when she was 80 years old. The packaging should also be labeled in a readable way, but overall the protection of the medicine is the most important aspect. The panelist favors packages which are easy to empty and which are well apportioned. According to the panelist, a package should not require any extra tools to open it.

For blister packaging, the panelist sees that they are not space efficient and they produce a lot of waste. On the other hand, blister packaging has the advantage of being good protection to the environment and are also easy when packaged in individual blisters.

B.2.3 Panelist 3

The panelist is 26 years old and lives in Switzerland. The panelist has neither children nor companion animals. The panelist is mainly used to blister packaging for oral dosage drugs. The panelist uses medications on a daily and weekly basis. The panelist is not concerned at all when he is purchasing drugs products. For the packaging to become a USP, it has to dramatically improve convenience and environmental friendliness of the product. The panelist prefers packaging made from glass and metal because he recognizes that these materials are more

environmentally friendly and safer in terms of plastic additives. The panelist has these same concerns with food products. The panelist didn't see a considerable disadvantage in double-packaging or over-packing.

Generally speaking, blister packaging is adequate because they are handy and convenient to use. By using blister packaging, single dosages can be carried around. The negative aspect of blister packaging is in their usage if they are hard to open and take a lot of space for such small quantities of products.

B.2.4 Panelist 4

The panelist is 36 years old and lives in France. The panelist uses medicaments approximately once a month. At the time of the interview, the panelist had not used pharmaceutical packaging for 2 weeks. The panelist has kids and three dogs, which she treats once a year for worms and ticks. The most important thing is the right dosage for the drug. So, for example, a drug in a liquid dosage form would be preferred less because the dose cannot be counted out. The cost, however, would be the main competitive advantage. The customer typically purchases drugs directly from the Vet due to negative experiences with OTC products in the past.

The panelist perceives blisters as a good packaging solution, but, depending on the usage method, she prefers bottles. Bottles have the advantage to be more volume efficient, but they can also become dirty. The panelist dislikes products which have too much packaging material compared to the tablet size. In addition, a transparent packaging solution would be preferable because it could be checked to see if it is possible to divide the tablets.

B.2.5 Panelist 5

The panelist is 43 years old and lives in Switzerland. The panelist has two children. The panelist uses medications about once a month, but prior to the interview, he had recently used a pharmaceutical product 3 days ago. The panelist is opening the packaging for himself and for his children (under 12). The panelist is most familiar with blisters, and glass and plastic bottles. The bottles are mostly used for liquid drugs, but also creams, powders, and suppositories for children. The panelist also lived in the USA, where he encountered tablets in bottles. For him, the most important thing in pharmaceutical packaging is ease of use and that they are easy to open. Generally, the panelist's biggest concern when it comes to packaging is that they are hard to open. Therefore, he generally dislikes any drug product that uses this packaging solution.

Child resistance for pharmaceutical products is of minor importance for the panelist because he does not trust the child resistance of pharmaceutical products. Overall, the panelist is not interested in the packaging as long as it does not add extra cost.

The panelist sees the main advantage of blister packaging in that they could easily be transported, especially in a single-dose without the secondary packaging.

For the panelist, it is necessary that the future blister packaging has a perforation to be separated easily into single doses. The main negative point for the panelist would be a hard-to-open feature.

The panelist sees great potential in strip pack solutions, as done by Bayer with Aspirin (see Figure 50), and the option to link digitally with the product in order to help at the administrative part.

Figure 50: Aspirin – Strip packing solution

B.2.6 Panelist 6

The panelist is 46 years old and lives in Switzerland. The panelist does not use medicaments often, but from time to time for dietary supplements. At the interview, the panelist had most recently used a pharmaceutical package the day before . Typically she opens the package for herself or, on occasion, for her partner. The panelist is familiar with glass and plastic bottles for food supplements, but pharmaceutical products are seen mostly in blisters. When it comes to pharmaceutical packaging, her main concerns are the protective barrier, the environmental friendliness of the packaging and its size. Overall the packaging of the drug is not important for the panelist and it would only be a USP if there is a major price difference and the product is the same.

The panelist finds blister packaging really easy to use and appreciates the amount of protection they confer. The products are protected in single doses until they are consumed. The major disadvantages are environmental issues and their size. The panelist does not see a reason why blister packaging has to have these huge dimensions.

During the interview, it was also mentioned that in some cases, the expiration dates could not be found on the primary packaging. The panelist would prefer to see tablets in bottles to the avoid over-packing. An important topic for the panelist is also that product is correctly apportioned.

B.2.7 Panelist 7

The panelist has no pets, but she has 2 children. The panelist is mostly opens pharmaceutical packaging for her children. She is not using medicaments herself on a regular basis except for some pills for lactose-intolerance, from which she has most of her experience with pharmaceutical packaging. In addition, the panelist is quite experienced in using children's medicaments. Therefore, the panelist is mostly accustomed to blisters and bottles, but creams in tubes are also commonly seen. For the panelist, the hygienic aspects and safety aspects of pharmaceutical packaging are the most important aspects. The panelist recounted cases in which blisters had to be squeezed, potentially damaging the tablet.

Still, blister packaging remains suitable for the panelist and improvements in packaging would not be a USP to her. In addition, the children's safety aspect for packaging is not a concern, because the children of the panelist have already learned to open child-resistant packaging. According to the panelist, the parents bear the responsibility to ensure that the medicaments cannot be reached by the children.

Generally, the main advantage of the blister packaging is in individually packaged doses. Here the hygienic aspects compared to bottle are a big plus. In bottles, the panelist has to touch more tablets before getting the right amount out. In blisters, the panelist had no problems with in-use stability, while for bottles, stability has been a concern. The biggest problem for the panelist with a blister is that they could damage the tablet. The environmental impact is a minor disadvantage for the panelist.

The panelist prefers packaging, which is easy to open, recyclable and easy to dispose. The panelist has had bad experiences with blisters that have required extra tools (namely a screwdriver) to open and would prefer to see packaging that can somehow be reused.

Appendix C List of Alternatives

The following table gives an overview of all explored alternatives.

Table 25: Overview of the different alternatives

Solution	Description	Description	Description
Solution 1A	Embossing A	Solution 5B	Rigid multi-dose bottle B
Solution 1B	Embossing B	Solution 5C	Rigid, multi-dose bottle C with application feature
Solution 2A	Blister shape A	Solution 6	Tubes
Solution 2B	Blister shape B	Solution 7	Flexible, single-dose solution A
Solution 3A	Colored blister A	Solution 8A	Flexible, multi-dose solution
Solution 3B	Colored blister B	Solution 8B	CR Flexible, multi-dose solution
Solution 4A	Active solution A	Solution 9A	Flexible, single-dose solution B
Solution 4B	Active solution B	Solution 9B	Flexible, single-dose solution C
Solution 4C	Active solution C	Solution 10	Rigid, multi-dose can A
Solution 4D	Active solution D	Solution 11	Rigid, multi-dose can B
Solution 5A	Rigid, multi-dose bottle A	Solution 12	Semi flexible solution

Appendix D Benchmarking

D.1 Animal Health Companies

Table 26: Animal health benchmarking study

No.	Brand	Product	Animal type	Picture	Primary packaging	Secondary packaging	Comments	Source	Picture source
1	Zoetis	Apoquel	Dog		Blister	Folding box		(Zoetis, 2020)	(Imart, 2020)

2	Zoetis	Apoquel	Dog		Bottle	No	Child resistance opening feature	(Zoetis, 2020)	(My Vet, 2020)
3	Zoetis	Banminth Plus	Dog, cat and horse		Blister	Folding box		(Zoetis, 2020)	(Heureka, 2020)
4	Zoetis	Cazitel	Dog and cat		Blister	Folding box		(Zoetis, 2020)	(Tokopedia, 2020)

5	Zoetis	Cazitel	Dog and cat		Blister	Display packaging		(Zoetis, 2020)	(Pet Circle, 2020)
6	Zoetis	Cerenia Tabletten	Dog		Blister	Folding box		(Zoetis, 2020)	(VetDispense, 2020)
7	Zoetis	Clamoxyl Tabletten	Dog and cat		Blister	Folding box	Chewable tablets	(Zoetis, 2020)	(DietVet, 2020a)

8	Zoetis	Cleorobe	Dog		Blister	Folding box		(Zoetis, 2020)	(Covetrus, 2020a)
9	Zoetis	Palladia	Dog		Blister	Folding box	Child resistant opening feature	(Zoetis, 2020)	(Sprzedajemy.pl, 2020)
10	Zoetis	Palladia	Dog		Bottle	No	Chewing tablets	(Zoetis, 2020)	(DietVet, 2020b)

11	Zoetis	Rimadyl	Dog		Bottle		Chewing tablets	(Zoetis, 2020)	(Petco, 2020)
12	Zoetis	Simparica	Dog		Blister	Folding box	Chewing tablets, Blister with 1, 3 or 6 tablets;	(Zoetis, 2020)	(Covetrus, 2020b)
13	Zoetis	Synulox	Dog and cat		Sachet	Folding box		(Zoetis, 2020)	(Pet Drugs Online, 2020)
14	Zoetis	Trocoxil	Dog		Blister	Folding box	Chewing tablets	(Zoetis, 2020)	(Tsokanos SA, 2020)

15	Bayer	Baytril	CA and FA		Bottle	No	Bottle in different sizes and with different quantities	(Bayer, 2020b)	(Bayer, 2020c)
16	Bayer	Drontal	CA		Bottle			(Bayer, 2020b)	(Bayer, 2020c)
17	Bayer	Drontal	CA		Blister	Display packaging	Chewing tablet, single blister;	(Bayer, 2020b)	(Bayer, 2020a)

18	Bayer	Drontal	CA		Blister	Folding box		(Bayer, 2020b)	(Santa Cruz, 2020)
19	Bayer	Drontal	CA		Blister	Folding box	Printed lidding foil	(Bayer, 2020b)	(VegaStore, 2020)
20	Bayer	Drontal	CA		Blister	Folding box	Embossing in the cavity	(Bayer, 2020b)	(Prado Mermoz, 2020)

21	Bayer	Profender	CA		Sachet	Folding box		(Bayer, 2020c)	(Bayer, 2020c)
22	Bayer	Profender	CA		Al Blister	Folding box		(Bayer, 2020c)	(Bayer, 2020c)
23	Bayer	Droncit	CA		Blister	Folding box		(Bayer, 2020b)	(Tienda Animales, 2020)

24	Bayer	Droncit	CA		Blister	Folding box		(Bayer, 2020b)	(Onubense, 2020)
25	Bayer	Advantus	CA		Bottle	Folding box	Chewing tablets	(Bayer, 2020c)	(Medi-Vet, 2020a)
26	Bayer	Alenza	Dog		Pouch	No	Chewing tablets; supplement product;	(Bayer, 2020c)	(Bayer, 2020c)

27	Bayer	Alenza	Dog		Bottle		Chewing tablets, supplement product;	(Bayer, 2020c)	(Jet.com, 2020)
28	Bayer	Quellin	Dog		Bottle		Chewing tablets	(Bayer, 2020c)	(Bayer, 2020c)
29	Bayer	Synovi G4	Dog		Box		Chewing tablets	(Bayer, 2020c)	(Bayer, 2020c)

30	Bayer	Synovi G4	Dog		Pouch		Chewing tablets, re-closable;	(Bayer, 2020c)	(Valley Vet Supply, 2020)
31	Merck Animal Health	Bravecto	Dog		Blister	Folding box	Child resistant opening feature, single blisters, chewable tablets;	(Merck Animal Health, 2020)	(Cheval, 2017)
32	Merck Animal Health	Incurin	Dog		Blister	Folding box	High cavity amount on the blister	(Merck Animal Health, 2020)	(Merck Animal Health, 2020)

33	Merck Animal Health	Orbax	Dog and cat		Bottle	No		(Merck Animal Health, 2020)	(Merck Animal Health, 2020)
34	Merck Animal Health	Panacur	Dog and cat		Bottle	No		(Merck Animal Health, 2020)	(Merck Animal Health, 2020)
35	Merck Animal Health	Safeguard	Dog		Sachet	Folding box	Product to put on food	(Merck Animal Health, 2020)	(Merck Animal Health, 2020)

36	Merck Animal Health	Salix	Dog and cat		Bottle	No		(Merck Animal Health, 2020)	(Merck Animal Health, 2020)
37	Merck Animal Health	Tri-Heart	Dog		Blister	Folding box	Chewable tablets	(Merck Animal Health, 2020)	(Merck Animal Health, 2020)
38	Boehringer Ingelheim Animal Health	Vetmedin	CA		Bottle	Folding box		(Boehringer Ingelheim, 2020)	(Medi-Vet, 2020b)

39	Boehringer Ingelheim Animal Health	Vetmedin	CA		Blister	Folding box		(Boehringer Ingelheim, 2020)	(DietVet, 2020c)
40	Boehringer Ingelheim Animal Health	Nexgard	CA		Blister	Folding box	White Blister with embossing	(Boehringer Ingelheim, 2020)	(Young, 2020)
41	Boehringer Ingelheim Animal Health	Prascend	CA		Blister	Folding box		(Boehringer Ingelheim, 2020)	(Performance Equine, 2020)
42	Boehringer Ingelheim Animal Health	Nexgard spectra	CA		Blister	Folding box	Cavity in special shape	(Boehringer Ingelheim, 2020)	(Shopee, 2020b)

43	Boehringer Ingelheim Animal Health	Heartgard Plus	CA		Blister	Folding box		(Boehringer Ingelheim, 2020)	(ShoppingLane, 2020)

D.2 Human Health Companies

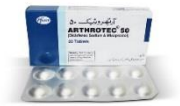
Table 27: Human health benchmarking study

Nr.	Brand	Product	Picture	Primary Packaging	Secondary Packaging	Storage Conditions	Comments	Source	Picture source
1	Pfizer	Accupril		Blister	Folding box	Store at controlled room temperature 15º–30ºC. Protect from light		(Pfizer, 2020c)	(Mims, 2020)

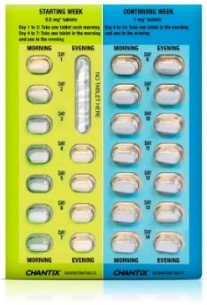
2	Pfizer	Accuretic		Blister	Folding box	Store at controlled room temperature 20°–25°C.	Die cutting at the edges	(Pfizer, 2020c)	(4NRX, 2020)
3	Pfizer	Aldactazide		Blister	Folding box	Store below 25°C.	Transparent Blister, al-lidding foil	(Pfizer, 2020c)	(Yaoota, 2020)
4	Pfizer	Aldactone		Blister	Folding box	Store below 25°C.	Colored forming foil	(Pfizer, 2020c)	(Practo, 2020)

5	Pfizer	Alesse 28		Blister	Folding box	Store at controlled room temperature 20°-25°C.	Highly colored blister packaging.	(Pfizer, 2020c)	(ChickAdvisor, 2020)
6	Pfizer	Altace		Bottle		Store at controlled room temperature 15°–30°C		(Pfizer, 2020c)	(Monthly Prescribing Reference, 2020)
7	Pfizer	Altace		Blister	Display packaging card	Store at controlled room temperature 15°–30°C	Interesting display packaging	(Pfizer, 2020c)	(Parker, 2020)

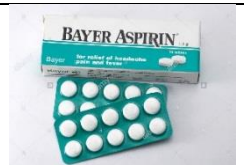
8	Pfizer	Altace		Blister	Folding box	Store at controlled room temperature 15–30°C		(Pfizer, 2020c)	(Budget Generics, 2020)
9	Pfizer	Aromasin		Blister	Folding box	Store at room temperature 20°-25°C.		(Pfizer, 2020c)	(Presta Shop, 2020)
10	Pfizer	Azulfidine®		Bottle	Folding box	Store at room temperature 25°C	Opening mechanism interesting	(Pfizer, 2020c)	(Pfizer, 2020a)

11	Pfizer	Azulfidine		Blister	Folding box	No special conditions required		(Pfizer, 2020c)	(PrescriptionGiant.com, 2020)
12	Pfizer	Arthrotec®		Blister	Folding box	Store at or below 25°C, in a dry area.		(Pfizer, 2020c)	(LiveWell, 2020)
13	Pfizer	Bosulif		Bottle	?	Store at 20°-25°C		(Pfizer, 2020c)	(Indiamart, 2020)
14	Pfizer	Bosulif		Blister	Folding box	No special conditions required		(Pfizer, 2020c)	(Indiamart, 2020)

15	Pfizer	Braftovi		Bottle	Folding box	Storage not over 30°C, storage in the original packaging	2 bottles in on box	(Pfizer, 2020c)	(Pfizer, 2020b)
16	Pfizer	Braftovi		Blister	Folding box	Storage not over 30°C, storage in the original packaging	Colored aluminum blister	(Pfizer, 2020c)	(Ono Pharmaceutical Co., 2019)
17	Pfizer	Viagra		Blister	Folding box	Store at 25°C	Colored blister	(Pfizer, 2020c)	(Smith, A., 2018)

18	Pfizer	Lo/ovral		Blister	Folding box	Store at controlled room temperature 20°-25°C.	Colored blister	(Pfizer, 2020c)	(Arneill, 2020)
19	Pfizer	Chantix		Blister	Display box	Store at 25ºC		(Pfizer, 2020c)	(eDrugstore.com, 2020)
20	Bayer	Aleve		Bottle	Folding box	Store at 25ºC	Unique shape	(Pfizer, 2020c)	(The Coca-Cola Company, 2020)

21	Bayer	Aleve		Tube	Display box	Storage not over 30°C, storage in the original packaging	Unique packaging	(Pfizer, 2020c)	(The Coca-Cola Company, 2020)
22	Bayer	Alka seltzer		Bottle	Folding box	Storage not over 25°C, storage in the original packaging	Transparent plastic bottle	(Bayer, 2020d)	(Pharmapacks, 2020)

23	Bayer	Alka seltzer		Pouch		Storage not over 25°C, storage in the original packaging	Re-cloasable with ziplock	(Bayer, 2020d)	(Bed Bath & Beyond, 2020)
24	Bayer	Aspirin		Blister	Folding box	Storage not over 30°C		(Bayer, 2020d)	(Alamy, 2020)
25	Bayer	Aspirin		Strip pack	Folding box	Storage not over 30°C		(Bayer, 2020d)	(Amavita, 2020)

26	Bayer	Aspirin		Strip pack	Folding box	Storage not over 30°C		(Bayer, 2020d)	(The Coca-Cola Company, 2020)
27	Bayer	Aspirin		Sachet	Folding box	Storage not over 30°C		(Bayer, 2020d)	(Framar Pharmacies, 2020)
28	Bayer	Berocca		Blister	Folding box	Storage not over 25°C, storage in the original packaging		(Bayer, 2020d)	(PromoFarma, 2020a)

29	Bayer	Berocca		Tube	Folding box			(Bayer, 2020d)	(PromoFarma, 2020a)
30	Bayer	Elevit		Blister	Folding box	Storage not over 25°C, storage in the original packaging, light sensitive		(Bayer, 2020d)	(Shopee, 2020a)
31	Bayer	Supradyne		Bottle	Folding box	Storage not over 25°C, storage in the original packaging		(Bayer, 2020d)	(PromoFarma, 2020b)

32	Bayer	Supradyne		Tube	Folding box	Storage not over 25°C, storage in the original packaging		(Bayer, 2020d)	(PromoFarma, 2020b)
33	Roche	Alecensa		Blister	Folding box	Store in the original package in order to protect from moisture		(Roche, 2020)	(KBR, 2012)

34	Roche	Alecensa		Bottle	Folding box	Store in the original package and keep the bottle tightly closed in order to protect from moisture		(Roche, 2020)	(PMLiVE, 2020b)
35	Roche	Cymevene		Bottle	Folding box	Storage not over 30°C		(Roche, 2020)	(Rosheta, 2020)

36	Roche	Esbriet		Bottle	Folding box	Storage not over 30°C		(Roche, 2020)	(PharmacyChecker.com, 2020)
38	Roche	Tamiflu		Blister	Folding box	Storage not over 20°C		(Roche, 2020)	(Pharmaceutical Technology, 2019)
39	Roche	Zelboraf		Bottle	Folding box	Keep the bottle tightly closed		(Roche, 2020)	(PMLiVE, 2020a)