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Beyond the Prototype: Exploitation Strategies for Proof of Concept Biomedical Devices

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Preface

The work presented in this thesis was performed at *Instituto Superior Técnico* (Lisbon, Portugal) and at *Instituto de Telecomunicações* (IT), during the period March-November of 2021, under the supervision of Prof. Hugo Plácido da Silva and Prof. Joana Serra da Luz Mendonça. Furthermore, in the scope of this thesis' case study, the work herein presented also counted with the support of e-CoVig project's partners: *Instituto Superior Técnico* (IST), *Faculdade de Medicina da Universidade de Lisboa* (FMUL), *Escola Superior de Tecnologia da Saúde de Coimbra* (ESTeSC), *Institute for Systems and Robotics* (ISR), *Instituto de Telecomunicações* (IT), *Centro Cardiovascular da Universidade de Lisboa* (CCUL), and BrainAnswer.

Declaration

I declare that this document is an original work of my own authorship and that it fulfills all the requirements of the Code of Conduct and Good Practices of the *Universidade de Lisboa*.

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I am forever grateful for all the support i received during the development of this work.

First, I would like to show my appreciation to all the incredible professionals of the e-CoVig team, who provided me the chance to be involved in their extraordinary project and were always willing to help me. I would also like to thank all the professionals that participated in the interviews conducted in this work. I appreciate your availability and knowledge, as your input enabled me to deliver the most accurate work possible. Moreover, I want to express my appreciation to the amazing technicians of the elderly home of *Aldeia da Luz*, who allowed me to conduct this thesis' experimental work in a place so close to my heart. Thank you for your effort, patience, and good mood throughout the whole experiment.

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Finally, I want to express my gratitude to my family, whose love and support allowed me to be where I am today, to be who I am today. To my mother and my father, who are my role models and encourage me, everyday, to pursue my dreams and to aspire for more, thank you for never letting me fall. To my brothers, who always kept me grounded and showed me how fun life can be, thank you for making me a fighter (in every sense of the word). To my grandfather, who will probably never read this but should know that his smile gave strength and comfort when I needed the most, thank you for making me appreciate the world, especially the small things, and for always cooking my favorite foods. And to my best friend, Magali, who I cherish with all my heart and consider as family, thank you for always taking care of me and make my life immensely better. I adore you all and dedicate this work to you.

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Resumo

A evolução tecnológica que se faz sentir nos dias de hoje, tem permitido a automação e optimização dos ciclos de desenvolvimento de muitas soluções, através de conceitos como a prototipagem rápida. Esta refere-se ao uso de tecnologias de fabricação acessíveis, capazes de acelerar o processo de criação e validação de inovações. Particularmente, em engenharia biomédica, a prototipagem rápida tem sido cada vez mais procurada, sendo usada quer na fabricação de instrumentação médica, ou de órgãos por bioimpressão 3D. No entanto, aquando da transferência de tais resultados para o mercado, os inovadores são muitas vezes prejudicados por aspectos estratégicos e regulamentares que se revelam difíceis de superar. Essa dificuldade advém, principalmente, da falta de um caminho claro que cubra toda a jornada desde a elaboração da solução até à sua chegada ao mercado, assim como da exigência intrínseca a este mesmo caminho. A presente tese visa então a caracterização e desenvolvimento de estratégias que possam, potencialmente, facilitar o caminho para o mercado de soluções biomédicas, particularmente, de dispositivos médicos. Será dada ênfase à proteção de dados, certificação, e ao processo de transferência de tecnologia da academia para a indústria, usando o projeto e-CoVig como caso de estudo. Neste mesmo âmbito, foram realizados dois estudos. O primeiro teve como objetivo avaliar a estrutura conceptual proposta neste trabalho, através da realização de entrevistas semiestruturadas com elementos-chave da indústria de dispositivos médicos. Nestas, foi destacada a importância da conformidade regulamentar e da participação do utilizador no ciclo de desenvolvimento dos dispositivos para os mesmos alcançarem, com sucesso, o mercado. O alinhamento destes, e outros resultados, com o conteúdo conceptual proposto, valida, assim, este último. O segundo estudo visou avaliar a usabilidade do sistema e-CoVig, seguindo a estrutura conceptual proposta neste trabalho. Para tal, o sistema foi implementado, durante três semanas, num lar de terceira idade, sendo utilizado pelas técnicas da instituição (sujeitos A e B) para registar e monitorizar a saúde dos residentes. Os resultados obtidos (qualitativos e quantitativos) permitiram identificar, não só possíveis melhorias no sistema (na sua maioria relacionadas com a utilização de tecnologia num ambiente dela desprovido), mas também os seus pontos fortes, tais como a possibilidade visualizar a evolução da saúde dos utentes ao longo do tempo. Apesar do feedback dos utilizadores ter sido positivo, os dados quantitativos obtidos revelam que, na perspetiva das técnicas do lar, é necessário um esforço significativamente alto para utilizar o sistema como demonstrado pelas pontuações obtidas na avaliação NASA TLX, de 55.00 (sujeito A) e 66.33 (sujeito B). Além disso, dependendo do conhecimento tecnológico do utilizador, haverá alguma dificuldade e/ou resistência em empregar o sistema o que foi revelado pelas respostas divergentes ao questionário SUS, do qual resultaram as pontuações de 77.5 (sujeito A) e 57.5 (sujeito B). A interpretação das conclusões obtidas será feita pela equipa do projeto, que entenderá quais as melhorias mais apropriadas de se fazer.

Palavras-chave: dispositivos médicos, regulação, caminho para o mercado, e-CoVig, caso de estudo, usabilidade

Abstract

Advances in technology have been allowing the automation and optimization of solutions' development cycle, with methods such as rapid prototyping. The latter pertains the use of easily available fabrication technologies to accelerate the creation and validation of proof-of-concept solutions. In the field of biomedical engineering, particularly, rapid prototyping has seen an increasingly growing interest over the past years, with applications ranging from medical device ideation, to organ production by means of 3D bioprinting. Nevertheless, when attempting to transfer the results of a rapid prototyping process to the real world, biomedical innovators are often hindered by strategic and regulatory aspects that prove to be difficult to overcome. This struggle mainly results from the lack of a clear path to deployment, as well as from the latter's demanding character. Therefore, this thesis aims to characterize and develop exploitation strategies that can potentially facilitate the path-to-market of biomedical solutions, particularly of medical devices created by means of rapid prototyping. Emphasis will be given to data protection, certification, and to the technology transfer process from academia to industry, using the e-CoVig project as a case study.

Furthermore, two experimental studies, conducted in the scope of this work, are described. The first aimed to validate the conceptual framework proposed in the thesis, by conducting open-ended semi-structured interviews with key players of the medical device industry. Results highlighted the importance of compliance and of a strong project foundation to perform a successful deployment, being in agreement with this work's proposed conceptual framework. Having approached most of the topics perceived by the interviewees as relevant in the medical device path-to-market, and having streamlined key matters (such as regulation), the validity of the conceptual framework was confirmed. The second experimental study aimed to assess the e-CoVig system's usability in a non-clinical setting, an elderly home. After using the monitoring system for a three-week period, to register the elders' clinical status, the feedback from the technicians that employed the system (subjects A and B) was collected, identifying both improvements points and strengths to the e-CoVig system. The first were mainly related to the use of technology in this specific setting, as technicians often lacked technology and/or technological knowledge. Nevertheless, the employment of the e-CoVig system in the elderly home was said to be beneficial and efficient, encouraging a more frequent performance of this type of clinical assessment. The ability to view, through the web-based platform, how each elder's health status has been evolving, and to assess different dimensions of their health, were some of the features highlighted. However, the results obtained from the evaluations performed show the system as having a significant workload associated to its use, as demonstrated by NASA TLX's scores of 55.00 (subject A) and 66.33 (subject B). Moreover, depending on the users' technological literacy, there could be difficulty and/or resistance to employ the system, as revealed by the divergent SUS's scores of 77.5 (subject A) and 57.5 (subject B). The results, to be further interpreted by the e-CoVig team, highlighted the need to improve the system for it to be applicable in this type of setting.

Keywords: medical devices, regulation, path to market, e-CoVig, case study, usability

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Glossary

biomedical engineering Application of engineering principles, practices, and technologies to the fields of medicine and biology, especially in solving problems and improving care (as in the design of medical devices and diagnostic equipment or the creation of biomaterials and pharmaceuticals). This field provides the connection between engineering and medicine. 1

biosignals Time-varying measures of the body's biological activities. Their collection (through several sources across the body) and tracking can provide essential insight regarding a living being's psychological and physical status. Categorized into physical signals - which measure biomechanical activity and allow to assess, for instance, respiration processes - and physiological signals - which relate to the vital functions of the body, such as cardiac and exocrine activities, and brain function; their nature can either be electrical (such as EEG, ECG, EMG and EDA) or non-electrical (such as oxygenation and MMG). 37

CAD Computer-Aided Design refers to the use of computers to create two-dimensional and three-dimensional designs; its software is used by designers and engineers to create 2D and 3D models of physical components. 17, 54

e-Health The application of electronic communication and information technology in health care activities, whether these are educational, informational or commercial. 19

health The state of complete physical, mental and social well-being and not merely the absence of disease or infirmity. 1, 2

health 4.0 Linked to the fourth industrial revolution "Industry 4.0.", represents the use of latter's technologies - such as Augmented Reality, Internet of Things, Big Data, and Machine Learning - to improve healthcare, providing more effective and efficient products, processes, and services, as well as becoming a more accessible and value-adding industry . 1, 36, 80

healthcare Efforts made to maintain or restore physical, mental, or emotional well-being especially by trained and licensed professionals. 37

healthcare sector The set of businesses that provide medical services, manufacture medical equipment or drugs, provide medical insurance, or otherwise facilitate the provision of healthcare to patients; it comprises six main industries: pharmaceuticals, biotechnology, medical equipment, distribution, healthcare facilities, and managed health care. 1, 3, 6

IoMT or Internet of Medical Things, consists of medical devices and applications that, by connecting to healthcare Information Technology (IT) systems through online networks, aim to improve the sector's outcomes. 1, 37

medical devices Products, processes, or services, intended for human use for one or more specific medical purposes (e.g. diagnose, prevention, monitoring, treatment, relief, investigation, modification and/or replacement). 1–3

MedTech or Medical Technology is the application of science to develop products, services or solutions to health problems or issues such as the prevention, delay disease onset, or the promotion and monitoring of good health. There are three main categories of medical technologies: medical devices, *in vitro* diagnostics medical devices, and digital health. 2, 37, 50

mHealth or Mobile Health, is referred to as the utilization of mobile technology, such as smartphones, laptops and tablets, to achieve improved health goals either relating to health services and research, as well as to self-care. It includes applications, programs, devices and other forms that allow the mobility of the user while enabling healthcare delivery. 1, 19

telemedicine The usage of telecommunications technologies to administer healthcare to remote patients, specially important in under served areas; while it refers to the practice of medicine, telehealth refers to all dimensions of healthcare (such as educational and informational) conducted by telecommunications technology. 1, 19

Chapter 1: Introduction

Our world changes at an outstanding pace, from technology innovation to society's mindset, it is notorious how each era never fails to shelter revolution, including ours. We have been witnessing a groundbreaking effort from the scientific community to deliver innovative solutions [150], to push for sustainable practices [156], and to improve society's quality of life [20]. However, providing solutions for some resource-intensive and highly regulated markets, such as those of the healthcare sector, may not be an easy task [121].

1.1 Deploying Healthcare Innovation

For its value to any human being, health has long been an object of scientific research and development activities. To innovate in health is to contribute for a greater cause: the well-being of society.

1.1.1 A New Era

We are now experiencing health 4.0, a more technological, patient-centred, and reachable era of health and its related industries [44][162]. Innovations with the power to face today's and tomorrow's challenges have been settling in the healthcare sector, allowing a higher quality care and precision to be delivered to patients, in both clinical and non-clinical settings [84]. Examples include: i) the digitization of health records, which, by increasing the volume of data collected per person, promotes the provision of a more tailored care; yet, simultaneously exposes each person's information to a possibly compromising level [142][164]; ii) the rise of deep medicine, employing artificial intelligence able to decide alike humans and to provide greater speed, precision, and efficiency, in its diagnose [150][154]; iii) the rapid prototyping technologies, used to create from medical instrumentation, to models of human organs [6]; iv) the Internet of Medical Things (IoMT), that enables the consistent communication between a network of medical devices (such as monitoring wearables (mHealth)) which collect and process their users' health data, and allow for health professionals to access and act upon it, even from a distance (telemedicine) [140].

The development of the aforementioned innovations was only possible due to the collaboration of multidisciplinary fields such as that of biomedical engineering. This field combines the knowledge of biology, biotechnology, and engineering, to surpass numerous challenges, namely those regarding society's well-being. For the importance of its solutions, the biomedical field has been evermore interested on employing facilitating strategies and technologies (such as those of rapid prototyping) that can accelerate their innovations' development and deployment in the market [4] (see Section 2.6). Nevertheless, the path-to-market of these products, processes, or service, can be challenging to outline given diversity of solutions that exist in the field. Take the example of a hydrogel scaffold for *in vivo* cell proliferation [67] and a monitoring wearable device [160], both biomedical solutions, yet, their development implies different stages, timelines, costs, and legal requirements. Therefore, since the development of a single

exploitation strategy, suitable to all types of biomedical solutions, is very hard to achieve, this work will focus on outlining a comprehensive path-to-market for just one of these many categories: the medical devices, a broad and intricate group of solutions, thus, worth streamlining.

1.1.2 Medical Devices

Medical devices are one of the three categories of medical technologies (or MedTech), and consist of products, processes, or services, that diagnose, monitor, prevent, treat, or care, for human beings [152]. For their impact on something as valuable as health, these devices can only be made available to society when undoubtedly safe and effective, which implies a close surveillance of their development and commercialization activities. In Europe, this industry is regulated by the Medical Device Regulation (or MDR) [49], in which definition medical devices fit thousands of solutions, from cardiovascular devices and hospital supplies, to monitoring devices - being an example of the former this thesis' case study, the e-CoVig system (see Chapter 3). Such diversity led to the classification of medical devices in four classes, following a risk-based classification system (see Subsection 4.3.2). Each class has its own set of pre- and post-market requirements driving the solutions' development and deployment. Additionally, with the rise of digital technology and of data processing activities at large scale, another concern emerged in the healthcare sector's industries: data protection [120][142][164]. With personal data of patients, health professionals, and the general public, being collected and processed by numerous medical (and non-medical) solutions (Section 5.2), a close overview of such practices was needed. In Europe, this task is carried out by the General Data Protection Regulation (GDPR) [48], which, along with the MDR, must be considered by medical device manufacturers throughout their activities.

Nonetheless, these same technological advances, combined with the world's evermore health-driven mindset [3][121], led to the success of the MedTech's industries (such as that of medical devices), now representing long-term valuable businesses [109][152]. However, few are those who manage to enjoy such success. To prove a medical device's viability in the market, and to ensure that it responds to all the necessary requirements, is a hard task to complete, especially for new entrants. The medical device path-to-market is filled with challenges, mainly resulting from the purpose and sensitive nature of these solutions. Matters like regulation, although of extreme importance, are very demanding with innovators often having to input a great amount of resources (e.g. time and financial) to become compliant, something not doable for all innovators, especially new entrants [56][32]. In fact, most startup companies end up failing to enter the medical device market [85] and, those that can, face a competitive environment plagued by huge costs able throw them out [152]. Thereby, it would be advantageous to characterize exploitation strategies that could help all types of innovators to mitigate the medical device industry's challenges and successfully deploy, and maintain, their innovations in the market.

1.2 Motivation

The medical device market is growing and becoming evermore enticing for both entrepreneurs and innovators [99][109]. New long-term opportunities were created from the increase of society's longevity, and

its consequent wish to, not only solve its emergent medical issues, but to seek new ways to improve its quality of living [121]. Furthermore, the healthcare sector is evolving and gradually moving towards a personalized model, focus on each individual's needs, tailoring the practice to the patient [20]. Today's digital era is providing innovative medical solutions that give all individuals a renewed control over their health, easily assessing and acting upon it [116][84]. The emergence of rapid prototyping technologies, particularly, allowed to accelerate the development cycle of these innovations, proving their viability and validity in the market faster than ever before [4]. However, such conquests can be overshadowed by the healthcare sector's multiple challenges. Its financial, time, and regulatory demands hinder the deployment chances of medical devices, trapping potential brilliant ideas in the shelves forever [135][56].

Thereby, the focus of this work is to study, in depth, the medical device path-to-market, identifying its main hurdles, as well as its key points for success, in order to help innovators, particularly new entrants, to deploy their medical devices in the market in an efficient, compliant, and successful manner. For this purpose, a conceptual framework of the medical device path-to-market is proposed in Figure 1.1. This is to be used as reference throughout this document, with adjustments being made as the present text develops. Further detail on each of the workflow's phases can be found in Table A.1 (Appendix A).

1.3 Objective

The objective of this thesis is to characterize exploitation strategies that can potentially facilitate the path-to-market of biomedical solutions created by means of rapid prototyping, particularly of medical devices. Emphasis will be given to the technology transfer process from academia to industry (which is often hindered, or even unattainable, by challenging barriers-to-entry [2][10]), the value of user engagement in medical device's development (aligning with the healthcare sector's gradual shift to a patient-centred model [20]), and the regulation covering both medical devices and data protection (which greatly impact path-to-market [121]). To both validate and apply the guidelines set in this work, two experimental studies are conducted, using the monitoring system e-CoVig as case study. Lastly, it is important to note that the path-to-market's hurdles relating to funding, although much relevant, are out of the scope of this thesis.

1.4 Contributions

The present work delivers comprehensive, and validated, guidelines on the medical device path-to-market for all innovators to resort to, particularly new entrants. Throughout this work, several approaches to the key stages of medical device development are described. Emphasis is given to the streamlining of the regulatory framework of both medical devices and data protection (Figures 4.5 and 5.7), and the final workflow covering, in detail, the medical devices' journey from concept to market (Figure 7.1). All the aforementioned aspects are believed to be able to help innovators on mitigating part of the industry's challenges, increasing the chances of deployment.

Furthermore, as mentioned before, part of the content herein presented derived from a symbiotic

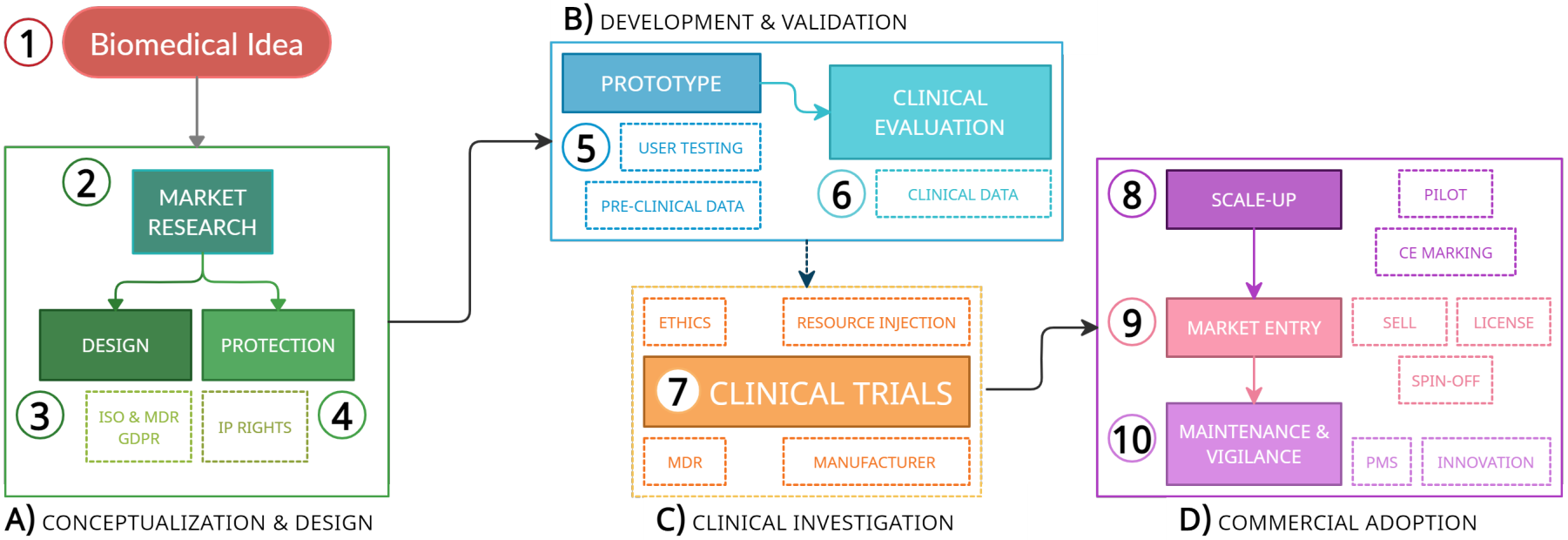

Figure 1.1: Proposed framework covering a medical device's journey from concept to market. Blocks A to D indicate the main phases of the path-to-market, each comprising essential stages indicated by the numbers 1 to 10.

relationship with the e-CoVig project, this work's case study (Chapter 3). Therefore, is it worth referring the direct contributions of the author, which include: the elaboration of data protection documents, such as the system's Privacy Notice and Data Protection Policy, that advanced their path to GDPR's compliance; the inventory and prioritization of both the MDR's and GDPR's requirements, creating important guidelines for their remaining journey; the evaluation, in an operational environment, of the e-CoVig system's usability, outcomes of which helped the e-CoVig team to identify the system's strengths and improvement points, and act upon it; and the summary of the essential matters to be tackled in the project's nearby future (Figure 8.3). Lastly, this work proved that, even with all the industry's challenges, all innovators are capable of deploying their innovations in the market.

1.5 Thesis Outline

This work is organised in nine chapters. The present chapter introduces the reader to this thesis scope and intents. Next, Chapter 2, presents the background research related to the topics of this work, such as technology's development and its transfer to the market. Chapter 3 introduces the reader to this thesis' case study (the e-CoVig), and to the interview study conducted with the medical device industry's key players to assess the validity of the conceptual framework proposed in this work. The results of such research, as well as the e-CoVig's journey so far, are detailed and discussed throughout the remaining chapters, at the appropriate moment, to better contextualize the reader.

In the next four chapters, this work's proposed conceptual framework is described. First, in Chapters 4 and 5, focus is given to medical device and data protection regulations, respectively. Besides streamlining their framework, the author provides strategies and tools to mitigate the challenges that both regulations may pose to innovators. Then, Chapters 6 and 7 approach Figure 1.1's proposed path-to-market as composed by two main phases. The first (described in Chapter 6) comprises the device's conceptualization and development activities (corresponding to stages 1 to 5, of Figure 1.1), while the second (detailed in Chapter 7), corresponding to Figure 1.1's remaining stages, addresses the device's scale-up activities and clinical validation, as well as its launch and maintenance in the market. The final proposed conceptual framework is provided in the end of the chapter, inputting the results of the interview study.

In Chapter 8, this work's second study is presented. Motivated by the conceptual framework proposed, consists of assessing the e-CoVig system's usability by implementing it in an assisted living setting. Both its qualitative and quantitative results are described and discussed throughout the chapter. Finally, Chapter 9 states this thesis' overall conclusions, and suggests future approaches to the present thematic.

Chapter 2: Background

As seen in Figure 1.1, the medical device path-to-market comprises several important stages, each with their own challenges [41][121]. This chapter will describe important concepts and results from literature that can help to make sense of, and mitigate, some of the medical device industry's hurdles.

2.1 The Innovation

Regardless of their field of application, all innovative projects start with an idea. Firstly, it is worth defining what is meant by innovation in the scope of this work. The latter concept is not consensual among the knowledgeable of the area, who argue about the level of novelty needed in a creation to be considered as so [125]. Nevertheless, one will hereinafter consider that both an incremental improvement of a previous creation and an entirely new concept created from scratch can be defined as innovations, as long as their adoption by the healthcare sector's industries creates value to society [21].

For long, innovation has been reinventing industries, shaping economies, and influencing society's behaviour and decisions. Nevertheless, not all innovations are equally revolutionary and/or impactful, being categorized accordingly into radical and incremental innovations. A radical innovation consists of a novel development where breakthrough and disruptive technologies implement a paradigm shift in the way products, processes, or services, are offered [13]. However, as a novelty, the audience needs to learn how to use it before fully enjoying it, a learning effort that makes the innovation take longer to be accepted [37]. An example of such disruption are the electronic tattoos, consisting of electronic devices, or systems, placed on the skin, to directly monitor the user's biosignals. These enable diagnostic sensing as well as the transfer of therapeutic drugs, thereby replacing previous bulky and expensive equipment [111]. Regarding incremental innovations, these aim to solely improve the performance and/or add new functionalities to previously developed solutions, downsizing their associated risk, yet, not changing their essence and purpose [88]. As an enhancement, both the development and acceptance of these innovations by the audience are more easily achieved. Examples are the wearable monitoring devices. These body-worn technologies allow the remote acquisition, analysis, and transmission of its user's personal data (including health records). Such characteristics are very enticing for many industries, such as those of the healthcare sector which, with just slight adjustments to the original backbone of these devices, can adapt them to different intents [91]. Although distinct, incremental and radical innovations have a symbiotic relationship in which the first stagnates without the second [37].

Furthermore, another differentiating factor in innovation is the force that drives its development, namely, a market-pull or technology-push force. When an innovation arises in response to a market need and/or customer demand, it is said to be driven by a market-pull force. This type of development generally starts with a comprehensive search for market opportunities and, only when these are identified,

proceeds to conceptualize the most appropriate solution [59]. One such example is the monitoring system e-CoVig (this thesis' case study), created by the need of a tool that could allow remote patient monitoring during the COVID-19 pandemic [8]. Conversely, developments driven by the solution's technology are said to be based on a technology-push approach. In this type of development, technology outweighs the needs of the users, neglecting market research and focusing on the materialization of the innovation. Examples include the employment of revolutionary technological concepts in medicine, such as those of artificial intelligence - providing a more accurate diagnose - and of augmented reality - supporting the physician in surgical interventions [5][58]. Note, furthermore, that the innovator should prioritize only one of these driving forces (at least in the beginning) since their philosophies and ideals may clash when mixed [139].

2.2 The Innovator

Regarding the creative minds behind the world's innovations, one can mention three important powerhouses: the companies, the users, and the academics. Companies (here understood as those with no academic background) were, for long, the dominant player delivering innovation to society. The costumer's opinion was, overall, neglected by the manufacturers during the solution's development, being only acknowledged on the commercial deployment stage [21][90][118]. However, a new type of innovation emerged in the last few decades, one in which the user is the key innovator: the user innovation [45][95].

The digital era establishing in the last few decades has allowed for knowledge and facilitating technologies to become accessible to everyone [14][63]. Furthermore, with the users' wishes gradually shifting from mass produced products to customized ones - an heterogeneous demand costly to meet by manufacturers - the users' felt encouraged to innovate by themselves [95]. This, combined with the valuable insight these individuals have on what is perceived as valuable, and wanted, by the market, established the users as capable innovators, able to impact industries [133][141][163]. This establishment had two important consequences. Firstly, it enabled the creation of open users' communities on which ideas, projects, resources, and knowledge, are shared between the members (usually in a free fashion), accelerating the development cycle of potentially good ideas [26][63]. Furthermore, even though this movement started in the software field - with the so-called Open Source Software communities - it quickly spread out to other sectors such as that of healthcare [25]. Platforms like Patient Innovation arise as a nurturing environment to develop creative projects within the medical context, allowing the collaboration between patients, caregivers, and other healthcare actors [92]. The second consequence of user innovation was within the companies. The users' knowledge caught the attention of established businesses and entrepreneurs, who recognized the value that the solutions' adopters could create for their businesses, which, otherwise, could be hard, and costly, to acquire [95][141]. Thus, companies started to consult with the users - particularly, with lead users who faces/identifies needs of the market earlier that the remaining audience [23][133]) - on early stages of research and development (R&D) activities, in order to get both their feedback and/or assess the potential of their own ideas. The users' involvement in the development cycle spread out across many industries, particularly on the healthcare sector's technological strands [119][130].

Another major contributor to the world's innovation is the academia. As an environment dedicated to the pursuit of knowledge through research, education, and scholarship, academia has long been a key contributor for territorial development, economical growth and, more importantly, on delivering innovation [147][148]. Whether the innovators are students, researchers, or teachers, from either universities, polytechnics, or research centres, these minds have the necessary advanced knowledge to create the most disruptive solutions of human history. For instance, the Google search engine and the social platform Facebook, were both created in universities, as well as the discoveries of penicillin and of recombinant DNA (rDNA), both revolutionizing for our society. Academia's innovations can face different challenges and be influenced by different factors on their path-to-market [35]. Motivation, resources, deployment strategies, and participating actors, can be quite distinct from those of users' and companies' innovations. Nevertheless, its developments, capable of changing the world, are constantly sought after by third parties through business agreements and/or collaborative programs. This cooperation, although extremely advantageous for society, can struggle to happen due to the poor alignment between the academics' motivations and strategies, and those of the businesses [10][121]. The lack of consensus can end up preventing the solutions' deployment, especially in competitive industries such as that of medical devices.

In sum, the technological landscape of today's world not only facilitates the sharing of knowledge and tools that allow individuals to nurture their innovative side, but also promotes the collaboration between different parties, each with their own set of skills. These are both important results, especially for intricate and competitive markets such as that of medical devices. Whether one is an academic, an user, or an employee in an innovative company, all innovators have the power to change society's ways for the better if the right tools and knowledge are accessed [21][95][156].

2.3 Technological Maturity

When developing a product, process, or service, many are the technology sets that can potentially fit the concept envisioned. The choice of which technology to integrate in the solution can determine the latter's success in the market, thus, a careful assessment must be performed. This passes by evaluating the technologies' maturity (i.e. the technology's readiness for operations across multiple environments), a procedure often supported by the Technology Readiness Level (TRL) scale [126].

2.3.1 Technology Readiness Levels

Technology Readiness Level (TRL) is a measurement system which promotes a more objective assessment of the technology's maturity [1]. As seen in Figure 2.1, it consists of a reference scale with nine levels, each corresponding to a maturity stage characterized by a group of parameters. The maturity assessment consists of evaluating the technology against these parameters and, then, assigning the appropriate TRL rating (being TRL 9 the highest maturity level). Typically, as the rating increases, the technology's associated risk decreases (with increasingly rigorous evaluations taking place), yet, the harder it becomes to to mature the technology since more and more resources are required to complete each stage's activities.

Although first developed for the space industry, the TRL is now being adopted (and adapted) by many industries, including that of medical devices. Figure 2.1, includes both the core stages of the standard TRL scale, and the adaption made to these same stages to suit the medical device industry (indicated in bold). The adjustments made are mostly related to regulation and clinical validity, the cornerstones of this industry.

TRL	Description
TRL 9	Actual system proven in operational environment (competitive manufacturing the case of key enabling technologies; or in space). **Medical device in its final form and in full commercial deployment. Post-market studies and surveillance.**
TRL8	System complete and qualified. **Medical device is in its final form. CE marking apposition.**
TRL 7	System prototype demonstration in operational environment. **Final product design is validated, and final prototypes are produced and tested in an operational environment.**
TRL 6	Technology demonstrated in relevant environment (industrially relevant environment in case of key enabling technologies). **Demonstration of the prototype in a relevant environment, such as high-fidelity laboratory and simulated operational environments. Safety of medical devices of higher risk classes is demonstrated. Technical Documentation and QMS are finalized.**
TRL 5	Technology validated in relevant environment (industrially relevant environment in case of key enabling technologies). **Validation of a higher fidelity model by testing it in a relevant environment. Beginning of clinical investigation processes, if needed.**
TRL4	Technology validated in lab. **Test of low-fidelity models in lab environment to prove that the different elements will work together.**
TRL 3	Experimental proof of concept. **Test of assumptions through analytical and laboratory-based studies. Demonstration of Proof-of-Concept. Beginning of Technical Documentation and QMS processes.**
TRL 2	Technology concept and/or application formulated.
TRL 1	Basic principles observed. **Conduction of scientific research to be translated.**

Figure 2.1: The Technology Readiness Level (TRL) scale comprising the nine stages of a technology's development process, being particularized, in bold, for medical device development. Source: US Army Medical Department [39].

Furthermore, since the illustrated maturity stages are meant integrate, and accompany, a solution's full development (as the one proposed in Figure 1.1), one can streamline this parallelism by associating the maturity levels to the development stages. Therefore, by analysing Figure 2.1, three groups were created: 1) "Ideation and Innovation": comprising TRL 1 to TRL 3, and corresponding to stages 1 to 4 (block A) of the proposed diagram; this phase is ruled by research and conceptualization activities which may include the development of a limited number of models stripped of any complexity. In this phase, assumptions and hypothesis are formulated (that will be later put to the test), and the solution's viability is demonstrated through Stage 2's market research (see Subsection 6.1.1); 2) "Translation and Validation": comprising TRLs 4 to 6, and corresponding block B's and C's activities, is the phase on which the previously defined concept comes to life through prototyping (see Subsection 6.3.2). Low and high fidelity models are tested in both laboratory and relevant environments, to evaluate their performance under conditions increasingly similar to those of their real world application. In the case of medical devices, technical and clinical assessments are conducted in parallel to ultimately collect all necessary data to prove the solution's effectiveness and safety (see Subsection 7.1.2), according to the main regulation's guidelines (Chapters 4 and 5); 3) "Scale-Up and Launch": comprising TRL 7, 8 and

9, corresponding to block D's activities; having found the features that value the solution, the design is validated, and final prototypes are developed to be tested and approved by the appropriate entities (further detailed in Section 7.1). In the European medical device industry, these entities will be both national supervising authorities and those that grant the European conformity seal: the CE marking. Regardless of the type of solution being developed, before launching it to the market to be adopted by the final user, testing activities are conducted in an operational environment since this, in theory, comprise all the requirements of the final application.

This correspondence between the TRL scale's maturity levels and the medical device path-to-market's phases is gonna be used to developed this work's proposed conceptual framework.

2.3.2 Valley of Death

All three mentioned phases ("Ideation and Innovation", "Translation and Validation", and "Scale-Up and Launch") will have their own challenges, demands, and intervening actors. For a new entrant, for example an academic, it can be particularly difficult to surpass some of these hurdles, namely those relating to resource demand. These innovators are often dependent on the efficiency of their relationships with third parties, namely the government (that provides them support through its official entities and initiatives) and the industry players (who provide them resources and business opportunities).

In the first phase of "Discovery/Innovation", academia uses its advanced knowledge to create an innovative concept, while governments are often in charge of providing the necessary capital to undertake part of the Research and Development (R&D) activities. However, since these include several resource-intensive processes and procedures, this public funding is often insufficient to cover all activities of medical device development, namely, from TRL 4 forward (see Figure 2.1). At this point, if the innovator can not afford the expenses in any way, she/he will probably turn to private funding to complete the R&D activities and value the solution. Unfortunately, private investors are usually only willing to invest later on the development cycle, particularly, from TRL 7 forward, when the solution's clinical validity is already demonstrated and deployment activities can be initiated. This poses a funding gap (from TRL 4 to TRL 6) that hinders the innovation's path-to-market in such a way that it can doom it to failure if the right approach is not adopted. This infamous gap is known as the "Valley of Death" (illustrated in Figure 2.2) and, unfortunately, represents the reality of many companies, particularly of new entrants [85]. In order to surpass this challenge, one must understand all the causes for this unfortunate fate. Although the lack of funding can justify part of it, the reality is that this "death" can also result from the misalignment between the basis of funding decisions and the developing team's motivation.

In the initial stage of R&D activities (the left side of the "Valley"), scientific merit is often the decisive factor for funding to be granted, and the innovation's development is often driven by a "technology push" force. Since this merit can easily be delivered by academia due to their technical knowledge and work method, the industry's interests are aligned with those of academia, making funding easier to get, especially when public initiatives, that allow their collaboration, arise. Conversely, on the right side of the valley - which is focused on the technology's scale-up and distribution - the basis of funding

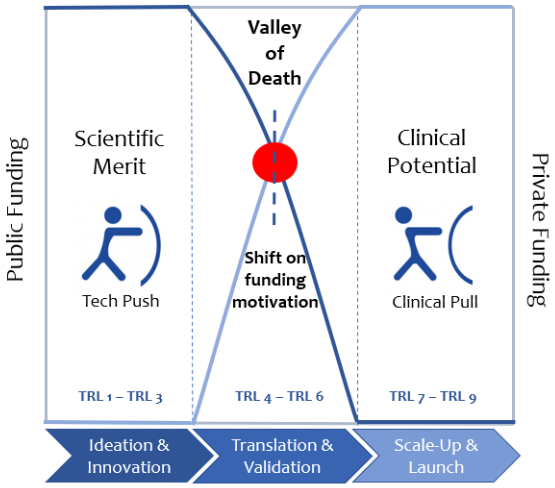

Figure 2.2: Representation of the "TRL Valley of Death". Public funding is represented with a dark blue line, whereas private funding is represented with light blue. Based on the webinar "The Healthcare Path from Idea to Market", John Collins (CIMIT) presentation.

decision changes becoming the technology's impact and investment potentials. What commonly happens is that the innovators do not change their motivation accordingly, remaining focused on scientific accomplishments instead of being driven by the market's demands, "clinical/market pull" approach.

Thereby, one encourages innovators to nurture their business perspective once validation activities are initiated, in order to entice investors and partners that can help deploy the technology in development. Furthermore, medical device entrants can surpass the "TRL Valley of Death" if they:

- Adopt core strategies tailored to the market: the medical device industry demands from the manufacturers extra care and attention when developing the solution. These have to act upon intricate matters such as regulation (Chapters 4 and 5) and ensure the device's safety and adequacy for their user (Chapters 6 and 7). One should know the market, its dynamics and users, and only then outline an appropriate strategy.
- Network from an early stage: market players are usually motivated by many initiatives to share their experiences and knowledge. Making the most out of these interactions may provide the innovator with good business and/or mentoring opportunities, facilitating the solution's integration in the market (see Section 6.1.3).
- Have a comprehensive plan: a timely structured plan displaying the business' objectives, projections, targets, and the solution's development journey should be outline early one, not only for the innovator to have a guiding tool throughout the path-to-market, but also to entice investors and other main stakeholders as these always appreciated a conscious and prepared innovator (see Sections 6.1.3 and 6.1.3).
- Employ facilitating tools throughout the development cycle: working philosophies, rapid prototyping technologies, multidisciplinary teams, are all facilitating tools that should be resorted to by the innovator in order to, firstly, avoid allocating vital resources in unnecessary actions and/or

wrong assumptions, and, secondly, decrease the intricacy and duration of the development cycle and, consequently, arrive sooner to the market.

- Integrate the end-users on the developing process: whether these are clinicians, patients, or a sales person, their insight can be key to create the most suitable solution (see Sections 6.1.1 and 6.3).

These and other strategies will be applied in the conceptual framework proposed in this work, as they benefit, not only the innovators, but the overall society. In fact, the "Valley" also symbolizes a loss for governments and its entities as important public resources (e.g. money and infrastructures) were allocated for solutions that didn't turn out meaningful and, thus, wasted. Thereby, all stakeholders must work to surpass this challenge, including governments empowering innovators with the tools and know-how that enable their technologies' deployment (as it will be described next). In the end, a successful deployment of innovation will translate into local and national growth, with more businesses and jobs being created around it, leading to both economic and demographic growth [35].

2.4 Technology Transfer: University-Industry

This work is focused on facilitating the transfer of innovation to the market, to the target audience. For that, one needs to make sense of the concept, its challenges and dynamics, especially when transitioning solutions between markedly distinct environments such as those of academia and industry.

Technology transfer consists of, as the name indicates, the transition of discoveries and knowledge to the public, which can be achieved, for example, through business agreements, conferences, or publications [100]. This educational flow typically occurs between the advanced knowledge producers (such as universities, R&D centres, and polytechnics) and the market (represented by expert companies/individuals and their costumers/users), and is this same transaction, between academia and industry, that will be, hereinafter, emphasized and meant by technology transfer.

The latter process is of extreme importance as it makes available to society outstanding solutions capable of improving one's quality of life, and which, otherwise, would have remained confined in the shelves of academia. However, the deployment of academia's solutions can be hard to achieve. Although its advanced knowledge permits to discover and develop exploitable innovations, the academia's lack of business know-how and resources can hinder the chances of commercializing such innovations. Thankfully, these two lacking factors are abundant in the industry, reason why their collaboration is highly encouraged [22]. In truth, academia is not the only party to benefit from such relationship. Industry recognizes that academia's valuable knowledge and developments are hard to match elsewhere. As both parties benefit from such collaboration, efforts have been made to nurture it, particularly within competitive and intricate markets such as that of medical devices, where any leverage one can have is important.

Academia-industry's technology transfer process is often based on business agreements - such as licensing deals, start-up creation, among others (see Section 7.3.1) [35]. Many renowned universities, such as MIT, Harvard, University of London, and Stanford, created a strong culture of entrepreneurship, where the commercial exploitation of their developments is strongly advocated for. Furthermore, technology

transfer agreements became a great source of income for these universities, allowing them to continue to invest on their R&D departments [9]. To help innovators go through the path-to-market, and correctly approach IP rights (see Section 2.5) and other technology transfer matters, these institutes provide their members supporting structures, such as Technology Transfer Offices (TTOs) [55]. Nevertheless, although advantageous, academia-industry collaboration is not always easily achievable. Academia is driven by scientific merit, by the possibility of advancing the state of art, whereas industry's motivation is often economical, the profitability, the chance of reaching millions of people and collecting even more dollars. With these two different perspectives on the innovation's value, which can be difficult to align [10][121], the technology transfer process can be hampered [55][122].

In order to guarantee that both their perspectives and objectives are respected, both parties must compromise. In fact, as mentioned before, the path-to-market often demands this same alignment between the innovators' mindset and the business' driven force in order to avoid the fate of many businesses: failure (see Section 2.3.2). Furthermore, the equilibrium of academia-industry's relationship also depends on other participating entities. For example, academia's TTOs play the role of mediators, guiding most of its technology transfer processes, and ensuring that the innovation's commercial exploitation becomes a reality. Other key entities are the governments and the regulators, which provide, not only resources and initiatives to bring together academia and industry (see Section 6.1.3), and stimulating innovation, but, through their legal power, greatly impact the technology transfer process [2][51][90], especially in highly regulated industries such as that of medical devices. In fact, regulators are essential on surpassing the "Valley of Death" [85], which highlights the importance of, not only understanding the technology transfer process, but of internalizing the industry's regulation.

In sum, as promoting technology transfer between academia and industry is to benefit the whole society, key opinion leaders must lead this cause, encouraging initiatives that join the two parties and facilitate their collaboration. Examples include to raise awareness and provide training on technology transfer matters (such as IP rights and business models) in academia, and to create partnering and networking experiences (see Sub-subsection 6.1.3).

2.5 Intellectual Property

Nowadays, any innovation is prone to be copied by other market players who wish to take advantage of non-proprietary solutions, thus, any innovator must understand the scope of property protection in order to safeguard her/his work when the time comes.

Intellectual Property (IP) includes all exclusive rights to intellectual creations. Seeking this protection for a product, process, or service, aims to, not only protect a creation against copycats and work-around solutions, but also to safeguard its creator(s) by conceding her/him with the rights to their own invention. Such IP rights are recognized world-wide with the objective of stimulating creativity and regional development, and their scope comprehends two main groups: copyrights and industrial property [155]. The copyright modality protects authors and their published, or unpublished, original work. This

can be referent to the areas music, literature, arts, drama, mathematics, and even informatics (as source code can be covered by copyrights). Industrial property refers to rights such as patents (and utility models), trademarks, industrial designs and models, among others. Focus will be given to three rights: trademarks, patents and utility models.

Trademark regards to anything that serves the purpose of identifying a manufacturer of goods, or a service provider. It can protect names, words, symbols, devices, or a combination of them, from being used or copied. Regarding patents and utility models, both rights can be used, in Portugal, to protect inventions (i.e. defined as novel technical solution for a specific problem), from which are excluded: presentations of information; surgical or therapeutical methods of treatment; the human body; discoveries, scientific theories and mathematical methods; plants varieties and animal breeds; and software as it is. Note, however, that in Europe software can be protected as a computer implemented invention, where the patent protects the process - how the software works within a system with hardware - and not the code itself (which, in turn, can be protected by copyrights). Both the patent and the utility model provide territorial protection and enable their assignees (the owners of the application's rights) to exclusively exploit the invention, and avoid its handling, in any way, by third parties. Nevertheless, their protection lasts for different time periods - 20 years for the patent and 10 years for the utility model - and their protection criteria are not equally rigours. A patent has stricter criteria to be complied with to be granted, namely: be new (meaning, it is not part of the state of the art), involve inventive activity (meaning, it is not be obvious to an expert of the field), and be susceptible of industrial application (meaning, it can be produced, or used, in the industry). The demanding criteria, together with the misinformation issues often surrounding these matters of intellectual property, can hinder the innovator's chances of protecting her/his innovation. For example, in the EU, to comply with the novelty criteria, no information can be disclosed (whether in a presentation, article, or a scientific meeting) until a patent request is filed. To avoid such mistakes, and to access expert advice throughout these costly, lengthy, and exhaustive protection journeys (see Section A.3), specialized entities should be consulted in a timely manner. National, and international, authorities, such as the European Patent Office (EPO) and World Intellectual Property Organization (WIPO), can help the innovator to make sense of the path to protection, as well as consulting companies and the Technology Transfer Offices (and related departments), often present in academia. Nevertheless, since the purpose of a patent is to be commercially exploited, this IP right is frequently sought after by innovators, particularly academics, who recognize both the value, and the business opportunities, it can create for their invention (see Section 7.3).

Furthermore, the patent system encourages technological innovation, dissemination of knowledge, technology transfer, and promotes competition and investment, and, although the protectability process often requires one to publicly disclose information on the innovation (see Section A.3), having a patent, or other form of protection, will allow the innovator to fight work around creations that may emerge from it, and access all the opportunities that protection unlocks.

2.6 Facilitating Development Tools

Today's dynamic world pressures industries to provide solutions the moment the need arises. This rhythm is only bearable if innovators access optimizing technologies and strategies that allow them to accelerate the development cycle and decrease the time-to-market [4][79]. Some of such facilitating tools will now be described. Their principles and methods will be applied in this thesis proposed framework.

2.6.1 Human Centred Approaches to Design

When approaching a medical device's design, the innovator must focus on both the industry's requirements (regarding technical performance, regulatory compliance, among others) and on human factors. In fact, being the healthcare sector evermore focused on the patient [20], is only natural to also reflect on the organic dimension of the devices, especially when it comes to their usability as usage errors may have serious consequences [83][163]. Thereby, approaches like Design Thinking and User Centred Design (UCD) should be integrated, to the appropriate extend, on one's design strategy. These will direct, from early on, the innovator's focus to the device's user, helping to develop, not only an effective device with good clinical outcomes, but a wanted and appreciated solution.

Design Thinking is a human-centred design process, applied at an early stage of the project's life-cycle, that efficiently exposes possible problems on the idea's foundations and stimulates the emergence of creative solutions through its five phases (see Figure 2.3): Empathize, where research is conducted to identify the users' pain points and unanswered needs; Define, where the information gathered is summarized and the problem one will solve is defined; Ideate, where the previously acquired teachings are used as an input in, for instances, brainstorming sessions, as to come up with a strong concept for the product/service; Prototype and Test, two symbiotic steps where prototypes are submitted to testing to assess their viability and performance, helping to shape each model until the solution's final form. This working loop, ideally, never seizes since a good project will always strive to evolve, thus, Design Thinking can be viewed as an organizational tool which principles are suitable to be integrated in any innovator's strategy, as they will in this thesis' conceptual framework (Chapters 6 and 7) [134].

Figure 2.3: Illustration of Design Thinking's five phases.

The User-Centred Design (UCD), on the other hand, is an approach to design focused on the users, their wishes and expectations. By contemplating all dimensions of healthcare, complementing quantitative (objective) data with insightful information on the user, UCD presents itself as improved alternative to the traditional approaches focused exclusively on the device's outcomes (its clinical value) [96]. The enriched data increases one's confidence in all decision-making processes and helps to create a suitable solution for the users, granting innovators a competitive advantage in the market [86][113]. Complementing UCD, is applied ergonomics, or Human Factors. This scientific branch dedicated to the human dimension, provides the tools necessary for one to design a more user-friendly product and, thereby, safer [83]. It

encourages the teams in charge to get to know the end-users and their surrounding environment, deeply enough that even their interaction with the solution can be predicted [98]. Although this approach is more frequently adopted in a solution's development stage, the integration of ergonomics (and all user-centred approaches) earlier on can bring an incredible value to the project since many considerations must be accounted for from as early as the design stage. For example, the way that users perceive the device's safeness and efficiency can be different than in reality, which presents a gap that, if not shorten by getting to know the users, their behaviour and surrounding environment, can lead to usage mistakes and wrong assumptions [83]. Even with such advantages and successful examples in medical device development [86], the medical device industry still offers some resistance on adopting user-centred approaches from an early stage [113], with technology performance and clinical results still outpacing user satisfaction. In truth, a medical device must be safe and reliable, meaning that regulatory matters, and both technical and clinical evaluations, are imperative and a priority. Nevertheless, one should not forget that medical devices are meant to serve their users, being only logic to design for them, with them [119][149].

2.6.2 Lean Development

Inspired by the lean manufacturing process, Eric Ries developed a new work philosophy sustained by validated learning [138], where consumers have a central role throughout the solution's development cycle. Simply put, in the lean startup model, the set of hypothesis made when conceptualizing and designing the solution, are constantly being tested by the users, whose feedback will then either validate, or invalidate, each hypothesis. In this process, known as the "Build-Measure-Learn" loop, the insight collected will be used to tune the tested prototype until a final solution that responds to the users' demands and technical requirements is achieved. The quicker one can go through the loop, the faster one learns and achieves the solution's final form, thus, one is encouraged to start the learning process as soon as possible. One shall start by developing, and testing, a simpler model with only the essential features that enable its function (designated as the Minimum Viable Product, or MVP), and, then, work through the loop. Testing activities can include A/B testing - on which two versions of the same feature are prototyped and evaluated by the user to identify the most appreciated- and straight forward methods such as in a launch-review system.

By adopting the lean model, the lesser resources are wasted in unnecessary features, and the faster one enters in market, a valuable advantage to have, particularly, in competitive markets such as that of medical devices. Nevertheless, not all the medical devices will be able to follow integrally this model since some solutions' prototypes can not be build at the speed the loop requires, nor the regulatory framework allows for the users to access devices that are not reliable, nor proven safe. Thereby, the extend to which the lean principles are employed depends on the innovators and the solutions they are developing, however, it is always advantageous to be driven by the model's advocated pillars: to value the user, the resources, and speed [137].

2.6.3 Agile Framework

The agile philosophy was created within the software industry to optimize the development and delivery of its products, processes, or services. Today, this framework is employed in many industries, such as those of healthcare, since its principles and tools are useful for any business. Agile, and its different methodologies (such as Scrum and Kaban), encourage developing teams to be flexible and creative, quickly responding and adapting to change through short development cycles, referred to as "sprints". The human element is also greatly valued, with multifunctional teams working as an unit to deliver value to the client (the product owner), with whom they are in constant communication. In sum, the agile framework is about being efficient and practical, replacing, for instance, lengthy case studies and documentation by simple "user stories" focused on the "who", "what" and "why" of solution's requirements [151].

2.6.4 Rapid Prototyping

On the prototyping stage, where the envisioned concept is materialized, the latter starts by taking the form of simpler experimental models which main goal is to validate and test the assumptions on which the idea was conceived, before spending significant resources on something unwanted, or unfit, for the market. Prototyping can be an expensive phase, since it requires resources (e.g. materials, expertise and machinery) that may not be accessible to all players. Furthermore, given how often the markets change their offer due to emerging technology and volatile costumer's needs, the advantage is of those who can deploy a good product before anyone else. Thereby, prototyping and testing activities must happen in a fast pace in order to deploy the solution as soon as possible, increasing its chances of success [79]. Enabling a quick, and affordable, delivery of solutions to the market are the rapid prototyping (RP) technologies. Rapid Prototyping is a relatively new approach that has reinvented the concepts of design and prototyping by providing fast, accurate, and affordable tools to materialize any person's idea. Such advantages are enticing for a whole new group of people that before didn't have the resources and/or know-how to employ traditional prototyping technologies (see Section 2.2). RP is, thereby, strongly propelling innovation, shortening the solutions' development cycles and increasing their delivery rate [4][38], features appreciated by most industries, including those of biomedical and health sciences [145].

Digital Fabrication

In 2D/3D fabrication, a structural model is constructed by first resorting to CAD software. This modelling tool will provide 2D/3D designs of the envisioned solution, allowing the innovator to experiment and visualize the models before actually spending resources on their materialization. When satisfied with the design provided by the software, the innovator will use the same design data as an input on manufacturing machinery that, finally, materializes the desired model. This type of RP technologies comprises two main methods: additive and subtractive fabrication. In additive manufacturing, commonly referred to as 3D printing, the desired result is obtained by slicing the 3D-CAD model into thin layers and then, with its geometric data, the manufacturing equipment proceeds to add multiple layers on top of one another. This method allows complex shapes with irregular features to be captured with high fidelity,

minimizing the waste of raw material. There is a variety of materials that can be used to print, from paper, plastic, metal and ceramic, to bio-ink, tissues or stem cells (in bioprinting) [6][89][145]. The subtractive techniques consist of removing material from an initial block of material, according to the CAD design, until the desired part, model, or assembly is achieved. There is a clear waste of material and problems can arise, reason why, through the years, additive methods have been favored in field such as the (bio)medical one, where these are employed in, for example, medical surgeries' pre-plannig, fabrication of prosthesis, implants, medical tools, hardware casing, among others, thus contributing to improve society's life [81][123]. RP printing technologies include techniques such as stereolithography (SLA) and selective laser sintering (SLS), which equipment and materials are gradually becoming more affordable, making them accessible to a bigger group of people, from researchers to students, and hobbyists [89].

Hardware

As mentioned before, innovative ideas do not only come from the expert minds, and since many fields of engineering can be quite hard to fully understand without a long educational journey and experience, a problem arises for those that lack the know-how but want to employ those same teachings in their creations. To respond to such problem, facilitating tools, such as toolkits, emerged in fields such as electronics, to give innovators the opportunity to create without worrying about the creation's complex core structure, saving them time to focus on innovating and to prototype in a timely manner [53]. For example, the BITalino, a low-cost, modular wireless biosignal acquisition system, is a versatile hardware toolkit designed to make accessible biosignals to whoever wishes to enter the world of physiological data [60]. It provides all the tools necessary to innovate, namely the BITalino credit-card sized development board which sensors enable the acquisition of several bioelectric and biomechanical measurements (such as electromyography and electrodermal activity) [61]. There are many platforms and toolkits available for one to resort to when prototyping a solution. Their characteristics and performances may be different, thus, one should study all options [80].

Software

Fast and affordable online prototyping tools arised to decrease software development cycles, and give designers and developers an important leverage [93]. Several platforms, with different purposes and features, are available to choose from. Such choice must consider: the intend the solution, the tool's learning curve and compatibility with others used in the project, the intend level of fidelity, the development budget, among others. Low code and open source platforms, such as Flutter and GitHub, provide their users the necessary tools to quickly create applications of different purposes in a simpler and intuitive manner, and to access an open source community where resources are share and development activities take place in a safe environment [54] [93][131].

Chapter 3: Case Study: e-CoVig

The present chapter presents the case study of e-CoVig, a remote monitoring health system developed by a team of both academics and non-academics, in response to the COVID-19 pandemic [8]. Besides introducing the system, this chapter also describes the qualitative research conducted with key players of the medical device industry, in the scope of the thesis' objectives.

3.1 An Overview of the e-CoVig System

e-CoVig is a monitoring system which collects, manages, and exposes physiological and clinical data of its users. This low-cost mHealth solution, coupled to a cloud-based e-Health platform, aims to automate and ease the follow-up and monitoring processes of patient's symptomatology, at scale. Its development was motivated by the COVID-19 pandemic, when a system was in need that could conduct the follow-up of those infected by the SARS-CoV-2 virus (which, at the time, was performed by the health professionals through time-consuming phone calls).

The e-CoVig's ecosystem, illustrated on Figure 3.1, consists of three elements: a web domain, a mobile application, and an acquisition device. This interconnected environment enables the communication between health professionals (and/or other relevant healthcare providers) and their patients, mainly interchanging information relating to the user's health status, such as personal annotations - often regarding the user's symptoms and/or thoughts, as in a diary - and physiological data - acquired through the sensing capabilities of, either the e-CoVig acquisition device and the smartphone sustaining the mobile application (see Figure 3.1), or of medical devices already possessed by the user. In fact, the use of the acquisition device is optional since common household devices, such as thermometers and oximeters, can perform the same measurements. Nevertheless, with the e-CoVig acquisition device, one gets to acquire critical data (including the user's temperature, oxygen saturation and heart rate) with just one object (which, otherwise, wouldn't be possible) and, due to its wireless connection to the e-CoVig mobile application, the communication and management of data becomes much easier. The aforementioned advantages should encourage its adoption [8]. Nonetheless, once collected, all data is displayed in a streamlined and intuitive manner (such as through dashboards and timelines) in each user's profile within the web-based platform. The former, developed by the company BrainAnswer, was designed to be applicable in multiple scientific research contexts [82]. Moreover, when the e-CoVig project started, in early 2020, the versatile platform was already in a mature state, which constituted an important advantage to the e-CoVig team, as it "only" meant to adapt the platform to the system's medical intend: to manage all collected personal data in an appealing and clear manner, and enable the streamlined communication between health care professionals and their patients (in a telemedicine approach). Overall, the automation and sensing capabilities of the e-CoVig system make it a promising system to be applied in both clinical and non-clinical settings, as its journey has been reveling.

Figure 3.1: e-CoVig mHealth system overview [8].

The path of the e-CoVig project has been distinctly unique, from its origin to its founders. It was created following a special call for R&D projects to address pressing needs of the COVID-19 pandemic (issued by the Portuguese National Science Foundation). Its development team was constituted by both academic and non-academic individuals of distinct backgrounds, including medicine, management, and engineering (detailed in Figure B.1). These two unique factors influenced the project's development in more ways than one. For example, the urgency of the pandemic scenario meant that: 1) the project's team had to conceptualize a system that could be delivered in a short period of time and, simultaneously, be ready to be applied at scale. The challenge was then, to encourage a mainly knowledge-driven team to divide its focus between research and the delivery of a practical effective solution; 2) the participating external entities had to be willing to facilitate typically slow procedures and processes, such as budget and legal decisions, in order to help achieve the project's timelines; 3) the team was handed an already defined problem and target audience, which led to the concept being defined quicker than when market scan is needed to identify and define opportunities, accelerating the solution's development cycle. Furthermore, the team's heterogeneity was vital to create a system that contemplated all the problem's main dimensions, including the solution's technical feasibility validation and its clinical purpose. For instance, the team counted with the participation of doctors which had a much greater understanding of the problem than the remaining team members.

During the system's design and development cycles, a limited number of prototypes of the acquisition device (Figure 3.2) were developed, and both the mobile application and the platform were matured. Further, the system's effectiveness and usability were often tested with the e-CoVig team's members and acquaintances, being formally performed, later on, in both clinical and domestic settings (from which good results were obtained). All of the participants were, within the scope of the project, considered healthy as they were not infected with the SARS-CoV-2 virus. As the project's development unfolded,

both the technical and clinical data were collected on the system. Furthermore, at the time this thesis is being written, the team had just received permission from the institutional ethical committee to conduct a clinical investigation on their acquisition device's performance, in a hospital setting with pathological subjects. Considering the e-CoVig's path so far, and this work's proposed path-to-market (Figure 1.1), the project seems to be standing in block B's verification and validation activities, while, simultaneously, initiating Block C's clinical trials, an important identification for later to respond to one of this thesis' objectives: the outline the e-CoVig project's future (Figure 8.3).

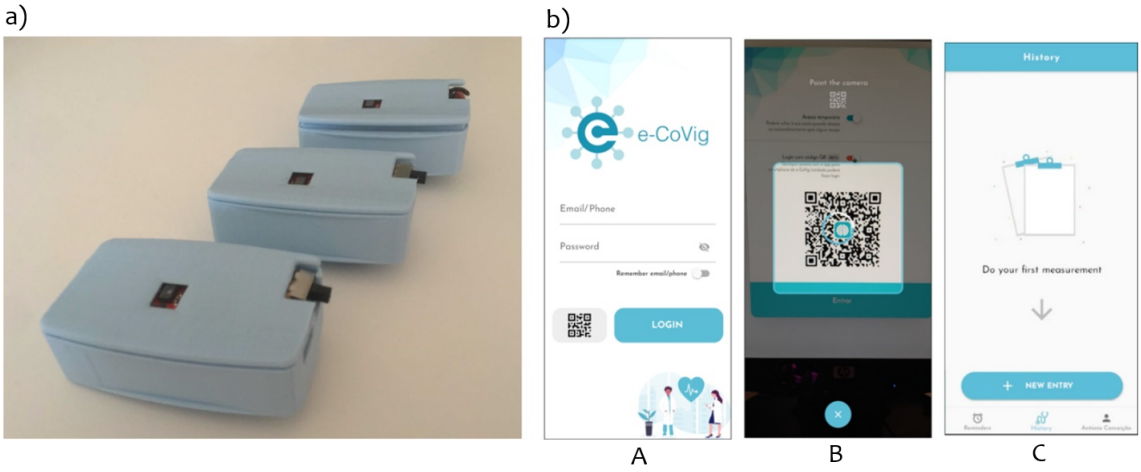

Figure 3.2: e-CoVig system's elements a) Prototype of e-CoVig acquisition device; b) e-CoVig mobile application (A: login screen; B: QR code; C: home screen) [8].

3.2 Interview Study: Method and Data Analysis

With this thesis' objectives in mind, one will now present the qualitative research conducted in the scope of this work's proposed conceptual framework. The latter, detailed throughout the next four chapters, will be evaluated by the input of key members of the medical device industry, including the e-CoVig team. Such feedback will be detailed as the framework is presented to, as stressed before, better contextualize the reader.

In order to conduct a sound study, and obtain insightful results, a timely and meticulous preparation was needed. This included, among others, the definition of the research main objectives, which were:

- To identify any barriers to safe and effective adoption throughout the path-to-market.
- To identify the key actions that must be performed to ensure a successful development, and deployment, of a medical device.
- To evaluate the contributions described throughout the present thesis.
- To characterize the e-CoVig's path so far, and identify potential improvement points.
- To outline a plan for the e-CoVig project's future, taking as input both its characteristics and the teachings attained throughout this work.

To accomplish the latter, a total of 16 open-ended semi-structured interviews were conducted, 9 of

which with key members of the e-CoVig project (the industry's new entrant, hereinafter mentioned as the group "e-CoVig") and the remaining 7 were conducted with experts belonging to the medical device industry's essential dimensions (hereinafter, regarded as "experts"). All interviewees, and corresponding organizations, are detailed in Figure B.1, in Appendix B. Within these two big groups of participants (e-CoVig and experts), extremely diverse backgrounds and roles in the medical device chain were identified prior to the conduction of the interviews. To approach such diversity in a streamlined manner, one chose to further divide the 16 participants into categories, according to what was expected to be their greatest contribution within the scope of the research. Thus, based on what is described in Chapters 1 and 2, five categories were created: "Ideation & Innovation", "Design & Development", "Technology Transfer", "Regulation" and "Entrepreneurship". Such categorization implied the development of five different scripts, each with their own objectives (detailed in Figure B.2), however, all scripts had the same core structure and followed the same interview protocol.

Since the results of the interviews aimed to evaluate this work's proposed framework, before conducting the research, the topics by it approached were summarized. Hurdles and key points of each of phase of the path-to-market (Figure 1.1) were gather and displayed as a reference "forecast" for this qualitative research (Figure 3.3). Note that the four categories created ("Ideation & Innovation", "Design & Development", "Pre-Clinical & Clinical Validation", and "Commercial Adoption") result from an adjustment of Figure 1.1's phases that aimed to optimize the interview process.

Category	Key points forecast	Hurdles forecast
Conceptualization	Clinical expertise Market research Technology Networking Planning	Undefined concept Technological maturity Incomplete budget Partnering
Design & Development	Work philosophies Team heterogeneity User-centred approach Intellectual Property (IP) Facilitating tools Data protection Medical device regulation	Regulatory awareness IP issues (misinformation) User inclusion Unchecked assumptions Suboptimizing development
Pre-Clinical & Clinical Validation	Timelines CE marking Clinical trials Financing	Regulatory workload Funding issues Misinformation Testing failure
Commercial Adoption	Regulatory surveillance Industry-University Market entry strategies Evolution	Market choice Production and distribution Initial customer traction Marketing

Figure 3.3: Forecast of the main hurdles and key points of the medical device path-to-market, based on this thesis' conceptual framework.

Having laid down what is to be validated (the hurdles and key matters approached by the proposed conceptual framework), the interviews could be conducted. For three months, 16 interviews were performed, lasting from 30 to 180 minutes. These were conducted online, and recorded amid the interviewee's consent. The results obtained are summarized in Figure 3.4, detailing the most mentioned matters of the medical device path-to-market perceived by the interviewees as key to achieve and succeed in the market.

This feedback was compared to the one's forecast and, thereby, to the framework proposed in this thesis in order to evaluate it. Furthermore, the results are displayed in a way that highlights the interviewees' consensual, or non consensual, opinion on each topic's relevance for a successful path-to-market. This separation in "e-CoVig team" and the industry's "experts" helped to understand if during the new entrant's path-to-market all the important actions and matters were approached, thereby, facilitating the detection of possible improvement points that could be acted upon in the project's future (one of the aims of this thesis). Once again, all results will be discussed in detail throughout this document, in the end of each pertinent chapter and/or section, to better contextualize the opinions and suggestions given by the participants.

Category	Mentioned matters	Perceived as relevant by the interviewees	
		Experts	*e-CoVig*
Conceptualization ***13 interviewees:*** *Ideation &Innovation (6)* *Tech Transfer (2)* *Regulation (2)* *Entrepreneurship (3)*	Level of innovation	✓	✗
	Market research	✓	✗
	Regulatory awareness	✓	✗
	Clinical expertise	✓	✓
	Intellectual Property	✓	✓
	Technology and its maturity	✓	✓
	Organize and plan	✓	✓
	Networking and partnering	✓	✓
Design & Development ***All 16 interviewees***	Work philosophies	✓	✓
	Usability	✓	✓
	Team heterogeneity	✓	✓
	User-centred approach	✓	✓
	Facilitating tools	✓	✓
	MDR	✓	✗
	GDPR	✓	✗
Pre-Clinical & Clinical Validation ***11 interviewees:*** *e-CoVig founders (5)* *Regulation (2)* *Entrepreneurship (4)*	Ethics	✓	✓
	Clinical trials	✓	✓
	CE marking	✓	✗
	Financing	✓	✗
Commercial Adoption ***7 interviewees:*** *Regulation (2)* *Entrepreneurship (5)*	Regulatory surveillance	✓	-
	Business plan	✓	-
	Industry-University	✓	-
	Market entry strategies	✓	-
	Evolution	✓	-

Figure 3.4: Interviewees' most mentioned matters of each category approached. Particularly, each group's ("e-CoVig" and "Experts") mention to the latter is indicated with intuitive symbology.

In the next two chapters the legal framework of the medical device industry will be discussed. The importance of both the Medical Device Regulation (MDR) [49] and the General Data Protection Regulation (GDPR) [48] was identified from early on, during this thesis' primary research (Chapters 1 and 2). Therefore, as two cornerstones of medical device development, their streamlining and detail was necessary (Chapters 4 and 5). The teachings attained will then be applied in Chapters 6 and 7, completing the proposed conceptual framework.

Chapter 4: Medical Device Regulation

Medical devices carry the big responsibility of dealing with the human health. This value, and simultaneous vulnerability, highlights the importance of risk assessment and good practices during the solutions' development and maintenance in the market. All key matters of medical device development are covered by regulations, such as the European Union's Medical Device Regulation (MDR) [49], which medical device manufacturers have to comply with, as well as other economical players, for the solution to be commercialized. Furthermore, whichever regulation is in force, governments and regulators must make sure that it is aligned with the current technological landscape, since new concepts and security hazards are constantly emerging [153].

Compliance can be a draining source of resources and difficult to make sense of, becoming, many times, a bottle-neck for innovators [36][56][135]. Thus, it is particularly important to address, and demystify, the medical devices regulation so that all innovators, especially new entrants, are aware of what the law requires from them and their solution, from early on. Such task will be take on by the present chapter, which will also approach some of Figure 3.3's forecast hurdles - such as regulatory awareness and workload, as well as the field's common misinformation and faulty performance issues - and the results of the conducted interview research study regarding the MDR (see Section 4.6).

4.1 Regulatory Entities

The European Union (EU) has official bodies in charge of regulating medical device trading activities within its territory, namely: the European Commission (which has the power of legislative initiative), the Council of European Union, and the European Parliament; being the latter two in charge of amending and approving the laws purposed by the Commission which, when approved, shall be adopted by the Union's member states, to which Portugal belongs. Each state will also designate a competent authority that acts in the name of the government to ensure that both common directives and regulations are adequately applied and respected within the nation. In the case of medical devices, this Portuguese authority is *Instituto Nacional da Farmácia e do Medicamento* (INFARMED) [68].

Other important entities to consider throughout this regulatory path are the Notified Bodies (NB) [28]. These are responsible for assessing the conformity of a product, process, or service, before being placed in the market. However, most countries (including Portugal) do not have a Notified Body for medical devices which can constitute a barrier for the manufacturers since, most times, a NB is required to intervene in the process of obtaining the CE marking, the conformity seal needed, in most cases, for commercial trade within the EU. Nevertheless, all member states have an accreditation authority - in Portugal, this is *Instituto Português da Qualidade*, or IPAC [71] - that assesses and recognizes the technical competence of conformity assessment bodies (such as laboratories, inspection or certification bodies) to

perform their duties and work to specified standards [27]. Particularly, the accredited certification bodies are exactly those that shall be consulted when the manufacturer wishes to be certified for a certain standard to help to demonstrate compliance with main regulations, including that of the MDR.

4.2 Standards

Standards are documents that set out agreed requirements and recommendations regarding products, processes, or services. They are not legally binding, however, in the scope of regulations (which are compulsory), these can be strongly suggested, or even compulsory to demonstrate compliance to the main legislation. Standards can be elaborated by the European Union, having to be included in the member state's law, or by International Standardization Organizations, such as ISO, developed to harmonise technical rules worldwide. The goal of developing standards is to achieve optimization by reducing costs, promoting the solutions' safety and high performance, and to promote, and simplify, international trade through their adoption at large scale [31].

In the medical device industry, there are several standards to be aware of in order to comply with the MDR. Firstly, one can highlight ISO 13845 [74], the international standard for medical device's quality management systems (QMS) - one of the two elements needed to conquer the CE marking (see Section 4.3.4) - which supports medical device manufacturers when designing their QMS, promoting the processes' quality and consistency (e.g. design, production, and delivery) and the device's safety. Other two important standards are the ISO 14971 [75], which approaches risk management - an important pillar of MDR - by identifying hazards of the medical device and providing methods to reduce the risk for all stakeholders; and the EN IEC 62366-1 [73], which describes an usability engineering process through which the device's usage errors (closely related with its risk and, thus, to risk management) are identified and minimised until an acceptable use-related risk is achieved. All these transverse standards, although extremely important, are still just standards, meaning they will only cover the core matters of each dimension, having to be complemented with the fulfillment of the MDR's specific demands and nuances.

Furthermore, depending on the type of medical device being developed, other standards may be needed to consider to demonstrate conformity with the MDR. For example, medical device software manufacturers should also comply with IEC 62304, a functional safety standard that covers the life cycle's process of medical device software (or of software embedded on a medical device), providing methods to ensure its safety [72]. Additionally, medical device manufacturers that process personal data (see Section 5.2) should as well respect the international standard ISO 27001, which sets out technical and organizational measures to decrease the risk of data breaches within the processing organization [76]. It is a particularly important standard in the scope of data protection and, thereby, its compliance is often advised to demonstrate conformity with yet another regulation: the GDPR (Chapter 5).

4.3 MDR Explained

The medical devices' regulatory landscape has been robustly changing over the last years, and with still more changes to come [33][40]. Previous directives were replaced by stricter and detailed regulations, outlining their urgency and importance, and digital technologies took the center stage along with their data protection issues. The current regulation covering the medical devices' placement on the market is the Medical Devices Regulation ((EU) 2017/745), or MDR [49]. This became effective on the 26th of May of 2021, and proves to be more detailed and comprehensive than its predecessors, demanding more quality, transparency and accountability from both the device and all involved in its deployment and maintenance to the market. It is worth mentioning another relevant regulation, the In-Vitro Diagnostics Regulation ((EU) 2017/746), or IVDR [50], that regulates the *in vitro* diagnostics medical devices and that will come into effect in 2022. Although important, this regulation is out of this thesis' scope.

If one's idea proves to be a medical device, a dense and compulsory regulation awaits, that should, furthermore, be tackled from any project's very beginning. Many of the regulation's requirements go back to as early as the design stage, and failing to comply with them may lead to costly and lengthy corrections that can hinder the device's whole journey to deployment. To help avoid such mistakes, guidelines and strategies were outlined, and made available by specialized organizations [65][66] and the European Commission [42], namely by the EU's Medical Device Coordination Group (MCDG), a group of individuals dedicated to the medical device sector's issues which guidelines, although not legally binding, are expected to be followed [29][30]. Nonetheless, the first step of the regulatory pathway of medical devices is to understand if one is indeed in possession of a medical device, which is already a challenge by itself since these type of devices can be tremendously different. To understand this matter, a brief summary of the categories and classification of medical devices will now be presented.

4.3.1 Material Scope

To know if one's solution is covered by the MDR, one must understand its scope. Starting with the definition, a medical device qualifies as such if three criteria are fulfilled: 1) is intended to be used on human beings; 2) it has, at least, a medical purpose - such as a diagnose, relief, treatment, monitoring and/or investigation intent; 3) its function can not be achieved by pharmacological, immunological and metabolic means [49]. The devices fitting this description can take the form of instruments, reagents, software, or implants, just to name a few. Classic examples of medical devices range from stethoscopes and oximeters, to wheelchairs, pacemakers and knee implants (see Figure 4.1). However, any solution that states a clinical intend can, and most probably will, fall under the scope of the MDR. For example, products belonging to categories that would not typically be considered medical devices - such as those of drugs, cosmetics, EPIs, food supplements, and biocides - can be if the manufacturer claims a medical purpose. Moreover, the intended use is of such importance that common household items, like a tooth paste, may have to comply with the regulation if it claims, for instance, to have a protective action against an oral health condition. Furthermore, even some non-medical products that not claim a medical

purpose will have to respect the MDR. Examples include cosmetic products, such as coloured contact lens (non corrective), liposuction equipment, anatomical modulators, and invasive devices like brain stimulation equipment, which may pose a significant risk to one's health if faulty, thus, worth watching over. The MDR details these, and other, exceptions being extremely important to read the regulation before outlining a development plan.

4.3.2 Medical Device Classification

The single most important action to do, once sure of being under the scope of MDR, is to correctly classify the device. Different classes will have different requirements, thus, the MDR's classification will drive the device's development. The regulation defines four main classes, based of the device's potential risk to the users' health as the result of fault in its functioning [152]. Class I medical devices are those of the lowest risk, however, within this class, three sub-classes were created - Class Is, Class Ir, and Class Im - which regard Class I devices of sterile reusable/reprocessed, and of measuring function, respectively. These three subgroups will have some different requirements then the remaining Class I devices, for example, their special features will have to be assessed by a Notified Body in order to get the CE marking (just like the remaining classes of risk), whereas Class I devices can self-declare their conformity for CE marking apposition. Next, there is the Class IIa, followed by Class IIb and, finally, Class III, of increasing risk and regulatory demand (see Figure 4.1).

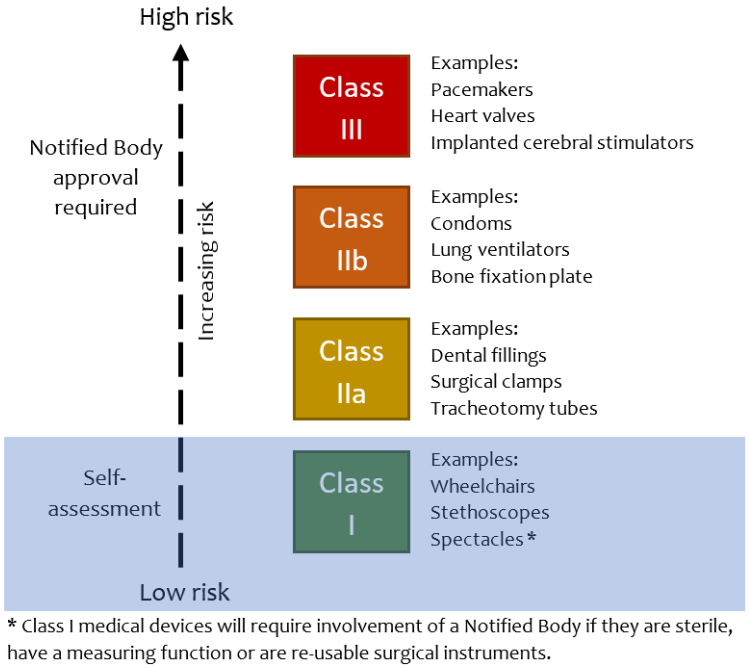

Figure 4.1: Classification of medical devices based on risk [64]. The intervention of a Notified Body, in the CE marking apposition process, is also displayed.

Given the scope of this thesis, it is worth streamlining the classification of medical device software into these four classes. Such categorization, simplified in Figure 4.2, is particularly dependent on the significance of the information provided by the software, and the clinical status of the patient.

Significance of Information provided by the MDSW to a healthcare situation related to diagnosis/therapy				
State of Healthcare situation or patient condition		**High** Treat or diagnose	**Medium** Drives clinical management	**Low** Informs clinical management
	Critical situation or patient condition	*Class III*	*Class IIb*	*Class IIa*
	Serious situation or patient condition	*Class IIb*	*Class IIa*	*Class IIa*
	Non-serious situation or patient condition	*Class IIa*	*Class IIa*	*Class IIa*

Source: MDCG 2019-11.

Figure 4.2: Medical device software classification (based on Rule 11 of the MDR) [102].

Furthermore, medical devices can be classified according to their duration of use in transient, short term, and long term and in, yet, three other categories: active, non-invasive, and invasive. To support the manufacturer in all these classification's processes, the MDR details all categories in its Annex VIII [49], providing twenty-two classification rules for one to resort to in order to do the best judgement possible. To complement the latter, the MDCG also provides guiding documents on classification matters relating to all classes of risk and for certain types medical devices, such as software [103][104][105]. Additionally, specialized companies and competent authorities can be consulted to clarify any doubts, especially regarding complex medical devices (either in structure, or function). For example, a device, such as biofunctional clothing, which intended use is to prevent a inflammatory crisis by integrating medicinal substances in its structure. Although it may be perceived as a medical device, it may not be one. Since the clothing has no medical intent, it would not be considered a medical device, and given that the prevention of the inflammatory crisis is likely to be achieved by pharmacological or immunologic means, this solution is, most probably, out of the scope of the MDR [17].

Once the device is correctly classified, the associated requirements can be identified and prioritized. Also, timelines and budget projections, as well as the overall business plan, can now appropriately contemplate the compliance journey of the device in question, contributing to its sounder path to deployment.

4.3.3 Territorial Scope

For one to know if it is under the MDR's scope, it is just as important to understand if the solution fits the regulation's material scope, as it is to know where the device's manufacturing and distribution operations are taking place. The MDR is directly applicable in the member states of the European Union (EU) and of the European Free Trade Association (EFTA). This being said, even manufacturers established outside this geographic range will have to comply to the MDR if, as stated in regulation, the medical device is to be commercialised and/or used by EU citizens [49]. Such manufacturers will, furthermore, have to designate an EU representative which ensures the regulation's compliance. Whether established in Europe, or with commercial activities running in the EU, the medical device manufacturer must, in most cases, acquire the CE marking, the "European passport" that will allow the device's commercialization. Achieving CE certification is a critical step on the path-to-market, and which demands time, funding, and dedication, from the manufacturer. Nevertheless, being accountability such an important pillar of

the MDR, also distributors, importers, EU representatives, and all economical players involved with the medical device, have responsibilities under the MDR. Thereby, the regulation must too be understand, and complied with, by these actors.

4.3.4 Key Matters

MDR is a dense regulation with several requirements, definitions, and suggested measures. To contextualize the innovator (and manufacturer) on the main steps that need to be taken to enter the medical device industry, the key points of the MDR are now summarized. Note that, for its importance in the medical device path-to-market, the CE marking will be detailed on its own section (Section 4.4).

- **Classification:** Medical devices can be extremely distinct, thus, being assigned to different categories with different requirements (see Section 4.3.2). Thereby, it is critical to correctly classify a device, being supported by regulation [49], guidelines [29], and reliable available information [17].
- **Technical Documentation:** Consists of a group of documents comprising all information on the medical device (validating it), namely: the device's description; its design and manufacturing information; compliance with performance and safety requirements; detailing on risk management and assessment dimensions; the device's verification and validation; and the technical documentation regarding the post-market activities. The Technical Documentation's requirements are expressed in the first three annexes of the MDR [49], particularly, Annex I details the regulation's essential requirements (General Safety and Performance Requirements, GSPR); Annex II describes, specifically, the content to be included in the Technical Documentation; and Annex III indicates the requirements of the Post-Market period to include in the documentation. The Technical Documentation must be made available to competent authorities or Notified Bodies (depending on the device's classification) and updated throughout the device's life cycle. These documents will be one of the two elements necessary to get the CE marking [87] [159].
- **Quality Management:** Together with the Technical Documentation, the Quality Management System (QMS) is a cornerstone of CE marking, being its implementation mandatory for every medical device manufacturer. It consists of a set of policies, processes, and procedures, covering multiple topics, such as process, production, and design controls, and the designation of the project's responsibilities (emphasizing the MDR's accountability pillar). The implementation of a QMS aims to approach the management of the numerous processes happening in the organization's daily basis in a sustained, safe, and rigorous fashion. Compliance with the QMS will validate the manufacturer. To achieve such conformity, her/him have to, not comply with the mentioned ISO 13485 (see Section 4.2), but also the MDR's particular requirements on the matter (such as the exceptions to conformity and the responsibilities of players other than manufacturers), implying a meticulous reading of the regulation. Besides the help provided to innovators by guidelines and standards [74], the implementation of a QMS can be facilitated by resorting to tools such as the electronic Quality Management System. The former's nature and features allow the automation of the whole process, which can bring greater benefits than those of the traditional paper-based method. For

example, the eQMS will detect errors more easily, support greater amounts of data, and facilitate the traceability and update of all documents, which is particularly important for the medical device industry's frequent audits.

- **EU Conformity Declaration:** A detailed file gathering all the important information regarding the medical device's identification and that, as the name indicates, claims the latter's conformity. It is demanded from all manufacturers and should be delivered by them when applying the device to CE marking in a Notified Body (NB), along with the QMS and Technical Documentation, or, if the NB approval is not necessary (see Figure 4.1), when preparing the actual apposition. Guidelines and templates are available in the EU's official page [159].
- **Clinical Evaluation:** Experimental evidence is needed as a way to guarantee the device's effectiveness and safety, and consequent compliance with regulation. Both before and after the device deployment in the market, clinical data will have to be collected, documented, and assessed, to demonstrate that the device performs as expected in both laboratory and real-world settings [30][106]. Clinical validity can either be obtained by claiming similarity with existing devices, or by conducting clinical evaluations and/or trials (depending on the amount of data needed to guarantee the device's clinical value and safety). Clinical trials are mandatory for devices that pose a higher potential risk, namely, Class III and implantable devices.
- **Vigilance and Post-Market Surveillance:** The importance of overseeing the medical device's performance in its operational environment is highly emphasized by the regulation, introducing dimensions such as Post-Market Surveillance and Post-Market Clinical Follow-Up. These have to planned out in advance and included in the appropriate documentation [107][108]. The manufacturer must elaborate and update reports, namely the post-market surveillance report and periodic safety update report (PSUR), that inform about possible safety measures implemented, as well as the analysis, and conclusions, of the new collected data.
- **Unique Device Identification (UDI):** An identification system to be integrated for all the medical device's classes, promoting the tracking and vigilance principles of the regulation [30]. Until 2028, appropriate entities will appose an UDI in all the devices.
- **EUDAMED:** The registration and tracking of medical devices is another important matter approached and currently being developed by European Union's work forces [33]. EUDAMED is an EU created database that works as a registration portal for medical devices, including all the important information about them and all main stakeholders (such as manufacturers, distributors, to EU representatives, and importers). Particularly in Portugal, the medical device competent authority (INFARMED) has already a system in place for the device's registration, which is expected to be performed by the Portuguese manufacturers before, and after, the EUDAMED's six modules - Electronic Systems on Actors registration, UDI/Devices registration, Notified Bodies and Certificates, Clinical Investigations and performance studies, Vigilance and post-market surveillance, Market Surveillance - are fully functioning (expected to be in 2022) [29][30].

4.4 CE Marking Pathway

The *Conformitè Europëenne* marking, or CE marking, is an European seal that demonstrates the conformity of the product, process, or service, with the main regulation and guidelines, being applicable in the same territorial as the MDR. For medical devices to acquire this seal, both the device and its manufacturer must be assessed and validated, by appropriate authorities. In Europe, and under the MDR, such validation will, respectively, depend on the conformity of two matters: the Technical Documentation and the Quality Management System (see Subsection 4.3.4). Furthermore, the manufacturer must also comply with the previously mentioned standards for medical device usability (EN IEC 62366-1), risk management (ISO 14971) and quality management (ISO 13485) (see Section 4.2).

Once the manufacturer acquires, and documents, the information required by the mentioned dimensions (including the clinical data), and implements the appropriate measures and procedures, her/him can submit them to be validated by the appropriate authorities, namely, the competent authorities and/or Notified Bodies (see Section 4.1). This process can be lengthy and costly, depending on the complexity of the device and the intervening entities. Several evaluations will have to be performed to access, and validate, the technical and clinical performance of the device, as well as its usability and aesthetics, and notifications will have to be frequently answered to by the manufacturer. Nevertheless, once both the manufacturer and the device are validated and said to be in compliance with the regulation, the CE marking can be apposed. This can be made by either the Notified Body - identified by a four-digit number in the device - or by the manufacturer by self-apposition, depending on the class of the device (see Figure 4.1). Having acquired the CE marking, the manufacturer can, finally, commercialize the medical device in the European market. It is worth mentioning that there are some exceptions in the medical device industry for the CE marking's compulsory status, namely, the custom-made devices, investigational devices (further detailed in Article 21 of MDR's Chapter 2 [49]), and any medical device under a special clause that, represented by another type of seal/reference, replaces the need for the CE marking.

In order to streamline the path to CE marking apposition, a workflow for all medical device classes is proposed in Section A.2, of Appendix A. These diagrams will be referred to in the proposed approach for MDR's compliance presented next.

4.5 Proposed Approached to MDR

As each class of risk presents different nuances throughout the regulatory pathway under the MDR, mainly regarding the CE marking certification process, a brief summary of such path, according to the device's class of risk, is presented in Figure 4.3. The latter is to be considered once the device is correctly classified and complemented by the provided CE marking's pathways.

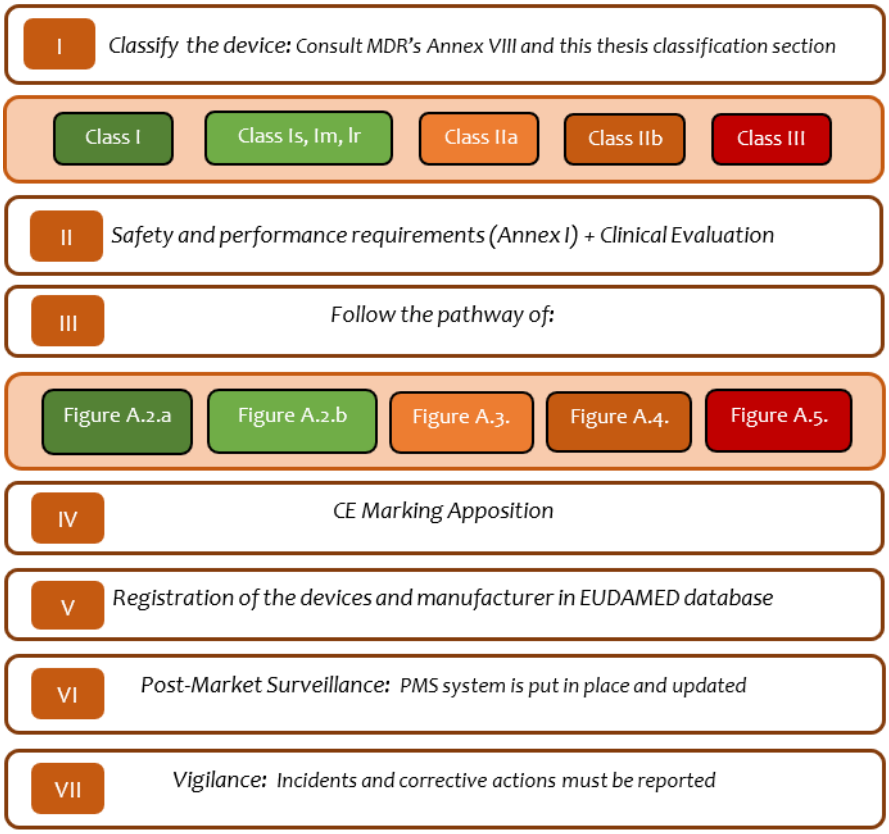

Figure 4.3: Proposed workflow for Medical Device Regulation compliance. Source: MDCG 2019 [105] [104] and MDR 2017 [49].

4.6 Interview Results: the MDR

Throughout the interviews, it was agreed by all participants, particularly the business-oriented and regulatory ones, that regulation, namely the MDR, presents itself as a huge challenge in the medical device path-to-market. High financial demands, accompanied by a high workload, were said to be unbearable for a standard new entrant, lacking of know-how and guidance. However, all experts acknowledged the regulation's importance to create a fair market and ensure the user's safety. The business-oriented experts highlighted the importance of seeking advise from early on in order to avoid costly hurdles in the future. The regulatory experts stated that most entrepreneurs of the medical device industry tend to underestimated the importance and workload of the legal issues, which may hinder their business on the long run. Furthermore, these legal knowledgeable also couldn't stress enough the importance of acknowledging the regulation from the first day of a project, not only to facilitate the compliance with main requirements (such as those demanding the traceability of the device's journey), but also to allocate the right amount of resources to compliance matters (the budget projections must meticulously detail the MDR's expenses). They also acknowledged some of the issues surrounding the MDR that are making it more challenging than it should be, particularly, the misinformation and lack of expert knowledge. Firstly, although the manufacturers should be aware of the regulation by their own initiative, it was

recognized that there is still a problem of communication between regulators and the manufacturers. Information does not seem to reach the industry players, particularly, the new entrants, with the urgency and value that it should. This was said to be an improvement point that should be worked on by the official entities and governments. Secondly, the regulatory experts also admitted that that information is sometimes not passed because is not yet fully understood by the actual regulatory entities. There is a alarming lack of human resources capable of supporting industry players, since regulators are themselves currently being trained for the matters of such recent (and in developing) regulation. A timely training for future dimensions of the regulation, such as EUDAMED (Subsection 4.3.4), should then be a priority.

Regarding, in particular, the results of each concept umbrella of Figure 3.4, one can notice that, during the conceptualization stage, the importance of the MDR was not perceived as relevant by the e-CoVig team, yet all experts participants agreed on its importance from this early stage. This lack of consensus may constitute a first warning sign on the path-to-market of the e-CoVig system. As stressed before the system was developed in unique conditions (see Chapter 3) which drove the team's total focus to the development stage, not putting legal matters such as the MDR (but not exclusively) as a priority as it should have been. During Design and Development (D&D) activities, all experts participants agreed on regulation being the biggest hurdle, much because it demands constant documentation and evaluations to be performed in parallel with the common demands of a D&D stage. The e-CoVig team, once again, did not mention any legal matters as key or challenging in this stage. Regarding the performance of pre-clinical and clinical evaluations, the CE marking pursuit was highlighted since it requires the collection of evidence on the device's safety and effectiveness through these evaluations (see Section 4.4). The complexity of clinical trials was also mentioned linked to the financial stretch necessary to prepare, perform, and analyse clinical evaluations. Strategies like claiming equivalence with pre-existing tested devices were suggested, along with the need to understand the regulation for medical devices since different paths exist for different categories of risk. Moreover, in the case of the e-CoVig system, regulatory experts highly encouraged the search for similarity data since, for their experience, the great number of mobile applications and acquisition devices being realised nowadays, typically have in common, at least, certain modules and components (respectively), which clinical data can be claimed, avoiding the performance of, at least, some evaluations. Regarding this same clinical investigations, the e-CoVig participants emphasized their struggle on getting approved by institutional ethical committee to conduct the trial in a hospital, as it took a lot of debating and, consequently, a lot of time to get the permission, delaying this stage several months. However, none of the remaining participants mentioned this matter as a pain point, on the contrary, even highlighted the importance of these considerations in today's world. Could be argued that experience on the field may ease this process by being prepared for all possible setbacks.

Lastly, in the scope of "Commercial Exploitation", the apposition of the CE marking was, logically, highly stressed by all experts (since it is the seal that allows trade activities to happen), however, the regulatory experts highlighted the importance of the awareness for national laws on commercialization. For instances, some countries, such as Portugal, demand for a product to be sold, it has to have its label written also in the national language. Such nuances much be accounted for. Concerning the device's

maintenance on the market, these participants emphasized the MDR's Post-Market Surveillance pillars (see Section 4.3.4), that should be planned out in advance and meticulously followed, as well as need to keep up with regulation as its constantly adapting to the technological landscape (regulatory uncertainty).

In sum, by comparing the forecast table's content (Figure 3.3) - which correspond to the matters approached in this thesis' framework - with that of the results table (Figure 3.4), one can affirm that both the importance and the challenging character of the MDR were correctly predicted. Furthermore, the insight collected, and discussed above, through the interviews was in concordance with the insight displayed throughout the present chapter, validating its conceptual approach.

4.7 e-CoVig and the MDR

Assuming that the e-CoVig system's aims to be applied out of the scope of the COVID-19 pandemic, and that its medical intent is set as monitoring one's health status, the first thing to do is to classify the system (see Section 4.3.2). Being the e-CoVig device a group of three elements, one must be cautious when classifying it since it will, most probably, require two, or more, certification processes. Firstly, the three elements are considered active devices by MDR, intended to monitor the user health status (medical intent stated). Thereby, in the case of the (optional) acquisition device, following Rule 10 of the regulation, this will probably be considered class IIa since, although it monitors vital physiological processes, the variations of those parameters may not result in immediate danger to the patient (where it would be class IIb). Nevertheless, a specialized entity must be consulted to clear such assumption.

Furthermore, if the manufacturer (in this case, the e-CoVig team) chooses to not pursue the acquisition device's certification, all other devices that can replace its function, working together with the remaining two elements (the platform and application) have, not only to be compliant, but also to be identified and disclosed to the user as a validated alternative. Regarding the application and web-based platform, although sometimes two different software may have to be classified separately (to be checked with the specialized entity), considering that both can be certified together, according with the Rule 11 regarding medical device software, the monitoring of physiological processes and provision of health information, together with the non-immediate danger of measurement variations to the patient, will lead to the classification of these elements as, also, class IIa, which implications are greatly detailed in MDR and official guidelines. Once classification is done and one knows what to do next, efforts and resources must be put into this journey, being the workflow suggested in Figure 5.7 a good place to start. This includes the timely implementation of a QMS and the elaboration of Technical Documentation to pursue the CE marking and commercialize the device (see Section 4.4). All MDR's measures to be implemented in the nearby future of the e-CoVig system are detailed in the Figure 8.3.

Chapter 5: Data Protection Regulation

As technology evolves, our lives become increasingly digitized, with moments being captured and shared, and large volumes of data being collected and stored [120]. The concept of Big Data refers to a great volume of data being generated every second, and perfectly mirrors the era we live on. The collection and processing of such an amount of information can be a great asset to businesses across all industries, however, a careless use of data poses a privacy and security risk for the data subject (see Section 5.3) [142][164]. Thereby, it became urgent to regulate the collection and use of data across the industry, according to the current technological landscape [40]. In Europe, particularly, the regulation covering data protection issues is the General Data Protection Regulation (GDPR) [48], topic of this chapter. Furthermore, one will also approach some of Figure 3.3's forecast hurdles, such as regulatory awareness and the GDPR's implementation within an organization. The results of the interview research study (see Section 3.2) regarding data protection and its regulation will too be discussed (see Section 5.8).

5.1 Enforcing the GDPR

In 2018, the GDPR became immediately effective in all member states of the European Economic Area (EEA), eliminating the disparities between their juridic regiments. The regulation regards all organizations that process personal data of EU citizens, or monitor their behaviour, regardless of whether they are established within the European Union's territorial scope, or not. The GDPR is sustained by its pillars of 1) lawfulness, fairness and transparency; 2) purpose limitation; 3) storage limitation; 4) data minimisation; 5) integrity and confidentiality (security); 6) accountability; 7) accuracy; which it promotes through its content. It, furthermore, aims to provide to the data subjects more control over their own information, safeguarding their privacy and integrity. For example, the GDPR limits the amount of data being collected to what is strictly needed, having to destroy the information after the purpose of the collection is fulfilled. The new regulation enforces more requirements and obligations for the processing organizations, as well as costly punishments for those who fail to comply, namely, fines up to 10 million euros, or 4% of total annual turnover (whichever is bigger). [48]

To ensure that the GDPR is implemented and respected across its territorial scope, each member state designates a Supervisory Authority for data protection - which in Portugal is the *Comissão Nacional de Proteção de Dados* (CNPD). A national law is also established - *Lei nº 58/2019*, in Portugal[11] - to, not only ensure the execution of the GDPR within the nation, but to complement the GDPR with the country's decisions over some of the regulation's sections that were left to be interpreted by each nation. Having done this brief presentation, the regulation's key matters will now be detailed.

5.2 Personal Data

Personal data is defined as any information that can allow to identify a natural person, either alone, or in combination with other information [48]. It is part of a subject's physical, physiological, genetic, economic, cultural, and social entity, and includes names, email addresses, locations, photos, and birth dates. There are also special categories of personal data, such as sexual orientation, health records, and religion, which can only be processed if special procedures and extra security measures are implemented (see Section 5.7). Figure 5.1 provides examples of personal data and sensitive personal data that fall under the scope of the GDPR.

Personal Data	Sensitive Personal Data
Identification Numbers *credit cards – mobile phone – ID card – social security number – plate number*	***Health Data*** patient medical history – illness – medical diagnosis, treatment, opinions – fitness tracker data
Home Address	***Genetic Data*** chromosomal – DNA analysis – RNA analysis
Names	***Biometric Data*** facial recognition – fingerprints – voice recognition – iris scanning – fitness tracker data – retina recognition
Internet Protocol (IP) Address	***Racial or Ethnic Origin***
Cookie ID	***Political Opinions***
Email Address	***Religious or Philosophical Beliefs***
Location Data	***Trade Union Membership***
Appearance	***Sex life or Sexual Orientation***

Figure 5.1: Personal data and sensitive personal data examples, under the scope of the General Data Protection Regulation (GDPR).

The sensitive character of data will depend on the hazard that can be created for its owners when this is breached and/or taking advantage of. An email, for instance, can effectively be used to identify someone, however, failing to protect it may not endanger someone's privacy as much as to allow improper access to one's medical records, such as Electrocardiograms (ECG) [62] or mental diagnoses [142]. Furthermore, by the GDPR [48], health data refers to information relating to the data subject's health status. Moreover, to be considered health data, one of the following criteria must be fulfilled: **i)** one can draw conclusions about the individual's health status from the acquired data; **ii)** in combination with other data, it can indicate the clinical status of the data subject; **iii)** the data collected as non-medical, can still relate to someone's physical or mental condition if it is acquired during long periods of time (such as the number of steps per day often collected by lifestyle mobile applications); **iv)** medical information is unavoidably attached to the data collected; **v)** the non-medical data, has a medical purpose for its processing. [48] Health data is, naturally, constantly being collected in the healthcare sector, particularly by medical devices and mobile applications, either inside medical facilities, or remotely through consumer products, processes, or services, such as fitness gadgets, smart devices and applications, brought up by health 4.0 [152][162]. With different settings, health data takes different forms. For instance, most information

collected and exposed by self-monitoring wearable devices [91] is considered health data, whether it is the users' heart rate measurements or their sleeping patterns, since deductions can be made about the user's past, present, and future medical condition, through such information. Furthermore, all biosignals acquired in both clinical and non-clinical settings (for instance, through smart IoMT devices [140]) are classified as health data and, thereby, also require a higher care and precaution from those in charge of their management.

However, one has being exposing only the predictable scenarios on which personal data is collected in healthcare, namely, through MedTech's digital solutions. Yet, medical device software and IoMT devices are not the only type of device collecting, processing, and storing the users' personal data. Solutions such as pacemakers, wheel-chairs, and diabetes monitoring devices, also do so from the very moment they are purchased. In fact, when acquiring a medical device, an individual's personal data is being collected, not only through its payment details, but through the device's warranty. For example, when purchasing a injection pump for diabetes, one can, furthermore, deduce the purchaser's clinical status from the warranty, making such information consistent with the definition of health data. In a broader perspective, all manufacturers of medical devices - in this scope, the data controllers (see Section 5.3) - will have one or more databases that store personal information of their clients (such as names, payment, and contact details), whether these are distributors or the final user. Most probably such data will be used to promote their device through marketing maneuvers that involve, for example, emails and newsletters, and which require the collection and processing of the customer's personal data. Being these just a few examples of how personal data is being acquired and processed in the medical device industry, it becomes evident the need of overseeing the organizations' processing activities and demanding from them a conscious use of data.

5.3 Main Actors

In order to understand data protection and its regulation (the GDPR), its main actors, and their interactions, must be considered. There are four main figures involved in data protection issues [48]:

- Data subject: the identified, or identifiable, natural person for which data is being processed. In the scope of GDPR this refers, mainly, to EU citizens.
- Data controller: the entity responsible for the data being processed, determining its purpose and means for its processing. This figure is in charge of demonstrating the organization's conformity with data protection requirements and principles, such as accountability and purpose limitation.
- Data processor: the entity that the data controller subcontract to process the personal data. Being a third-party handling personal information, it must be compliant with the GDPR, thus, a contract known as "Data Processing Agreement" must signed between the controller and the processor to provide, among other things, those same guarantees (see Subsection 5.5.1).
- Supervisory authority: the national entity responsible for the enforcement of personal data protection laws and regulations. It intervenes mostly on issues covering data security, such as data

breaches, and data protection impact assessments decisions.

Another important actor that may participate in data protection matters is the Data Protection Officer (DPO). This individual (either external, or internal to the organization), is responsible for guaranteeing the enforcement of the GDPR within the company. The DPO must have training in GDPR matters, and should actively seek its compliance by, for instance, promoting staff training sessions. Moreover, in cases of products, processes or services that have an international outreach, matters such as international transfers and partnerships with third countries, will come up and further technical knowledge will be required from the DPO and/or designated teams. This figure is only mandatory in some contexts (see Subsection 5.5.1), however, it is strongly suggested to perform such designation since it will help, not only to demonstrate compliance with the GDPR, but also to facilitate the work around this intricate matter that is regulation, helping to create a strong privacy framework within the organization, useful in both short and long terms.

5.4 Legal Basis

Organizations can only process personal data if they have a valid reason to do so, more specifically, one of six lawful basis [48]: 1) contractual obligations: where the processing is necessary to fulfill a contract to which the individual is a party, or processing is required to create a contract at the individual's request (generally, the strongest basis for processing); 2) legal obligation: when processing is required to comply with the law; 3) vital interest: when processing is necessary to protect life or to supply essential services; 4) public interest: when the processing of personal data is in the public interest; 5) legitimate interest: the most flexible lawful basis, most likely to be appropriate when we use people's data in the ways they would expect us to do; 6) consent: appropriate when one can offer the individual real choice and control over how the data controller will use their data. The data subjects explicitly agree on their data being collected and processed. Consent is mandatory for sensitive classes of personal data, such as for the collection and processing of health data. The lawful basis is only one of many information that must be simply, and explicitly, documented and provided to the user (and other pertinent third-parties), namely through Privacy Notices, necessary to demonstrate conformity with the GDPR. Therefore, this choice must be carefully made. One must consider both context of processing and the type of data being collected, as well as the rights that each lawful basis provided to the data subject (Figure 5.2).

Right to / Legal basis	Erasure	Portability	Object
Contract	✓	✓	✗
Legal obligation	✗	✗	✗
Vital interests	✓	✗	✗
Public interest	✗	✗	✓
Legitimate Interests	✓	✗	✓
Consent	✓	✓	✗*

* But right to withdraw consent

Figure 5.2: Data subject's rights, under the GDPR, according to the legal basis chosen by the data controller to sustain processing activities.

5.5 How to Comply with the GDPR?

First and foremost, regardless of the regulation in question, compliance is never an one-time job. It is a process that accompanies the whole life cycle of a product, process, or service, being constantly evolving and requiring attention. Nevertheless, one can wonder if, similarly to the medical device regulation, the GDPR has a certification of its own that assures the controller's (and processor's) full conformity to the regulation. In truth, the GDPR does not predict a direct certification of its legal compliance, however, there are other types of certification that can be sought after. For example, one can seek certification to approved certification schemes, as well as to codes of conduct [15] [114]), made available by official entities once an option, providing sufficient appropriate safeguards, is submitted. Furthermore, controllers and processors may seek conformity by complying with standards that attest for compliance with data treatment and control processes, such as the international standard ISO 27001 that provides the specifications to implement a sound information security management system (see Section 4.2).

In general, the GDPR establishes the organizational and technical measures that one should implement in order to demonstrate compliance. Although these can be dense and challenging to implement, one has numerous tools to resort to facilitate this journey, including compliance guidelines created by the EU and its specialized entities [16] [158], as well as toolkits that can help controllers to organize and keep track of the necessary documentation for conformity [46][57]. Furthermore, complying with the data protection regulation can be simple if one faces the it as a work philosophy, and not as a dense list of requirements. In fact, the GDPR "only" requests that controllers and processors keep privacy and security in mind at all times. For example, those that develop mobile applications, wearable devices, websites, and any solutions that deal with a great amount of data, must ensure that the GDPR's pillars are integrated in all their operations, such as in the solution's design. In the latter, the regulation advocates for "data protection by design and default", a principles which encourages companies to embed data privacy options in the product's design and in its default settings, such as by resorting to encryption, pseudonymisation, user authentication, and even international ISO standards (such as ISO 27701) can be used to demonstrate conformity with this cause [48][115].

Furthermore, technical and organizational measures such as encryption, data protection awareness sessions, limiting the collection of data to what is strictly necessary, and erasure it when no longer serves its purpose ("right to be forgotten"), are a few examples of actions that proves one's effort to protect the data subjects' rights and freedoms [157][158]. These should be documented and updated to both demonstrate compliance with the regulation and to keep track of what is done internally. One will now describe in detail some of these measures. To ease their exposure, they are divided according to their nature in "compulsory" and "encouraged". A comprehensive privacy framework will, then, be proposed.

5.5.1 Compulsory Compliance

In the GDPR, there are core compulsory items that can have to be checked by all data controllers. Their fulfillment is often achieved through the elaboration of documents and procedures that, alike MDR's

standard compliance, are mostly not explicitly mentioned by the GDPR. These include:

- Privacy Notice: a public document (commonly made available in the organization's website) that justifies the collection and processing of personal data to data subjects, and displays the company's commitment to respect and comply with the GDPR.
- Data Processing Agreement: a legally binding contract signed between the controller and processor, and which lays down confidentiality and liability terms, and guarantees the processor's compliance to the GDPR,
- Records of Consent: registry of all data subjects' declarations on how they agreed to the use of their data by the organization.
- Documentation regarding technical and organizational measures for processing security (such as encryption), and procedures implemented for data breaches, notifications to other entities, subjects' requests, and non-EU data transfers.

Other actions are only compulsory for some contexts, however, their employment is strongly suggested for all controllers that want to have a strong privacy framework and be compliant. Such actions include the elaboration of the Records of Processing Activities and of the Data Protection Impact Assessment (DPIA), and the designation of a DPO. These are, furthermore, mandatory for when: 1) the organization has more than 250 employees; 2) the processing activities are not occasional; 3) the organization processes special categories of data (such as health records); and/or 4)the processing of data results in a high risk to the rights and freedoms of the data subjects.

5.5.2 Encouraged Compliance

Conversely, there are actions, mainly promoting organization and awareness within the organization, for which implementation is highly encouraged, however, not mandatory. Examples of such are:

- Data Protection Policy: an internal document which summarizes GDPR's main pillars, and provides orientation to the whole staff regarding data protection matters;
- Sessions of Awareness: in order to promote a cohesive view towards data protection within the organization, webinars and training for all the members should be advocated;
- Internal Audit: an assessment and inventory should be performed to understand what type of data an organization possesses, and how is the latter organized, thereby helping to identify and solve possible issues that arise that prevent total alignment with the regulation.
- Templates and Action Procedures: several scenarios may arise when dealing with personal data, for which an organization must be prepared. Action procedures (as well as templates of documents that may be necessary to fulfill in such procedures), should be in place to deal with issues such as security breaches and data subjects' requests.

5.6 Why to Comply with GDPR?

Other than the obvious reason of its compulsory status, the regulation brings many benefits for both the data subject and the organizations covered by it. A quick look into the GDPR can seem like the compliance will demand an absurd effort and resources from the controller. However, the reality is that, on a long term, the advantages it can bring are much greater than the possible hurdles. For instance, focusing on the GDPR from the start will:

- Make it much easier to implement its (mandatory) framework and will avoid the burden of having to reformulate designs and the readjust the company's mentality;
- Make the compliant project more attractive to possible partners and investors, since this possible legal hurdles no longer constitute an obstacle for business to be made;
- Create greater levels of information governance and cyber resilience, helping mitigate possible malicious attacks to the data stored by organizations and to improve the overall structure of it;
- Since the foundations of GDPR are based on integrity, honesty and safety regarding data subjects, complying with it can help organizations to renew public trust and improve costumer relationship, through marketing moves.

In short, all projects should take a risk-based approach to data protection, and create a strong privacy framework on which administration and employees can lean on when pursuing and maintaining GDPR's compliance.

5.7 Proposed Approach to the GDPR

Any organization to which the GDPR applies should, not only put an effort on complying with its mandatory rules, but to always act demonstrating how seriously it takes the regulation and, above all, the integrity of its users. To do so, a strong privacy framework must be built from day one.

The first step is to be aware of the regulation. GDPR [48] and related guidelines [16] [115] must be carefully analysed in order to do a proper preparation of their compliance, avoiding any costly mistakes. Moreover, whenever possible, one should seek specialized advice from consulting companies of the matter, as well as guidance from national (and international) entities in charge of implementing such regulation (such as the Portuguese supervisory authority, the CNPD), to ensure all key elements are being acknowledged, namely, consulting company of the matter and the member state's supervisory authority. To know the regulation's exceptions, demands, and actors, to understand, and prepare for, its future direction, are just a few questions that one should have clarified. Also, an internal audit should be prepared and performed as to organize, learn, and evaluate the data that one's organization processes. With this knowledge, and all the tools and information available [46][57] [115][157], one can outline a proper compliance plan - ideally including both the compulsory and suggested items displayed in the previous sections - act correctly upon matters such as the choice of the lawful basis for processing. However, before doing so,

one must make sure that the GDPR applies to her/his activities. To clarify such matter, a decision tree is also provided in Figure 5.3. Once clarified, the proposed data protection workflow of Figure 5.4 can be consulted and implemented. This is specifically designed for a hypothetical health data' processing organization (such as that of Chapter 3's case study), being its particular requirements identified with " * ".

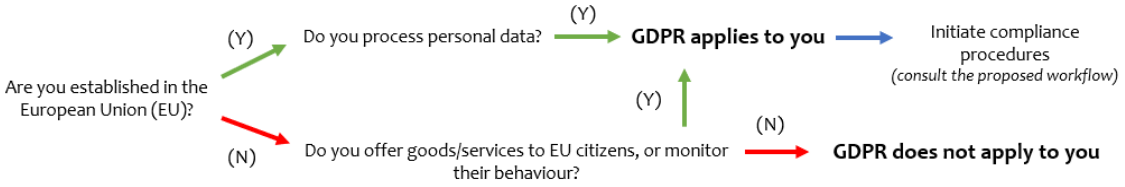

Figure 5.3: Decision tree regarding the obligation to comply with the GDPR. "Y"= yes; "N"= no.

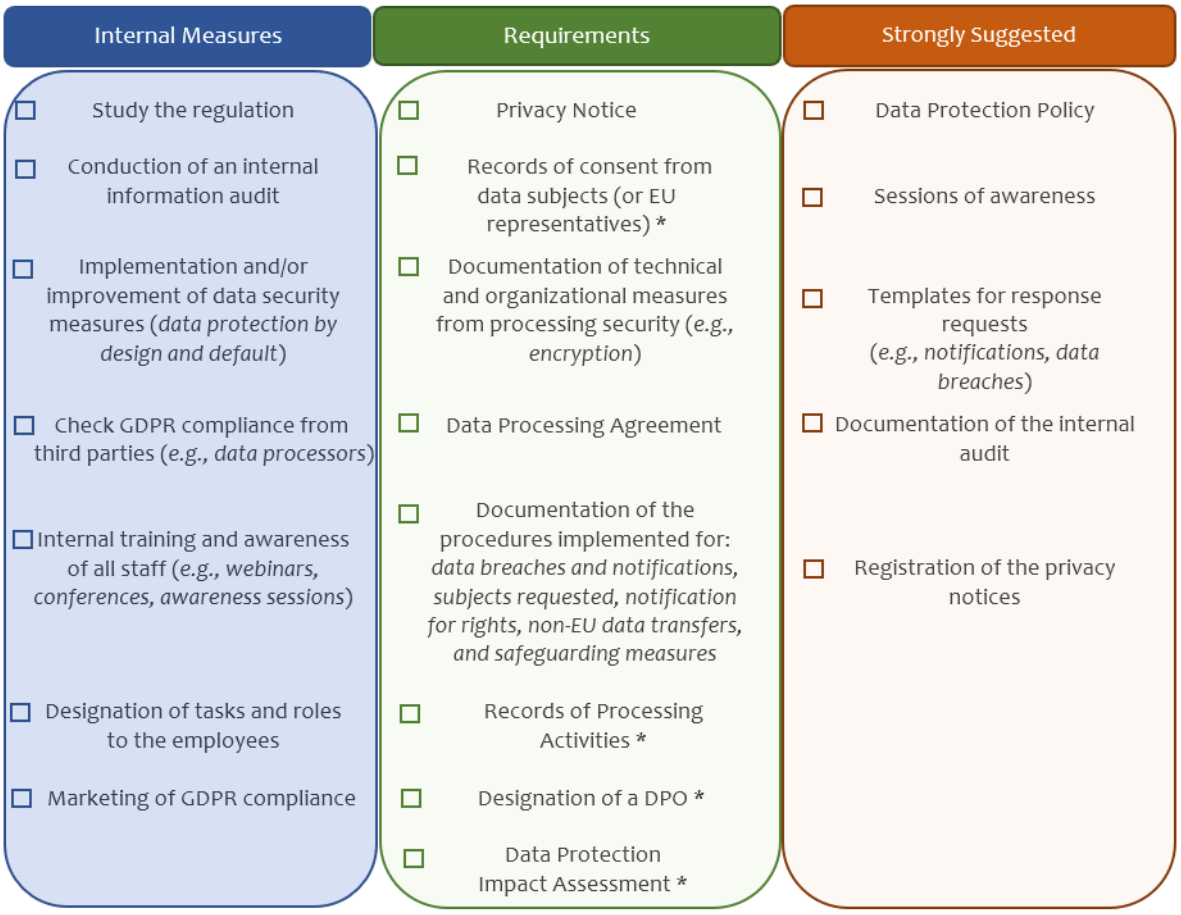

Figure 5.4: Checklist for GDPR compliance, particularized for health data processing organizations.

5.8 Interview Results: the GDPR

Data protection and, particularly, the GDPR, were approached by all the 16 participants, who, at all times, stressed the importance of data protection regulation, specially in the technological world one lives on. The "boom" of digital technologies was viewed by the experts as essential to make regulators reflect upon the dangerous of collecting personal information indiscriminately. Although all regulations tend

to be perceived as challenging and a synonym of workload and high costs, the business-oriented experts had a different view on the GDPR. Besides recognizing the need of controlling data transactions in the all healthcare sector's industries, including that of medical devices, these interviewees affirmed that they faced the GDPR as a natural working method, which pillars are already expected to be integrated in the organization's principles and mission, and the tools to implement them to be present in any good professional's skill set. The users' safety was emphasized as a priority for any organization with good practices, thereby, it was not hard for the business individuals to understand and implement the GDPR. Such statements were aligned with those of the regulatory expert on matter, although this interviewee also acknowledged that there is a long path to follow when it comes to make organizations aware of their duties, as well as their data processors, since there is still a lacking of understanding of the extension of the GDPR and the personal data definition. Moreover, the GDPR's expert emphasized that compliance is a continuous process on which one will have to be constantly working on, and not a one-time effort.

Regarding the e-CoVig team members, these did not mention GDPR as a relevant matter when remaining interviewees did (Figure 3.4), particularly during Conceptualization and D&D's early stages, however, once they acknowledge the importance and need to comply with the GDPR, the team searched for expert support by seeking outsourcing options. Unfortunately, at the time, the financial resources available could not cover these actions and the pursue of GDPR's compliance was postponed. This being said, the team's good professionals, alike what was said by business-oriented experts, implemented data security measures from the very start. The platform and mobile application were designed to mitigate security risks, and, later on, other technical and organizational measures were implemented to approach the remaining requirements of the GDPR, particularly those mentioned in the next section. In sum, by comparing one's forecast (Figure 3.3) with the interviews' results (Figure 3.4), one can affirm that both the importance and the challenging character of the GDPR were correctly predicted. Furthermore, the insight and and conceptual framework proposed in this chapter appears to be in validated by the interviewees' knowledge.

5.9 e-CoVig and the GDPR

Considering the path of e-CoVig so far (see Section 3.1), and both the proposed approach and interview results regarding the General Data Protection Regulation, it made sense for one to work on advancing the e-CoVig's GDPR journey, and, consequently, its path-to-market. To do so, a comprehensive reading of the regulation was conducted, which helped to prioritize, based on the workflow of Section 5.7, which actions could be (and were) immediately performed. These included: the conduction of an internal information audit to facilitated the identification of the appropriate legal basis for each type of data collected (detailed in the privacy notice); the elaboration of the Privacy Notice; the elaboration of the Data Protection Policy. All implemented GDPR's measures, and those yet to be implemented, are detailed in the Figure 8.3.

Chapter 6: Research and Development

As stressed before, the medical device path-to-market is filled with challenges, not only those relating to standard product, process, or service development, but also those arising from the sensitive nature of this industry's solutions (such as regulation and clinical validity). Recognizing such intricacies of such path, one proposes to approach the solutions' development as a set of two phases (as illustrated in Figure 6.1): the "Research and Development" (R&D) phase - addressed in the present chapter and approaching the stages 1 to 5 of the proposed conceptual framework (Figure 1.1) - and "Deployment and Maintenance" - detailed in Chapter 7 and approaching the framework's remaining stages.

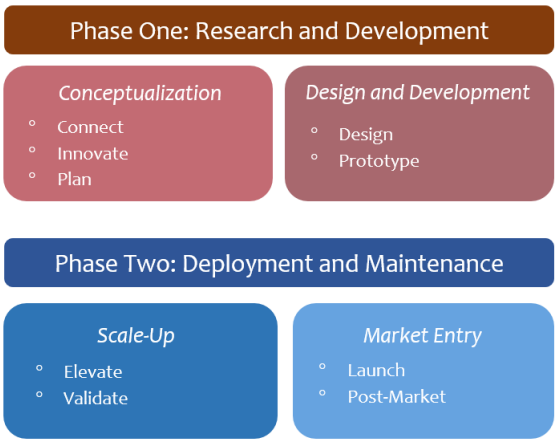

Figure 6.1: Illustration of the proposed development cycle of a medical device.

The approach here proposed aims to complement the literature by combining two important matters of medical device development: user engagement and regulation. Thus, in both phases, focus will be given to the legal framework of the industry, being this enriched by an user engagement roadmap. Furthermore, both phases will integrate the facilitating strategies and tools previously described (Chapter 2). Emphasis goes to the Lean Development model (see Section 2.6.2) which "learning loop" will serve as base to this approach's "optimizing loop". Although both encourage a cyclic tuning of solutions, leaning on user feedback, the loop here proposed is adapted to the industry's characteristics and limitations. For instance, knowing that for most medical devices high-pace learning cycles are not doable (as prototyping takes times and resources, and safety must be ensured at all times), this work's loop will focus less on speed and more on doing comprehensive evaluations so that it takes less iterations to achieve the solution's final form; and on compliance, the cornerstone of medical devices and key to successfully mature the device. Furthermore, the development approach proposed, unlike the Lean development, combines two tools as the optimizing loop is to be used to climb the maturity ladder that is the TRL scale for medical devices (Figure 2.1).

This being said, in the present chapter, the Conceptualization and D&D stages of path-to-market will be described, including their hurdles and key points to consider. In the appropriate sections, the

results of this work's interviews, regarding the same stages, will too be approached (Sections 6.2 and 6.4).

6.1 Conceptualization

Conceptualization is to be understood as the process on which an idea grows to become a strong concept sustained by reliable data and realistic goals, and which will be approached as a group of three stages, created based on those of Design Thinking (Section 2.6.1): 1) Connect: where the innovator seeks to identify and characterize the user and the market/industry, gathering all the solution's requirements. 2) Innovate: where the data collected is inputted in a creative environment on which the solution's main stakeholders craft a strong concept. All the important dimensions regarding the device and its application are defined and documented. 3) Plan: where an action plan is outlined considering all that was defined and contemplating the key matters of the medical device path-to-market.

6.1.1 Connect

The medical device innovator should start by connecting. To connect with the market, the industry, and the user; to understand their needs, expectations, and behaviour; are all essential actions to perform in order to develop a wanted and/or needed solution. To acquire such data, market research must be conducted. Whether this is focused on the user or on the industry, the innovator should seek to respond fundamental questions regarding the project's foundations, before jumping into the development stage and potentially allocating important resources to unstained assumptions.

User Research

User research is particularly important on the healthcare-related industries, such as that of medical devices, since these are gradually shifting to a more patient-centred model [20]. Furthermore, in this particular industry, not only are the customers' needs constantly evolving and becoming evermore demanding, but the end-users can be of markedly different profiles - from an ordinary individual of the general public, to healthcare professionals or healthcare institutional decision makers (private and public) - each impacting the path-to-market in their own way. For example, if one chooses to conquer the general public, the device should, most probably, be widely appealing and able to be quickly mass produced, which requires to have a creative D&D team and to guarantee a well-oiled production-distribution operation. Nevertheless, these challenges are balanced by the benefits of a greater costumer base. On the contrary, if the solution targets a niche audience, such as individuals of a certain clinical profile, the downsized number of potential users may difficult costumer acquisition and provide a limited revenue stream. However, having a clearly defined clinical intend and target audience will accelerate both the conceptualization and development cycle of the solution. Furthermore, besides different profiles, the user's role in the market chain will impact one's path-to-market. The user can, in some contexts, take on all three roles of purchaser, handler and beneficiary of the device (as it happens, for example, when purchasing a wearable device that is directly sold to the general public), or it may happen that these three roles are taken by different entities, such as in this thesis' experimental study (Chapter 8) where

the beneficiaries are, in theory, the elders; the handlers of the device are the institution's technicians; and the purchaser is the institution itself. With just a few examples, it becomes clear that the device's path-to-market will greatly depend on the chosen target user. Thereby, it is important for innovators to, not only identify and characterize suitable users for their devices, but to prioritize them according to their business value and fit in the project's vision.

First and foremost, as in any sound research, one will define the questions to seek answer to, in this case, to define the solution's target. These may include: 1) "Who are the end users?": identify all possible end users and characterize them by collecting both metrics and subjective data on them (regarding their backgrounds, decision-making, behaviour, purchase power, demographics, among others); 2) "What are their needs?": gather all the requirements and expectations that, in their perspective, would have to considered in the device's D&D activities for it to be adopted (level of complexity and efficiency expected from the solution; aesthetics and usability); 3) "What is type of setting where the device is to be applied (clinical or non clinical)?": identify and characterize the application environment and assess the users' roles in the application's chain. The way such answers are acquired will depend on both the project and its resources, as well as on the type of data necessary to acquire (if subjective and/or objective). Nevertheless, many research methods are available for one to resort to (see Section 6.1.1).

Once the innovators characterizes the main users of the device, these should then be prioritized (along with their requirements). Such prioritization will based on their business value, their adequacy for the project's goals. A set of variables should be chosen by the innovator against which each potential user (and setting) will be evaluated. Such variables may include the user's: background, environment, purchase power, skill set, demographics, role in the healthcare chain, behavioural metrics, among others. Since initial customer traction is very important in the medical device industry (see Section A.4), the choice of the device's targets is extremely important and should be well thought out.

Industry Research

Another imperative action to perform at this point is to make sense of the industry to which device belongs in order to do a comprehensive planning of the solution's path-to-market. The medical device industry, particularly, is both competitive and demanding, two features that can be dooming for any innovator, if not properly prepared. Thereby, a comprehensive industry/market research must be conducted, assessing, among others: 1) the industry behaviour over time and its projected future: quantitative data will help the innovator understand what does the industry seem to be walking towards, what were its past challenges, what technology is being used and/or trending; 2) the industry's past, present, and future, regulatory landscape: regulatory uncertainty must be considered [85] and mitigated; regulation must be timely understood and prepared for; 3) the most suitable market to approach first: consider factors such as demographics and culture, economical power and healthcare investment, legal framework, hypothesis to partner within the industry, ability to access other markets; 4) the device's competitors: which technology are they using; how can one differentiate from them; 5) the sustainability of the business: can one conquer a space in the market? Is it sustainable? Once again, to acquire such answers many research methods

can be resorted to, as it will now be described.

Market Research Methodologies

There are many methodologies for one to adopt in market research activities, depending on the type of information/answer the innovator is hoping to acquire. User and industry researches will benefit from resorting to both quantitative and qualitative research methods. Among the quantitative type, one highlight the conduction of surveys and questionnaires - commonly used by companies as it allows, for instance, to measure satisfaction and/or expectations across a large population, over specific matters- and data analytics' approaches - where big data is analysed and dashboards provide bulk answers on the user's behaviour and industry's dynamics. The metrics provided by these methods will only inform about how the user behaves and not the reason for such behaviour, thus, should always be complemented by subjective and spontaneous data that can in fact justify such behaviour. Qualitative data can be collected through, for example, interviews - typically performed with smaller groups of users, nevertheless, being very insightful - and direct observation - on which the users are asked to interact with either past versions or simple prototypes of the solution in order to assess what they perceive as useful, dispensable and/or upgradeable. Each methodology is unique in its design, conduction, and type of results provided, thereby, should be timely, and accordingly, prepared. A workflow, composed of five stages, to conduct market research is now suggested: 1) Definition: define the research objective, choose the research methodology, accordingly. Based on the former's characteristics, design the experience, namely, establish the population, the protocol (questions to make, logistics, *etc*), and the analysis method; 2) Execution: conduct the research based on what was previously defined. Organize the data to be analysed; 3) Analysis: Assess the collected data and draw conclusions. Did it answer the research objective?; 4) Report: document the findings - a data base of reliable insight will be helpful for both present and future projects - and present them to main stakeholders - it helps building a trusting relationship and facilitates the communication among all members. 5) Act: input the knowledge attained on the solution's development. Adjust the concept, design, and/or the overall strategy, if needed.

Many are the questions that one should answer with market research, including those previously referred (Sections 6.1.1 and 6.1.1). Nevertheless, as it can be complicated to approach all of them right away, one should begin by addressing those that forge the foundations of the project. An useful exercise for such is the "Five W's" [112], a guiding method which encourages the innovator to start by answering five core questions: "What" is being developed and "Why"; for "Who", and by whom, is this solution being created; and "When" and "Where" is it to be deployed. This prioritization, also advocated in the agile framework (see Section 2.6.3), will allow the innovators to consciously allocated their resources to the most important matters, and build her/his further research from there. Note that, particularly in the medical device industry, establishing the clinical need (the "Why") is a sensitive and critical process. Research can highlight multiple demands in the market that require devices' of different levels of complexity, different market sizes, and, most importantly, different regulatory requirements (see Section 4.3.2). Thereby, one should also reflect upon such factors before any costly decision is made.

6.1.2 Innovate

Having answered most of the project's main questions, one shall apply the information attained to create a strong and reliable concept, basis of the solution's development. In this innovation stage, a nurturing environment is created to encourage the innovators' creative side. Brainstorm and sketching activities take place, ideas are exchange and, gradually, based on all the data from research, the solution's core pillars are sanded and strengthen. Furthermore, this innovation stage may include the elaboration of mockups to better visualize the established concept. As one innovates, assumptions will, naturally, be made. These will be put to test later on, when the solution is formally materialized (Section 6.3.2). After such collaborative ideation, and having all participants agreed on the concept's main dimensions, the innovators shall clearly define it and document it. Such streamlined information will not only provide guidance on the solution's development and promote a homogenized vision within the company, but it will also facilitate the communication between the innovator and key participants of the market (such as investors). Examples of the concept's main dimensions to define, include: the problem to be solved by the device; the device's clinical intend, target user and market; the application setting; the main requirements of both the industry and the target user, and the technology to be used in the project. The latter choice will be detailed next due to its importance for the medical device success in the market.

Technological De-Risking

Choosing the technology to be employed is an impactful decision to make [126]. The chosen technology has to, not only allow an efficient performance according to the device's defined intend, but to fit the users' requirements and their intellect. Furthermore, the collected user data (Section 6.1.1) will help establish the device's working principle - what is the device expected to do - and their profiling will allow the innovator to choose the technology which complexity is most suitable for the users' capabilities. This being said, the innovator must conduct a de-risking exercise through which the most appropriate technology set is identified, diminishing the project's development risk and increasing user functionality.

To do so, one shall start by identifying number of potentially suitable technologies sets, based on the requirements previously defined through research. The next step on this de-risking exercise is to assess the technologies' maturity and readiness to be employed in one's project. To start, the core functionality of the technology must be characterized and assessed on its own. Then, once the functionality proves to be appropriated for the device's application, the innovator will want to evaluate the technologies' readiness and feasibility in the scope of the project, which passes by, firstly, defining a set of variables against which the technologies will be evaluated (that can include cost and development acquisition, compatibility with other technology sets, among others), and, secondly, to direct the resulting stricter group of technologies to a development loop based on lean development's principles (Section 2.6.2) and the TRL scale's stages (Section 2.3.1). Since this last step of the de-risking exercise will be sustained by prototyping activities, it will be described together with the latter, in Section 6.3.2.

6.1.3 Plan

When an innovator chooses to develop an medical device idea, she/he must understand that a long journey awaits, filled with challenges and a panoply of dimensions to consider. One will now mentioned some of the key considerations to have, and act upon, in the very beginning of the medical device path-to-market.

Networking

With no secret recipe available to surpass the medical device path's obstacles, an helpful action to do so is to work on your network from the very beginning. Participation in conferences, interface centres, collaborative laboratories, field-specific clusters, and other knowledge-sharing initiatives, can be an action of great value, particularly for new entrants since business opportunities and know-how can be freely acquired. In industries like the medical device one, to be well connected and aware of all sensitive matters from early on is incredibly important, not only to surpass the industry's hurdles regarding fierce competition and intricate path-to-market, but to improve healthcare, its quality and safety [22][52]. Such networking initiatives exist both at national [69] [129] and international level [12][43][127], thereby, one has many chances to link and evolve in the healthcare sector. Other than searching for contacts and advise, these same hurdles of the healthcare sector can be overcome with the establishment of a partnership. The chosen strategic partners must have a strong knowledge in the area, either by possessing medical and/or technical insight (such as the health professionals do), or by complementing the innovator's skill set with a great business vision (as it is the case of business-oriented individuals).

Whether one chooses to formally partner, or just to invest on growing her/his network and knowledge, having a third party's input from early on in the medical device's journey, will prevent the innovator from making some costly mistakes due to her/his inexperience in the industry, and end-up facilitating the solution's development, adoption and dissemination in the medical device market [22]. One should then start by approaching players already establish in the market by participating in knowledge sharing initiatives and seek to evolve through collaborative networks and clusters.

Team and Mindset

Building a team to fulfil your vision can be challenging but also very rewarding. In the medical device industry is critical to have a creative multidisciplinary team to be able to attend all the solutions' requirements and deal with all hurdles that may arise from this industry's distinct dimensions. However, medical device innovators tend to devalue some critical areas of activity for not being explicitly connected to value brought by the innovation. For instance, one will knowledgeably recognize the need of professionals with a background in management and medicine, yet, do not recognize the immediate need of a regulatory expert, a professional with a background in innovation, or an industrial designer educated on ergonomics. Thereby, one suggests what can be viewed as a "Minimum Valuable Team", a team composed by the key profiles of medical device development that, ideally, should not be outsource. This core team is composed by experts on: biomedics, management, and design (ideally someone that intends to introduce human-centred strategies). This knowledge should be complemented with regulatory experts (both regarding

MDR and GDPR), computer science professionals and/or industrial designers (depending on the type of device), and health professionals, who generally have an elevated understanding of the problems that one is trying to solve. The add-ons can be, for example, outsourced, consulted with (as in the case of a physician), or integrated through collaborative initiatives between industry and academia. The latter is of special importance, since the relationship between industry and academia is being nurtured, which, as stressed before, is essential to grow the sector (improving patient care), the communities and their economies. A cooperative, knowledgeable, and driven team can go a long way, thus, when recruiting, one must prioritize, not only those who bring knowledge, but the ones that will balance the team. A good way to do that would be to prioritize those of belonging to the profiles mentioned in the "Minimum Valuable Team", and to add members as it is needed (which will depend on each project's development journey). To thrive and impact the sector, the project's team must also work to align both the project's economical and regulatory goals with those stipulated, nationally and internationally, for MedTech [47].

Business Model

A business model is an integral part of the business plan - which exposes the journey, goals, and strategy, of one's business - that displays the essential information on how business will be done. How will one sell the product, process, or service, to whom and through which channels, what (if any) partners will help on the solution's commercialization, and how is one gaining and spending resources, are some of the questions to be reflected upon when designing a business model. Furthermore, the answers to these will be showcased in what is known as the "Business Model Canvas". This summary of one's business model is a simple, yet, very useful tool to have in order to homogenize the business' vision among the main stakeholders. The business model will not be constructed right away, it will, in fact, be the result of a gradual process that accompanies the life-cycle of each solution. As the solution gains shape and sustainability, the business model gets a foundation to be built on. Furthermore, it will be designed according with the market where the solution is to be deployed since different territories will have their own laws, demographics, beliefs, and economical power, features that can, and most probably will, impact how business will be made. To design the business model, one can start by answering the business model canvas' key questions. Once a reliable answer is acquired and agreed upon, the next should be approached and so on.

Compliance Plan

Once the solution's concept is clearly defined, market is assessed and objectives are established, it is time to plan for regulation compliance. In the case of medical devices commercialized in Europe, as mentioned in Chapters 4 and 5, a dense legal framework will accompany their whole life cycle. Whether this regards the device quality and technical safety (contemplated in the MDR), and/or its personal data processing activities (covered by the GDPR), the innovator must prepare, in a timely and rigorous manner. To do so, a compliance plan must be outlined once the innovator correctly identifies all the requirements and actions needed. Innovators can start by conducting a meticulous reading of both regulations from which they must conclude if, firstly, they are under the scope of the regulations and, secondly, if so,

perform a correct classification of the device (MDR) and the processing activities (GDPR). An inventory of all conformity demands is then done accordingly, upon which the innovators shall act. The proposed workflows of this thesis can be a great point to start the journey to become compliant with the MDR (Figure 4.5) and the GDPR (Figure 5.7). Nevertheless, there is guiding information available to support the innovator on the journey [29][157][158].

The compliance plan should be drawn early on, including, not only immediate matters such as the implementation of the QMS and the elaboration of the Technical Documentation (Section 4.3.4) and of Privacy Notices (Section 5.5.1), but also matters of the post-market period such as post-market surveillance (PMS) activities (Section 4.3.4) and response templates for data subject interaction with the processing organization (Section 5.5.2).

IP Rights

Early on the path-to-market, one important consideration must be made, the Intellectual Property (IP) protection. This should be contemplated in two perspectives: regarding the violation of IP rights while manufacturing the solution; and the acquisition of such protection for your own device. Regarding the first, when defining the solution's structure, one should check if any of the technologies considered to integrate and/or build it are legally protected, meaning that choosing to use them can cause a conflict of interests between the innovator and the entity who owns the IP rights. A state of the art research can easily dissipate any doubts surrounding this issue, and should be conducted before making costly mistakes. Databases such as "Google Patents", WIPO's "PatentScope", USPTO's "Patents Database", and EPO's "Espacenet", contain information about millions of worldwide patent applications and can be freely consulted. Similarly, other modalities like trademarks are also compiled into databases which are equally easy to find online. At a national level, every country has entities responsible for such matters (such as industrial property and copyrights offices), that support innovators in their journey to protection and provide them with databases with such protection registries. These national entities can be consulted online [117].

Concerning the pursue of the solution's protection, important reflections should be made. The innovator should start by assessing if any of the IP rights fits her/his solution's characteristics (see Section 2.5). To do so, one shall conduct a insightful research on the subject and, if possible, search for specialized advise. For example, Technology Transfer Offices, commonly present in universities and research centres, can be consulted, as well as the national entities of each country, and consulting companies. After understanding on which modality the solution may fit, one must understand if all criteria is fulfill. Particularly with patents, one may see her/his chances of protection be hindered if any information was already disclosed to the public before the patent application is submitted. Once again, consulting with specialists will provide a correct answers to any doubts. Then, if protection reveals to be a possibility, the innovator must assess, before pursuing it, if it is suitable for the business. Protection is not only a costly and lengthy, but demands focus and dedication from the innovator, all features that may not suit right away the resources available and, thereby, should be carefully evaluated. An example of a protection

journey, conducted within academia, is provided in Appendix A, Section A.3, along with the timelines and costs of both a national and international protection application.

6.2 Interview Results: Conceptualization

To be questioned about the path-to-market's initial phase of conceptualization, 12 participants (see Figure 3.4) were selected based on their experience on projecting a medical device from scratch, and knowledge on innovation and the legal landscape of the medical device industry. All interviewees agreed on the importance of accessing clinical expertise when conceptualizing a medical device. Whether this knowledge is acquired within the team (through the inclusion of a health professional, for example) or externally (such as a consultant), such insight on health science and its related industries was stated as "critical" to develop an adequate medical device. The interviewed group of experts also mentioned innovation as an important factor to consider, not only because it promotes the creation of something new and/or exciting - which helps to differentiate the device from competition - but also because the novelty factor often intrinsic to innovation facilitates a solution's protection (see Section 2.5), thus providing new business opportunities (see Section 7.3.1). The e-CoVig team also highlighted the importance of innovation but for its ability to advance the state of art and evolve science, which, in fact, was not the focus of the team in this project. Furthermore, the members were asked to provide, not a disruptive novelty, but a practical and effective solution. Nevertheless, although not focused on scientific merit, the team ended up advancing the state-of-art, which helps to sustain the conceptual framework here developed: a quick loop of assessment and incremental improvement may be as effective on delivering an innovative solution as traditional approaches leaning on extensive research and poor user engagement.

Furthermore, innovation- and business-oriented experts could not stress enough the importance of performing market and user research before jumping into development. To understand the industry, and to define both the device's target audience, and respective clinical need, was said to be essential to allocate the available resources on the most important matters of the project. Another consensual opinion among these particular experts was the need of acknowledging regulation and other legal matters (such as intellectual property rights), from as early as the conceptualization phase. Suggested actions included: to understand the regulations' scope; to do a compliance plan; and to include expert advice in the team. The regulatory experts, in particular, mentioned the urgency of implementing both the GDPR's and the MDR's principles in the organization's framework, and of consulting with specialized entities during the first decision-making moments. Regarding IP rights, the technology transfer experts highlighted the importance of contemplating the solution's legal protection as soon as possible, since simple mistakes can ruin such possibility. During the interview with the TTO office leader, the main challenges of technology transfer from university to industry were highlighted. Misinformation between the public and the specialized entities (like the TTO), the researchers' urgency to publish their discoveries before the IP's application submission, and the current lack of trained individuals on IP matters, were some of the hurdles said to hinder the academia's efforts to become, not only a place where advanced knowledge is created, but a place where this is commercially exploited and made available to society. Nevertheless,

this interviewee mentioned being witnessing an increase on the quality of academic innovations and of the number of protection requests, mirroring the effort being made by national entities to support research, and promote innovation and entrepreneurship within academia.

The e-CoVig members did not mentioned market research, nor legal matters, as fundamental points to consider during conceptualization (see Figure 3.4), which may be a first red flag in the e-CoVig project. Generally speaking, many of the differences identified between the e-CoVig path and the experts view on the ideal journey can be, partially, justified by the urgency, and overall context, of the e-CoVig project (see Section 3.1). The short timeline demanded by the funding call possibly influenced the team's focus - directing them for the development activities from which they could present tangible results - and made it difficult to reserve time for bureaucratic and theoretical matters (such as IP rights, MDR, and GDPR, and meticulous market research), that, in other circumstances, would have been approached. Also, with both the target user and the clinical need defined prior to the e-CoVig project's beginning, the team's efforts were automatically directed to follow the already outlined plan, an unconscious decision that revealed to be structurally damaging latter on, when the perspective of the system's adoption at national scale gradually lost strength and support by national authorities. Such scenario forced the team to abruptly adjust, which was only possible due to the their versatile backgrounds and agile minds which made them realize that the monitoring system could be used for more than the pandemic purpose. Furthermore, the e-CoVig members also admitted that the project's urgency prevent them to carefully contemplate their IP options and, those that reflected upon it, assumed that system's elements were not protectable as most technologies integrated and/or developed were of worldwide use and, thereby, difficult to appropriate. Finally, all participants mentioned the importance of the technology's choice. This was said to be able, together with the market's opinion, to make or break a project, since its maturity and adoption levels in the industry can determine the solution's longevity in the market.

Overall, the main mentioned hurdle of the conceptualization stage was the definition of the clinical need and of the device's users. Understanding what is needed but, simultaneously, viable and feasible, was said to be the real challenge. Nevertheless, the content previously exposed (Section 6.1) proposed some strategies to overcome such hurdles, which meets this thesis' intends. Furthermore, results obtained are in accordance with those forecasted (Figure 3.3), thus, with the content exposed so far in this chapter.

6.3 Design and Development

In this phase, all the data acquired through qualitative and quantitative research is used to design and develop the most appropriate solution. Both activities will be leaning on the end users, whether by keeping their interests and requirements in mind while developing, or by consulting with them throughout optimizing loops supporting both design and development stages. The regulatory dimension intrinsic to the medical device industry will also be highlighted.

6.3.1 Design

Designing a medical device is not an easy task. More than finding out the users' preferences and needs, and responding to them in something aesthetically pleasing, this process is about creating a safe, effective, and compliant design which, when materialized, serves its purpose [96]. The balance between efficiency, compliance, and usability, is the real challenge of the design stage. Nevertheless, many strategies can be employed to facilitate this task, namely, the formation of a multidisciplinary team (see Section 6.1.3), resorting to facilitating design tools (see Section 2.6.4) and methodologies (see Section 2.6.1), among others. The aforementioned will integrate this thesis' proposed approach to the design stage. Furthermore, note this stage's activities will extend to the scale-up phase of the development cycle, when this first design is applied to a low-fidelity prototype, evolving together until the solution's final form is achieved (see Section 7.1.1).

A poor and/or unconsidered design can have negative consequences on the device's development journey. Not considering the users' wishes and needs will hinder costumer acquisition and create unnecessary risk for wrongful use of the device [83]; not considering regulatory issues will hinder the chances of acquiring the CE marking and/or commercialize the device. Thereby, medical device design must be timely prepared, as well as sustained on human-centred principles that emphasized usability and user participation, since healthcare-related industries are evermore focused on the patient [20]. Furthermore, since the packaging of the technology is, arguably, as important as the device's technology for its commercialization, design must also be de-risked and validated. Throughout the design cycle, ergonomics' principles will be applied, putting usability first and helping the innovator create something that adds value to the user [44].

This being said, with the information previously collected through research (Section 6.1.1), and prioritized according to its business value and the project's intends (Section 6.1.2), the innovator has now a core set of requirements (both non functional and regulatory) which are inputted to create different design options. These same designs will be introduced in a optimizing loop on which both the innovator and the end user participate. The latter may include from physicians, patients, and the general public, to sales people and distributors. Performing this iterative exercise that is the optimizing loop not only minimizes the expenditure of resources and highlights the value brought by user, but also allows the innovator to arrive to conclusions regarding the design' adequacy much sooner, accelerating the overall development cycle [113][137][163]. Starting with the loop's building phase, the designs are drawn up resorting to facilitating tools such as CAD software, or to, as previously mentioned, online platforms and toolkits (see Section 2.6.4). The employment of such technologies will provide designers the opportunity of experimenting different configurations and/or settings, possibly detecting structural mistakes, before allocating resources to the concept's materialization [97]. Once the different design options are achieved, these proceed to the second phase of loop, the testing phase. In the latter, each design will be tested and its appropriateness for the project will be assessed. This evaluation phase will, ideally, count with the end users' participation, as advocated in human-centred frameworks (see Section 2.6.1). User engagement can have many formats, from more intimate and subjective (such as through interview research), to

more objective ones like lean development's A/B testing (see Section 2.6.2). The former, although more commonly used in prototyping, can also be conducted in the design stage to test simple attributes, such as the solution's shape and configuration. To do so, low-fidelity prototypes (stripped of much detail and looking nothing like the envisioned solution) are developed to test high-level concepts of design [130]. Once tested, the results and feedback collected will help the innovator to discard some of the design options and improve those with potential to become the solution's final commercial design. After a few iterations, one will, ideally, have a design that respects the users' requirements, as well as the industry ones (whether these are relating to its legal framework or its standards), being ready to be applied to the selected technology.

Importantly, as stressed before, medical device design implies the consideration of intricate dimensions than other products do not have to worry about, namely, the regulatory framework under which they are under. The MDR, for instance, requires from medical device manufacturers a meticulous description of the design cycle. Both design inputs and outputs, its outlined plan, and all assumptions and drawings made, must be documented and included on both the Technical Documentation and the QMS (see Section 4.3.4) [49]. This traceability will translate the manufacturer's discipline and dedication to comply with the industry's good practices and requirements, and can be later audit. Particularly, the medical device's usability (a dimension on which design is focused on) is much emphasized in the MDR, so much so that manufacturers will also have to comply with the European usability standard, the EN IEC 62366-1 (see Section 4.2). Alike the MDR, data protection regulation (Chapter 5) must also be tackled in the design stage. Technical and organizational measures must be implemented to integrate the regulation's principle of "privacy by design and default" (such as through data pseudonymisation and encryption), as well as its pillars of accountability, transparency, among others (Section 5.7).

In the case of the e-CoVig team, the device's usability was much considered in all its three elements' design. The mobile application included features that improve the intuitiveness of its use by the handlers and mitigate the chance of misclicking or wrong use. Examples of such comprehensive choices included the implementation of big buttons, intuitive naming of the functions, login QR codes, and visual registries (Figure 3.2). These decisions were sustained both on the target audience's characteristics - which could be from caregivers to elders, having very different technological capabilities - and on the setting where the system was to be applied. The mobile application's design was guided by "Material Design"'s principles and resources, a design system created to help teams build high-quality digital experiences for Android, iOS, Flutter, and the web [101]. Regarding the platform, this was adapted to the device's application. All tabs were optimized and adjusted to support the communication between health professionals and patients, as well as to display the users' data in a streamlined manner. For both the mobile application and platform, data protection's principle of security by design and default was implemented and the good practices of Information and Communications Technology's field were respected. Finally, concerning the e-CoVig system's third element (the acquisition device), this was intended to be portable and practical in all settings, thus its design focused on meeting such requirements, being of small dimensions and with few, intuitive, buttons (Figure 3.2).

6.3.2 Prototype

Prototyping is a key stage of the development cycle, where ideas are materialized. It serves multiple purposes such as demonstrating the idea's feasibility, in a technological de-risking exercise (see Section 6.1.2), and to validate both the assumptions made during conceptualization and the model's technical performance. In one's proposed approach, this stage will be occurring parallel to design and sustained, once again, by a optimizing loop on which both the users and the industry's requirements are kept in mind (see Figure 6.2), as advocated in both the lean and agile frameworks (see Section 2.6). Moreover, prototyping will comprise all activities until the TRL scale's fourth level of maturity (see Figure 2.1), thus until the technology's low-fidelity prototype is validated in a laboratory setting. The remaining levels will be approached in Chapter 7. This being said, at this point, the innovator has initiated the de-risking exercise of the solution's technology, having selected a group of sets which individual performance proved their potentially suitability for the project (see Sections 6.1.2 and 6.3.1). The final step of this exercise is to gradually discard each of these options based on their technical performance under environments with increasingly similar parameters and constraints to those the device's real application, respecting the TRL system working principle (see Figure 2.1). To do so, an iterative loop will be used to test and tune the technology's prototypes, such as advocated by the lean framework [137].

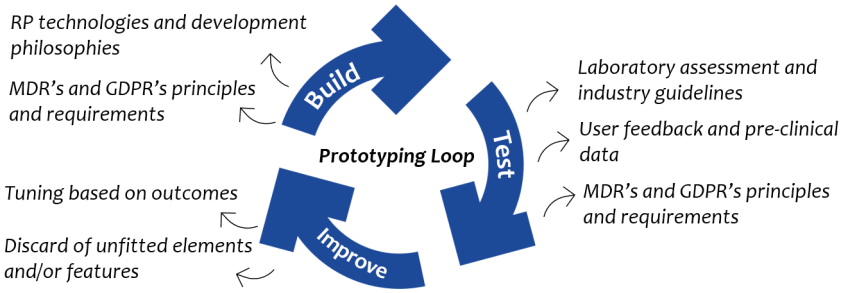

Figure 6.2: Proposed optimizing loop for medical device prototyping activities, based on lean development's framework [137].

Build

In the first stage of the optimizing loop ("build"), the innovator occupies herself/himself with the development of a prototype of each of the technology sets previously selected. These should start by being stripped of aesthetic details and complex features, including solely the minimum set of characteristics that allows their technical evaluation and evolution (known in lean development as the Minimum Valuable Product, MVP - Section 2.6.2). As the loop proceeds, the prototypes will become increasingly complex and similar to the solution's final form.

Naturally, developing a model, even the simplest, demands time, technologies, materials, and/or human resources, an expenditure that may not be bearable in a cyclic manner, nor be feasible in due course. Moreover, in the medical device industry, where devices can be of markedly different natures, the prototyping stage can distinctively demanding. In software engineering, it is easier to reach to change, to make adaptions as the development stage proceeds, since software can be made as flexible as one wishes

if the right measures and approaches are taken (such as those advocated in the agile philology [151]). On the contrary, other types of engineering, such as those creating hardware solutions and fabrications, will depend on more materials, on distribution and/or manufacturing operations, and, overall, on bigger timelines, to create a single unit. Thereby, lean's development loop must be employed to the extend, and frequency, that the innovator finds most suitable. Nonetheless, the use facilitating technologies and tools, such as rapid prototyping technologies, may balance the demands of prototyping. Medical device software can count on development frameworks, such as Agile [151], and tools like open-source code [25], to help create its prototypes. For example, tools such as GitHub that facilitate the organization and communication within a project, were employed by the e-CoVig team when developing the system. These were said to ease the construction of the mobile application's code since developers could work simultaneously without having to concern that the code may be altered or erased accidentally. Regarding the e-CoVig platform's development, this was sustained by principles present on the lean framework, such as the deployment of its different versions to the user whose input was applied into the platform's improvement [82]. The open-source communities of ICT were also resorted to by the team's developers, when necessary, accelerating the application's development cycle.

However, one must pay attention to their use on the device's final form. Using code that was not developed by the device's makers can represent a big problem when seeking certification if the team can not properly evaluate its risk, nor predict how it will behave in multiple scenarios. Furthermore, because the MDR demands for any medical device to be safe and reliable, data must be shown to prove the former, which may be hard to achieve when one did not develop part of its code. Thereby, any piece of a device must have an owner and, if open source code has necessarily to be included in the final version, one must: firstly, check if the source code has a license agreement where it authorizes people to use it on their own projects and, secondly, if exclusive property rights can be bought, the code's developer shall acquire such rights, becoming a licensee. In both cases, the team acquiring the property must always, as mentioned, be able to guarantee the reliability of the source code and make sure it knows how it will interact, in any, context, with the remaining code. If a team happens to have no control over the code and this gets altered in a way that influences its product, process, or service, many problems, other than regulatory, may arise, such as breaking the interaction between the module that integrates the code and all the others of the network, leading to the solution's malfunction [25].

For medical devices which materialization is physical, rapid prototyping technologies, toolkits and standard parts should be employed to accelerate the development cycle [4] (see Section 2.6.4). Take as example, the e-CoVig's acquisition device that resorted to 3D printing technology to develop the casing of the hardware, and standard development boards and chips to develop the hardware and test initial assumptions [60][61] (which, furthermore are beginning to be replaced by personalized ones as the e-CoVig system approaches its final form).

Test and Improve

For any product, process, or service, to be released in the market, it must perform well both structurally and technically. Malfunctions, inaccuracy, or any inadequacies, must be prevented to the extent possible to avoid costly corrections, the solution's removal from the market, or worst, endangering someone's life. Thereby, during a medical device development cycle one must conduct evaluations on its technical performance, to ensure it follows the industry's guidelines and standards. Such testing activities will be conducted in this second phase of the prototyping loop, where the pre-clinical data requested by regulation (see Section 4.3.4) will also be collected. Each prototype will be evaluated under increasingly faithful environments until a technology set performs as intended and required. Note that the device's clinical validity (and respective evaluations) will be approached in the next chapter (Section 7.1.2).

The testing activities performed at this stage will, at first instance, aim to assure the technology's quality. For example, in software development, is extremely important to assess its quality since failures can have tremendous consequences on the real world, especially in the medical device industry where lives may be dependent on their proper functioning. Software testing include the assessment of its maturity, data-flow, precision, among other metrics [7][94], but also of its usability and intuitiveness by including the users. Such evaluations will focus more on the user interaction with the technology, and less on its effectiveness, and can include from counting the number of clicks made by the user to access a certain functionality (to access the software's intuitiveness), to identifying their favorite features through a lean development's A/B testing (see Section 2.6.2). This split test is particularly useful for a software solution since elaborating two software prototypes is significantly easier (and less costly) than to create two prototypes of fabrications and hardware devices, nevertheless, it can too be feasible for other type of devices, especially when their prototypes are of low fidelity. Furthermore, medical devices of other natures, such as hardware and fabrications, will too be prototyped according with good practices guidelines and improve with technical testing activities, although somewhat distinct from those of software. For example, a wheelchair, a medical device designed to sustain an individual's weight, will be evaluated in its physical dimension, namely, the force tests that assess if the maximum wight supported matches the required. Wearable device hardware pre-clinical evaluations, on the other hand, will have to guarantee that the electric flow running through the device is between the standard maximum and minimum values, ensuring both its functioning and safety for the user [161].

Whichever evaluations are performed, regulation has to be kept in mind, both the MDR and the GDPR. As stressed before, validation of one's Technical Documentation and QMS (Section 4.4) is necessary to be granted the CE marking and, thereby, be able to commercialize the medical device. Both of them must include, not not clinical data proving the solution's clinical validity, but pre-clinical data regarding the device's structure, technical performance, usability, among others [49]. Thereby, medical device technical testing is not just a good practice, it is critical to commercially exploit a device. Furthermore, whenever third parties, such as users, participate in these pre-clinical evaluations, data protection measures must be applied to safeguard one's personal data, such as limiting the data collection to what is strictly necessary, encrypt the data when stored, obtain consent from the data subject, inform her/him

about the data's processing purpose, among others. As the loop proceeds, the prototypes are tested and validated in increasingly complex laboratory settings. The results and feedback of each loop are inputted to improve the past tested models (improvement phase), as well as to discard, among the group of technology sets previously selected as potentially suitable, those that do not fulfill the expectations (of both the industry and the users) [7][94]. In the end of the prototyping loop, one will have, ideally, a low-fidelity (lacking of its commercial design) functional prototype of the solution's technology (corresponding to TRL 4). This is now ready to be combined with the developed design, and tested in relevant and operational settings, until the solution's final form is achieved (Section 7.1).

6.4 Interview Results: Design & Development

During the design and development (D&D) stage, the most frequently mentioned key point for a device's success was the inclusion of the user in the D&D activities. All interviewees referred the great value brought by such individuals when aiming to create the most appropriate solution, in a timely and efficient manner. Furthermore, a design made with the user in mind (such as that of the e-CoVig system), was said to be evermore important in the healthcare industry. Other consensual key matters were the usage of facilitating technologies and work philosophies to accelerate the development cycle and decrease the time-to-market. Although the value of lean and agile philosophies on optimizing the D&D process, avoiding wasting resources, was agreed upon, the extent to which rapid prototyping technologies should be used brought up divergent opinions between the interviewees. The most business-oriented experts considered them as an useful tool for the whole medical device development, however, some alerted for the danger of including non-proprietary technologies, especially, open source code in the final form of the medical device software solution. Similarly, regarding the industry's digital fabrications and hardware solutions, although the small-sized batches enabled by the rapid prototyping techniques was said to be a perfect match for prototyping activities, the solution's mass production should, in their opinion, be conducted by industrial means and lean on custom design, whenever one's resources allow.

Additionally, the importance of setting-up a multidisciplinary team was also emphasized by the majority of the participants. Conversely, legal matters regarding medical device manufacturing and data protection were only considered relevant by the experts of the field, namely by the business- and legal-oriented participants. The former pointed out that most entrepreneurs of the medical device industry tend to underestimated the importance and workload of the legal issues, which can hinder their business on the long run. Furthermore, regulatory matters were considered as the main challenge of the D&D stage, representing a bottle-neck from most interviewees' perspective. However, the source of such hurdle differed. While the legal experts claimed misinformation and lack of quality professionals as such origin, the business experts indicated that the regulations' high-resource demands are the most harmful for innovation deployment (see Sections 4.6 and 5.8 for further detail on regulation matters).

In sum, all matters considered as relevant by the interviewees (Figure 3.4) were contemplated in this section and, thereby, correctly forecasted (Figure 3.3). With the validation of this particular content, and the streamlined of the D&D stage, this section's objectives are fulfilled (Chapter 1).

Chapter 7: Deployment and Maintenance

The present chapter will approach what is to be considered the second phase of the medical device path-to-market, comprising Figure 1.1's stages 6 to 10. As seen in Figure 6.1, "Phase Two" comprehends two sub-phases: "Scale-Up" (Section 7.1) and "Market Entry" (Section 7.3). In turn, each of these attains their own stages - respectively, "Elevate" (Section 7.1.1) and "Validate" (Section 7.1.2), and "Launch" (Section 7.3.1) and "Post-market" (Section 7.3.2) - which describe the journey of transforming a technically functional low-fidelity model on a high-fidelity one that fulfills all stipulated requirements and intends, and which is then to be deployed and appropriately maintained in the market. Furthermore, the chapter focuses on discussing the key matters and hurdles highlighted in both the Pre-Clinical and Clinical Evaluation, and Commercial Exploitation phases (Sections 7.2 and 7.5), during the conduction of the research study (see Section 3.2). Finally, in the last section of this chapter (Section 7.6), a final path-to-market workflow is proposed.

7.1 Scale-Up

The scale-up process (corresponding to Figure 1.1's stage 8) of a development cycle consists of putting together a mature technology with a comprehensive design, and evolve it until a model that comprises all technical, legal, and usability requirements is obtained. To do so, it is encouraged the adoption of, yet again, a optimizing loop (such as that of Figure 6.2) to climb the remaining TRL scale's maturity levels - namely, TRLs 5 to 9 (see Figure 2.1) - and the parallel pursue of the device's clinical validity.

7.1.1 Elevate

At this point, the innovator should have in her/his possession a technically reliable system, which technology - selected based on the users' expectations and the device's defined intend - is technically validated in the laboratory (see Section 6.3.2), as well as a commercial design in ongoing development (see Section 6.3.1). In order to elevate one's creation, these two dimensions - the technology and the design - are combined and put to test in both relevant and operational environments. Each iteration of the optimizing loop (Figure 6.2) shall count with the participation of the target user, who will, ideally, validate the innovator's efforts so far. Users will now be particularly effective on identifying issues regarding the device's usability and aesthetics. Furthermore, the moment of scale-up is to apply ergonomics' principles (see Section 2.6.1), and adjust any features that may facilitate the usage of the device, mitigating the chance of usability errors and making the device safer [83]. Additionally, scale-up is also the moment to turn low-fidelity prototypes into high-fidelity models. Standards and/or non-proprietary parts, such as development boards and open-source software, respectively, should be replaced, if possible, by personalized elements. This will not only allow to gain efficiency in production, reduce costs, and increase the model's robustness, but will provide the innovator more control over the solution's functioning, which is

always ideal. Moreover, purpose-built, higher quality materials, software's optimization, are all elements that must now be considered, and integrated, to construct the device's final form. Nevertheless, personalization will, most probably, introduce other elements to the business' dynamics, such as the dependence on other manufacturers to produce the tailored pieces, factors that must be considered and weighted when taking these next steps. One should also note that, although users may suggest to add new technology forms to the model, one may not want to value such feedback at this point since introducing such elements without a new de-risking exercise may add unnecessary risk to the project. Instead, one should continue to focus on the device's core requirements, earlier established.

The testing activities conducted in this stage can include in-person interviews, A/B testing, direct observation, software's alpha and beta releases, or more representative forms of real-world assessment such as usability tests and pilot studies. The former, particularly, are conducted later on the scale-up phase, when the safety and effectiveness of the device are sufficiently secured for it to be put to test in an operational environment, with real users, in order to assess its clinical performance and/or usability in detail. In particular, a pilot study consists of selecting a group of individuals representative of the device's target audience and provide them the medical device under development for a stipulated period of time. The pilot's small sample prevents generalizability of results, however, allows to anticipate, in general, the results of a (costly) larger trial (such as a clinical investigation). The pilot study will enable the innovator to identify improvement points and/or adjustments that neither laboratory, nor relevant environments could identify, and collect the clinical data required by the medical device regulation to prove compliance (see Section 7.1.2). Nevertheless, whichever the study selected, this must be timely prepared, having time to define the research's objectives and protocol, including its quantitative and qualitative indicators. A proper example of this type of studies can be consulted in Chapter 8, where the usability test conducted with this thesis' case study is described.

Throughout the optimizing loop, the solution's prototype will be improved based on the each test's outcomes, having an increasingly higher fidelity and performance. In the end of the scale-up loop, when few corrections are pointed out, the design achieves its final form and being its correspondent models produced in greater volumes (possibly, by industrial means). However, while prototype is elevated and its usability checked, its clinical value must also be assessed and validated in order to commercialize the developed medical device. Such verification and validation activities (corresponding to Figure 1.1's stages 6 and 7), will now be approached. These will be conducted keeping regulation in mind, particularly, the MDR's clinical requirements for CE marking (see Section 4.3.4 and 4.4), and GDPR's pillars (Section 5.1).

7.1.2 Clinical Validity

In the medical device industry, the best asset, and the ultimate goal, is to develop a clinically effective device fitted to the audience's needs. In order to sustain the device's safety and clinical effectiveness, clinical data must be collected through research and experimental studies, before (and after) market deployment. This data is, furthermore, essential to acquire the CE marking since it must be included on

both the manufacturer's Technical Documentation and QMS (see Section 4.4).

To collect such data, the medical device manufacturer has three options: 1) to conduct state-of-art research and claim similarity; 2) to conduct clinical evaluations on high-fidelity environments; 3) to conduct clinical investigations (clinical trials). The employment of all three may be needed for high risk devices, while simple, low-risk ones may just have to conduct state-of-art research. This is why, before starting to collect clinical data and spend resources, the manufacturer has to be sure of her/his medical device's classification by the MDR (see Section 4.3.2), since different classes have different requirements.

Once a correct classification is guaranteed, one may start to acquire clinical data on the device's performance. Regarding the first modality, the similarity claim, is highly encouraged to be pursued by all manufacturers in a first instance since it can dismiss the conduction of some experimental studies, thus, saving important resources. It consists on claiming (part of) the clinical data of state-of-the-art solutions based on their similarity to one's device (see Section 4.3.4). This claim has to be well sustained, having the manufacturer to provide irrefutable evidence of such equivalence to official bodies. To do so, the manufacturer should start by conducting a meticulous state-of-the-art research in order to find validated solutions which working principle and/or functionalities match those of one's device. Most probably, this claim will not be total, having the non-equivalent dimensions to be evaluated separately through other modalities (clinical evaluations and trials). Nevertheless, this option must always be contemplated, specially when dealing with a medical device software, since these are often developed by modules which functions and characteristics are often the same as those of other already developed solutions.

The next modality are the clinical evaluations, which comprehend the conduction of multiple experimental studies in environments which constraints and parameters are increasingly closer to that of the device's application. It includes the conduction of the previously mentioned engineering tests to assess the device's technical performance (see Section 6.3.2), the device's evaluation on laboratory settings such as those of simulated use and/or animal testing, as well as the evaluation of the device under relevant and operational environments. All these evaluations aim to, not only prove the device's safety and effectiveness, but also its usability and added-value to the intended user. The results will be documented, together with each study' design - including the research objectives, protocol, conditions and parameters, participants, among others. Additionally, conclusions regarding electrical safety, biocompatibility, software verification and validation, to name a few, are expected to be included in the documentation, as stated in the MDR [29][49]. The final option for clinical data acquisition is clinical investigation (clinical trials), resource-intensive and complex scientific experiments on which the solution's prototype is tested on human (or human samples). This type of experiment is conducted to predict, and assess, the device's performance in the real world with more accuracy since the results one gets from other types of evaluations (such as from *in vivo* experiments) do not always translate the solution's effectiveness on the human system. Although all manufacturers may perform such investigations to further validate their devices, by the MDR, such performance is compulsory for higher risk devices - namely those of Class III and implantable - since their faulty performance poses a larger risk to the users' health, thereby deserving a more detailed evaluation. Nevertheless, as the regulation predicts exceptions to this compulsory status

(described on Article 61 of the MDR [49]), a careful reading is strongly suggested before allocating a large amount of resources to conduct the trials.

Besides being costly, clinical trials can take several months or years to be completed, thereby their preparation must not be rushed. To reinforce this idea, the MDR requires the development, and availaility, of a Clinical Investigation Plan (CIP) that comprises the study's design, objectives, method of analysis, as well as the information lay down on Annex XV of the regulation [49], in order to guarantee that such investigation will be properly carried over. The intention of conducting the clinical investigation must also be communicated to the appropriate authorities, including the ethical committees - since the trials are to be conducted on human beings - and the national competent authority, who have, as well, to approve it. Furthermore, similarly to all evaluations on which the user participates, the GDPR's requirements and principles must also be respected. Once the clinical data is acquired and properly integrated (including in both the manufacturer's Technical Documentation and QMS), the medical device can be submitted to further assessment by the appropriate bodies, such as the Notified Bodies (see Section 4.4). The ultimate validation will be given when granted the CE marking that enables the device to be trade within EU.

In sum, clinical value acquisition can be a very demanding process. As scrutinized by the regulation, any scientific approach must be robustly conducted, from research studies to clinical evaluations and/or clinical investigations. These require focus on their preparation, a clear view on regulatory demands (regarding both MDR and GDPR), financial power to perform it, and time to successfully complete it. Such resource-intensive activities can be very challenging to support, especially by new entrants of the medical device industry. Nevertheless, as advocated throughout the thesis, these are essential, not only to become compliant with regulation, but because such evaluations guarantee the device's safe and effectiveness, mitigating their risk to human health, and fulfilling the ultimate goal of any innovation: to be useful. In fact, all testing activities are important, whether these regard the device's clinical value, usability, aesthetics, or technology, evaluating and validating the solution's different dimensions in different settings (such as laboratory, relevant and operational environments), will lead to the creation of the best device possible.

7.2 Interview Results: Pre-Clinical and Clinical Evaluation

In the stage of pre-clinical and clinical evaluation, questions were directed to the medical device companies, the regulatory experts, and the founders of e-CoVig. However, note that the e-CoVig project is only now acquiring clinical data and preparing the conduction of clinical trials, thus, only superficial questions were posed to these participants. The interviews' main outcomes will now be detailed.

In the scope of the clinical data acquisition, the MDR expert highlighted the importance of such collection in the scope of CE marking, as well as the extend of these activities for the post market period. Claiming equivalence with pre-existing tested devices was strongly suggested by this interviewee, along with the need of comprehending the regulation before jumping into assessment. In fact, the regulatory expert highly encouraged the e-CoVig team to search for similarity data given the great amount of

similar solutions being released nowadays. Furthermore, the need of a proper compliance plan was also emphasized, specially for the manufacturers of high risk classes medical devices since these will probably have to conduct clinical trials, which can be a long, costly and bureaucratic process. In this same scope, the data protection expert also highlighted the importance of following the GDPR's relation when conducting all kinds of research, especially, during clinical investigations, pointing out that these should, among other measures, limit the personal data collection to what is strictly necessary to fulfill the investigation's purposes. Ethics was also a topic approached, this time by both the business-oriented experts and the e-CoVig founders, however, their feedback diverged. The e-CoVig team mentioned their struggle on getting approved by institutional ethical committee to conduct a trial, taking a lot of back and forward and, consequently, a lot of time to get their permission, delaying this stage several months. On the contrary, none of the business-oriented experts mentioned this matter as a pain point, in fact, even highlighted the importance and need of this type of considerations in today's world. Could be argued that the latter's experience on the field may have facilitated the process of ethical approval. Finally, the experts emphasized the importance of conducting both pre-clinical and clinical evaluations for one to acquire the CE marking. Business-oriented experts mentioned the challenges posed by such assessments, pointing out the financial demand. The e-CoVig team did not mentioned neither the CE marking, nor the financial burden, mostly because the project is yet to enter this demanding stage. In sum, the collected feedback, once again, seems to be in concordance with both what was forecasted (see Figure 3.3 and described throughout the thesis (Section 4.4, and Subsections 4.3.4 and 7.1.2).

7.3 Market Entry and Maintenance

A medical device's entrance and maintenance in the market is yet another challenging phase of the path-to-market (corresponding to Figure 1.1's Block D, stages 9 and 10). This comprises deployment and post-market activities, and demands a strong business and regulatory perspective from the innovator.

7.3.1 Launch

For one to launch a medical device this needs to be completed, meaning that it has to be safe, effective, appealing, and, most importantly, validated. Launching a medical device is a critical time to any entrepreneur and must be carefully planned. The deployment plan must comprise matters such as the medical device's marketing (further detailed in Section A.4), the entrant's business strategy, the post-market activities, as well as production and distribution operations which have to be in sync to be able to respond to any shift on the market's demand. For one to prepare such dimensions, the device's deployment market must be already chosen. This choice is essential for the device's success in the market since a good post-deployment feedback can be just the needed advertisement to skyrocket one's business, whereas bad results can close many doors for business to be made, especially, in the healthcare sector. Thereby, as stressed before, variables such as demographics, culture, financial investment on healthcare, and regulatory landscape, must be considered before making a choice. The best decision will come from prioritizing the market which characteristics better align with one's vision.

Once the market is chosen, one can identify and outline the best strategy to enter it. Given this thesis' scope, mostly focused on helping new entrants, such as academics, to get their medical device to the market, one will focus on three main market entry approaches (although others exist): the license agreements, start-up, and spin-off [122].

Licensing

Commercializing a product, process, or service, can, many times, pass by licensing the solution's intellectual property to third parties, who can then commercially exploit it (see Section 2.5 and 6.1.3). The IP right's owner (the licensor), thereby, grants other entity (the licensee) permission to use the innovation (to whatever extend agreed) and, in turn, the first receives a stipulated revenue from the solution's commercial outcomes. Additionally, the licensee may require benchmarking tests and other types of evaluations, before negotiating such agreement, to ensure that the solution meets her/his expectations.

Licensing deals, mostly focused to exploit patents, are particularly popular within academia, making up most of its technology transfer agreements [9][122]. This favoritism is not only due to academia's ability to create patentable inventions from its advanced knowledge, but because of the revenue stream and resources it can secure by licensing the rights to third parties (the industry). Furthermore, such funding and resources acquired are critical to both enable the commercial exploitation of the invention, and to support academia's further R&D activities. Nevertheless, licensing agreements have some downsides, namely, the innovator will be dependent on a third party and let go of some control over the technology, which may not be ideal. In truth, the control over the actual rights may also be in danger since, in the licensing agreement, information regarding the technology is disclosed, increasing the risk of this to be replicated and/or stolen if the IP right's protection is not the strongest.

As most technology transfer deals, licensing agreements are filled with bureaucratic and legal matters which can be lengthy and challenging to make sense of. Thereby, any innovator should make use of specialized structures, such as the universities' Technology Transfer Offices and associated departments (such as those for business partnerships). These can, not only provide contacts and advice, but will accompany the innovator throughout the whole journey, helping her/him to select the most appropriate partner and to negotiate the deal.

Spin-Off

A spin-off is a company that is created within another organization (the parent organization), which can be an academic institution, a research institute, or a company. The decision to break off is often based on the need to focus on a certain product, process, or service, of their portfolio that otherwise, for more than one reason, would not grow as much. By creating a new entity, efforts and resources are solely allocated into developing and exploring the new technology. Furthermore, if the business strategy of the parent organization does not fit into what that most suitable for the solution in question, creating a spin-off could be a smart choice since this has its own management and business independence (until certain extend). In the case of academic settings, pursuing the spin-off strategy can be essential to keep developing

the technology innovation created on campus, and to stimulate an entrepreneurship environment within academia. To do so, a timely preparation must be carried on - including all mentioned steps of Chapter 6 - with, most likely, the participation of the academic TTOs to help transition the technology's rights from the institution to the spin-off. The participation of expert regulatory knowledge is also essential to expedite the formation of the new entity, as supported by literature [124]. Examples of successful spin-offs with a corporate parent, within the healthcare sector, are Siemens and General Electric's spin-offs, Siemens Healthineers and GE Healthcare, respectively.

Start-Up

Startups are a thriving type of business, which definition has been topic of much discussion. Nevertheless, these can be seen as businesses capable of impacting the world through the deployment of their, often, high-value innovation. Furthermore, the concept of startup is associated to the initial stages of a business, being considered as such for its 3 to 5 years. Being, commonly linked to advanced technological developments, these new innovative enterprises are, generally, focused on exploiting the solution sustaining their business, avoiding spreading their attention to other developments. Their funding sources include family and friends, venture capitalists, business angels, among others. A proper preparation is required to establish a startup considering all business challenges of today's world [132]. In academia, there are many successful examples of startups born from universities. Such success stories include Facebook, Google and FedEx, all of which benefited from the advanced knowledge provided by academia.

7.3.2 Post-Market

A safe and efficient device is now available in the market. Any manufacturer having reached this phase can be considered herself/himself successful since so few are able to do so [121]. However, her/his work does not finish here. As mentioned before (Section 7.1.2), the device's performance in the market must be continuously assessed and overseen, with its clinical validity having to be proven throughout the solution's whole life cycle. This Post-Market Surveillance (PMS) dimension is much advocated in the current medical device regulation, being, in fact, one of the marked differences between the MDR and its predecessor [66][65]. The MDR only allows the commercialization of a medical device while proof of its effectiveness and safety is made available to the appropriate entities. Since the PMS' requirements must be included in both the Technical Documentation and the QMS (Section 4.3.4), these must be prepared as soon as possible (certainly, before deployment), supported by appropriate guidelines [49][107][108][136]. Furthermore, in the post-commercialization period, PSUR and PMS reports informing about possible safety measures implemented, as well as the analysis, and conclusions, of the new collected data, must be provided by manufacturers of larger and smaller risk devices, respectively.

On this post-market journey, the innovator must also keep active in other fronts besides regulation. As innovative devices and concepts will keep emerging in the healthcare sector and, particularly, in the medical device industry [70][99], medical device innovators should work to keep relevant in the industry. To do so, innovation must be a constant within an organization and the industry's landscape should be

kept up to date at all times. New markets, devices and functionalities must be sought after, in order to keep the business meaningful. To choose another market to deploy to, for example, one should greatly consider regulation as a deciding factor since, as stressed before, different markets may have different demands than that on which the device was first commercialized. Also, new partnerships could be established between the organization and universities, as students can provide fresh new ideas and one can provide them a structure to flourish that otherwise would not. Furthermore, users' feedback should be closely monitored in order to (re)act in a timely manner, if necessary. Overall, both market trends and regulation should be continuously analysed and keep up with, since misinformation can catch a business off-guard and make real damage to it. Therefore, as business grows, teams should equip themselves with knowledge relating to these matters, for example, by attending scientific conferences and webinars that train them on how the industry works and evolves.

Post-market activities may seem relatively easy to conduct considering the challenging journey that precedes it, however, this is normally a misconception. Post-market means to have simultaneous control over management, development and human factors. Firstly, being in a market means to take on the pressure of deadlines, and to deal with possibly third-parties in distribution and manufacturing activities. Also, having an established business means to have an infrastructure that sustains all your operations and qualified staff to ensure these run smoothly, both costly procedures. Operating in the healthcare sector means that, firstly, one probably can not afford to have flaws or unpractical features in the devices, making design and development a continuous up and running stage. Also, dealing with health means that the organization must have a strong customer engagement mechanism in place, to guarantee a quick response to possible arising problems. These and many more factors must be dealt with while seeking after innovation and maintenance of the business. Thereby, the entrepreneur must plan this post-market stage with double the focus and care, to ensure that all the effort done in vain and to prepare the business to the market's volatile behaviour. Preparation will include: elaborating GDPR's response mechanisms for costumer engagement and data breaches (see Section 5.5.2); prepare for MDR's surveillance activities (see Section 4.3.4 and 6.1.3); document all research and activities conducted throughout the device's development to guide future endeavours and the solution's remaining pathway (see Section 6.1.3).

7.4 e-CoVig and Market Entry

The ultimate goal of any solution is to be employed, and the e-CoVig is no exception. At this moment, the future of e-CoVig seems to be on monitoring chronic patients, particularly those with cardiovascular and/or oncology conditions. Also, being difficult to entice and/or finalize a deal with the higher power of the national health system, the most appropriate choice appears to be on solidifying the usage of the system in the elderly homes across the country. Portugal has an aged population, many of which institutionalized in facilities that often struggle to keep track of all their residents, thereby, being open to introduce solutions that could help them to be more efficient. Furthermore, cardiovascular diseases are a commonly identified clinical status among the older age groups which further draws the e-CoVig team focus to this type of settings [109][121].

This being said, the e-CoVig's strategy to enter the market - once the system is fully validated- will pass, firstly, by getting Portuguese elderly homes (and similar non clinical settings) to implement the system and recommend it to other institutions. Once a significant amount of experience and results are collected, the next step would be to bring this more sustained and reliable project to more demanding and/or apprehensive users such as private and public hospitals (clinical settings). This commercial expansion, if accomplished, will imply an adjustment on the implementation protocol - since the device's new handlers will now be health professionals and the environment on which it is to be employed will be more demanding and stressful - and changes on the actual system - as new features may be required to ease the professional's experience, and some of those already implemented may not be suitable for the context. Importantly, one must keep in mind there is still a long way to go until the e-CoVig system's deployment in the market, thus, this strategy can become inappropriate later on.

Regarding the project itself, the e-CoVig, as of right now, comprises both academic and non-academic professionals, each belonging to their own organizations (see Figure B.1). In the future, the creation of a start-up could be appropriate to solidify the focus on the project and on its exploitation.

7.5 Interview Results: Commercial Exploitation

This last stage of the path-to-market was approached by the business-oriented and regulatory experts. The e-CoVig team did not deepen this matter since they are not in this phase yet. The most mentioned matters of commercial adoption were regulatory compliance, the establishment of a good business plan and strategy to enter the market, and the importance of reinvention and innovation after establishing it. The latter evidences the need of having a continuous process of D&D, as well as of preparing compliance for any hurdles of arising from market traction (see Subsections 4.3.4, 5.5.1 and 5.5.2). Furthermore, the importance of academia on providing innovation and expertise to the industry was quite stressed and recognized by all interviewees, nevertheless, one business expert mentioned academia's common lack of business perspective as possibly hindering when trying to enter the market and/or make agreements with the industry. Finally, all participants agreed that the ability to adapt and keep up with the industry is critical to thrive in the market, mentioning the importance of reinventing the solutions, to search for new markets, technologies and applications, after securing a place in the industry. The aforementioned challenges were said to be mitigated if, for instances, one partners, ideally before deployment, with a key opinion leader who can facilitate the integration of the device in the market. Overall, all mentioned matters were approached, with more or less detail, thereby validating one's conceptual framework.

7.6 Proposed Development Framework

It is now presented, in Figure 7.1, the final proposed framework to accompany any innovator on her/his journey from concept to market. This is to be understood as an improved version of the this thesis' first proposed workflow (Figure 1.1) since it not only addresses all the key matters approached throughout this work, but is also complemented with the insight obtained from the conducted interviews.

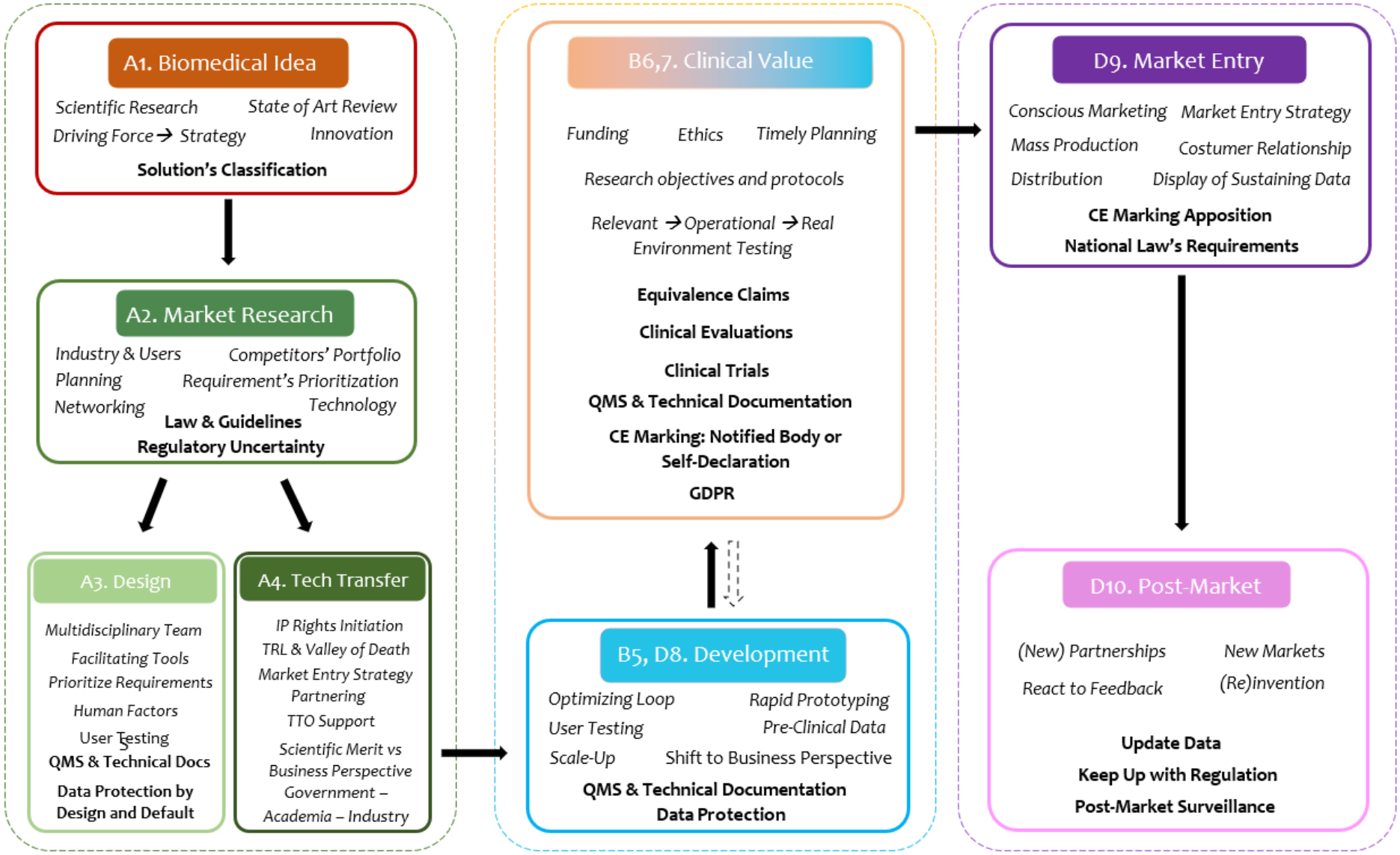

Figure 7.1: Final proposed framework for the medical device path-to-market. Correspondence with this thesis initial workflow (Figure 1.1) is performed by the prefix in each block's name. Matters regarding regulation are highlighted in bold.

Chapter 8: Usability Study

This chapter describes the usability testing conducted with the e-CoVig system to assess its usability and added-value for the user. This assessment was motivated by this work's proposed conceptual framework.

8.1 Experimental Setting

The e-CoVig system was implemented, during a three-week period, on a non-clinical operational setting, namely, an elderly home. This institution was located in a small village of Évora's district (Portugal) named *Aldeia da Luz*. Included in the study were all 19 residents of the elderly home, with ages between 49 and 101 years old, and of different clinical profiles (none of which including previous, nor current, infection with SARS-CoV-2 virus). Furthermore, to employ the system and perform all this study's related tasks (detailed in Figure B.4), two technicians of the institution were selected, referred to hereinafter as Subjects "A" and "B" (of, respectively, 28 and 50 years old). Note that, given the experimental setting, and e-CoVig system's working principle, the true beneficiary of the employment of this monitoring system are the technicians, thus, all the study's results relate to their feedback.

Prior to the experiment, the assessment of the elders' clinical status was, normally, only performed when a resident presented some clear sign of discomfort, thereby, not periodically. Further, the acquisition of all pertinent physiological data was done by the technicians through the institution's own devices (such as thermometers and oximeters), while the registry of such data was done in paper. In the scope of this study, was this same paper-based method that was replaced by the e-CoVig system, particularly, by its registry/diary modality consisting of both the mobile application and platform (see Figure 3.1). The e-CoVig's acquisition device (Figure 3.2) was not included in the usability study, being used to acquire the physiological data the institution's own devices.

8.2 Method

In order to assess the quality of the user's experience when interacting with the system, an usability study was conducted. Firstly, an institution was identified and contacted for the possibility of implementing the system in its installations. The e-CoVig project was exposed and, once the institution agreed to participate in the study, the two mentioned technicians were selected based on their role in the care home and availability to participate. Then a survey was conducted aiming to identify the physiological measurements usually acquired from the elders, as well as other health data that the technicians would like to see collected. Their feedback was used to create the protocol to be displayed in the mobile application at each acquisition. Next, the e-CoVig system was implemented, installing the mobile application on the elderly home's own tablet, and the web-based platform was made available in its computer (through its own login account).

In the implementation day, the identified technicians were also trained on the working principle of the application and platform, as well as the research objectives. Each of technician was then asked to perform and time a monitoring activity per week, making a total of two monitoring days per week, six monitoring activities over the course of the study. Each activity consisted of: 1) accessing, on the computer, the elder's profile thorough the platform (Figure 3.1); 2) scanning (with, in this case, the tablet's camera) the associated QR code to enter her/his profile on the mobile application (Figure 3.2); 3) selecting, performing, and submitting, the appropriate protocol. The latter contained the requests and questions needed to be answer for that particular elder to complete its health assessment. The data inserted could regard either elder's mental health (such as her/his comfort, motivation and personal thoughts) or her/his physiological measurements (collected through the oximeter and thermometer of the care home). This process was to be repeated in all 19 elders, in each activity day, however, one had to adapt to the time constraints of the institution, thereby, only half the elders (9 or 10 residents, depending on the activity day) was assessed in each monitoring activity.

In sum, over the study's three-week period, six monitoring activities were conducted (and timed) using the e-CoVig system and the institution's complementary devices. Each resident had three health assessments performed on her/him during this time, making a total of fifty-eight health assessments for *Aldeia da Luz*'s elderly home. The data collected in the six assessments was complemented by the conduction of formal evaluations (either before, during, and after, the three-week period) in order to enrich the study and its conclusions. These are further detailed Section B.2, of Appendix B.

8.3 Results and Analysis

From this experimental study, both quantitative and qualitative results were obtained. The first regard all the formal evaluations performed during the three-week period (detailed in Figure 8.1). Concerning the qualitative results, these were obtained by posing open ended questions, and further debating each raised matter, with the study's technicians. The collected feedback can be consulted in Section 8.3.5, right after the analysis of the results obtained in the five evaluations performed that are now presented.

8.3.1 Technology Literacy

As to assess the technicians' knowledge on digital technologies and their ability/easiness to use them, as well as to identify possible literacy differences between both technicians, three proficiency measurements were identified according to the study's context. The first group of scaling questions posed to the technicians, was the eHealth Literacy Scale (eHEALS) [24], aiming to understand the user's perceived capacity at using information technology, and other electronic resources, for health matters. By analysing Figure 8.1's results, one can verify that the technicians scored similarly in this assessment, with subject B surpassing subject A's result by one point. Although these scores showcase a similar (perceived) knowledge on electronic health resources, their middle-range character also highlights a significant lack of confidence when using online resources to support their own health decisions. The latter may influence the confidence and/or resistance to adopt solutions like the e-CoVig system in the future.

<table>
<tr><th>Evaluation</th><th>Description</th><th>Results</th></tr>
<tr><td>Technology Literacy</td><td>To respond to three questionnaires that assess the user's technology literacy:
✓ eHEALS
✓ MDPQ-16
✓ FACETS</td><td><table><tr><th>Test</th><th>Subject A's Score</th><th>Subject B's Score</th></tr><tr><td>eHEALS</td><td>25/40</td><td>26/40</td></tr><tr><td>MDPQ-16</td><td>40/40</td><td>34/40</td></tr><tr><td>FACETS</td><td>49/60</td><td>34/60</td></tr></table></td></tr>
<tr><td>Learning Curve</td><td>To time the performance of the monitoring activity (when employing the e-CoVig system), of all residents, every time it is done.</td><td><table><tr><th># Week</th><th>Time (≈ minutes)</th><th># Residents</th><th>Date</th><th>Subject</th></tr><tr><td rowspan="2">1st</td><td>36</td><td>10</td><td>10/08/2021</td><td>A & B</td></tr><tr><td>32</td><td>9</td><td>12/08/2021</td><td>A & B</td></tr><tr><td rowspan="2">2nd</td><td>45</td><td>9</td><td>17/08/2021</td><td>B</td></tr><tr><td>35</td><td>10</td><td>19/08/2021</td><td>A</td></tr><tr><td rowspan="2">3rd</td><td>40</td><td>10</td><td>24/08/2021</td><td>B</td></tr><tr><td>28</td><td>9</td><td>26/08/2021</td><td>A</td></tr></table></td></tr>
<tr><td>Performance Time</td><td>To time the acquisition-registry activity's duration in two moments: one when using the paper-based method and other when resorting to the e-CoVig system.</td><td>Paper- Based Time: ≈ 30 minutes *
*Excluding mental health assessment
e-CoVig Time: ≈ 36 (± 5.9) minutes</td></tr>
<tr><td>Usability Assessment</td><td>To respond to two questionnaires: SUS and NASA TLX.
Further feedback was collected by posing open-ended questions</td><td><table><tr><th>Test</th><th>Subject A's Score (out of 100)</th><th>Subject B's Score (out of 100)</th></tr><tr><td>SUS</td><td>77.5</td><td>57.5</td></tr><tr><td>NASA TLX</td><td>Raw: 40.83
Weighted: 55.00</td><td>Raw: 65.83
Weighted: 66.33</td></tr></table></td></tr>
</table>

Figure 8.1: Quantitative results of the evaluations performed during the elderly home's usability study.

Next, two scales were employed to assess, firstly, mobile device's proficiency - the Mobile Device Proficiency Questionnaire, MDPQ [110], particularly, its shorter version (MDPQ-16) - and, secondly, to assess the frequency with which an individual resorts to commonplace current information technologies to tailor and improve her/his care provision - the Functional Assessment of Currently Employed Technology Scale (FACETS) [19]. The MDPQ-16 scores were significantly different across the subjects, particularly when regarding the files transferring and email domains. Subject A (the younger technician) achieved a perfect score of 40/40, while subject B had a six- point difference. These results present subject A as more comfortable and aware of mobile device's functions that subject B, foreseeing a possible difference among their user experience with the e-CoVig system. Nevertheless, both scores are, in fact, high, indicating ease and confidence on dealing with mobile device for both subjects, a positive result since this study's implies using two mobile devices (a tablet and a computer). Finally, the FACETS' results were those that most evidenced technology literacy differences between the handlers, having subject A obtained the high score of 49/60, demonstrating confidence when dealing all digital technology's dimensions. With less 15 points is subject B, who demonstrated apprehensiveness and lack of confidence when performing some tasks in mobile devices, again anticipating some difference in the usability results.

Overall, subject A presented better results on the technology literacy assessments, showcasing readiness and availability to to use technology, such as those of the e-CoVig system. Subject B's results, although proving a good level of comfort and ease when dealing with commonly used technology, also demonstrate some level of resistance when facing more complex and/or novel tasks and functions. Even though in today's world, technology is widely spread and employed by most age groups, the evaluations'

results (and the informal talk had to expose the project) evidence that age may influence one's confidence to employ new digital tools and concepts. Nonetheless, *a priori*, both technicians are fitted to conduct the experimental study. Furthermore, the e-CoVig system's intuitiveness and user-friendly design is expected to help both technicians to quickly adapt to it.

8.3.2 Learning Curve

Before analysing the results of timing the task's performance (Figure 8.1), one must disclose important details. Firstly, to time the results in a precise manner, an individual would have to begin the countdown in the exact moment of the first log-in and finish it in the exact moment of last one's closure. Given that neither the working atmosphere, neither the human resources allowed for such precision, one must take all time values as approximate measurement of the actual performance. Furthermore, depending on the group of residents being analysed (both in number and profile), and their mood and/or availability to express themselves, the time taken to assess them can be significantly different than that of other activity days. In fact, even the technician's working schedule in the activity day in question, and their personal relationship with the residents, influence the activity's outcomes. Therefore, all these factors must be considered when interpreting the results. Nevertheless, an effort was made to keep the same two groups of residents throughout the study, and for both sets to be analysed by each technician, approximately, the same number of times.

Regarding the time results, as seen in Figure 8.1, these show, after the first week, a decreasing trend for both technicians, with the maximum value being reached on the first activity day of the second week (17/08/2021), and the minimum being achieved on the last activity day of the overall experience (26/08/2021). Contrary to expectations, the first week did not comprise the maximum value(s). This was due to the fact that, during this week, the technicians chose to team up, performing the task together. While one acquired the physiological measurements and posed the questions to the residents, the other technician registered and performed the logins. This initial choice was justified by the fact that both subjects did not feel completely confident (nor comfortable) on performing the task individually, an important input to consider later on since, not only indicates resistance (even from the most technological literate technician) but because teaming up actually optimize the task. From the time values, one can verify that took less time to complete the task when two subjects were performing it (first week results) than when they "adventured" alone (second week results), even after being already familiar with the system. Moreover, the best week results were, overall, the first one's, supporting even more the choice of partnering during the task. Additionally, results show that subject B appears to benefit the most from the collaboration, having registered the biggest increase of time when left alone to perform the activity (about 9 minutes), whereas subject A only took an extra 3 minutes when acting alone. This result could be partially sustained by the technology literacy's results - where subject A (the younger technician) showed to be more receptive and at ease with technology than subject B - however, such a (small) difference can also be due to the setting's particularly characteristics as previously mentioned.

When focusing solely on the second and third weeks, which followed what was first stipulated,

the collected data provides us two important insights: firstly, the learning curve of both technicians significantly improved over time, with both performing better (taking less time) as they gained experience with the e-CoVig system, and, secondly, performance-wise, the younger technician (Subject A) did better than the second technician, with, about, a 10 minute difference between their best result. Once again, the prediction made based on their technology literacy results seems to be correct, given that the subject with a more extended and enriched background in technology adapted best to the system. Moreover, note that, even though the number of residents analysed in each activity day may have been different, the segmentation was done as to guarantee that each technician would operate the device on the same number of elders as the other, decreasing the relevance of this factor on the results' analysis. Nevertheless, when comparing the time values of the activities days on which the same number of residents was assessed, they still present a difference of, about, ten minutes which also validates the previous analysis.

8.3.3 Performance Time

Regarding the performance times that compared the time-consumption of the traditional registry modality (the paper-based method) with that of the new e-CoVig system, Figure 8.1 showcases a difference of, about, six minutes between both, favorable to the paper-based method. However, this result must be carefully analysed given each method's nature. Firstly, one must mention the origin of each result. The e-CoVig's representative time value corresponds to the average time of all six monitoring activities, a total of 36 (+/- 5.9) minutes. Concerning the paper-based method, this value was provided by one of the technician that measured one of her previous paper-based monitoring assessment as taking, approximately, 30 minutes to perform. The results may come has a bad surprise to those who believed on the benefits brought by technology on optimizing antiquate procedures such as this one. However, the results are actually favorable to the implementation of digital systems in these type of settings, at least when it comes to optimize the task's temporal demand. In fact, if one acknowledges that the traditional method does not comprise a mental health evaluation, and solely focuses on registering each resident's physiological measurements (such as blood pressure, oxygen saturation, temperature and/or blood glucose), the performance time's results turn out to be favorable to the e-CoVig system since, with only, about, six minutes more (less then one minute per elder), it can assess mental health, an evermore important dimension to assess in today's society and which enables, to some extend, the timely diagnose of both physical and psychological health conditions.

In sum, although the traditional method, formally, leads to lower execution times, a less than ten-minute difference of the e-CoVig system allows the exploration of a new, and imperative, dimension. A fair trade, one may argue.

8.3.4 Usability Assessment

As to respond to this study's main objective (assessing the system's usability and added-value to its user), both technicians were inquired in the end of the experience, having provided their feedback through both scaling questions and open ended ones. Firstly, two scaling questionnaires were posed to both technicians

- the ten-item's System Usability Scale (SUS) [77] and the NASA Task Load Index (TLX) [144] (see Appendix B) - in order to assess their experience with the system and the workload these represented to them, respectively. As seen in Figure 8.1's last group of results, the scores of the SUS questionnaire for the younger and older technicians were, respectively, of 77.5 and 57.5, out of 100, significantly different results. The first one, of 77.5, is well above the average (defined in literature as a SUS score of 68 [78][146]), closely approaching the top usability grade (corresponding to a SUS score of 80.3 or higher), which translates into a high perceived usability of the system by the younger technician. The latter was appreciative of the system's functioning and was comfortable when dealing with it. Furthermore, according to literature [146], the 77.5 rating makes the technician highly likely to recommend the system to her peers, a positive result for e-CoVig team as mouth-to-mouth marketing is highly important in the healthcare sector. Contrary, the second technician's score of 57.5 out of 100, distances itself negatively from the average score and dangerously approaching the lowest grade possible (a score of 51 or lower). This disparity between both subject's SUS scores is somewhat predictable considering the technology literacy assessments, as perceived usability is connected to both the knowledge and ease one has when dealing with technology. Thereby, the younger technician adapted to the e-CoVig system much easier than the older one, being open to change and to encourage others to change too, which was not the case of the older technician, who struggle on adjusting to the new work environment.

Importantly, one must consider that, although the SUS scale has proven to be efficient with small samples [78], this study's population may be too small for one to make generalized conclusions. Nevertheless, it was clear, by both SUS scores, that the system has room for improvement. Particularly, although intuitive and easy to work with, both technicians felt that other less technological individuals, very much present in these elderly home's contexts, could have difficulty and/or present resistance to change their paper modality to a digital one. In the technicians' opinion, other peers would probably need more training to deal with the system and, since most institution do not have the technological resources to perform the tasks with the e-CoVig system, could be difficult, even if these technologies were provided, to adapt to the use of equipment such as tablets and/or smartphones. Nevertheless, the biggest barrier was considered to be, by both technicians, to learn how to use the system in a timely manner, which, consequently, led to a slight lack of confidence when handling it.

Regarding the NASA TLX, the younger technician scored a weighted total [143] of 55.00, out of 100, while the older technician obtained a 66.33, out of 100. According to literature, the both scores represent a high workload [144]. This effort, in the case of the younger technician, mainly regarded physical and temporal dimensions, while the other technician highlighted mental effort and temporal efforts as the major demanding sources. The mental effort pointed out mostly refers to the level of focus needed to perform the task, especially when dealing with residents of challenging clinical backgrounds. The mentioned physical demand regards the fact that the technicians had to juggle between the computer (where the platform was displayed) and the tablet (where the mobile application was installed) to perform the task which, considering the resources and the setting of the institution, was not always an ideal scenario, as it will be later approached. Finally the temporal demand, mentioned by both the subjects

was, logically, due to the time spent on performing the task, which, as said by the users, will always take significant time when assessing many elders of multiple profiles.

In sum, both usability evaluations evidence the need to improve the system for it to be applicable in this assistant living settings, namely adjusting it to the type of technological literacy of the technicians.

8.3.5 User Feedback

Finally, the technician's feedback was obtained in the end of the study, through a series of questions that encourage both technicians to freely speak their mind about the experience and the possibility of using the e-CoVig system as their new registry modality. Firstly, a summary of what the technicians considered to be the system's pain points is displayed in Figure 8.2, together with their suggestions of what to improve in both the system and the implementation experience. These are mostly related to the technological dimension of system as elderly homes often lack of equipment that can support such digital solutions, as well as of professionals capable and/or comfortable to use them.

Pain points	Suggested Improvements
Working with two devices	To be able to access all residents' profiles (the platform) in the mobile application, avoiding the use of a computer.
Equipment deficiency and log in method	To create a new log in method that avoids having to rely, in the case of the QR code, on the device's camera – that may not have the best quality, slowing down the whole task – or on an email and password method – which is not feasible in a universe of elders.
Technology Literacy and Experience	To conduct a more detailed formation on the system and its working principle (ideally, including the performance of a test monitoring activity) and to have available technical support on demand. These initiatives aim to mitigate the resistance and/or difficulty that could be easily felt by a technician, of any standard elderly home house, when learning how to handle the new system. This barrier, most probably related to the technicians' lack of experience and/or knowledge on advanced devices, and their capabilities, leads to another suggested initiative (that may be out of this project's scope): to provide a comprehensive formation on technology.
Equipment availability and quality	Although the COVID-19 pandemic has forcibly implemented technology in the Portuguese elderly homes, most of these are, overall, not in possession of advanced technology - such as tablets, mobile phones and/or computers - that fit this task's characteristics, meaning that, last case scenario, these may have to be provided by the e-CoVig team.
Temporal and Human Demand	To fit the care house's technicians often tight schedule, the time taken by the task may benefit from a collaborative work between two technicians; nevertheless, this is not always an option given the limited human resources of a standard care house. Another solution could be to designate the performance of this task solely to the institution's full-time nurse; however, several care houses do not have this employee. This information must be collected, in each elderly home, prior to the conduction of any studies and/or implementation, to tailor each protocol to the institution.
Technicians' own tab in the platform	To design a personalized tab in the BrainAnswer platform reserved for technicians and their work within the elderly house. Organization of supplies and of their schedules, to do lists and a calendar where appointments of any kind could be registered and made available to all the staff, are some of the features suggested.

Figure 8.2: User's feedback summary.

Regarding the identified strengths of the e-CoVig system, many were the features of the system positively emphasized by the technicians. Firstly, the design and architecture of the system (both the platform and application) were considered very well done, being intuitive, simple, appealing and well organized, giving everything needed for a successful assessment. Although the structure provided by the system has already the essential elements to cover most issues, the technicians would like to have some space to fit the system to themselves, for example, having a section dedicated to the technicians

and their work organization. Also, the registration of the collected data was considered very practical, having to only fill in the spaces and move on to the next question/page. The feature the technicians liked the most was, without a doubt, the ability to observe the progress of each patient. The dashboards with the timelines for each question, were considered tremendously handy since, many times, the health professionals requested some information over a certain time period and, through the e-CoVig platform, this information can easily be made available to them, which does not happen with the paper-based method since this required a posterior organization and analysis of all collected data, for each patient.

Furthermore, the system allowed to personalized the protocol to the institution's and each resident's needs, which meant that domains such as mental health could now be assessed periodically. Although liked, this feature was actually difficult to thrive since most residents: 1) did not want to talk; 2) did not feel comfortable to talk with a certain technician; 3) responded but did not deepen their responses, either by inability or lack of will; or 4) had some sort of clinical condition that made the communication between the resident and the technician difficult. To improve these issues it was suggested that, first, the technicians(s) would be, as much as possible, always the same as to make the resident feel comfortable over time on sharing her/his problems, and to include, instead of scaling question, other type of evaluations that could assess the mental state of more difficult patients. Nonetheless, the ability to assess this other very important domain of one's happiness, the mental health, was very appreciated and encouraged to continue to be developed, since the paper-based method did not assess such dimension.

When questioned about the conduction of the task with, and without the system, both technicians indicated the digital method to be more practical and insightful on the long-run, namely after optimizing its handling process and having a enough data on the residents, to create a comprehensive timeline that provides them an overview the elder health evolution. Furthermore, the e-CoVig system was said to: 1) demand slightly less time than the paper-based method to perform the task, considering the extra information provided by system regarding the resident's mental health; 2) to be more comprehensive of all the resident's health dimensions (mental and physical); 3) to encourage the technicians to perform these important assessments more often (and not only when the patient is in need of one) given its appealing aesthetics, its dynamic functioning, and playful side. In fact, the technicians mentioned that even the residents were more excited than before to be clinically evaluated as the system was an exciting novelty to them. In sum, the e-CoVig system collected good feedback, with emphasis on its features and design. The main pain points identified were, as expected, related to the employment of novelty technology, and to the technological resources available in the elderly homes.

8.4 Discussion

The data collected in the elderly home of *Aldeia da Luz* was tremendously helpful to get the e-CoVig's development team a clearer picture of what is indeed needed in a care home setting, and what is dispensable. The study demonstrated that:

- Subjects with more experience and knowledge on technology will be more receptive, and capable of

handling the e-CoVig system and managing its features. It is strongly suggested that, if possible, a technology literacy assessment is done prior to implementation, to identify the most suitable technicians and/or mitigate their limitation.

- Care home's technicians will probably be apprehensive on employing new tools in their workplace (especially those related to already long-duration tasks such as that of the study). Support, both technical and emotional, should be provided by the e-CoVig team to guarantee their participation.
- Collaborative tasks are more attractive than individual ones. The care home's resources must be assessed in advance to prepare the most suitable implementation.
- The e-CoVig system is intuitive and easy to work with, once one has enough experience with it. Furthermore, the learning curve can be relatively short, as demonstrated by this study, in which a three-week experience seem to be sufficient for both subjects to, at least, increase their level of comfort when handling the system and optimize the time spent on the task.
- A registry system like e-CoVig is useful and facilitates the technicians' job, on the long run, by allowing to have access to the health profile evolution of every resident. This central repository of timelines and personal data, improves the care provided to the elders by both the care home's technicians and any other health professional.
- The traditional paper-based methods does not provide all the (considered) useful features and information that the e-CoVig system modality does. Moreover, the performance time with the new method is favorable considering the significantly greater insight gained in the same amount of time as that of the traditional method's performance, which seems to support the gradual replacement of traditional approaches with those digital for the monitoring and registry of institutionalized elders' health. However, as age, alone, appears to influence the success of the implementation, uneven technological resistance will be a barrier for such transition. Thereby, only with custom assessment, preparation, and training, for each institution one can mitigate such disparities and provide strong evidence for the employment of digital technologies in such settings.
- Mental health is definitely important to access, especially in those who saw their acuity decreased over time, however its evaluation has to be fitted to each resident, since the predisposition, emotional availability and/or ability to share their mental status will differ across subjects. Furthermore, the sensitive nature of the matter demands extra care and attention on planning the evaluation.
- The e-CoVig system's registry/"diary" modality needs to have some adjustments done to both the application and platform to guarantee the implementation in more institutions (Section 8.3.5).
- External entities will directly, or indirectly, influence the course of the e-CoVig project. For instance, access to technological equipment that supports these solutions will, on the long-term, depends on the government's (and other supporting organizations) initiative, thus, being able to influence the availability of new institutions to implement the system. Thereby, it will be essential for the e-CoVig members to expand their network, not only to find new costumers, but also to connect with key economical players that may provide advise and/or resources to surpass such challenges.

In sum, the usability testing experience was successfully performed in the sense that the necessary insight was collected and can now be used to tune the e-CoVig system. Regarding the system's usability, there was some non-consensual results. Although the feedback collected in the final interviews with the technicians regarded the e-CoVig system as efficient, needed, and exciting to work with, the results of the usability evaluations (NASA TLX and SUS) show that, when it comes to the user's experience when employing the system, there is a clear to adjust the system to the setting as a high workload was associated to its use (NASA TLX scores), as well as a low perceived usability by one of the technicians (subject B's SUS score).

8.5 Planning the e-CoVig's journey

Considering all the insight attained throughout this thesis, one can envision a more suitable and realistic plan to cover the e-CoVig's remaining path. Figure 8.3 presents the key measures/procedures already executed by the e-CoVig team, as well as the author's suggested actions for the project's near future. Evidently, more actions have to be undertaken to create a sustainable and compliant business (described throughout this work), however, a timely and careful approach to these immediate matters will strengthen the business and, perhaps, empower the innovators to pursue long-term objectives.

Dimension	Executed Actions ✓	Next Steps 🕐
Ideation	• Conduct Market Research • Prioritize adopters and requirements • Define the device's purpose	• Clearly define clinical intend (when choose to pursue CE marking) • Document all decisions
Design & Development	• Test usability of the system's "diary" function, in a relevant environment • Obtain permission to conduct clinical trial on the acquisition device	• Tune the software elements according to user feedback • Validation of the acquisition device, in an operational environment • Enhance the system to its final form • Produce unities of the acquisition device
MDR (When choose to pursue CE marking)	• Classify the e-CoVig device • Acquire technical and performance data • Research for equivalence claims: software and sensing devices	• Check classification with specialize entities • Display information on Technical Documentation and implement a QMS • Identify which other measuring devices can be use together with app and platform • Acquire further clinical data through the conduction of the clinical trial • Train staff on regulation matters
GDPR	• Elaboration of Data Protection Policy and Privacy Notice • Implement appropriate security measure for sensitive data	• Designate a DPO • Create response procedures and templates • Sign a Data Protection Agreement with third parties • Train staff on regulation matters
Market Entry & Post- Market	• Create a protocol of the system's implementation activities • Reach out to elderly houses • Create an ongoing technical support system	• Document the strategy in the business plan • Design a comprehensive training for the handlers • Partner/Connect with key market players • Collect clinical data and display through the appropriate channels • Proceed with learning loop

Figure 8.3: Planning of the e-CoVig project's remaining journey to the medical device market, displaying recent actions undertaken by the team and those to be performed in the near by future.

Chapter 9: Conclusion

The objective of this work was to provide a conceptual framework for medical device development and deployment that could be employed, with confidence, by all innovators, especially by the industry's new entrants. Throughout this work, the main cornerstones of the medical device industry were addressed, namely, the regulation under which is it ruled (the Medical Device Regulation) and that of data protection (the General Data Protection Regulation) for its increasing importance in today's technological landscape (Chapters 4 and 5, respectively). The streamline of both legal frameworks, as well as the provision of strategies to mitigate their challenging character (such as the workflow's of Figures 4.3 and 5.4), met this thesis' objectives. The conceptual framework proposed by this work (Figure 1.1) was thoroughly described in Chapters 6 and 7. It comprised all matters understood by the author as key to successfully develop and deploy a medical device in the market, as well as one's suggested development approach based on an optimizing loop and the proposed TRL scale for medical devices.

The validation of the aforementioned framework was performed by the interview study's results (displayed in Figure 8.1 and detailed throughout this thesis' sections), as they were consistent with what was the content of the conceptual framework (summarized in Figure 3.3). Furthermore, any lacking content emphasized as key in the medical device path-to-market by the interviewees was included in the final version of the conceptual framework for medical device deployment (Figure 7.1), providing the most complete work to the reader. Although one may argue that the interview study's sample was relatively small (16 participants) and, thereby, not representative of all the medical device industry's opinion, the participant's fields of expertise matched, in their grand majority, with those encompassed in the medical device path-to-market (such as biomedics, medicine, design, regulation, computing, management, intellectual property, among others), thus representing a significantly big scope of knowledge that, being in concordance with the proposed approached, gives the author confidence on the work developed and on its validity, fulfilling this thesis' ultimate objective. Nevertheless, since financial matters were out of this thesis' scope, the author suggests to strengthen this framework by conducting future research on their impact in the path-to-market.

This being said, some of main teachings of this work's conceptual framework were that:

- Anyone can be an innovator in today's world. The fourth industrial revolution is, among other things, allowing to accelerate the developing cycles of most solutions and highlighting the need of collaborating with one another while innovating. User engagement and acknowledgement has been particularly advocated in the healthcare sector's own revolution (health 4.0).
- Compliance with both the MDR and the GDPR can be less of a burden if: 1) regulation is interpreted as an ethical work methodology on which integrity and quality reign; 2) it is timely prepared for; 3) governments and official entities provide facilitating tools and know-how to innovators. Regulatory knowledge should, perhaps, be taught in innovative centers such as universities, as part as

their curriculum.

- The collaboration between academia and industry must be nurtured for the technology transfer processes to succeed. Entrepreneurship must be promoted in academia, focus on revenue must be balanced by focus on the society's well being.
- Matters such as those of IP rights, technology transfer, MDR, and GDPR, would greatly benefit if more trained and competent individuals would be available to integrate their human resources. Furthermore, regulators should push to provide streamlined information regarding such intricate matters.
- The innovator who will succeed on achieving and thriving in the medical device market will not be necessarily the most experienced, intelligent, nor resourceful, but that who better adapts to the industry.
- The proposed framework can be employed by all innovators as a tool to guide them through the industry, nevertheless, each innovator will have adapt it to fit her/his context and solution.

Regarding the experimental research conducted on the e-CoVig system's usability, this was performed based on the proposed framework. The research was successful in the sense that all the research objectives were achieved. The feedback obtained from the technicians was satisfactory, as they recognized the system's value and utility. However, the quantitative results, from the formal evaluations, proved that the system needs to be improved for it to be employed in this type of setting with success. The technicians suggestions for improvement should, thereby, be considered. Concerning the study's limitations, since the institution's paper-based registry activity, used as reference throughout the study, did not assessed the resident's mental health that the e-CoVig's modality did, the reliability of results of their direct comparison are limited. Thereby, the author also suggests to perform an usability test in which the paper-based method addresses exactly the same dimensions as the digital modality. Furthermore, because the study was conducted for only three weeks (due to the availability of the institution) the learning curve and technicians' adaptability to the e-CoVig system could not be properly assessed, thus, any future experiment should, if possible, extend in time. Similarly, depending on the institution's resources, any future research should be designed to include more monitoring activities per week. Additionally, since the assessment of usability only regarded the system's registry modality (the mobile application and platform), the author purposes the conduction of the same type of study (making the mentioned adjustments and suggested improvements) with all three elements: mobile application, platform and the acquisition device.

Finally, having successfully performed the outline of the e-CoVig's future (Figure 8.3), all of this thesis' proposed objectives are now fulfilled.

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Appendix A: Conceptual Support

A.1 Proposed Path-to-Market

A summary description of each stage of Chapter 1's reference framework of the medical device path-to-market (Figure 1.1) is provided in Figure A.1.

A.2 MDR Conceptual Support

The CE marking pathway for each class of medical devices, referenced in the proposed workflow for MDR compliance (Figure 4.3 of Chapter 4, are now presented in Figures A.2 to A.5). These were created based on the Medical Device Regulation [49].

A.3 Intellectual Property Path

It will now be presented an example of a protection pathway for one to follow considering that the inventor is an academic (particularly, a university student) looking forward to patent her/his invention developed in the university (implying her/his collaboration with the campus' Technology Transfer Office (TTO)). Importantly, all the described procedures, timelines, and values were attained from both the interview performed with the IST's TTO leader (see Figure B.1), and from the webinar promoted by the same Office ("Patenting", attended on February 17th, 2021).

The patenting journey here considering will pass by: 1) Conducting a state of the art research, before even disclosing any information to the TTO. Once the inventor concludes that there are not similar creations described, she/he shall approach the office; 2) TTO assesses if the invention used the university's resources. If so, the university is included in the process. The extend of its participation depends on the type of inventor. If the inventor is an employee (such as a researcher) that came up with the creation during the labor schedule, the labor entity (the university), by the Portuguese law, has the right for the ownership of the invention (the assignee) and the obligation to financially compensate the inventor(s) (which values are stated on the university's policy). If the inventor is a student, having no labor contract, such ownership is not binding, however, given the financial, time, and expertise demand of the patent process (most times unbearable for an academic), she/he can voluntarily transfer the ownership rights to the university and become the financially compensated inventor. Any inventor will be mentioned by the assignee in the patent and will participate in the whole protection process. If the voluntary transfer is chosen a declaration is submitted to the TTO; 3) The university is now in charge of the process' procedures, fees, response to notifications, to name a few. It will start by submission of the patent application Choices like the international extension of the application internationally will be made based on reports provided punctually by official entities and the commercial exploitation potential (the

Block	Step	Description
A. Conceptualization& Design	1. Biomedical Idea	Envisioning of a product, process, or service, driven by market demand and/or technology. Initial assumptions are made.
	2. Market Research	Market analysis. Getting to know the target audience, the competition, the industry's pain-points, and timings. The collected information will help establish a strong concept and plan for the remaining journey of the project and help evaluate early assumptions.
	3. Design	An interdisciplinary team compiles the requirements of both the industry and the users, previously defined, in an appealing, safe, effective, and compliant, design. Medical device and/or data protection regulations will be strongly considered. A learning loop based on user feedback will be performed until a comprehensive design is achieved, ready to be materialized. The solution's viability is proven at this point.
	4. Protection	Intellectual Property (IP) rights must be considered in both perspectives of seeking protection to one's own creation, and of avoiding breach others' IP rights, during design and development.
B. Development & Validation	5. Prototype	Potentially suitable technology sets take the form of low-fidelity prototypes, developed by means of rapid prototyping technologies, to be tested and technically matured through a learning loop. Testing activities, both of quantitative and qualitative nature, provide pre-clinical data. The solution's feasibility is validated and demonstrated.
	6. Clinical Evaluation	Parallel clinical data collection activities, to demonstrate compliance with the main regulation, are conducted. Pursue of equivalence claims, through state-of-art research, and conduction of clinical evaluations which test the device in increasingly faithful environments (theoretical, relevant, and operational settings). The device's clinical value is demonstrated and validated by official bodies. CE marking apposition.
C. Clinical Trials	7. Clinical Trials	Non-compulsory, by regulation, for most devices (exceptions being higher risk devices). Conduction of clinical investigations to collect further clinical data. Approval must be granted by ethical committees and competent authorities. CE marking apposition.
D. Commercial Adoption	8. Scale-Up	The commercial design is applied in the technically functional low-fidelity prototype. A learning loop, leaning on ergonomics' principles and user feedback, is conducted until the solution's final form is achieved. Pilot studies may be conducted to further evaluate the device's usability and effectiveness.
	9. Market Entry	A fully compliant and complete solution is deployed in the most appropriate market. The previously established market entry strategy is put in place, as well as the post-market plan.
	10. Maintenance & Vigilance	According to the real-world feedback, the project adapts. Innovation, reinvention, and new markets are considered. Post-market surveillance activities are responding to both the user and regulation's needs. The device's clinical validity must be, continuously, proven, thus, data collection activities shall continue after the device's deployment.

Figure A.1: Description of each stage of the workflow suggested in Figure 1.1, for the medical device path-to-market.

ultimate goal of a patent). Note that if the university chooses to not pursue the extension, the rights can be returned to the inventors and these may pursue it, being in charge of all costs and procedures. The detailed timeline and costs will be approached next; 4) The TTO will communicate with the inventors all the decisions and actions made, also consulting with them throughout the process. Once the patent is granted and the invention is commercially exploited, through licensing deals or spin-off and start-up

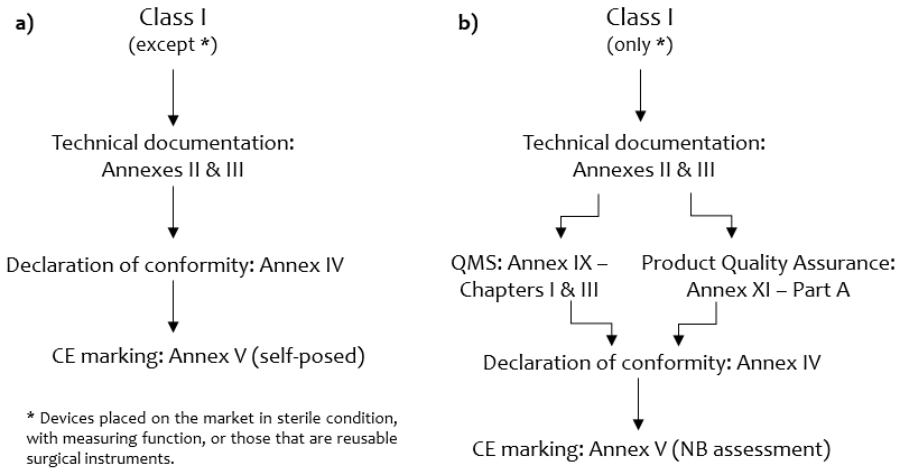


Figure A.2: CE marking journey for medical devices of Class I. a) Class I; b) Subclasses Is, Im, Ir.

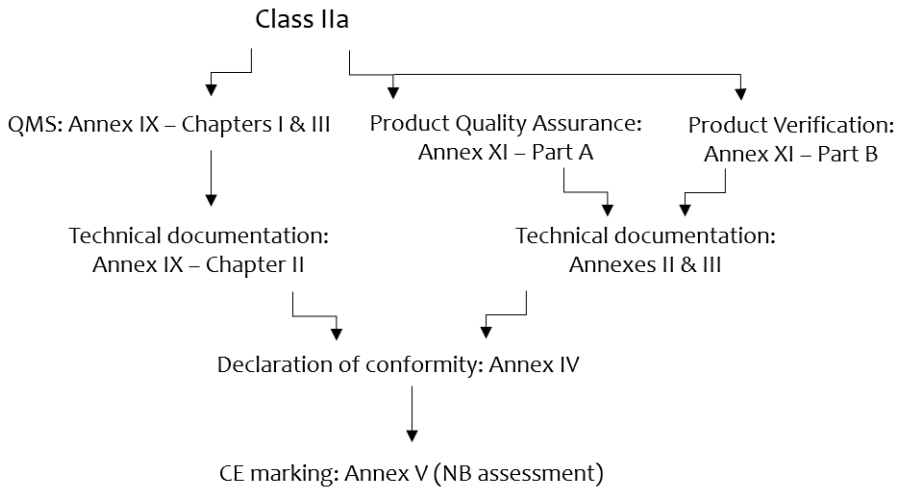


Figure A.3: CE marking journey for medical devices of Class IIa.

creations (see Section 7.3.1), the financial compensation is conceded to the inventors.

Regarding the patenting process' timelines, one can mentioned both the national and international journeys, according with the wish to file a patent that covers only the national territory or other countries to. Concerning the national application, one must know the following time points: 1) Patent application submission: known as priority date, and used as a reference throughout the protection process, refers to the day the application is submmitted to the national entity for patenting matters (which in Portugal is *Instituto Nacional da Propriedade Industrial*, or INPI). The draft is normally done by a patent attorney; 2) Next, a formal examination period, until the 18th month (counting from the priority date), moment when the application is published; 3) Opposition phase: A two month period follows where opposition to the patent's grant can be communicated to the national entity. An examiner analyses the application, considers any opposition filed, and assesses if the invention fulfills all the criteria to be patentable. Notifications will need to be answered by the owner (and inventors). Such answers must be considered valid by the examiner for the patent to be granted. This period can take many months or years; 4) Patent

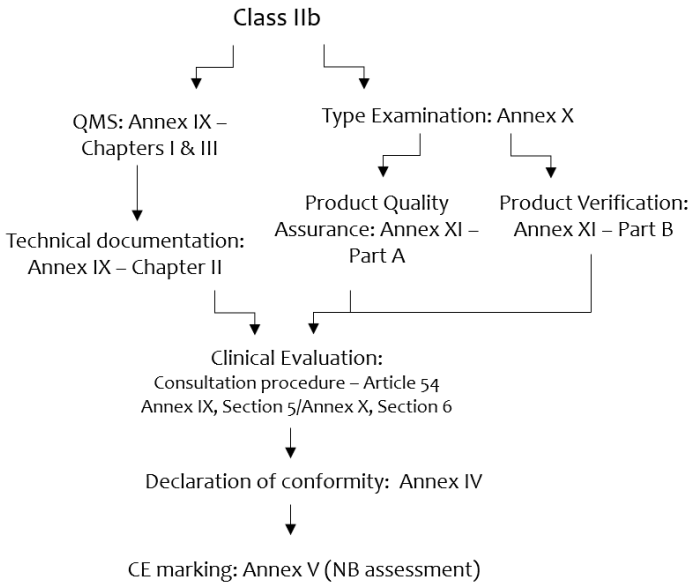


Figure A.4: CE marking journey for medical devices of Class IIb.

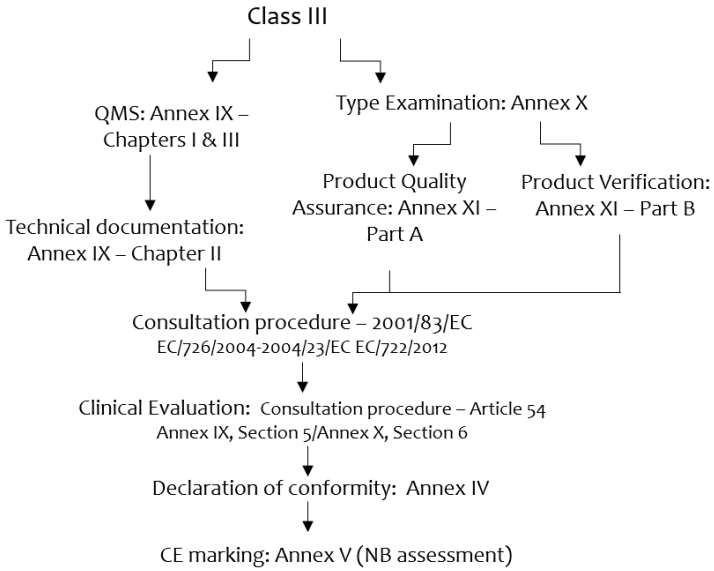


Figure A.5: CE marking journey for medical devices of Class III.

is granted. It is valid for 20 years, counting from the priority date.

Concerning the international application, one is here considering the pursue of such protection via Patent Cooperation Treaty (PCT) application. This is a less expensive and more streamlined method to do extend the patent to other countries and regions as enables the owner of the application to apply to more than 150 states at once. For international application, one must consider other time points that those of national scope, namely: 1) At the 12th month, from the priority date, the owner of the application must decide if it extends the application internationally. One must choose the territories most relevant for her/his invention. If international protection intention is not communicated until this date, the PCT ceases and the patent will only be valid nationally; 2) At the 16th month, one gets a search

report with the written opinion of the international searching authority (one in each country) for the assignee to know if the patent fulfill the criteria or not; 3) At the 30th month the application enters the national phase. Begins the validation of the patent in the countries selected and the payment of regular fees (often annual) to keep the patent "alive" (these exist both before and after the patent is granted.

The cost of this protection process considering, for instance, that the patent is granted in the 5th year, 4 extensions are pursued (such as Europe, Canada, Japan and China), and the patent is kept "alive" during its 20 years validity, is of, approximately, 123 500 euros, between fees, patent attorneys, procedures,to name a few.

A.4 Medical Device Marketing

The medical device industry is, as much stressed throughout this document, very unique. Many challenges are posed during the development, including marketing related ones, as it strongly depends of mouth-to-mouth recommendation. Commercialising a device implies timing, a deep understanding of the market, its laws, and its audience, and to emphasize and sustain the right features to the right audience. The sensitive nature and increased risk of a medical device implies that the purchaser will, forcibly, take extra care when buying, including comparing all available options. Thereby, efforts must be made by the marketing teams to evidence the device's advantages over its competitors and to support such claims with reliable research data that can be easily made available to the target audience [18][34]. This being said, catching the attention of the right audience, and creating a trusting relationship with it, demands a timely preparation of the marketing activities. Traditional marketing plays need to encounter modern marketing tactics, in an ethical and conscious advertising "battlefield". Internet, for example, presents itself, nowadays, as the main "show window" for any product, including the medical devices. Any buyer (entity or individual), will, most likely, look for solutions online before reaching out to any distributor and/or manufacturer. Thus, a strong website that clearly displays the solution's advantages, its compliant character, and that presents the manufacturer as a trustworthy entity, will be a good start in a well-founded marketing plan [128]. Furthermore, other initiatives such as search engine optimization and the displaying of the device's clinical evidence acquired through research, may turn out to be a decisive purchase factor for the buyer. The latter's expectations and criteria can be assessed by consulting the data collected in the early stage of market and user research. This insight will be essential to create the most appropriate marketing strategy, according to the adopters previously prioritized.

Appendix B: Case Study

B.1 Part One: Interviews

Sixteen semi-structure and open-ended interviews were conducted in the first part of the two-fold research that this thesis' case study comprehended.

B.1.1 Sample

The interviewees, detailed in Figure B.1, were selected in order to cover the medical device's path-to-market main matters and stages. Due to the COVID-19 pandemic, the interviews were conducted through an online platform and recorded, after consent was given. The interviews lasted between thirty (30) and one hundred and ten (110) minutes. The objectives of each of defined blocks of the interviews are displayed in Figure B.2.

B.1.2 Concept Umbrellas

The analysis of all conducted interviews implied the segmentation of their content into key concept umbrellas, given the marked differences between each of the discussed subjects. Thereby, based on this thesis' path-to-market suggested initially (see Figure 1.1), four concept umbrellas were created to accommodate the interviews' data and which are detailed in Figure B.3.

B.2 Part Two: Usability Testing

During a three-week period, the e-CoVig mobile application and platform were implemented in an elderly home, in *Alentejo*. To respond to the research objectives, qualitative and quantitative indicators were defined and elaborated to assess user satisfaction and the system's added value for its handlers and, to some extend, to the residents. Each of these assessments was performed in different time-points, having different purposes. The institution's long adopted paper-based registry modality was used as reference throughout the analysis. The evaluations are detailed in Figure B.4. Note that the results of all these assessments were calculated through proper methodology described in literature.

Furthermore, four types of questionnaires were posed to both technicians to access both their technology literacy and feedback on the system, namely: the eHEALS, NASA TLX, SUS, and the MDPQ-16. These are displayed bellow.

eHealth Literacy Scale (eHEALS)

Source : https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1794004/

I would like to ask you for your opinion and about your experience using the Internet for health information. For each statement, tell me which response best reflects your opinion and experience *right now*.

1.How useful do you feel the Internet is in helping you in making decisions about your health?
1) □ Not useful at all
2) □ Not useful
3) □ Unsure
4) □ Useful
5) □ Very Useful

2. How important is it for you to be able to access health resources on the Internet?
1) □ Not important at all
2) □ Not important
3) □ Unsure
4) □ Important
5) □ Very Important

3. I know what health resources are available on the Internet.
1) □ Strongly Disagree
2) □ Disagree
3) □ Undecided
4) □ Agree
5) □ Strongly Agree

4. I know where to find helpful health resources on the Internet.
1) □ Strongly Disagree
2) □ Disagree
3) □ Undecided
4) □ Agree
5) □ Strongly Agree

5. I know how to find helpful health resources on the Internet.
1) □ Strongly Disagree
2) □ Disagree
3) □ Undecided
4) □ Agree
5) □ Strongly Agree

6. I know how to use the Internet to answer my questions about health.
1) □ Strongly Disagree
2) □ Disagree
3) □ Undecided
4) □ Agree
5) □ Strongly Agree

7. I know how to use the health information I find on the Internet to help me.
1) □ Strongly Disagree
2) □ Disagree
3) □ Undecided
4) □ Agree
5) □ Strongly Agree

8. I have the skills I need to evaluate the health resources I find on the Internet.
1) □ Strongly Disagree
2) □ Disagree
3) □ Undecided
4) □ Agree
5) □ Strongly Agree

9. I can tell high quality health resources from low quality health resources on the Internet.
1) □ Strongly Disagree
2) □ Disagree
3) □ Undecided
4) □ Agree
5) □ Strongly Agree

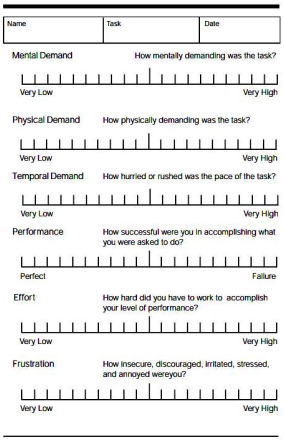
10. I feel confident in using information from the Internet to make health decisions.
1) □ Strongly Disagree
2) □ Disagree
3) □ Undecided
4) □ Agree
5) □ Strongly Agree

Thank you!

** Note: Questions #1 and #2 are recommended as supplementary items for use with the eHEALS to understand consumer's interest in using eHealth in general. These items are not a formal part of the eHealth Literacy scale, which comprises questions #3-10.*

NASA Task Load Index

Hart and Staveland's NASA Task Load Index (TLX) method assesses work load on five 7-point scales. Increments of high, medium and low estimates for each point result in 21 gradations on the scales.



System Usability Scale (SUS)

1. I think that I would like to use this system frequently.
2. I found the system unnecessarily complex.
3. I thought the system was easy to use.
4. I think that I would need the support of a technical person to be able to use this system.
5. I found the various functions in this system were well integrated.
6. I thought there was too much inconsistency in this system.
7. I would imagine that most people would learn to use this system very quickly.
8. I found the system very cumbersome to use.
9. I felt very confident using the system.
10. I needed to learn a lot of things before I could get going with this system.

Mobile Device Proficiency Questionnaire (MDPQ-16)

Please answer each question by placing an X in the box that is most appropriate. If you have not tried to perform a task with a mobile device or do not know what a task is, please mark "NEVER TRIED," regardless of whether you think you may be able to perform the task. Remember, you are rating your ability to perform each of these tasks specifically using a mobile device (tablet or smartphone).

1 - Mobile Device Basics

Using a mobile device, I can:	Never tried (1)	Not at all (2)	Not very easily (3)	Somewhat easily (4)	Very easily (5)
a. Navigate onscreen menus using the touchscreen					
b. Use the onscreen keyboard to type					

2 – Communication

Using a mobile device, I can:	Never tried (1)	Not at all (2)	Not very easily (3)	Somewhat easily (4)	Very easily (5)
a. Send emails					
b. Send pictures by email					

3 – Data and File Storage

Using a mobile device, I can:	Never tried (1)	Not at all (2)	Not very easily (3)	Somewhat easily (4)	Very easily (5)
a. Transfer information (files such as music, pictures, documents) on my mobile device to my computer					
b. Transfer information (files such as music, pictures, documents) on my computer to my mobile device					

4 – Internet

Using a mobile device, I can:	Never tried (1)	Not at all (2)	Not very easily (3)	Somewhat easily (4)	Very easily (5)
a. Find information about my hobbies and interests on the Internet					
b. Find health information on the Internet					

5 – Calendar

Using a mobile device, I can:	Never tried (1)	Not at all (2)	Not very easily (3)	Somewhat easily (4)	Very easily (5)
a. Enter events and appointments into a calendar					
b. Check the date and time of upcoming and prior appointments					

6 – Entertainment

Using a mobile device, I can:	Never tried (1)	Not at all (2)	Not very easily (3)	Somewhat easily (4)	Very easily (5)
a. Use the device's online "store" to find games and other forms of entertainment (e.g., using Apple App Store or Google Play Store)					
b. Listen to music					

7 – Privacy

Using a mobile device, I can:	Never tried (1)	Not at all (2)	Not very easily (3)	Somewhat easily (4)	Very easily (5)
a. Set up a password to lock/ unlock the device					
b. Erase all Internet browsing history and temporary files					

8 – Troubleshooting and Software Management

Using a mobile device, I can:	Never tried (1)	Not at all (2)	Not very easily (3)	Somewhat easily (4)	Very easily (5)
a.Update games and other applications					
b.Delete games and other applications					

Group	Participant identification	Participant description
e-CoVig	*Instituto Superior Técnico* **(IST)**	University of Engineering (Lisbon).
	Faculdade de Medicina da Universidade de Lisboa **(FMUL)**	University of Medicine (Lisbon).
	Escola Superior de Tecnologia da Saúde de Coimbra **(ESTeSC)**	Coimbra Health School (Coimbra).
	Institute for Systems and Robotics **(ISR)**	RD&I institution, affiliated with IST.
	Instituto de Telecomunicações **(IT)**	Private, non-profit, R&D institution specialized in telecommunications.
	Centro Cardiovascular da Universidade de Lisboa **(CCUL)**	Research centre regarding the cardiovascular disease's processes and mechanisms.
	BrainAnswer	Established company that provides services and tools to be applied in research environments.
Experts	*Emitu*	Established company that provides enterprise-grade Internet of Things (IoT) solutions combining smart sensors and software.
	HopeCare	A Digital Health company that develops mHealth concepts and support services that allow the remote collection and monitoring of vital signs and, thereby, a disruptive provision of health care.
	Glintt	Iberian Peninsula's leaders in the health market. Focused on developing and implementing solutions for hospital, clinical and pharmaceutical settings.
	Technology Transfer Office **(TTO)** *of IST*	The TTO focuses on the exploration of IST's knowledge base, managing the university's intellectual property and serving as its point of contact for entrepreneurship and corporate relations.
	Instituto Pedro Nunes **(IPN)**	Private and non-profit institution that targets innovation and technology transfer processes by establishing collaborative relationships between the scientific and technological fields and the corporative domain.
	Comissão Nacional de Proteção de Dados **(CNPD)**	Independent entity with authority powers, endowed with administrative and financial independency, which works together with the Portuguese Republic's Assembly. Focused on matters of data protection.
	Société Générale de Surveillance **(SGS)**	World's leading inspection, verification, testing, and certification company.

Figure B.1: Detailing of the interview study's participants.

Scope	Group	Function	Objective
Ideation & Innovation	**e-CoVig (5)** *FMUL | IT (&IST) | IRS (&IST) | BrainAnswer | ESTeSC (&CCUL)* **Experts (1)** *SGS*	e-CoVig's project founders Innovation responsible	To discuss: idea's drivers; team's value; importance of market research and planning. Key points and struggles of this phase.
Design & Development	**e-CoVig (3)** *IT (& IST) (2)* *BrainAnswer*	App and acquisition device developers Platform developer	To discuss: adoption of facilitating tools; inclusion of the user; team's composition; compliance issues; expenditures. Key points and struggles of this phase.
Technology Transfer	**Experts (2)** *IST (TTO)* *Emitu*	Technology Transfer leader CEO of Emitu (On the establishment of MedTech company and partnership with e-CoVig)	To discuss: academia-industry collaboration; the infrastructure and human resources; the knowledge-spreading process; possible agreements and rights; expenditures. Key points and struggles.
Regulation	**Experts (2)** *IPN (medical devices)* *CNPD (data protection)*	MDR expert of IPN General Secretariat of CNPD	To discuss: bottle-neck *vs* innovation driver; misinformation and communication channels; expenditures; architecture and support. Key points and struggles.
Entrepreneurship	**e-CoVig (1)** *BrainAnswer* **Experts (4)** *Emitu* *HopeCare* *Glintt (2)*	CEO of BrainAnswer CEO of Emitu CEO of Hopecare Team leaders	To discuss: business perspective inclusion in academia's projects; market entry strategies; partnering and networking. Key points and struggles.

Figure B.2: Detailing of the interview study's objectives and participant's role on the path-to-market.

Category	Description
Ideation & Innovation	Conceptualization phase where assumptions and hypothesis are formulated. Market research is conducted to help answer the core questions regarding the envisioned solution. Strategic planning of all phases, and both timeline and budget projections, are outlined.
Design & Development	Design activities are conducted considering the previously established concept and available facilitating tools. An interdisciplinary team is put together to define the best way to translate the idea and demonstrate its viability and usability. Having chosen the technology and defining the feasible design, the prototyping cycle is initiated and elapses through a learning loop, or a waterfall method, according to the type of solution. Users are ideally included throughout this phase.
Pre-Clinical & Clinical Validation	Low and high-fidelity models of the envisioned solution are tested both under laboratory and relevant environments to prove the solution's safety and effectiveness. The clinical value acquired will contribute to demonstrate compliance with main regulation, particularly, to get the CE marking that enables commercialization within the European Union.
Commercial Adoption	The previously chosen market entry strategy is put in place, with production and distribution activities being outlined accordingly. Having checked all regulatory requirements, the solution is launch to the target audience and initial costumer traction is acquired. The scaling plan is then executed, counting on a clear marketing strategy. Post-market surveillance activities must be carefully executed to ensure the maintenance of the solution's compliance with main regulation. Innovation and ideation activities should as well be (again) considered to keep being relevant in the market.

Figure B.3: Detailing of the four concept umbrellas used in interview study's data analysis.

Evaluation	Description	Objective	Subjects	Timing
Technology Literacy	To respond to three questionnaires that assess the user's technology literacy. The proficiency measurements performed regard eHealth (eHEALS) and technology usage (MDPQ-16 and FACETS).	By comparing the questionnaires' results with the ones of the "Learning Curve" evaluation, this assessment aims to understand how the handler's prior technological knowledge impact her/his experience with the system.	Care House technicians (Subjects A and B)	Prior to the study's beginning.
Learning Curve	To time the performance of the monitoring activity (when employing the e-CoVig system), of all residents, every time it is done.	To assess the impact that experience and habituation has on handling the system, meaning, to assess the user's learning curve evolution.	Care House technicians (Subject A and B)	Every activity day (a total of six days over the study's three-week period).
Performance Time	To time the monitoring activity's duration when, firstly, using the paper-based method and, secondly, when employing the e-CoVig system for the last time during the study.	To understand, by comparing the paper-based time and the last e-CoVig's time (to balance the experience factor), if the implementation of this new system shortens the activity's duration.	Care House technician (Subject A)	**Paper-based:** prior to the study's beginning. **e-CoVig:** subject A's last registry day of the three-week period.
Usability Assessment	To respond to two scaling questionnaires which address the system's usability (SUS) and workload issues (NASA TLX). The handlers' feedback is also collected through the placement of open-ended questions.	To collect the user's feedback on the e-CoVig system, namely, the advantages and disadvantages brought to the handler/user, and its possible improvements. The data acquired will be used to, if needed, tune the system to meet the user's expectation.	Care House technicians (Subjects A and B)	Once the study is finalized.

Figure B.4: Description of the qualitative and quantitative evaluations performed during the elderly house's usability study.