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Study of the usability of a Dry Powder Inhaler among people aged 12 to 75 years with the aim of creating Instructions for Use

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Study, development and analysis of the usability of a Dry Powder Inhaler among people aged 12 to 75 years with the aim of creating Instructions for Use

Abstract

This thesis presents the development of a comprehensive **Instructions for Use (IFU)** for a Dry Powder Inhaler (DPI), following a structured process aligned with regulatory standards such as **ISO 13485**, **ISO 14971**, **IEC TR 62366-2** and **FDA Regulations**.

The **final version of the IFU** showed improved safety and usability, as reflected in the reduced incidence of errors during follow-up testing. This research underscores the importance of a rigorous, user-centred approach in the development of medical device documentation, ensuring both safety and efficacy in real-world use, ultimately **providing a better quality of life for our patients**

Abbreviations & Terms

Abbreviation	Description
AEMPS	Agencia Española de Medicamentos y Productos Sanitarios
CC	Capsule Chamber
COPD	Chronic Obstructive Pulmonary Disease
DI	Design Inputs
DPI	Dry Powder Inhaler
FDA	Food and Drug Administration
FMEA	Failure Mode and Effects Analysis
FMNC	Failure Mode Not Classified
HPMC	Hydroxy-propyl-methyl-cellulose
IEC	International Electrotechnical Commission
IFU	Instruction/s For Use
IP	Intellectual Property
ISO	International Standards Organization
MDI	Metered Dose Inhaler
NPDC	New Product Development Center
PPT	H&T Presspart Tarragon Site (Arboç)
SMI	Soft Mist Inhaler
SVI	Small Volume Nebulizers
TLD	Treatment of Long Duration
UN	User Needs

1 Introduction

1.1 Problem Context & Motivation

H&T Presspart is a company that is focused on bringing solution to pharmaceutical market improving people's quality of life. As biomedical engineer working in H&T Presspart allowed me to get a better comprehension of medical device development process inside pharmaceutical industry. One of the main areas that attracts me it how usability studies are performed and why they are necessary. Therefore, the main motivation behind this Final Degree Project is to generate a set of IFU that not only improve the patient-device interaction, but also optimize the performance of the Sunriser dry powder inhaler. This approach will not only benefit end users by facilitating correct and effective use of the device but will also lay the foundation for future developments and improvements in similar medical devices.

1.2 Project Goals

The primary objective of this study is to develop and validate a complete set of instructions for use (IFU) for the Sunriser DPI.

In addition to developing clear and precise IFU, this project also aims to establish a systematic process for validating these instructions through user testing. Obtaining and analysing user feedback will ensure that IFU are intuitive and effective, addressing the specific needs of end users and continually improving the user experience of the Sunriser device.

Figure 1: Presentation and rendering of the Sunriser device – H&T Presspart [30]

1.3 Background for the relevance of DPI in drug administration

Drug delivery via dry powder inhalator devices has revolutionized the treatment of respiratory diseases by providing a direct and efficient route to deliver medications in powder form directly to the affected lungs. These devices are especially beneficial in conditions such as asthma or chronic obstructive pulmonary disease (COPD), where precise inhalation of medications is crucial to relieving symptoms and improving lung function.

The principle behind DPIs lies in their ability to transform dry powder medications into fine particles that can be inhaled and deposited directly into the lungs. This ensures precise dosing and rapid therapeutic action, thus optimizing treatment efficacy and minimizing systemic side effects.

However, the effectiveness of DPIs depends largely on the patient's ability to correctly administer the medication. The complexity of the device and the lack of clear instructions can lead to errors in the inhalation technique, compromising the delivery of the medication and reducing its therapeutic efficacy. Additionally, treatment adherence may be negatively affected if patients encounter difficulties in using the device appropriately.

Therefore, optimizing instructions for use (IFU) for devices like the Sunriser is crucial not only to improve the user experience, but also to ensure optimal clinical outcomes. By establishing clear and accessible standards in IFUs, accurate and effective administration of inhaled medications can be facilitated, thereby improving the quality of life of patients and ensuring the long-term success of respiratory treatments.

2 Overview of Inhalation Therapy Devices and Market Context

2.1 Drug Delivery Mechanisms

In the field of inhaled drug delivery devices, drug delivery mechanisms are critical to ensuring treatment efficacy and proper delivery of the drug to the airways. These mechanisms can be classified into three main categories: user-aspirated delivery mechanisms, semi-automatic mechanisms, and automatic mechanisms.

User-Aspirated Delivery Mechanisms

This type of mechanism relies on the user's ability to generate the airflow necessary to disperse and deliver the drug through the inhaler. In this case, the user takes a deep and rapid inhalation, causing the drug in dry powder form to be released and carried into the lungs. The effectiveness of these inhalers depends largely on the strength and consistency of the user's inhalation, which can vary depending on age, lung capacity, and technique used. These devices are common due to their simplicity and portability but require proper patient education to ensure effective use.

Semi-Automatic Mechanisms

Semi-automatic mechanisms combine user action with design features that facilitate drug release. In these devices, although the user must still take an inhalation, the device is equipped with internal mechanisms that help prepare or release the drug more efficiently. For example, some devices may incorporate springs or pressure chambers that trigger the release of the dry powder by sensing the airflow generated by the user's inhalation. These mechanisms are designed to reduce dependence on inhalation technique and improve consistency of the administered dose, being especially useful in patients with difficulties in generating the necessary flow.

Automatic Mechanisms

Automatic mechanisms represent the most advanced category in terms of technology and automation in inhalation devices. In these systems, drug release does not depend on the user's active inhalation but is completely controlled by the device. These inhalers are equipped with sensors and mechanisms that detect when the user is ready to receive the dose, automatically releasing the drug at the optimal time. This type of device is ideal for patients who have difficulty coordinating or generating adequate airflow, ensuring accurate and consistent delivery of the medication regardless of the user's skill.

In summary, drug delivery mechanisms in inhalation devices can be divided into three main types: user-aspiration-dependent mechanisms, semi-automatic mechanisms that assist the process, and automatic mechanisms that fully control drug delivery. Each of these mechanisms has its own advantages and applications, and the choice of device type should be based on the patient's needs and capabilities to ensure effective and safe delivery of the inhaled treatment.

With the information obtained, Sunriser is classified within the "User Aspiration Delivery Mechanisms" type.

2.1.1 Mechanisms for delivering medicines in inhalers.

According to a study by H&T Presspart regarding the units per million inhalers sold in 2020 we find out how much medication the device can cover. The following graph shows three types of delivery mechanisms: Combo, Mono and Triple.

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Figure 2: Device Units sold 2020 in million pcs by API - H&T Presspart [30]

On the other hand, following the same study, we find in the line of the mechanism, the type of doses that can be implemented according to the design and medicines intended for the inhaler. This subdivision of dose types is classified into; Dose in capsule, Dose in blister/disc and Dose in reserve.

The diagram shows the quantity, in percentages (%), of inhalers according to the type of dose for which the device is qualified:

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Figure 3: Percentages of existing inhalers by type of delivery rate - H&T Presspart [30]

Finally, Figure 4 is observed as a summary of the advantages and disadvantages of each of the 3 subdivisions mentioned.

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Figure 4: Advantages & Disadvantages of the 3 subdivisions- H&T Presspart [30]

2.1.2 Comparison between different types of inhalers (MDI, DPI, nebulizers & SMI).

Nowadays there are thousands and thousands of inhalers on the market, but not all of them are the same. All of them have the same purpose, which is to improve people's quality of life by inhalation of a drug in order to carry out the correct treatment needed. However, they are classified into 4 main groups. Note that MDIs, DPIs, and SMIs are called *inhalers*, whereas the SVN is called a *nebulizer*.

When used correctly, all 4 types of aerosol devices can provide good breathing treatments. However, there are differences in how each device makes the aerosol. What follows is a brief description of the devices and how differ from each other. A more detailed explanation of how DPI type of device works appears later in this project.

Metered Dose Inhaler (MDI)

An MDI is a small, aluminium canister that contains a mixture of both medication and pressurized propellant. The pressure from the growing propellant forces the medication from inside the canister through the device each time the canister is pushed down into the plastic container or boot/actuator. [14], [15]

Figure 5: Metered-Dose Inhaler [14]

Soft Mist Inhaler (SMI)

A soft-mist inhaler (SMI) is an inhaler that produces a mist with a slower speed than a pressurized metered-dose inhaler, so there may be less aerosol remaining in your mouth when you breathe in. The mist that comes out of the SMI is referred to as a "soft mist". As seen in the picture to the right, it comes in two pieces: a medication cartridge and the inhaler. Instructions for loading the cartridge into the inhaler and taking a dose of medication from the SMI are below. The SMI is not used with a spacer. [14], [15]

Figure 6: Soft-mist inhaler [14]

Nebulizers (N)

A small-volume nebulizer (SVN) is a device that turns a liquid medication into a mist that can be breathed in. SVNs are often used by respiratory therapists in the hospital to deliver breathing treatments to patients. Home-use SVNs can also be used outside the hospital. [14], [15]

While there are many different types of SVNs, they all do the same thing. A dose of liquid medication is changed into an aerosol. SVNs do this in 1 of 2 ways — by using gas (the traditional way), or by using a power source (the newest way). The traditional SVN is actually 2 separate parts — a tabletop electric air compressor and a small plastic medication cup (see Figure 4). The 2 parts are connected together with a piece of tubing. The compressor provides the pressurized gas that the nebulizer needs to turn the liquid into an aerosol mist. The newer electronic SVNs use sound waves or vibrations to turn the liquid medication into an aerosol mist. This type of nebulizer is called a vibrating mesh nebulizer. However, electronic SVNs cost 2 to 3 times more than traditional SVNs. [14], [15]

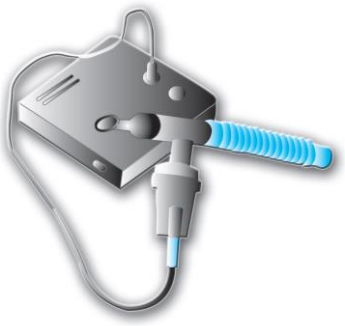

Figure 7: Small-volume nebulizer (SVN) [14]

2.2 Respiratory Diseases Treated with DPIs

Dry Powder Inhalers are widely used in the treatment of various respiratory diseases due to their effectiveness in delivering medication directly to the lungs. These devices are particularly beneficial in managing chronic conditions where long-term treatment is necessary.

Dry Powder Inhaler (DPI)

A DPI is a different type of inhaler that delivers medication as a fine, dry powder. Instead of a forced propellant, you provide the energy needed by taking a deep and fast breath through the DPI mouthpiece. This deep breath also helps to carry the powdered medication farther into the lungs. [14], [15]

Figure 8: DPI Devices - Different Type of Dose Administration [14]

2.2.1 Principal respiratory diseases treated with inhalers (asthma, COPD).

The two primary respiratory diseases commonly treated with DPIs are asthma and Chronic Obstructive Pulmonary Disease (COPD). These conditions significantly impact the respiratory system, and inhalers, particularly DPIs, play a crucial role in their management.

- *Chronic Obstructive Pulmonary Disease (COPD)*: COPD is a progressive lung disease characterized by persistent airflow limitation, often due to chronic bronchitis or emphysema. Symptoms include chronic cough, sputum production, and shortness of breath, particularly during physical activities. DPIs are an essential component of COPD treatment, providing bronchodilators that relax the muscles around the airways, making it easier to breathe. Inhaled corticosteroids delivered via DPIs can also help reduce inflammation in the airways, improving lung function and reducing the frequency and severity of COPD exacerbations. [15], [17]

- COPD INHALED MEDICATIONS & INHALATORS

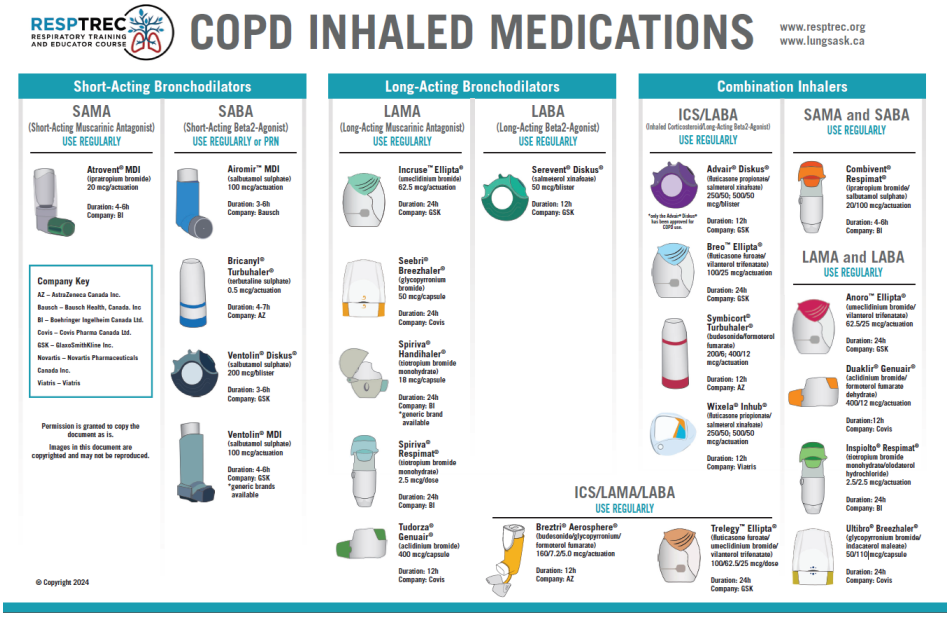

Figure 9: COPD Inhaled Medications [16]

- *Asthma*: Asthma is a chronic inflammatory disease of the airways that leads to episodes of wheezing, breathlessness, chest tightness, and coughing. These symptoms are triggered by various factors, including allergens, exercise, and stress. DPIs are commonly prescribed for asthma management because they allow for quick and direct delivery of bronchodilators and corticosteroids to the lungs,

helping to reduce inflammation and open the airways during an asthma attack. Regular use of DPIs can also help prevent asthma exacerbations by maintaining control over airway inflammation. [15], [17]

- ASTHMA INHALED MEDICATIONS & INHALATORS

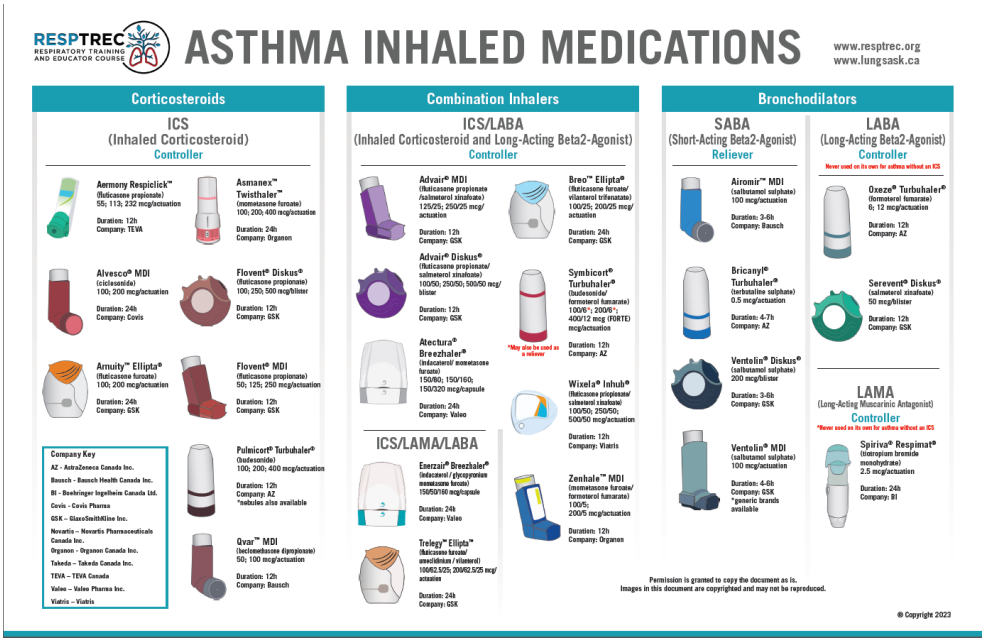

Figure 10: Asthma Inhaled Medications [16]

In both figures 9 and 10 we find the classification of the different inhalers according to a new criterion.

When treating asthma and COPD, the effectiveness of DPIs hinges on proper inhaler technique and adherence to prescribed treatments. DPIs offer the advantage of portability and ease of use, making them a preferred option for many patients. Their ability to deliver medication directly to the lungs ensures that the treatment is fast-acting and minimizes systemic side effects, making them an integral part of the therapeutic regimen for managing these chronic respiratory diseases.

2.2.2 Impact of DPIs on the improvement of patients' quality of life.

Dry Powder Inhalers (DPIs) offer several significant advantages in the management of respiratory conditions, which can lead to notable improvements in a patient's quality of life. Compared to traditional oral medications or needle injections, DPIs have distinct **benefits**: [13], [14]

- *Smaller Doses*: DPIs generally require smaller doses of medication to achieve therapeutic effects. This means that patients are exposed to lower amounts of medication compared to oral or injectable forms, which can reduce the risk of systemic side effects.
- *Quicker Action*: The medication delivered through DPIs acts faster because it is inhaled directly into the lungs. This rapid onset of action can be particularly beneficial during acute episodes of respiratory distress, providing more immediate relief compared to other forms of medication.
- *Direct Delivery to the Lung*: DPIs ensure that the medication is delivered directly to the target area—the lungs. This targeted delivery increases the efficacy of the treatment by focusing the medication precisely where it is needed, which is particularly useful for managing conditions such as asthma or chronic obstructive pulmonary disease (COPD).
- *Fewer Unwanted Side Effects*: Since DPIs use smaller doses and deliver medication directly to the lungs, there is a reduced likelihood of experiencing systemic side effects. This localized delivery helps minimize the risk of adverse effects that can occur when medications circulate throughout the entire body.
- *No Pain*: Unlike needle injections, DPIs are painless. The absence of needles makes the use of DPIs more comfortable and less intimidating for patients, enhancing their adherence to the treatment regimen.

Despite these advantages, there are some **challenges and limitations** associated with DPIs that can impact their effectiveness and the overall patient experience: [13], [14]

I. *Limited Absorption*: The lung's ability to absorb medication is not perfect. Typically, only about 10-15% of the medication delivered through a DPI is absorbed by the lungs. This means that correct inhaler use, and technique are crucial to maximize the amount of medication that reaches the intended site.
II. *Breathing Technique*: Effective use of a DPI often requires a specific breathing technique, such as inhaling slowly and deeply. Patients experiencing a flare-up or those who have difficulty coordinating their breath with the actuation of the device may find it challenging to use the inhaler properly.
III. *Device Operation*: Some patients struggle with the mechanical aspects of using a DPI, such as pressing the device and breathing simultaneously. Difficulty with these actions can hinder the effective delivery of the medication.
IV. *Variety of Devices*: The wide range of DPI designs and types available can create confusion for patients. Each device may have different instructions and operational mechanisms, which can make it difficult for patients to understand how to use them correctly.

V. *Lack of Standardized Information*: There is a lack of standardized technical information across different manufacturers. Each drug company may use its own terminology and explanations, which can add to the confusion for patients trying to understand how to use their specific DPI.

To achieve the best possible outcomes with aerosol medications delivered via DPIs, it is essential for patients to follow the instructions and guidance provided by their healthcare providers. Proper education on the use of the inhaler, including technique and device operation, is critical for optimizing the effectiveness of the treatment and improving overall quality of life. By addressing these factors, patients can benefit from the advantages of DPIs while mitigating potential challenges associated with their use.…

2.3 Market Analysis and Competitors

The analysis of the dry powder inhalers market focuses on assessing the current situation of the global market, identifying the main competitors and key players, as well as the emerging trends that could influence its future evolution. Through an exhaustive study of different sources and market reports, it seeks to provide a comprehensive view that helps to understand the dynamics of this sector and its medium- and long-term projections.

2.3.1 Analysis of the global inhaler market.

The global market for inhalers, particularly dry powder inhalers (DPIs), is showing significant growth, driven by the increasing prevalence of chronic respiratory diseases such as COPD, asthma, mentioned in the previous sections, and cystic fibrosis (*Cystic fibrosis (CF) is an inherited disease. It is caused by a defective gene that leads the body to produce an abnormally thick, sticky fluid called mucus. This mucus builds up in the airways of the lungs and pancreas causing life-threatening lung infections and serious digestive problems.* [17]). The increasing adoption of dry powder inhalers is due to their advantages over other types of inhalers, such as nebulisers and metered dose inhalers (MDIs). DPIs are preferred due to their ease of use, portability, absence of propellants and lower environmental impact.

Furthermore, the global digital respiratory devices market, of which DPIs are a part, was valued at USD 43 billion in 2022 and is expected to reach USD 400 billion by 2032, at a compound annual growth rate (CAGR) of 25% during this period. This growth is driven by the increasing prevalence of respiratory disorders and the need for more accurate drug delivery devices. Various market reports, including those provided by Fact.MR and Verified Market Research, highlight that the global inhaler market is projected to expand

significantly over the next decade. This growth is underpinned by technological innovation, digitisation of inhaler devices and an increase in demand for more effective and personalised solutions for the treatment of respiratory diseases. [18], [19]

2.3.2 Key market players and competitors.

In the competitive market for dry powder inhalers, several key players dominate the landscape, consolidating their position through innovation and a strong product portfolio. **Prominent competitors** include *GlaxoSmithKline plc*, *AstraZeneca plc*, *Boehringer Ingelheim GmbH, and Novartis AG*. These companies have established a strong global presence through their expertise and continued investment in research and development. **GlaxoSmithKline**, for example, has led the market with innovative products that have raised the standards of treatment for respiratory diseases. **Boehringer Ingelheim** has stood out for its focus on advanced inhalation therapy. [18], [19], [30]

The Handihaler® and the RS-01® are both dry powder inhalation devices (DPI) used for the delivery of inhaled medication but have notable differences in their design and operation compared to Sunriser.

Handihaler®

The Handihaler, developed by Boehringer Ingelheim in Germany, is a capsule-based DPI device. For dosing, the user tilts back the mouthpiece and inserts a size three capsule into the capsule compartment. Before inhalation, the device needs to be primed by pressing a button, which causes two pins to pierce the capsule. During inhalation, the capsule rotates inside the compartment, which facilitates the expulsion and deagglomeration of the dry powder contained in the capsule. The capsule is held in place by a metal grid at the bottom of the mouthpiece. This device produces a buzzing sound during inhalation, which serves as a positive feedback control to ensure that inhalation is being performed correctly. [27], [33]

RS-01®

The RS-01, manufactured by Plastiape in Italy, is part of a family of DPI devices with very similar designs that employ the same deagglomeration technology. Plastiape specialises in the production of medical devices and plastic packaging, not pharmaceuticals. The RS-01 is marketed in two versions, one with low resistance, which allows a nominal airflow, and one with intermediate resistance, which generates a pressure drop. Similar to the Handihaler, to apply the dose, the user must tilt back the mouthpiece and insert a size three capsule. A key difference is that the capsule orientation

on the RS-01 is horizontal, while the Handihaler is vertical. To prime the RS-01, two buttons located on the sides of the device must be pressed, which causes the capsule to be punctured by two opposing pins (or four pins, depending on the configuration). During inhalation, air is drawn through tangential slots in the device's housing, causing the capsule to rotate, thus facilitating the expulsion and deagglomeration of the dry powder. Like the Handihaler, a buzzing sound created by the rotating capsule serves as an audible feedback control. [32]

In summary, while both devices share similar operating principles, such as capsule piercing and the use of sound as feedback, they differ in key aspects such as capsule orientation, intrinsic resistance, and activation mechanisms. These details are important when considering usability and efficacy in inhaled drug delivery.

See below for images of the respective devices:

Figure 11: Spiriva® Handihaler® [33]

Figure 12: RS-01® [32]

2.3.3 Market trends and future projections.

Currently, the dry powder inhaler market is in a phase of rapid evolution, with several emerging trends that could have a decisive influence on its future development. One of the most prominent trends is the digitisation of respiratory devices, which has led to the development of smart inhalers equipped with remote monitoring functions and digital connectivity. These devices not only improve patients' adherence to treatment, but also provide physicians with real-time data to adjust and optimise therapies.

The global digital respiratory devices market is also benefiting from drivers such as the increasing prevalence of respiratory diseases, favourable reimbursement policies, and the COVID-19 pandemic, which has accelerated drug approvals and new product launches. Digitalisation and personalisation of treatment are key forces driving innovation in this market. [18], [19]

In addition, regional growth in North America is projected to remain significant due to its advanced healthcare infrastructure, increasing population awareness and continued technological advances. In the UK, reforms in the National Health Service (NHS) are expected to drive an increase in the use of digital respiratory devices, improving personalised and accessible care outside hospitals. [18], [19]

Projections indicate that current trends will not only continue but intensify, resulting in sustained market growth over the long term, benefiting both manufacturers and patients seeking more effective and accessible treatments.

3 Theoretical Framework

ISO is an independent, non-governmental international organization. It brings global experts together to agree on the best ways of doing things. From climate change and healthcare to quality management and artificial intelligence, our mission is to make lives easier, safer and better – for everyone, everywhere. [1]

3.1 Development Regulations

The Development Regulations (Development Activities 4.1) refers to the set of regulations and standards that guide and control the medical device development process. These regulations ensure that devices are designed and manufactured according to quality standards that ensure their safety, efficacy, and regulatory compliance.

Within Development Regulations, the following key regulations are included for the current usability study:

3.1.1 ISO 13485

ISO 13485 is an international standard developed by the International Organization for Standardization (ISO), which sets out the requirements for a quality management system (QMS) specifically designed for the medical device industry. This standard is crucial to ensure that medical devices comply with relevant regulations and meet customer needs and expectations. Although not mandatory, the implementation of a QMS compliant with ISO 13485 is highly recommended for organizations that wish to ensure the quality and safety of their products and maintain consumer confidence. [2]

Since safety and quality are critical aspects in the manufacturing of medical devices, ISO 13485 plays a fundamental role by establishing precise guidelines for the creation and maintenance of a robust QMS. The standard applies to organizations of all sizes that design, produce, install and distribute medical devices. In addition, ISO 13485 is used by certification bodies and third parties in auditing and inspection processes, helping companies to control and continually improve the quality of their manufacturing operations. [2]

Key Components of ISO 13485: [2]

- *QMS Documentation*: The standard requires the creation of a documented system that includes quality policies, manuals, procedures, work instructions and records. This documentation is essential to ensure that all quality-related activities are clearly defined and controlled.

- *Resource Management*: It must be ensured that the necessary resources, such as personnel, infrastructure and work environment, are available and adequate to carry out the processes effectively. This includes the training and competence of personnel, as well as the maintenance of equipment and environmental conditions.
- *Product Realization*: This covers everything from product design and development to production, distribution and after-sales. Each stage of the process must follow strict quality protocols to ensure that the final product meets regulatory requirements and customer expectations.
- *Measurement, Analysis and Improvement*: The standard emphasizes the importance of internal auditing, control of non-conforming products, data analysis and continuous improvement. These processes enable the organization to identify areas for improvement and take corrective and preventive actions to maintain and raise quality standards.

In the context of a usability study for a DPI, ISO 13485 has significant relevance. Implementing a QMS based on this standard will ensure that the dry powder inhaler meets the required quality and safety standards, which is vital for the creation of accurate and effective instructions for use.

I. *Manufacturing Control*: The standard requires that the DPI manufacturing process be strictly controlled to ensure that each device produced meets the established quality standards. This includes ensuring that materials, equipment and processes are consistent and safe.
II. *Functional Testing*: Rigorous testing must be conducted during and after production to ensure that each DPI performs as intended. These tests are essential to validate the effectiveness of the device across a wide range of users, especially considering variations in lung capacity, inhalation technique, opening and closing of the device and other steps compared between different age groups and with or without IFUs.
III. *Internal Audits*: Conducting regular audits of the production process is critical to identify any deviations from quality standards and correct them in a timely manner. This is particularly important at the DPI development stage, where adjustments to design and manufacturing may be necessary to improve usability.
IV. *Continuous Improvement*: ISO 13485 encourages a focus on continuous improvement, which involves collecting and analysing user feedback and product performance data. This information will be crucial to refining both the inhaler design and the instructions for use, ensuring that the final product is safe, effective and easy to use by people of various ages.

In summary, ISO 13485 not only lays the foundation for a robust quality management system, but also provides a framework that is directly applicable to the development of medical devices, such as the dry powder inhaler, and the creation of instructions for use that improve user experience and treatment effectiveness.

3.1.2 21 CFR 820.30

21 CFR 820.30 is a specific section of the FDA (Food and Drug Administration) regulations that focuses on design controls for the development of medical devices. This regulation is part of the FDA's Quality System Regulation (QSR) and establishes mandatory requirements that manufacturers must meet to ensure that medical devices are safe and effective. [3], [4]

The main objective of 21 CFR 820.30 is to ensure that the medical device design and development process is rigorous, systematic and properly documented. Therefore, this specific section of the regulation focuses on the design controls that medical device manufacturers must implement and maintain to identify and mitigate risks throughout the product life cycle. [3], [4]

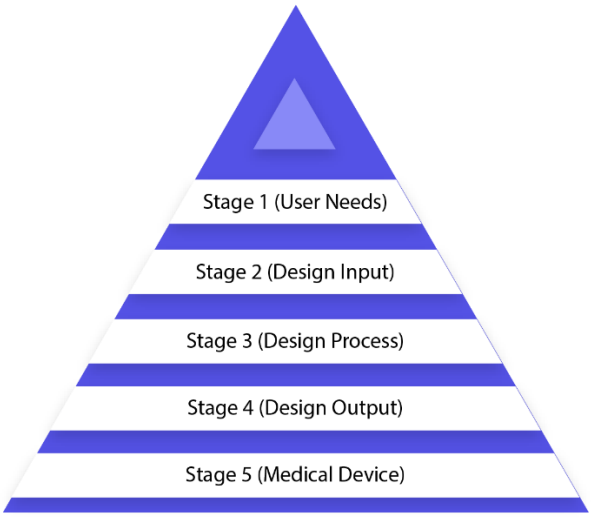

Figure 13: Medical Device Development Process - Design control process flow chart. [5]

In order for medical device manufacturers to establish and maintain procedures to control the design of the device, ensuring that the specified design requirements are met, the regulations classify medical devices into three classes according to risk:

Following the same thread, the development process is broken down into 10 steps including class II division. The steps to be followed are: [3], [4], [5]

I. General:

Class I: Low risk (e.g. surgical gloves).

Class II: Moderate risk (e.g. glucose monitors)

Class III: High Risk (e.g. pacemakers)

Because of this classification, the FDA requires that these devices meet rigorous safety and efficacy standards before marketing. It is crucial to ensure that the instructions for use (IFU) are accurate and clear, thus facilitating the correct use of the device by patients and minimising the associated risks.

II. Design and development planning:
Manufacturers are required to establish and maintain plans describing or referencing design and development activities, defining responsibilities, and ensuring review and updating of these plans as the design evolves. [3]

III. Design input:
Manufacturers must establish procedures to ensure that design requirements are appropriate and address the intended use of the device, including user and patient needs. [3]

IV. Design output:
Design outputs must be defined and documented in a manner that allows for adequate evaluation of conformance to the design input requirements. [3]

V. Design Review:
Formal, documented reviews of design outputs shall be planned and conducted at appropriate stages of development. [3]

VI. Design Verification:
Design verification should confirm that the design output meets the input requirements. [3]

VII. Design Validation:
Design validation is performed on initial or equivalent production units under defined operating conditions to ensure that the device meets user requirements and intended uses. [3]

VIII. Design transfer:
Procedures must be established to ensure that the device design is properly translated into production specifications. [3]

IX. Design Changes:
Design changes must be identified, documented, validated or verified, reviewed, and approved prior to implementation. [3]

X. Design history file:
Manufacturers must maintain a design history file (DHF) containing or referencing records necessary to demonstrate that the design was developed in accordance with the approved design plan and the requirements of this regulation. [3]

The medical device development process in the waterfall design process (design control process flowchart), Figure 4, is a methodology that covers the entire plan with the 5 stages that can be seen in this figure. However, despite being broken down into these stages, its procedure is complex and continuous in order to build a product that is usable for a customer and, therefore, for the proposed FU, always considering the progressive changes in the design of use and, in addition, dissecting the defective aspects. [5]

3.2 Risk Management Regulation

The Risk Management Regulations (Risk Management Activities 4.1) refers to the regulations and standards that guide the identification, evaluation, control, and mitigation of risks associated with the use of medical devices throughout their life cycle. Risk management is critical to ensuring that medical devices not only meet their design requirements but are also safe for users and patients.

3.2.1 ISO 14791

ISO 14971 is an international standard that outlines a comprehensive framework for risk management in medical devices, ensuring safety throughout the product's lifecycle. This standard emphasizes a systematic approach to identifying, assessing, controlling, and monitoring risks associated with medical devices. [6]

Key Components of ISO 14791: [6]

- *Hazard Identification*: This step involves identifying potential situations or events that could lead to harm. For a Dry Powder Inhaler (DPI), hazards may include improper inhalation technique, device malfunction, or dosage inconsistencies.

- *Risk Assessment*: This involves estimating both the probability and severity of potential harms. For example, evaluating how likely it is for a user to incorrectly use the inhaler and the potential consequences of such misuse.
- *Risk Control*: This step involves implementing measures to reduce identified risks to acceptable levels. For a DPI, this could involve design improvements, clearer Instructions for Use (IFU), or safety features that prevent incorrect usage.
- *Residual Risk Evaluation*: After implementing risk control measures, any remaining risks are assessed to ensure they are within acceptable levels. For instance, even with improved IFUs, there may still be a residual risk of incorrect inhalation that needs to be evaluated.
- *Review and Monitoring*: Continuous review and monitoring of the risk management process and the effectiveness of implemented controls are essential. This includes ongoing evaluation of user feedback, post-market surveillance data, and updates to risk management practices as new information becomes available.

In the context of a usability study for a DPI, ISO 14971 is directly applicable and integral to ensuring that the device is safe and effective for a broad age range of users. Here's how the standard relates to a project:

I. *Risk of Inhalation*: The usability study helps to identify risks associated with incorrect inhalation techniques, which is critical to ensuring that users from different groups with and without instructions for use can use the DPI correctly. Identifying these risks early in the study phase aligns with the hazard identification component of ISO 14971.
II. *Dosage Evaluation*: The study assesses the consistency and accuracy with which the DPI and instructions for use are able to help the user perform the action correctly, which is crucial for risk assessment. This ensures that the device works reliably for different users, minimising the risk of overdose or harm.
III. *Quality Controls*: Based on the findings from the usability studies, quality controls can be implemented to address identified risks. This could involve refining the design of the DPI or improving the instructions for use to make it easier for users to understand and follow the correct usage steps.
IV. *Post-Market Surveillance*: In the future, following the usability study after the DPI is launched, ongoing monitoring and review of user feedback will be necessary to identify new risks or issues that arise during real-world use. This process aligns with the review and monitoring aspect of ISO 14971, ensuring that the device remains safe and effective over time.

3.3 Usability Regulation

Usability Regulation refers to regulations and guidelines that establish how products should be designed and evaluated to be easy to use and safe for users. These regulations seek to ensure that products, especially in critical areas such as medicine, meet usability criteria to avoid errors and improve the user experience. Therefore, IEC TR 62366-2 helps manufacturers comply with usability regulations by offering a structured approach to design and evaluate the usability of medical devices, being in summary a key tool. [7]

3.3.1 IEC TR 62366-2

IEC TR 62366-2 is a technical report that provides guidance on the application of usability engineering to medical devices. It is designed to ensure that devices are developed with a strong focus on the user, prioritizing safety and effectiveness. The standard emphasizes creating devices that are easy to use and reducing the likelihood of user errors. [7]

Key Components of IEC TR 62366-2: [7]

- *User-Centred Design*: This principle involves focusing on the needs, limitations, and contexts of the users throughout the design process. For a Dry Powder Inhaler (DPI), this means designing the device with consideration for the wide range of users, from adolescents to elderly adults, ensuring it meets their diverse needs.
- *Usability Evaluation*: Methods are outlined for evaluating how users interact with the device, including usability testing and task analysis. These evaluations help identify areas where the DPI may be confusing or difficult to use, guiding improvements.
- *Usability-Related Risk Management*: This involves identifying and mitigating risks that arise specifically from how the device is used. For example, recognizing that a poorly designed mouthpiece or confusing instructions could lead to improper inhalation and subsequently implementing design changes to reduce such risks.
- *Usability Validation*: The standard emphasizes validating that the device can be used effectively by the intended user population under expected conditions. This ensures that the DPI works as intended across different scenarios, whether used by a teenager with asthma or an elderly person with COPD.
- *Documentation*: All usability activities must be thoroughly documented to meet regulatory and quality requirements. This includes keeping detailed records of usability tests, risk assessments, and any design changes made based on user feedback.

In the context of a usability study for a DPI, the IEC TR 62366-2 standard is highly relevant and directly applicable. Here is how this standard can be integrated into a project:

I. *Ease of use*: The study aims to ensure that the DPI is easy to use for a wide range of ages. By applying the user-centred design principles of IEC TR 62366-2, the focus can be on creating intuitive instructions and a device that adapts to the different physical and cognitive abilities of users aged between 12 and 75 in the current case.
II. *Usability testing*: As part of the study, usability testing is essential. These tests, aligned with the guidelines of IEC TR 62366-2, help to identify challenges that users may face when using the DPI, such as difficulties in opening the dust cap or correctly inhaling the medication. Based on these findings, you can refine the device and the instructions for use (IFU) to improve user interaction.
III. *Usability error mitigation*: Usability also involves identifying potential usage errors that could compromise the safety or effectiveness of the DPI. Following the risk management principles of IEC TR 62366-2 will proactively address these risks and ensure that the final product minimizes the possibility of user error.
IV. *Usability documentation*: To comply with regulatory standards and ensure traceability, all findings from a usability study, including test results and any design modifications, must be meticulously documented. This documentation process is in line with IEC TR 62366-2 and ensures that your project meets all necessary regulatory and quality standards.

3.4 FDA (Food & Drug Administration) Guidance for IFU's

The FDA is an agency of the U.S. Department of Health and Human Services. It is responsible for protecting public health by ensuring the safety, efficacy and safety of medicines, biological products, medical devices, food, cosmetics and products that emit radiation. [9], [20], [21]

FDA - Applying Human Factors and Usability Engineering to Medical Devices [20], [21]

The FDA's guidance titled "Applying Human Factors and Usability Engineering to Medical Devices" (2016) provides a framework for applying human factors and usability engineering principles in the design of medical devices. This regulation is essential to ensure that devices are safe, effective, and easy to use, addressing potential user errors and improving the overall experience. [9]

Detailed information:

I. *User-Cantered Design Principles*:

Description: The FDA stresses the need to design medical devices with a user-cantered approach, considering the capabilities and limitations of end users throughout the design process. This includes conducting research on the context of use, user tasks, and potential errors. [9]

II. *Usability Assessment*:

Description: The guidance recommends conducting thorough usability assessments, including real-world use tests and simulations to identify issues and improve the design. These assessments should cover different scenarios and user profiles to ensure the device is safe and effective. [9]

III. *Usability Risk Management*:

Description: The FDA stresses the importance of identifying and mitigating risks associated with usability. This includes analysing how the design of the device can lead to usage errors and developing strategies to minimize these risks. [9]

IV. *Usability Validation*:

Description: The guideline states that manufacturers must validate that the device is effective and safe for the intended user population under normal conditions of use. This implies that the device must function correctly and be used safely by the target group. [9]

V. *Documentation and Communication*:

Description: The guideline also emphasizes the importance of documenting all usability-related activities, including test findings and design modifications. This documentation is essential to meet regulatory requirements and for traceability. [9]

In summary, the current study establishes a relationship with the FDA where FDA guidance provides a crucial framework to ensure that the DPI usability study aligns with regulatory standards. By applying user-centred design principles, conducting thorough evaluations, managing usability risks, validating the device under normal use conditions,

and maintaining detailed documentation, it will be ensured that the DPI is safe, effective, and easy to use for all targeted age groups.

FDA – Instructions for Use | Patient Labelling for Human Prescription Drug and Biological Products | Content and Format [20], [21]

The FDA's guidance titled "Instructions for Use | Patient Labelling for Human Prescription Drug and Biological Products | Content and Format" (2022) provides recommendations for developing the content and format of Instructions for Use (IFU) documents aimed at patients using pharmaceutical or biologics with complex instructions for use. These recommendations seek to ensure that patients receive clear and concise information for the safe and effective use of these products, as well as to provide consistency in the content and format of IFUs. [8]

The recommendations in this guide do not apply to labelling of stand-alone devices or parts of devices in combination products that are marketed under device authorisation, or to products whose device is the primary mode of action, or to labelling intended for healthcare professionals. In addition, the content of this guide has no force of law and should be considered as recommendations, unless specific regulatory or legal requirements are indicated. [8]

3.4.1 FDA Content

In order to develop an "Instructions for Use" (IFU) according to the FDA recommendations, it is crucial to follow an organized and clear structure that facilitates the understanding and safe use of the product by patients. The most important aspects and the main structure to follow are detailed below:

The **general content** of the IFU is mainly intended to guide the patient in the safe and effective use of the pharmaceutical product. These instructions should include detailed, step-by-step instructions on how to prepare, administer, handle, store and dispose of the product. In addition, it is advisable to accompany the written instructions with visuals, such as illustrations or photos, to improve understanding. It is essential that the IFU be consistent with the FDA-approved Prescribing Information (PI), ensuring that they are accurate and coherent. The IFU should include relevant information from the PI and additional details that facilitate the safe use of the product. [8]

Regarding **language and readability**, the IFU should be written in simple language, understandable even for people with low literacy levels. It is advisable to avoid jargon. Language should be direct and use the active voice and imperative style, beginning with action verbs (e.g., "Wash your hands" instead of "You must wash your hands"). It is also important to avoid abbreviations to reduce the risk of interpretation errors. Clarity in

dosing is also crucial, so misleading dosage designations, such as unnecessary trailing zeros (e.g., "1 mg" instead of "1.0 mg"), should be avoided. [8]

The FDA recommended structure suggests clear organization with specific headings for each section. The main recommended sections include: [8]

I. *Title*: The "INSTRUCTIONS FOR USE" heading should appear centred and prominent on the first page.

II. *Product Name*: The trade name, generic name, dosage form, and route of administration should be included. These elements should be clearly identified and aligned with FDA regulations.

III. *Statement of Purpose*: A brief statement indicating the purpose of the IFU, for example, "These Instructions for Use contain information on how to inject [Name of Drug]."

IV. *Product Visual*: A clear image of the product and, if applicable, the associated device should be included. Images should be clearly labelled and should help identify parts and their use.

V. *Important Patient Information*: This section should include key warnings or critical information that the patient should be aware of before using the product, such as instructions on how to properly administer the drug or how to avoid usage errors.

VI. *Preparation Instructions*: Details specific steps to prepare the product before use, such as mixing, checking for particulate matter, or warming to room temperature.

VII. *Administration Instructions*: This section should provide detailed instructions on how to administer the drug, including the correct site of application, the technique to follow, and any variations in administration methods.

VIII. *Storage Instructions*: Provides guidance on how to store the drug properly, such as refrigeration conditions or protection from light.

IX. *Disposal Instructions*: Provides directions on how to safely dispose of the drug or its components, especially to avoid risks such as needlestick injuries.

X. *Additional Information*: Should include contact information for further details or to report adverse events, as well as details of the manufacturer, distributor, or licensee.

Finally, at the conclusion of this FDA document, a statement indicating that the IFU has been approved by the FDA should be included, along with the initial approval date or the most recent revision date. [8]

After the most important sections have been mentioned, it is worth highlighting that after a benchmarking (see section 2.3.1 and 2.3.2) comparing the different IFUs and prospectuses on the market by the competition, some criteria have been established in the IFU of this study, supported in turn by the FDA.

The criteria will be found throughout the project mentioned, such as their clear appearance in the User Needs and in the Design Inputs. As a general idea, the following has been established:

- An **index** to be implemented for the final IFU. Because for the versions for the experimental tests it has been reduced to make a more focused approach to the usability of the device (see section 4.3.3 in DI-25).

- A clear differentiation of the **highlighted messages and illustrations** that have been considered necessary to write with a different format (messages: bold, capital letters, italics, etc. & illustrations: cross, ticks, colours, arrows, etc.).

- A correct and legal **mention** and documentation within the confidentiality of the study by the identification of the **responsible company** together **with** the personal data of the **person responsible for the usability study**.

- An implementation of dashed lines referring to sections within the IFU that should be included, but since they are not the focus of the study or accepted by the company, the privacy of said information is respected (mostly **pharmacological details**).

- A **regulatory reference** to the **FDA**, simulating the approval of the IFU proposal, **and** to the **AEMPS** as the Spanish representative of the product.

IFUs should be carefully designed to be easy to understand, ensure accuracy, and reflect FDA-approved information. By following these structural and content recommendations, you ensure that patients have the tools they need to use medications safely and effectively.

3.4.2 FDA Format

The following formatting recommendations are designed to make Instructions for Use (IFU) easier for patients to read and to help them use drug products safely and effectively.

A. Typographic Style Recommendations

Font and Font Size

The FDA recommends using a sans-serif font for all text in IFUs, as sans-serif fonts are easier to read than serif fonts. Some recommended sans-serif fonts include Verdana and Arial. The FDA discourages the use of reverse typefaces (such as white or neutral-coloured text on a dark background), light fonts, shadowed, highlighted, condensed, or narrow fonts, as these techniques may make reading difficult for patients. [8]

- Regarding font size, the FDA suggests that it be no smaller than 10 points (where 1-point equals 0.0138 inches) in any section of the IFU, except in the following cases, where up to 8-point font may be used: [8]
  - The name and address of the manufacturer, packager, and/or distributor for products marketed under an NDA or ANDA.
  - The name, address, and license number of the manufacturer (and, if included, the distributor) for products marketed under a BLA.
  - The literal statement: "These Instructions for Use have been approved by the U.S. Food and Drug Administration."
  - The month and year of the initial FDA approval or revision of the IFU.

Capitalization

The FDA recommends that the heading "INSTRUCTIONS FOR USE" appear in capital letters. In addition, the brand or generic name used in the body of the IFU (excluding the product title) should match in style its appearance in the Prescribing Information (PI). Other headings in IFUs should appear in title case. It is advisable to avoid excessive use of capitalized words or phrases in the body of IFUs, as an abundance of capitalized text can make reading difficult and detract from the importance of terms that should be capitalized. [8]

Bold, Italic, or Underlined Text

The FDA recommends that the following information be displayed in bold: the heading "INSTRUCTIONS FOR USE," the product title (including the drug name, pronunciation, dosage form, route of administration, and, where applicable, the controlled substance

symbol), headings, step numbers, and figure titles. Bold headings help patients find information quickly and easily. However, it is suggested that the use of bold, italics, and underlining in the body of IFUs be limited and applied only to important phrases or concepts (e.g., "For oral use only"). [8]

B. Page Layout and Design Recommendations

Step-by-Step Instructions

The FDA recommends that instructions be numbered sequentially, with each step heading boldfaced and noted as Step 1, Step 2, etc. In addition, it is suggested that continuous numbering be used throughout the document, avoiding multiple instances of Step 1. [8]

The FDA also suggests that action-oriented instructions appear before any supporting information related to performing a step. Supporting information should be presented in bullet form on a separate line immediately following the appropriate step. [8]

If the patient needs to skip a specific step or set of steps that are not necessary for each dose, the FDA recommends that IFUs refer the patient to the next appropriate step. If a step or set of steps needs to be repeated, it is recommended that IFUs refer the patient to the appropriate step. [8]

Visuals for Step-by-Step Instructions

Visuals are helpful for patients to understand instructions. They can be useful for action tasks and information that help the patient understand and safely prepare, administer, store, or dispose of the product. The FDA recommends that visuals be easy to understand, appropriately sized to allow patients to see the focal point and demonstrate one concept or idea per visual. Photographs are helpful because they show the most accurate visual representation of the product. However, in some cases, using drawings or illustrations may be more effective in simplifying complexities and highlighting key components. [8]

The FDA suggests that visuals be placed immediately next to the related instructional step. Additionally, it is recommended that visuals be labelled alphabetically in bold (e.g., Figure A, Figure B, etc.), and that steps with corresponding figures refer to the appropriate figure at the end of the step. [8]

Spacing

The FDA recommends maintaining a sufficient balance of text, visuals, and white space in IFUs. White space can be used to prevent the document from appearing cluttered,

overwhelming, or too scattered. To facilitate reading, the FDA suggests using white space or blocks of text to separate concepts and indicate changes. Consideration should also be given to increasing the amount of white space around important text and visuals to make them stand out. [8]

Colour

The FDA recommends that IFUs be presented in black text on a white background to facilitate readability. This combination maximizes contrast and readability, and also makes it easier to consistently reprint the document. Using colour text and visuals can be helpful, as long as all text and visuals maintain clarity and remain legible when printed in black and white or grayscale. [8]

4 Usability – Centred Development Process

This section will explain the process that has been followed during the project to achieve the objectives set by focusing on the usability process contemplated in the blocks that can be observed in the next section in Figure 4:

I. User Needs (UN)
II. Design Inputs (DI)
III. uFMEA (User Failure Mode & Effects Analysis)
IV. Usability Study

All this interacts together in order to obtain a Design Output for the project that is correlated with the instructions of use (IFU).

4.1 Usability Process Definition

The Usability Process Definition has been structured and broken down as can be seen in the Figure 4 flow diagram.

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Figure 14: Usability Process Definition

4.2 User Needs (UN)

The User Needs document for the Sunriser DPI is based on the intended use and end users of the device. These needs provide the basis upon which the Design Input Requirements (DI) will be developed, and the corresponding Design Output Requirements (DO) will begin to be developed.

4.2.1 Standard concepts of DPI use

Standard concepts of DPI use are essential to ensure efficacy and safety in the administration of inhaled medications.

This section provides the User Needs Requirements for Sunriser DPI based on the intended use and users.

In terms of user, the device is intended to be suitable for use by patients across broad age range (e.g., 12 to 80 years old) across target medical conditions, including elderly patients who may have limited dexterity and cognitive ability with compromised eyesight, and healthcare professionals.

Goal

The goal of this section is to document the User Needs (UN), that have been identified considering intended use and users. They will be the base on which to build the Design Input (DI) Requirements and start developing the corresponding Design Outputs (DO).

4.2.2 Identification of user needs

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4.2.3 Targeted User Needs to be addressed

Following **User Needs** have been identified:

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Table 1: User Needs Definition

4.3 Design Inputs (DI)

The development that H&T Presspart is carrying out, as mentioned in the User Needs, requires a major commitment. In the same line, therefore, in the second principal place, Design Inputs must be studied on the basis of the UN, which serve as a structure and basis for the usability study.

4.3.1 Standard concepts of DPI use

This document provides the Design Inputs (DI) Requirements for Sunriser DPI based mainly on the defined user needs and the applicable standards.

Goal

The goal of this section is to document the Design Inputs, which have been defined considering the user needs and the applicable standards. They will be the base for the development process and defining the corresponding design outputs.

4.3.2 Identification of design inputs

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4.3.3 Targeted Design Inputs to be addressed

Following **Design Inputs** have been identified:

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Table 2: Design Inputs Definition

4.4 Risk Analysis

Based on the knowledge already known from the rules and regulations applied at the beginning of the study, we know that risk analysis is a systematic and comprehensive process used to identify, assess and mitigate the risks associated with a medical device, in this case a dry powder inhaler (DPI). This analysis is crucial to ensure the safety and effectiveness of the device, minimising potential risks to the end user. The aim of risk analysis is to detect all possible failure modes that could arise during the use of the device, as well as the adverse effects that these failures could have on the user. This allows for the implementation of appropriate control measures that reduce the likelihood and severity of these risks.

4.4.1 Definition of User Steps with the DPI

Following **User Steps** have been identified:

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Table 3: User Steps Definition

This table sets out the steps that the user must follow in order to use the dry powder inhaler safely and effectively.

4.4.2 Risk identification associated with the use of the DPI

This section focuses on the identification and analysis of potential risks associated with the use of the DPI. **Risk identification** is a critical component in the development and improvement process of medical devices, as it allows for anticipating potential failures in the use of the device and designing strategies to mitigate them.

Following **Risk Analysis** have been identified:

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Table 4: Risk Analysis Definition

4.4.3 Initial Control Measures

In the context of risk analysis and identification of critical steps in the operation of a dry powder inhaler, a series of **Initial Control Measures** have been developed aimed at mitigating potential failure modes and improving the usability of the device.

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Table 5: Initial Control Measures

4.5 Usability study

The traceability carried out to date has allowed us to establish a precise correlation between each of the previous sections and the development of the dry powder inhaler, closely linking these aspects with the usability process. This systematic approach has led us to structure the final usability study, which has been meticulously designed to address all the methodological aspects necessary for the execution of the experimental phase of the project.

4.5.1 Usability Methodology

The usability methodology used in this study is divided into two main blocks:

5 IFU Development

The main objective of this section is to outline the recommendations for format and content that facilitate understanding by the patient, ensuring correct and safe use of the dry powder inhaler. According to previous studies (Buck 1998; Koo et al. 2003), *IFUs should be clear, concise, and accessible, considering factors such as the user's level of health literacy, simplicity of language, and the inclusion of visual instructions that complement the written text*.

5.1 Generation of the IFU for the usability study

The generation of the IFUs for the usability study was carried out following an iterative process that included several phases of design, review and testing. Initially, a draft was prepared and subjected to a preliminary evaluation process (Pre-Testing) by a group of experts in the NPDC department, which allowed refining and adjusting the content and format of the instructions.

The "Version 001" IFU obtained can be seen in Annex 9.7. Next, the "Version 002" (see in Annex 9.8) generated after the Pre-Testing modifications was developed and prepared for the main experimental tests (Testing).

The approach to the creation of these IFUs included the following steps:

- *Requirements Analysis*: The usability requirements were analysed to identify the specific needs of the users, considering factors such as age, level of familiarity with medical devices and possible physical or cognitive limitations.

- *Content Design*: Instructions were developed using simple and direct language, complemented by illustrations and diagrams to facilitate understanding of each step necessary for the correct use of the device.

- *Comprehension Testing*: Test sessions were conducted with representative users to assess the clarity of the instructions, adjusting based on the feedback received.

- *Final Review and Validation*: The revised IFUs underwent a final validation process, ensuring that they met usability standards and were accessible to all potential users.

Finally, after the results obtained in the following sections, an analysis will be carried out again, but this time in a more exhaustive, controlled and data-rich manner.

The final result is a set of instructions that not only meets regulatory requirements, but also maximizes ease of use and minimizes the risk of errors. View the final instructions for use in section 6.

5.2 Usability Testing

Usability analysis during the experimental phase of the study was performed using **Power BI software**, an advanced tool provided by the company for data visualization and analysis. This software allowed for a thorough statistical analysis, facilitating dynamic interaction with the data and allowing the creation of intuitive and straightforward graphical representations.

Using **Power BI** in this context offered several advantages:

- *Data Filtering and Segmentation*: Specific filters could be applied to segment the data according to variables of interest, such as the group of users with or without instructions, age, and level of experience with medical devices. This allowed for a more precise and focused analysis of the results obtained.

- *Dynamic Visualization*: The dynamic graphical representations provided by Power BI allowed for patterns and trends to be identified more clearly, facilitating the interpretation of the results and data-driven decision making.

- *Deep Interaction Analysis*: Power BI's ability to manage large volumes of data and perform interaction analysis between multiple variables allowed for detailed insights into user behaviour during inhaler manipulation.

Next, in sections 5.2.1, 5.2.2 and 5.2.3, the specific results of the usability analysis will be presented, highlighting the failure modes observed, the effectiveness of the instructions for use, and the areas for improvement identified during the study. This analysis will be supported by the graphs and data generated using Power BI, providing a comprehensive and detailed view of the device's performance under real-life conditions.

5.2.1 Results & Discussion: User Steps

The User Steps are evaluated in the following table in order to analyse each of them individually, generating a discussion between the group of users with instructions and the group without instructions.

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5.2.2 Results & Discussion: Potential Failure Modes

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5.2.3 Results & Discussion: Design Inputs

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5.3 Final Control Measures & IFU Review

This section details the final control measures adopted following a rigorous review and thorough evaluation of the device's instructions for use (IFU), as well as the results obtained in the pilot phase of the usability study.

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6 Final Packaging/Leaflet Proposal

In the final proposal of the instructions for use, the design of the IFU in package leaflet format has been additionally implemented together with a potential design approach to a future Sunriser packaging.

7 Conclusions

The present study has provided an in-depth understanding of dry powder inhaler usability, highlighting both strengths and areas for improvement. The main conclusions drawn from the results obtained are detailed below.

7.1 Main Outcomes from Results

I. *Significant Improvement between Groups with and without Instructions*
II. *Identification and Mitigation of Potential Failure Modes*
III. *Knowledge Acquisition for Future Projects*
IV. *Identification of Limitations and Areas for Improvement*

In summary, the study has provided valuable insights into the usability of the dry powder inhaler, highlighting both advances made and areas requiring further attention and refinement. These results lay the foundation for continued optimization of IFUs and medical device design, ensuring safer and more effective use by patients.

7.2 Future Development Proposals

In order to mitigate the limitations identified in the usability study and improve future product development, several key strategies and considerations are proposed that could be integrated into subsequent studies.

8 Acknowledgments

Sincerely, this project would not have been possible without the support and encouragement of many people. First and foremost, I would like to thank my advisor from H&T Presspart S.A., Daniel García, for their invaluable guidance, teaching and constructive feedback. In the same line, I would like to thank my university tutor for the support in parallel during this period, Marc Lázaro. Nevertheless, the present project could not have been carried out without the approval and support from the outset of H&T Presspart's Technology Director, Paloma Herrera.

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Finally, I acknowledge the resources and facilities provided by H&T, which played a key role in the completion of this project.

9 Annexes

9.1 Usability Testing Study - Raw Data

The main experimental part of the project has been carried out by collecting all the above-mentioned data from the patients in the following raw data table:

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9.2 Usability Pre-Testing Study - Raw Data

The previous experimental part of the project has been carried out by collecting all the above-mentioned data from the NPDC members in the following raw data table:

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9.3 Potential Failure Modes - Raw Data

The raw data of all PFMs evaluated in the usability study are filtered according to the number of times committed, with comparison between the group of participants with and without instructions, achieving results in percentages to be analysed. The raw data are shown in the table below:

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9.4 uFMEA - Database

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9.5 Standard Regulation of the Packaging - AEMPS

The explanation of the regulations established by the Spanish Agency for Medicines and Health Products (AEMPS) in the design of the packaging of an inhaler is briefly explained below.

Section	Details
1. Drug Name: The name of the drug is an essential component of the labelling, since it guarantees the correct identification of the product and avoids possible confusion with other drugs. The regulation establishes that:	- **Composition of the Name**: Must include the drug's fancy name, dosage, and dosage form, presented as a visual unit on the main face. This format should be present on at least three non-consecutive faces of the outer packaging.
	- **Positioning of the Dose**: For mono-drugs, the dose must immediately follow the name without breaking onto another line.
	- **Braille**: Must be included on the outer packaging, except for drugs administered exclusively by healthcare professionals.
2. Active Ingredient(s) and Excipients	- **Active Ingredient(s)**: Mentioned below the drug name. The base of the active ingredient should be highlighted over the salt to avoid dosing confusion.
	- **Excipients**: All excipients with recognized effects must be declared. Mandatory to specify all excipients in drugs administered parenterally, topically, or ophthalmologically.
3. Route of Administration and Pharmaceutical Form	- **Route of Administration**: Should appear on the main face, clearly indicating the method of administration.
	- **Pharmaceutical Form**: Specified using current standard terms, indicating the drug's presentation (e.g., powder, liquid, capsules).
4. Symbols, Acronyms and Legends: Labelling should include symbols and acronyms that provide crucial information about the drug, such as:	- **Symbols**: Such as prescription requirements or refrigerator storage, placed in the upper right margin of the two main sides.
	- **Legends**: Include warnings like “Keep out of sight and reach of children” and “Read the package insert before using this medicine”. For NHS-financed drugs, include the seal coupon.
5. Safety Devices, Batch, and Expiration Date	- **Unique Identifier and Anti-Tampering Devices**: Must include a unique identifier in a two-dimensional barcode and an anti-tampering device.

	- **Batch and Expiration Date**: Clearly indicated on all containers, including those with reduced stability after opening or reconstitution.
6. Special Storage Conditions: Special storage conditions should follow the standard phrases in Appendix III of the QRD template, for example:	- **Temperature**: "Do not store above 25°C" or "Store in refrigerator".
	- **Protection**: Keep the product in its original packaging to protect from light or humidity.
7. Authorization Holder and Local Representative Information	- **Marketing Authorization Holder (MAH)**: Name and address must be clearly indicated on the outer packaging. Optionally, telephone or corporate email can be included.
	- **Local Representative**: If applicable, include the name and preferably the contact details. The representative's logo is optional if it does not affect legibility.
8. Security Devices and Blue Box	- **Blue Box**: For centrally approved drugs, must include a box with nationally required information like the national code, SIGRE symbol, and other applicable legends. Ensure design harmonization with the rest of the labelling.
9. QR Codes and Pictograms	- **QR Codes**: Can be included for additional information but must comply with authorization procedure recommendations.
	- **Pictograms**: Optional to enhance understanding of the drug, such as the driving pictogram warning about effects on the ability to drive or operate machinery.

Table 5: Main Regulatory Aspects of Packaging Design - AEMPS [9], [10], [11]

An example provided by the agency itself is the following draft guidance to follow along with the information provided above:

Figure 15: Important information included on medicine packaging – AEMPS [10], [11], [12]

9.6 Rubric – Usability Study

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9.7 Version 001 - IFU

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9.8 Version 002 - IFU

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9.9 Sunriser Leaflet Proposal - IFU

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9.10 Sunriser Packaging Proposal – IFU

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