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**Certification of a Blood Management and Analysis Software
as a Medical Device: A Comprehensive Study on the
development of Technical Documentation and a Quality
Management System under MDR and IVDR rules**

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Abstract

This dissertation focuses on the certification of Software as a Medical Device (SaMD) following the Medical Device Regulation (MDR) and *In Vitro* Diagnostic Medical Devices Regulation (IVDR). It provides all the information needed to develop a Technical Documentation (TD) and Quality Management System (QMS), which are crucial for a medical device (MD) certification. This work addresses the main challenges usually faced by companies of all sizes when certifying an MD, focusing on SaMD and demonstrating how these challenges affect decision-making when obtaining the CE marking.

A multifaceted approach to research methodologies was employed to strengthen the reliability of the information, offer different viewpoints, and broaden the study scope. This work employed three principal qualitative research approaches: case study, literature review, and framework development. The case studies examine the use of QMS and TD in two distinct companies. At the same time, the literature review emphasizes the primary requirements for TD development in MDSW projects and QMS implementation, along with the digital technologies used to improve both processes. A framework was established to assist all organizations in implementing a QMS, particularly for MD design and development, following ISO 13485 requirements.

Digital technologies are essential in developing and certifying MDSW, aiding documentation management, assuring traceability, and allowing adherence to regulatory requirements. Nevertheless, particular challenges remain concerning the customization and integration of these technologies, particularly in highly regulated industries such as MD development. The analysis reveals that smaller organizations face difficulties due to limited resources, while larger, more established companies struggle with challenges related to data integration and security concerns. Digital technologies are crucial in addressing these challenges and enhancing compliance processes. Nevertheless, additional adaptability is necessary to meet different sectors' specific requirements and fully integrate into an organization and its policies.

Keywords: Medical Device Software; Medical Device Regulation; Quality Management System; Technical Documentation; Digitalization

Resumo

A presente dissertação centra-se no processo de certificação de Software como Dispositivo Médico, em conformidade com a Regulamentação de Dispositivos Médicos e de Dispositivos Médicos para Diagnóstico *In Vitro*. Este estudo foca-se no desenvolvimento da documentação técnica e de um sistema de gestão da qualidade, que são fundamentais para a certificação de dispositivos médicos. O principal objetivo é clarificar sobre todos os requisitos necessários para a certificação, analisar os desafios diariamente sentidos pelas diferentes empresas durante a certificação de um software médico, e perceber a forma como estes afetam a tomada de decisões ao longo do processo de obtenção da marcação CE, obrigatória para a comercialização de dispositivos médicos na União Europeia.

O estudo baseia-se na combinação de vários métodos de investigação para garantir uma maior fiabilidade dos resultados, fornecer diversas perspetivas e ampliar o alcance da pesquisa. As três abordagens principais usadas foram casos de estudo, revisão da literatura e desenvolvimento de um *framework*. Os casos de estudo focam-se na implementação do sistema de gestão da qualidade e da documentação técnica em duas empresas distintas, com diferentes níveis de maturidade e recursos, o que permite uma maior compreensão dos obstáculos enfrentados por ambas. Um dos casos estudados aborda a implementação de um sistema de gestão da qualidade numa empresa envolvida no desenvolvimento de software médico e de um IVD, onde são mencionados os principais obstáculos enfrentados na adaptação dos processos internos e na criação de um sistema que cumpra com os requisitos da norma ISO 13485, essencial para garantir a conformidade com os padrões de segurança e desempenho exigidos pela regulamentação europeia. O outro caso de estudo centra-se no desenvolvimento da documentação técnica necessária para a certificação de um software médico e obtenção da marcação CE, com detalhe nas etapas envolvidas e os desafios enfrentados pela empresa ao desenvolver a documentação exigida para provar a conformidade com a regulamentação. A revisão da literatura concentra-se nos principais requisitos para o desenvolvimento da documentação técnica e a implementação do sistema de gestão da qualidade essenciais para a certificação de software médico na União Europeia. Foca-se ainda na importância que as plataformas digitais apresentam e dos seus benefícios no desenvolvimento destes dois processos. O *framework* desenvolvido tem como principal objetivo orientar empresas na implementação do sistema de gestão da qualidade, ajustando esta implementação a cada uma das fases de desenvolvimento de um dispositivo médico. Este foca-se em três áreas essenciais, sendo estas, o desenvolvimento do producto, gestão de risco e usabilidade. Apesar de este seguir uma sequência lógica, o presente *framework* pretende ser usado como uma ferramenta flexível, permitindo revisões constantes entre as diferentes fases de forma a mitigar potenciais erros ou realizar alterações necessárias. O *framework* tem como objetivo ser adaptável a diferentes tipos de dispositivos médicos e projetos, de forma a ajudar diversas empresas, com níveis de maturidade distintos.

Foram ainda formuladas duas perguntas de investigação para mitigar os principais obstáculos mencionados nos casos de estudo. A primeira foca-se na dificuldade em manter a documentação técnica sempre atualizada e de acordo com os requisitos impostos pela regulamentação europeia durante todo o ciclo de um software médico. A segunda pergunta de investigação foca-se em como adaptar a implementação de um sistema de gestão da qualidade às diferentes fases e níveis de maturidade das empresas.

O papel das tecnologias digitais é destacado ao longo de toda a dissertação, sendo fundamental no desenvolvimento e certificação de software médico. Estas tecnologias são cruciais para a gestão eficaz da documentação, asseguram a rastreabilidade necessária para cumprir com os requisitos impostos pela regulamentação, e facilitam a conformidade com normas como a IEC 62304. Ferramentas digitais como o Jira, Confluence, Polarion e Greenlight Guru são atualmente amplamente usadas por diversas empresas devido à sua elevada flexibilidade e eficiência ao longo dos processos de

desenvolvimento e certificação. Estas ferramentas revelam-se particularmente úteis em contextos de desenvolvimento de software médico, onde os requisitos se tornam cada vez mais específicos e rigorosos com o passar do tempo.

Contudo, apesar das vantagens evidentes proporcionadas pelas tecnologias digitais, existem também desafios significativos relacionados com a personalização e integração destas ferramentas em setores altamente regulamentados, como o dos dispositivos médicos. Embora estas tecnologias ofereçam benefícios na gestão de documentação e na garantia de rastreabilidade, a adaptação destas ferramentas às exigências específicas do setor da saúde e dispositivos médicos nem sempre é um processo simples. A necessidade de personalização de plataformas digitais para garantir que estejam em conformidade com os requisitos impostos pela regulamentação é um desafio constante, especialmente para empresas de menor dimensão que nem sempre possuem todos os recursos para esta adaptação. A integração de soluções digitais exige também um elevado grau de esforço, especialmente em empresas com processos e políticas já definidas há largos anos. Adicionalmente, o elevado custo das tecnologias digitais, associado à necessidade de adaptação das mesmas, é um dos maiores desafios para as empresas. Outras preocupações associadas à segurança de dados e a conformidade com as normas de proteção de dados, são também fatores críticos para organizações que lidam com grandes volumes de informações sensíveis. Outro desafio identificado é a falta de protocolos padronizados para a implementação de ferramentas digitais. A ausência de normas claras para a utilização destas tecnologias pode gerar incertezas nas empresas, que temem investir em soluções que, no futuro, possam não estar em conformidade com regulamentações ou normas atualizadas. Assim, a adaptação tecnológica deve ser planeada cuidadosamente, considerando a evolução das exigências regulatórias e a necessidade de garantir a conformidade a longo prazo. Antes de implementar novas tecnologias, as empresas devem realizar uma avaliação de riscos para compreender os potenciais benefícios e desafios da digitalização no contexto da certificação de software médico.

Os casos de estudo revelam que as empresas de menor dimensão enfrentam dificuldades organizacionais e desafios relacionados com a falta de recursos, tanto financeiros como de infraestruturas tecnológicas, o que pode limitar significativamente a sua capacidade de cumprir os requisitos impostos. Organizações que se encontram no mercado há mais tempo lidam com questões relacionadas com a segurança e integração de dados. O desenvolvimento de um sistema de gestão da qualidade e da documentação técnica para um software médico envolve processos bastante complexos, que muitas vezes ultrapassam as capacidades das empresas de menor dimensão ou das que estão numa fase inicial de maturidade organizacional. No entanto, as ferramentas digitais, quando bem implementadas, podem mitigar muitos desses desafios, demonstrando eficácia na gestão da documentação, assegurando a rastreabilidade e melhorando a comunicação interna entre as equipas. Ferramentas como o Jira e Confluence, por exemplo, permitem uma gestão mais eficiente dos requisitos de software e da documentação técnica, assegurando que as equipas de desenvolvimento conseguem controlar todos os processos que são críticos para o desenvolvimento de dispositivos médicos e futura certificação.

Em suma, a presente tese pretende demonstrar que a digitalização desempenha um papel crucial no processo de certificação de software médico, especialmente no que diz respeito à gestão da documentação e à rastreabilidade. Ferramentas como Jira, Confluence, Polarion e Greenlight Guru demonstram ser essenciais na otimização dos processos, garantindo que as empresas possam trabalhar de uma forma mais eficiente e reduzir custos. No entanto, a adaptação destas ferramentas às exigências de diversos fatores, especialmente a nível de produção e certificação de dispositivos médicos ainda exige esforços consideráveis, tanto em termos de personalização quanto de integração tecnológica.

Palavras Chave: Software como Dispositivo Médico; Regulamentação da União Europeia; Sistema de Gestão e Qualidade; Documentação Técnica, Digitalização

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Nomenclature

Abbreviations and Acronyms

AI	Artificial Intelligence
AIMDD	Active Implantable Medical Devices Directive
CA	Competent Authorities
CAPAs	Corrective and Preventive Actions
CE	Conformité Européene
DoC	Declaration of Conformity
EC	European Communities
EEA	European Economic Area
EPO	European Patent Office
eQMS	Electronic Quality Management System
eTD	Electronic Technical Documentation
EU	European Union
EUDAMED	European database for medical devices
GSPR	General Safety and Performance Requirements
IFU	Instructions For Use
IMDRF	International Medical Device Regulators Forum
ISO	International Organization for Standardization
IVDD	<i>In Vitro</i> Diagnostic Medical Devices Directive
IVDR	<i>In Vitro</i> Diagnostic Medical Devices Regulation
MD	Medical Device or Medical Devices
MDCG	Medical Device Coordination Group
MDD	Medical Device Directive
MDR	Medical Devices Regulation
MDSW	Medical Device Software
NB	Notified Bodies or Notified Body
PHA	Preliminary Hazard Analysis
PMS	Post-Market Surveillance
QFD	Quality Function Deployment
QM	Quality Manual
QMS	Quality Management System
SaMD	Software as a Medical Device
SGS	Société Générale de Surveillance
SiMD	Software in a Medical Device
SOA	State of the Art
SOP	Standard Operating Procedures
SRN	Single Registration Number
TD	Technical Documentation
UDI	Unique Device Identifier

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1 Introduction

1.1 Context and Motivation

Over the past few years, there have been significant changes in the qualification, classification, and certification of medical devices (MD) due to the progress of technology and its crucial role in the production and improvement of these devices [2]. Indeed, the number of patent applications for medical technology increased by 32.5% between 2010 and 2019, and in 2021, more than 15 300 patents were filed with the European Patent Office (EPO), an organization responsible for granting European patents, marking a 0.8% growth over the previous year [3], [4]. Medical technology contributes 8.1% of all applications, ranking second among all European industrial sectors [4]. They are vital for patient health and currently embrace a critical role in the healthcare system, constantly adapting to provide better and more effective care [5]. Currently, more than 500,000 medical technologies are accessible in hospitals, community care settings, and at home [4]. There is then a significant motivation for manufacturers, healthcare professionals, and patients to obtain new and potentially superior medical technology that is currently entering the market at a swift pace [6].

Like other industries, the healthcare sector has witnessed an upsurge in digitalization. This led to the widespread use of software in hospitals and care centers for administrative processes and to support clinical decisions [6]. The European medical technology market, projected to exceed €150 billion in 2021, is estimated to account for 27.3% of the global market [3]. Today, mobile and web applications are integral to these technology-based MD, playing a crucial role in diagnosing, monitoring, and treating patients. These applications, falling under the MDSW category, have proven helpful in the interconnectivity, management, and maintenance of patient medical information and clinical decision-making [7]. This underscores the role of technology in improving patient care, providing reassurance about the positive impact of technological advancements in the healthcare sector.

Medical device regulation in Europe dates back to the early 1900s, with rules governing the production, commercialization, market-entry, and surveillance always in place. As technology and science advanced, updating and tightening these regulations became necessary. Consequently, the EU MDR and IVDR were published in 2017 and had their date of application in 2021 and 2022, respectively [8]. Compliance with these regulations is crucial for all companies in the MD industry.

At present, the production of MD is strictly monitored by authorities, and it is the responsibility of manufacturers to follow the regulatory requirements that address the proper safety and performance of the device in the country where it is being CE-marked for use. This certification indicates that the device meets the essential requirements of all relevant European Medical Device Regulations [9],[10]. Software is currently included and is also required to comply with these rules. Putting a device into the market takes an average of 3 to 7 years, compared to other industries like pharmaceuticals, which require an average of 12 years to certify drugs. Research indicates that the EU focuses on guaranteeing that only reliable and secure devices enter the market [2]. Therefore, to provide efficient clinical care, organizations and manufacturers must implement a system capable of documenting all the necessary procedures throughout the lifecycle of each MD. This proves compliance with EU regulations and helps companies and manufacturers adopt good practices, ensure quality, and avoid possible non-compliance risks in this highly regulated environment. For successful market entry, organizations must then apply and develop a well-structured and well-regulated system that complies with the regulation, such as a QMS [8]. Further processes are also mandatory to affix the CE marking to an MD, to prove conformity with the applicable legislation and to justify and support an EU declaration of conformity, being then crucial to have exhaustive TD to provide information about design, manufacture, and operation of a device [9].

1.2 Aim of the Work and Dissertation Outline

This work provides a comprehensive overview of certifying Software as a Medical Device (SaMD), according to the MDR and IVDR. The focus of this study is on the implementation of a Quality Management System, the development of Technical Documentation for software in the medical field, and the digitalization of both processes. The various chapters delve into these topics, focusing on the major challenges encountered in establishing these procedures. This work aims to demonstrate how these challenges significantly impact MD certification in the EU, highlighting the relevance of the certification process compliance.

This dissertation has been developed to obtain a Master's Degree in Biomedical Engineering and Biophysics. The research was carried out in collaboration with Compliance Tech, Sociedade Unipessoal Lda. (referred to hereafter as Complear), a company that facilitates regulatory compliance with medical device software for market entry. Therefore, all actions align closely with the company's objectives and needs. The dissertation framework may not follow the conventional academic outline and may be customized to meet the organization's needs. However, each chapter is well-explained and justified concerning its relevance within the research context.

The current chapter provides a context and motivation for this work's purpose and primary goals.

The second chapter provides an overview of the definition of an MD, the changes in the EU Regulation throughout time, and the criteria for qualifying and classifying MD according to MDR and IVDR, which also covers the MDSW. The background also covers the regulatory requirements, encompassing details about CE marking, conformity assessment, regulatory authorities, and the steps required to bring an MD to market. Finally, this chapter details the requirements for QMS per ISO 13485 and TD as per the MDR.

Chapter three centers on the proposed methods for this study, encompassing an in-depth examination of both qualitative and quantitative research approaches. This overview aims to determine the most effective research strategies for this dissertation.

Chapter four focuses on two case studies presented in this work. One case study refers to developing a TD for MDSW, while the other addresses the implementation of a QMS. The purpose of these case studies is to highlight the primary difficulties and constraints that manufacturers encounter when developing such processes for both MD and IVD. To address the primary challenges uncovered in the case studies, chapter five centers on the research questions that will ultimately guide this dissertation. Chapter six presents a comprehensive literature review addressing the research questions provided in the previous chapter. The focus lies on the required documentation in MDSW projects, the QMS requirements, and understanding how the phases and maturity of companies impact QMS development. It concludes with information about the implementation of digital tools in digital development.

Chapter seven outlines the framework for implementing a QMS and developing a TD. This framework was carefully developed and adjusted over several months based on the work conducted for the companies stated in the case studies. This section provides an overview of the framework, which is then divided into several stages encompassing the design and development of the QMS. The purpose is to clarify the specific documents, procedures and information necessary at each level of a MD's development. By testing the framework in the two organizations described in the case studies, challenges and learnings could be extracted to better understand the primary issues encountered at this level.

Chapter eight discusses its final remarks about QMS frameworks and the integration of digital tools in MD certification. The last chapter synthesizes the key concepts and findings discussed throughout this dissertation. This chapter summarizes the work performed, the conclusions drawn from the case studies, and the implementation of the framework. It also examines the influence of digitalization on the implementation of QMS and TD. Lastly, it suggests future directions, emphasizing MD certification's ongoing development and opportunities for future research.

2 Background

2.1 Regulatory Frameworks of Medical Device

2.1.1 What are Medical Devices?

Access to high-quality, readily available, safe medical products is critical for improving patient care, responding to health crises, and preserving community health. Certain medical procedures, such as monitoring the heart rate, applying a bandage, and performing any surgery, would be impossible without an MD. These are used in various circumstances and environments, including assessing illnesses, monitoring treatments, aiding disabled patients, or treating diseases [10]. During this dissertation, MDs may be referred to as MDs and IVDs.

MD span a broad spectrum of categories, each with a unique applicability to various healthcare needs. These range from the most familiar ones, like pacemakers, wheelchairs, thermometers, and MRI machines, to the less conventional ones, such as medical device software. They can be used in hospitals, medical centers, and additional health facilities to assist healthcare professionals in providing superior patient care and enhance the precision and efficacy of medical procedures [11].

The MD sector is continually growing and innovating, with new technologies and products constantly emerging. This contributes to healthcare development and guarantees patients obtain the latest sophisticated treatments. Over the previous decade, MDs have displayed significant developments and rising technologies, that have provided them with several benefits. They became lighter and more portable, making them more accessible and simpler to use. They included wireless technology, allowing for the transmission of medical data or remote monitoring of specific conditions, and they incorporated AI technology, aiding in the analysis of data and identification of diseases [12]. As a result, MDs have become crucial in contemporary healthcare systems, providing patients with less invasive treatments, and better control of their conditions. Creating new MDs will continue to modify patient care and explore the boundaries of what is achievable in health.

2.1.2 Evolution of Medical Device Regulation in the EU

Throughout the 1960s and 1970s, the Member States of the European Communities (EC) believed that the unification of product regulations was the best approach to establishing regulatory consistency across the Community. Therefore, each EC member released a set of rules to prove that these harmonized policies existed. Even though this legislation benefited the commercialization of certain products, some countries weren't complying with it [13].

The EC's approach to product regulations experienced significant changes in the 1990s, along with the sudden growth of the MD market, as it began to rely on mutual acceptance of device certification. This period saw the introduction of three directives that laid the foundation for the MD law in the EU. These directives, which came into force from 1990 onwards, shared crucial aspects such as preserving free trade, public protection, and harmonizing standards [11]. Directive 90/385/EEC on Active Implantable Medical Devices (AIMD), published in July 1990, was a landmark in this journey. It was applied to any powered device "intended to be totally or partially introduced, surgically or medically, into the human body or by medical intervention into a natural orifice, and which is intended to remain after the procedure" [12]. It mandated that starting on January 1st, 1994, all Member States should adopt legislation and regulations to comply with this Directive, with a transitional period up to December 1994 [11]. The second directive, Directive 93/42/EEC on MD (MDD), published in July 1993, was equally significant. It was applied to almost all medical devices, except *in vitro* diagnostic devices, active implantable devices, cosmetic products, and any product of human or animal origin [14]. The adoption of regulations according to this Directive was intended to start on January 1st, 1994, with

a given transitional period extended to 13 June 1998 [13]. The last directive to be applied was Directive 98/79/EC on *In Vitro* Diagnostic Medical Devices (IVDD), published in October 1998 and intended for medical devices used in laboratory tests of human functions [15].

At that time, all Member States had to adopt new rules according to the Directives and ensure the well-functioning of the market. Non-compliance issues related to safety, performance, health protection, and process authorization would create trade barriers between the countries. To prevent that, all MDs had to follow essential requirements related to the commercialized devices' manufacturing, design, and packaging procedures as part of the conformity assessment process [13].

With the MD market growing and with significant scientific and technological advancements, there was a need to develop stricter sets of regulations. As a result, the MDR and IVDR were approved in 2017 by the European Council and the European Parliament to replace the EU Directives. It is currently mandatory for companies and manufacturers to comply with these regulations when selling their devices in the EU, to guarantee the proper safety of all commercialized MD.

2.1.3 Qualification of Medical Devices according to MDR/IVDR

In the same way European regulations have changed throughout the years and adapted according to the market needs, the definition of MD and IVD has also evolved (**Figure 1**).

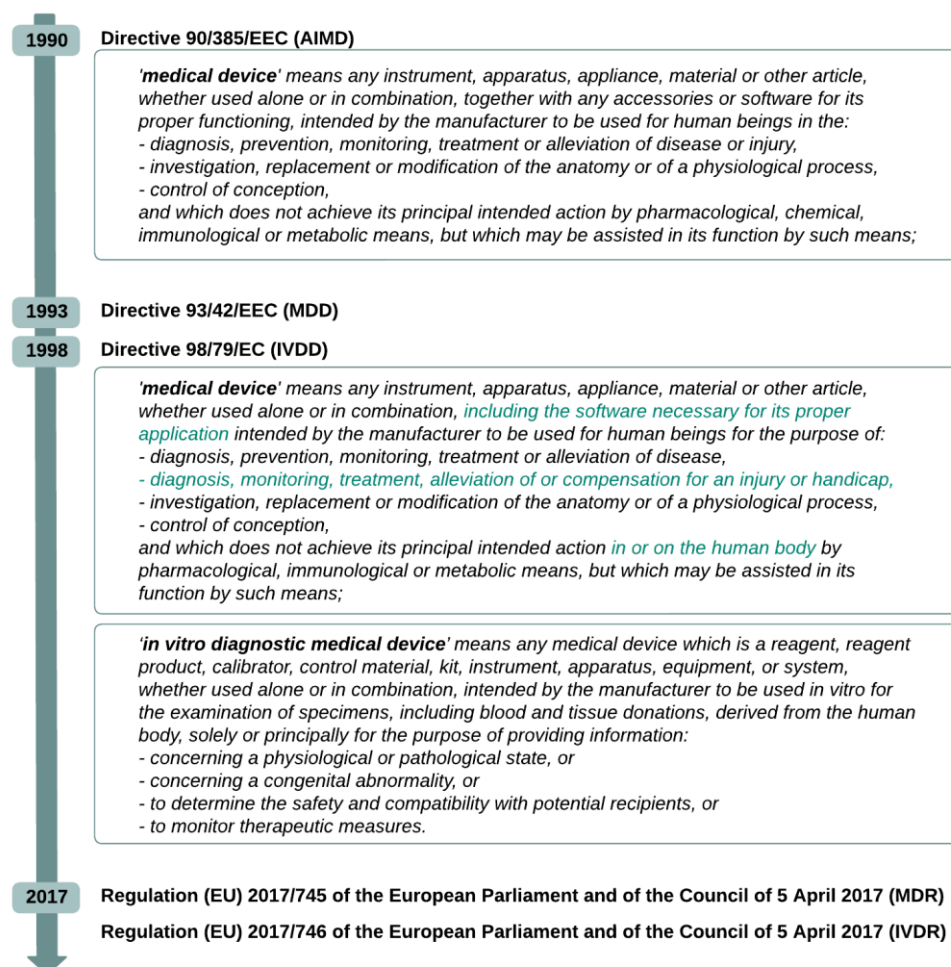


Figure 1. Overview of the Medical Device definition in the EU (changes are represented in green) (information from [13], [14] [16]).

Nowadays, MD encompasses a wide range of technologies, from low-tech and straightforward devices, such as dressings or disposable needles, to more complex systems, such as pacemakers, prostheses, imaging devices, and even software. To qualify a product as an MD, it must serve a medical purpose and comply with other essential requirements, underscoring the complexity of this field.

According to the Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017, a medical device is defined as “any instrument, apparatus, appliance, **software**, implant, reagent, material or other article intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the following specific medical purposes: (i) diagnosis, prevention, monitoring, prediction, prognosis, treatment or alleviation of disease, (ii) diagnosis, monitoring, treatment, alleviation of, or compensation for, an injury or disability, (iii) investigation, replacement or modification of the anatomy or of a physiological or pathological process or state, (iv) providing information by means of *in vitro* examination of specimens derived from the human body, including organ, blood and tissue donations, and which does not achieve its principal intended action by pharmacological, immunological or metabolic means, in or on the human body, but which may be assisted in its function by such means.” [17]. This regulation entered into force in May 2017 and has been applicable since May 26, 2021. In addition, Regulation (EU) 2017/746 of the European Parliament and of the Council of 5 April 2017 was created also in May 2017 and put into practice since May 26, 2022. This regulation concerns *in vitro* diagnostic medical devices, which are defined as “any medical device which is a reagent, reagent product, calibrator, control material, kit, instrument, apparatus, piece of equipment, **software** or system, whether used alone or in combination, intended by the manufacturer to be used *in vitro* for the examination of specimens, including blood and tissue donations, derived from the human body, solely or principally for the purpose of providing information on one or more of the following: (a) concerning a physiological or pathological process or state; (b) concerning congenital physical or mental impairments; (c) concerning the predisposition to a medical condition or a disease; (d) to determine the safety and compatibility with potential recipients; (e) to predict treatment response or reactions; (f) to define or monitoring therapeutic measures.” [16].

These regulations were established to ensure the users’ safety through higher transparency and traceability of MD [18].

2.1.3.1 Medical Device Software (MDSW)

Healthcare is becoming increasingly reliant on software and other valuable applications. This is seen by the growing popularity of complex technological devices and software for healthcare professionals and consumers, especially within health facilities. This represents a massive impasse for lawmakers who question whether software should be regulated similarly as an MD, given that it can injure and hurt humans in the same way as physical equipment does, leaving no uncertainty that it must be regulated with an identical level of disparity [19].

Given that software is often an essential part of MD technology, it is crucial to establish secure and effective procedures to ensure the safety of these devices. It is then critical to understand the software's intended purpose and provide evidence that using it doesn't cause any additional unacceptable risks [20].

The MDR and IVDR state that any software, alone or in combination, designed for use by a human being can be considered a medical device as long as it serves the specific medical purposes stated in these regulations, regardless of whether the software is independent, driving or influencing the use of a device [20]. The software's purpose determines whether it qualifies as an MD and strongly influences its classification and pathway to the market. As a result, it is crucial to have a well-defined intended purpose that is thought of, consistent throughout the development and documentation of the device, and aligned with a company's or manufacturer's business strategy.

There are many terminologies to qualify software used in the healthcare industry. Software is defined according to its intended purpose and function within a device, as seen in **Figure 2**.

SaMD is internationally defined by the International Medical Device Regulators Forum (IMDRF) as software intended to fulfill a medical purpose without being part of a hardware MD. This type of software can operate independently of the device but can still be embedded in or run on hardware as long as it isn't necessary for that hardware to achieve its medical purpose. SaMD can be employed with general-purpose IT equipment or a hardware MD's computing platform. However, it remains SaMD as long as the hardware isn't required to fulfill its medical function [22].

On the other hand, MDSW is an EU term, as the European Commission does not use the term SaMD. It pertains to software intended to be used, either alone or in combination, for purposes outlined in the definition of MD as per the EU MDR and the EU IVDR. MDSW is used to classify software according to Rule 11 of the EU MDR, which applies to software-only MDs and hardware devices that include MDSW as an integral part [22].

The key difference between SaMD and MDSW is that MDSW includes software necessary for a hardware device to achieve its medical purpose, while SaMD excludes software essential for a hardware device to function. Another key difference is that MDSW includes software for specific medical purposes, such as "support of conception" or "alleviation of disability", which are part of the EU MDR's definition of an MD but not covered in the definition of SaMD under the IMDRF [22].

Another worldwide designation for software is Software in a Medical Device (SiMD). This applies to software embedded within a hardware MD, where the software is essential for the hardware to fulfill its intended medical purpose. SiMD would be classified as MDSW if necessary for the MD's function in the EU [22].

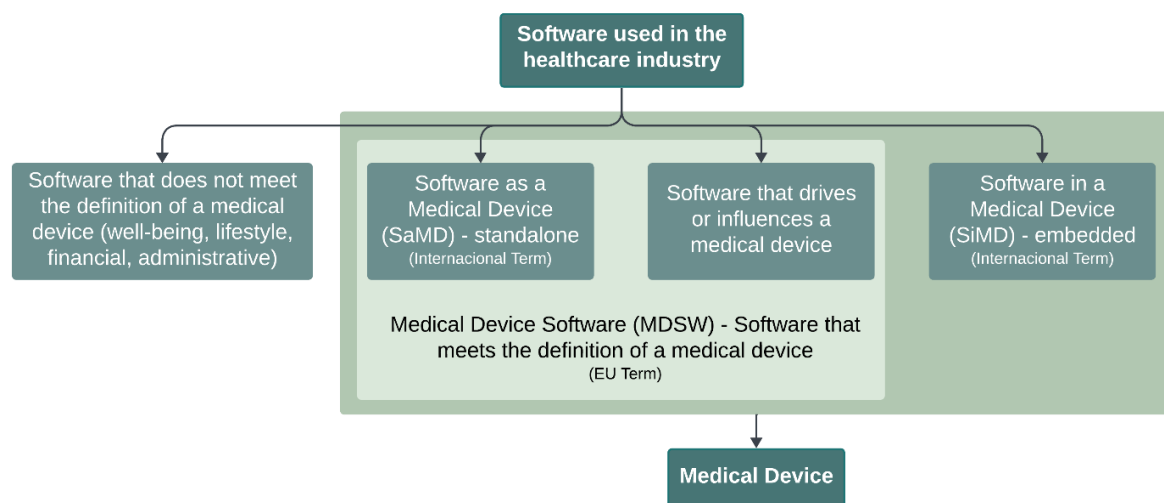


Figure 2. Qualification of Health Software (information from [22]).

To qualify software as MDSW, manufacturers can follow the MDCG 2019-11 created by the Medical Device Coordination Group (MDCG). This document serves as guidance when developing a new product and states the necessary decision steps for qualifying software as MDSW according to MDR and IVDR requirements (**Figure 3**).

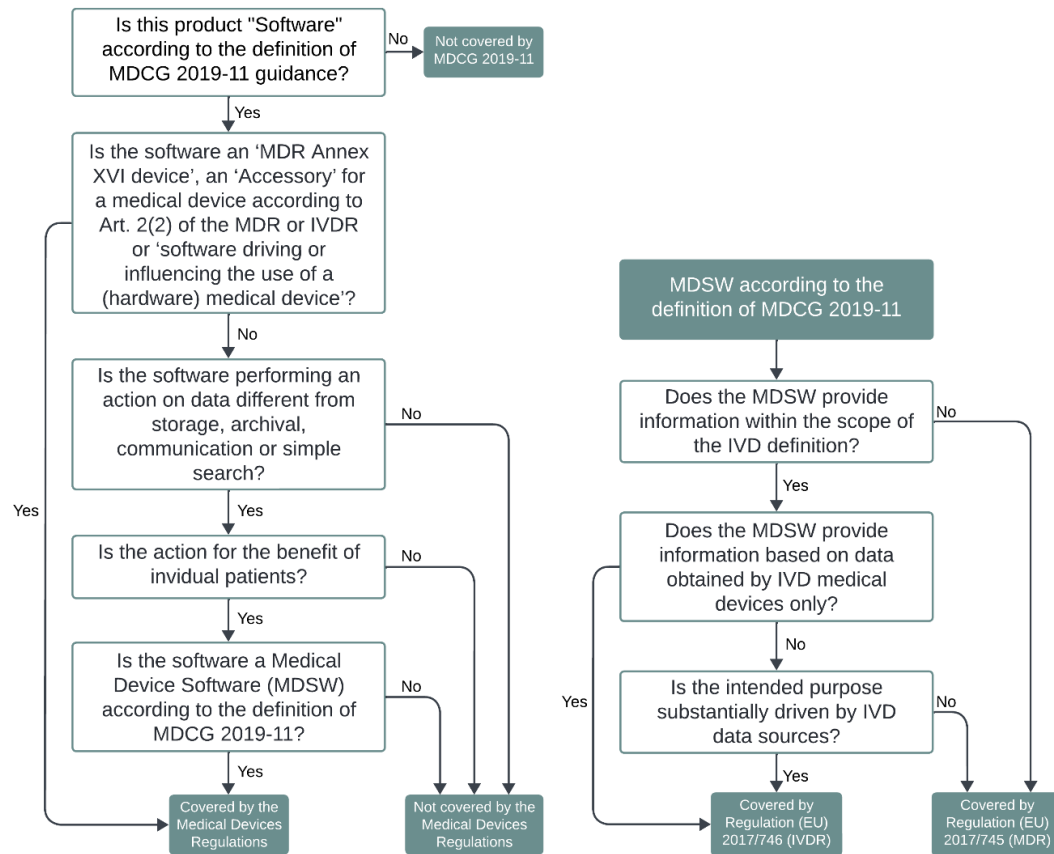


Figure 3. Decision steps to assist qualification of MDSW (a) according to the MDR and (b) according to the IVDR (adapted from [23]).

2.1.4 Classification of Medical Devices according to MDR/IVDR

The challenges of classifying MD stem from their diversity and multiple applications in healthcare. In the EU, devices are classified according to their intended time of use, their interaction with the body while in use, and whether they are active MD, meaning they require an external power source. Also, devices used in the central cardiovascular and nervous systems are separated from other devices, potentially due to their higher risks [24].

MD can be classified as Class I, II, or III in the EU. Non-invasive devices and the ones that result in low risk for patients are mainly classified as Class I. These constitute the majority of the MD in the EU market and can be further divided into the following subclasses:

- **Class I:** Non-sterile and with no measuring function, such as bedpans or wheelchairs;
- **Class Is:** Placed on the market with a sterile condition, either sterile transportation or sterilized upon receipt, such as personal protection kits;
- **Class Im:** Devices with a measuring function, such as thermometers or stethoscopes;
- **Class Ir:** Reprocesses or reused devices, such as surgical instruments.

Class II devices are divided into two groups: the ones that constitute a medium risk to patients, are typically invasive and installed in the body for less than 30 days are usually classified as **Class IIa** devices. This category includes ultrasonic diagnostic equipment and hearing aids. This class also comprises **Class IIb** devices that pose a medium to high risk to patients, are primarily invasive, and are usually installed in the body for more than 30 days, such as infusion pumps and radiotherapy equipment. At last, the **Class III** MD represents the highest risk to patients and includes breast implants, pacemakers, or heart valves [25], [26]. All rules applied to the classification of an MD according to the MDR are presented in **Table 1**.

Table 1. Classification of Medical Devices (adapted from [24])

Type of Medical Device		Description	Classification	Exceptions
Non-invasive		Either do not touch the patient or contact with injured skin or mucous membrane as a mechanical barrier, compression, or absorption exudates.	Class I	
		Intended for channeling or storing blood, body liquids, cells or tissues, liquids, or gases for eventual infusion, administration, or introduction into the body; Connected to an active device in class IIa or higher; Intended to manage micro-environment of injured skin or mucous membrane.	Class IIa	Unless intended for channeling and storing blood bags (Class IIb).
		Intended for modifying the biological or chemical composition of human tissues or cells, blood, other body liquids, or other liquids intended for implantation or administration into the body; Intended for wounds which have breached dermis or mucous membrane and heal only by secondary intent.	Class IIb	Unless treatment consists of filtration, centrifugation, or exchanges of gas and heat (Class IIa).
		Intended to be used <i>in vitro</i> in direct contact with human cells, tissues, or organs taken from the human body or used <i>in vitro</i> human embryos before their implantation or administration into the body.	Class III	
Invasive	Non-Surgical	Transient use (<60 minutes).	Class I	
		Short-term use (60 minutes to 30 days) or connected to an active MD in class IIa or higher.	Class IIa	If only in the oral cavity, in the ear canal, or the nasal cavity (Class I).
		Long-term use (>30 days).	Class IIb	If only in the oral cavity, in the ear canal, or the nasal cavity, and not liable to be absorbed by the mucous membrane (Class IIa).
	Surgical	Transient use.	Class IIa	Unless it is a reusable surgical instrument (Class I); Intended to administer medicines in a potentially hazardous manner and to supply energy/ionizing radiation; Biological effect-mainly of wholly absorbed

				(Class IIb); For use in direct contact with the heart and central circulatory or nervous systems; Used to control/diagnose/monitor/correct a defect of the heart or central circulatory system through direct contact (Class III).
		Short-term use.	Class IIa	Unless intended to undergo chemical change in the body (not in teeth), to administer medicines (not in teeth) and to supply energy/ionizing radiation (Class IIb); Intended for use in direct contact with the central nervous system, heart, or central circulatory system; Specially to monitor/control/diagnose/correct defect of heart or central circulatory system by direct contact; Biological effect-mainly or wholly absorbed (Class III).
	Implantable	Long-term use.	Class IIb	Unless intended to be placed in teeth (Class IIa); To be used in direct contact with heart or central circulatory/nervous system; Biological effect or are wholly or mainly absorbed; To undergo chemical change in body (not teeth); To administer medicinal products; Active implantable devices or their accessories; Breast implants, surgical meshes (Class III); Total or partial joint or spinal disc replacement or implants in contact with spinal column; Except components such as screws, wedges, plates and instruments (Class IIb).
Active		Active therapeutic devices intended to administer or exchange energy.	Class IIa	Unless intended to control/monitor or directly influence the performance of a class IIb active therapeutic device; Administer or exchange energy in a potentially hazardous way; To emit ionizing radiation for therapeutic purposes, to control or monitor active therapeutic devices intended to administer or exchange energy, or directly influence their performance (Class IIb); For controlling/monitoring or directly influencing the performance of active implantable device (Class III).
		Active therapeutic devices with an integrated or incorporated diagnostic function that determines the patient management by the device (closed loop systems and automated external defibrillators).	Class III	
		Active devices for diagnosis and monitoring or supplying energy to be absorbed by the body or to image in vivo distribution of radiopharmaceuticals	Class IIa	Unless intended to illuminate the patient's body, in the visible spectrum (Class I); Devices emitting ionizing radiation for diagnostic or therapeutic radiology, including interventional radiology devices and devices which control or monitor such devices; Intended to monitor vital

	or allowing direct diagnosis or monitoring of vital physiological processes.			physiological parameters where variations could result in immediate danger to the patient or for diagnosis in clinical situations where the patient is in immediate danger (Class IIb).
	Software (Rule 11)		Class I	Unless intended to provide information used to make decisions with diagnosis or therapeutic purposes (Class IIa); Decision impact can cause serious deterioration in health or surgical intervention (Class IIb); Impact can cause death or irreversible deterioration of health (Class III); Monitor physiological processes (Class IIa); Decision impact can cause serious deterioration in health or surgical intervention (Class IIb).
	Active devices to administer and/or remove medicines & other substances from the body.		Class IIa	Unless this is a potentially hazardous way (Class IIb).
	All other active devices.		Class I	
Device Exceptions	Devices incorporating integral medicinal substances and that have an action ancillary to that of the devices.		Class III	
	Devices used for contraception or prevention of sexually transmitted diseases.		Class IIb	Unless they are implantable or long-term invasive devices (Class III).
	Devices that are intended specifically to be used for disinfecting or sterilizing medical devices.		Class IIa	Unless they are specifically intended for disinfecting, cleaning, rinsing, or hydrating contact lenses (Class IIb); Disinfecting solutions or washer solutions specifically to be used for disinfecting invasive devices, as the end point of processing (Class IIb).
	Devices intended for recording X-ray diagnostic images.		Class IIa	
	Devices utilizing non-viable human or animal tissues, cells, or their derivatives (unless such devices are intended to contact with intact skin only).		Class III	
	Devices incorporating or consisting of nanomaterials or	Negligible potential for internal exposure.	Class IIa	
		Low potential for internal exposure.	Class IIb	

	High or medium potential for internal exposure.	Class III	
	Devices invasive concerning body orifices (not surgical) to administer medicinal products by inhalation.	Class IIa	Unless the mode of action has an essential impact on the efficacy and safety of the administered medicinal product (Class IIb); Intended to treat life-threatening conditions (Class IIb).
	Devices composed of substances or combinations of substances to be introduced into the human body via a body orifice or applied to the skin and absorbed by or locally dispersed in the human body.	Class IIb	Unless they are applied to the skin or in the nasal or oral cavity as far as the pharynx and achieve their intended purpose on those cavities (Class IIa); They, or their products of metabolism, are systemically absorbed by the human body to achieve the intended purpose (Class III); They achieve their intended purpose in the stomach or lower gastrointestinal tract and they, or their products of metabolism, are systemically absorbed by the human body (Class III).
	Active therapeutic devices with an integrated or incorporated diagnostic function that significantly determines the patient management by the device, such as closed-loop systems or automated external defibrillators.	Class III	

IVDs are also classified based on the risk they represent to public or individual health, with classes ranging from A to D, being class D the ones with highest risk. This classification is essential as it dictates the level of engagement of a third party in evaluating IVDs, pre- and post-market. **Class D** devices provide the highest individual and public risk, with the potential to cause life-threatening infections. These include devices that detect highly contagious and dangerous pathogens, such as SARS and Ebola, that assess tuberculosis patients' infection levels or detect HIV status in blood reserves. **Class C** devices present a high individual and moderate public risk and may include, for instance, diagnostic tests alongside cancer treatments, cancer screening and diagnosis, and genetic tests in humans. Devices with a moderate individual and low public risk are often classified as **Class B**, such as control devices with no specified quantitative or qualitative function. Lastly, **Class A** devices present the lowest individual and public risk. These include, for instance, devices designed particularly for *in vitro* diagnostics or laboratory accessories with no critical features, washing, or buffer solutions [27].

2.1.5 Requirements for Medical Devices according to MDR/IVDR

Millions of people in the EU rely on an ever-winding range of MDs for disease management and diagnosis, demanding high standards for the MD's quality, safety, and performance. To sell their products legally in the EU market, manufacturers must meet the minimum requirements demanded by the EU Regulations, which include a set of processes to ensure the product's safety and efficacy. However, these procedures alone are not enough to ensure quality. It is through the adoption of a constant improvement approach, facilitated by a well-developed QMS that companies can truly be effective. A well-developed QMS enables manufacturers to maintain these strict standards over the entire lifecycle of the MD, thereby enhancing patient safety and trust. It is the QMS that controls MD quality and fosters the continuous growth and innovation that companies strive for in the MD industry.

Before launching an MD into the EU market, manufacturers must provide technical documentation proving the device's compliance with the applicable legislation. The legal requirements that manufacturers must follow have significantly changed due to the modifications in the EU regulations. As a result, competent authorities and notified bodies became stricter while auditing the technical files for soon-to-be-launched MDs. Manufacturers are currently responsible for developing technical documentation required for all MD classes and providing access to these documents when required by regulatory authorities. Certain sections of the technical documentation are used by the manufacturer when submitting the device to the chosen Notified Body while obtaining the CE mark [28].

2.1.5.1 CE Marking

When a device is classified as an MD in the EU, it must conform to the EU Regulations before it can be placed on the market. The CE mark is not just a quality label, but a crucial legal requirement. It declares that the device conforms with all applicable requirements related to safety and quality, ensuring that the device can be freely commercialized in the European Economic Area (EEA). It's important to note that many non-medical products, such as personal protective equipment or toys, also bear the CE mark. The CE marking is designed to harmonize regulations, provide a uniform standard for high-level security, health, and environmental protection, and enable the mobility of goods within the EU market. This not only ensures product safety but also promotes trade [29], [30].

The CE marking is a certification mark that indicates product conformity with an EU regulation, which can be for example, for security, health, and environmental protection. It shows that the product has been tested and verified by the manufacturer to show compliance with the applicable requirements. The CE mark, which stands for *Conformité Européene*, allows a product to be legally commercialized in the EU. The mark has a specific graphic design and shall be placed by the manufacturer legibly and visibly on all products claiming compliance, including MDs, according to **Figure 4** [17].

For a manufacturer to obtain the CE marking, it must demonstrate that the device meets specific requirements, which differ depending on the product but often include health and safety features. All electrical equipment, MD, construction products, and toys, among others, must bear the CE marking to show that they comply with the current regulation.

The process of obtaining a CE mark demands manufacturers to describe all relevant information about the product's design, production, and operation and the manufacturer's testing and conformity assessment procedures in a well-developed and transparent technical file. The conformity assessment process is crucial for a device to be CE-marked, as it comprises all necessary details about the product's features, design, and performance testing. According to the device's risk level and applicable regulation, it can be self-certified or third-party certified.

CE marking is required for a product to be legally sold in the EU market and to ensure compliance with the minimum health and safety standards. Its use must be controlled and not deceive customers or imply sponsorship by any regulatory organization [31].

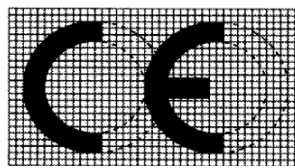


Figure 4. CE Marking (extracted from [32]).

2.1.5.2 Conformity Assessment

The conformity assessment procedure is crucial for a manufacturer to obtain the CE marking, as it guarantees that the device operates according to the requirements demanded by the EU Regulation. This procedure is adapted to each product and its designated level of risk. It is also intended to determine whether the device fulfills the appropriate level of quality and environmental management system criteria. Manufacturers can self-evaluate the low-risk devices before affixing and demonstrating conformity with the CE mark by showing the documentation related to the product's design, technical reports, and risk assessment. For high-risk devices, a third-party conformity assessment procedure is required, including the work of a Notified Body (NB) that will perform tests to verify the conformity of the product.

The conformity assessment procedures may vary according to the device and its classification, so the manufacturer must understand which method is the most appropriate for obtaining the CE mark. All processes must be standardized and suitable, and the technical documentation must contain technical specifications, testing results, and instructions for use, addressing all crucial requirements, hence speeding up and simplifying the CE marking process [31].

2.1.5.3 Regulatory Authorities

2.1.5.3.1 Competent Authorities (CA)

In every EU Member State, a competent authority facilitates the implementation and application of the Regulations on MD and *in vitro* diagnostic medical devices, ensuring that all medical equipment complies with the EU Regulations and national law. The CA, chosen by the Government of each member state, identifies and monitors notification agencies, conducts inspections to assess manufacturing standards, and reviews the technical file for the MD while also informing the Member State's Minister of Health. These organizations additionally offer training and exchange of best practices and are primarily responsible for the lowest-risk MD [26].

2.1.5.3.2 Authorized Representative

When a device's manufacturer is not based in a Member State, the device can only enter the EU market if the manufacturer appoints an authorized representative, who consists of any legal or natural

person centered in the Union who has granted and accepted a written mandate from a manufacturer established outside the Union. They have the duty of operating on behalf of the manufacturer concerning specific duties following the latter's obligations under EU legislation. If a manufacturer's devices fit into several generic categories, they might have more than one authorized representative, nevertheless, for a specific generic device group, the manufacturer should only nominate one [32].

The authorized representative ensures that the EU declaration of conformity and TD have been prepared and that the manufacturer has completed a suitable conformity assessment procedure if required. They must also notify the manufacturer if there is any concern that the conformity assessment procedure is inappropriate for the device. The designated person must also preserve a copy of these documents while in charge of the device in question, meaning at least ten years after the previous device was placed on the market and 15 years for implantable devices [32].

2.1.5.3.3 Notified Bodies (NB)

Notified Bodies are government designated companies that take over official duties on behalf of national authorities to assess that specific products comply with all legal requirements before they enter the market and play a crucial role in helping manufacturers obtain the CE marking. These authorities conduct tasks essential for the conformity assessment procedures prescribed by the applicable legislation when a third party is requested and work as a bridge between manufacturers and the MD regulatory system. This process may include evaluating the relevant TD, reviewing technical design and product testing, auditing the manufacturer's QMS, and drawing evaluation reports. NBs are responsible for offering their conformity assessment services, crucial to placing a product on the EU market, to any economic operator in any EU or non-EU country. They must act in a non-discriminatory, impartial, open, autonomous, and neutral way to ensure the confidentiality of the conformity assessment information. All companies and manufacturers can choose any NB legally approved to conduct the conformity assessment process [33].

The New Approach Notified and Designated Organizations (NANDO) website¹ provides an updated list of the NB operating in the EU countries, including each NB's identification number and the responsibilities for which it has been notified. Each NB is uniquely identified by a 4-digit code that must be placed below the CE Marking on the product and/or its packaging and the user manual [26], [34].

Class I MD and Class A IVD devices can be certified without an NB since they are deemed low-risk devices; however, devices with other classifications, such as Class Im, Is, Ir, and above, require their assessment. In a simplified manner, Class Is, Im, and Ir requires the involvement of an NB for assessment limited to the special functions. Class IIa MD and Class B IVD must submit the technical file and conform to the tests performed by NB. Class IIb MD and Class C IVD devices require the same procedures as Class IIa or a device type examination by an NB. Finally, Class III MD and Class D IVD devices require a full QMS audit or device type examination by an NB [33].

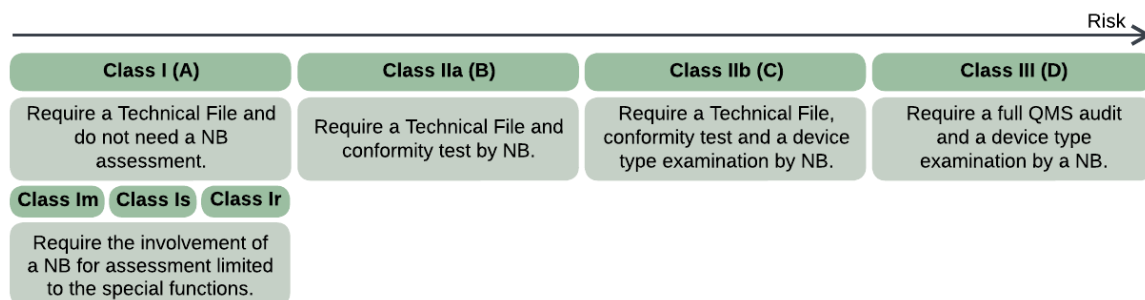


Figure 5. Action of Notified Bodies according to the device classification. Bracketed codes refer to in vitro diagnostic medical devices as defined by the IVDR (adapted from [26]).

¹ NANDO website: <https://webgate.ec.europa.eu/single-market-compliance-space/notified-bodies/by-legislation>

2.1.5.4 Steps to the Market

Developing and releasing a MD into the EU market is a complex, challenging, and deliberate process. It requires not only coming up with the idea and creating a functional prototype but also guaranteeing that all procedures, from the initial concept to the device's launch into the market, comply with the EU Regulations and meet the minimum safety and health requirements. Therefore, formulating and strictly following a plan is crucial for bringing a device to market without disobeying European law.

According to the step-by-step approach advised by Société Générale de Surveillance (SGS) (Figure 6), the first stage is to formulate the device's intended purpose, which is the primary step in determining whether a product qualifies as a MD. Along with this process, it is crucial to understand the clinical benefits that the device brings to a patient (individual or group) or public health, identify the target population, and highlight the main indications and contra-indications of the device. It is vital to demonstrate that the product is safe for all patient populations in the intended use environment. This step ends by establishing if the device is a MD under the MDR (EU) 2017/745. Stage two involves classifying the device according to the rules of Annex VIII of the MDR into one of the following classes: Class I, Class I (sterile, measuring, reusable surgical instrument), Class IIa, Class IIb, or Class III. During this phase, it is recommended that the company or manufacturer contacts the CA to understand the potential requirements for national registration and to acquire a Single Registration Number (SRN) from the CA or the European database for medical devices (EUDAMED). The implementation of the QMS should begin in the third stage and comply with Article 10 of the MDR. For this, most companies apply the ISO 13485² standard to meet the requirements established by the EU Regulation. Step four is related to developing the Technical Documentation to provide evidence that the MD conforms with the MDR Annex I – General Safety and Performance Requirements (GSPR). It is crucial to emphasize that all Class III and active implantable devices must have a Design Dossier and undergo a Clinical Investigation. All MDs must include a Clinical Evaluation in the Technical Documentation. A company based outside the EU must appoint an Authorized Representative (EC REP), an organization competent in managing regulatory issues in the EU through a written agreement. This is the primary step in stage five. In stage six, all MDs except Class I (non-sterile, non-measuring, non-reusable surgical instruments) must select an NB to audit and analyze the QMS and Technical Documentation or Design Dossier from the NANDO database. In stage seven, if both the NB audit and the TD assessment are successful, all devices, except the ones specified before, must require a European EC Certificate. An ISO 13485 certificate, usually valid for five years, is recommended during this phase. A surveillance audit is performed annually, and the certification must be renewed every three years. In step eight, each MD must obtain a Unique Device Identifier (UDI) and register in the EUDAMED system. Stage nine requires the preparation of a Declaration of Conformity (DoC), which consists of a legally binding document signed by the manufacturer's authorised representative. It comprises a list of necessary information and ensures the device complies with the relevant Regulations, Directives, and other Statutes. The final step is affixing the CE Marking, which is only possible once all preceding steps have been done successfully. All Class Im, Is, Ir devices or higher must include the NB number in the CE Mark [35]. A similar process is followed for IVDs, that must comply with IVDR (EU) 2017/746.

² For simplification reasons, EN ISO 13485:2016 + A11:2021 will be shortened to ISO 13485 throughout this document.

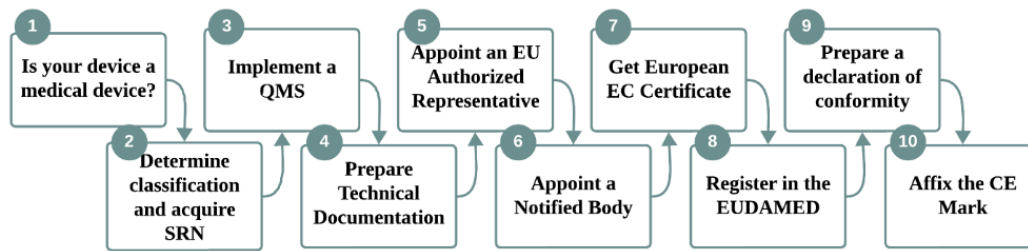


Figure 6. Steps to the EU Market and CE Marking Process (information from [35]).

2.2 Requirements for Quality Management System according to ISO 13485

Medical devices are increasingly important in providing high-quality healthcare to the general population. They include a wide range of products, resulting in ever-winding complex and exhaustive regulatory and certification processes. As a result, manufacturing companies have paid close attention to standardization and implementation procedures in the past few years to ensure that safety and quality criteria are met throughout the device manufacturing process. The importance of obeying standards and acquiring proper certification stems from the MD's primary purpose of increasing patient safety, enhancing clinical results, and promoting public health.

Regulations do not always cover every required technical aspect. Therefore, complying with them leads to the industry's state of the art (SOA) and/or standards that cover those aspects. Some of these standards are harmonized to provide conformity assessment criteria that align with the essential requirements of EU directives and regulations, such as ISO 13485.

Although standards have a vital role in a globalizing society, both in terms of quality of life and economics, their application within a company still remains a sensitive issue. There are currently no definitive answers to how the implementation and compliance with quality systems and standards might benefit organizations [36].

2.2.1 Quality Management Systems from Quality to Medical Devices

Quality management refers to how a company, organization, or manufacturer oversees the interrelated parts of a specific operation or task that must be performed. It is used to manage and ensure that a given process is carried out according to the regulations and to accomplish acceptable quality goals. Given the company's area and dimension, the extension ranges from only having effective leadership to having considerable documentation and a variety of procedures that meet regulatory obligations to ensure stakeholders' security and fulfillment, a process known as QMS [37].

A QMS is a set of strategies, principles, and procedures that help a company achieve quality excellence and meet the customer's requirements. It is based on several guidelines, established processes, and records that help specify how an organization produces and delivers a product or service intended to be used by a particular consumer. A QMS should always be tailored to a specific product or service. Thus, a company must specify its significant goals and adjust them to meet the organization's needs [38]. The primary motivations and benefits of implementing a QMS rely on internal and external factors. While internal motives stem from a company's desire to enhance its methods of performing tasks and different procedures, external motivations arise when a company or manufacturer is interested in entering a new market, exporting new goods, and fulfilling clients' needs. The benefits are considerably more remarkable when quality standards are established to improve the efficacy of an organization's structure, system, and processes. Several motives and benefits can be presented as examples of why an organization might want to implement a QMS. Internal motives include improving processes and procedures, increasing the quality of products or services, decreasing errors, rejections, and concerns, lowering internal expenses, and facilitating communication inside a company. External motivation stems from an organization's need to preserve or expand market share, gain competitive

advantage, have direct access to a new market, be trustworthy, and promote a good company's image. Companies and manufacturers that prioritize actual quality improvements and corporate demands achieve greater advantages from their QMS implementation [36].

To assist manufacturers in fulfilling all expected requirements while enhancing quality within an organization, several guidelines help standardize the development of a QMS. The International Organization for Standardization (ISO) is a well-known, independent, non-governmental international organization with standard bodies in 169 countries and the author of 25 111³ international standards. Among their most recognized standards is the ISO 9000 family, which addresses several aspects of quality management and consists of the world's best-known standard for QMS, ISO 9001 [37], [39]. This standard enables companies of all sizes and areas to enhance performance, meet user expectations, and prove their commitment to quality. It addresses all requirements for initiating, developing, maintaining, and continually improving a QMS. ISO 9001 covers a wide range of topics that focus on seven crucial principles: context of the organization, leadership, planning, support, operation, performance evaluation, and improvement. Based on these categories, ISO 9001 requires companies to establish the internal and external variables that impact the capacity to accomplish the desired results of their QMS and highlights the value of leadership in adopting and maintaining a QMS. According to this standard, the QMS must incorporate measures to reach an organization's quality goals while continuously improving the system's performance. It also covers some areas involving resources, awareness, competence, recorded information, communication, and the processes required to fulfill customer expectations and satisfaction, which must be planned, executed, and monitored. ISO 9001 demands a QMS's performance and efficacy be consistently regulated, monitored, examined, and updated, relying on performance evaluation outcomes and other information sources. Every company should be interested in complying with and being certified with 9001, as it offers several benefits, including guidance for enhanced customer satisfaction, increased efficiency, better risk management, improved competitiveness, cost savings, and productivity gains [40].

ISO provides various QMS standards based on ISO 9001 and tailored to specific industries and business sectors. ISO 18091, for instance, offers guidelines for local governments to understand and implement a QMS to satisfy their citizens' expectations and needs; ISO 22163 specifies requirements for railway QMS; and ISO/IEC/IEEE 90003 guides companies in the purchase, supply, creation, and maintenance of computer software. In the MD field, ISO 13485 establishes QMS requirements in which a company must show its capacity to offer MD and related services that consistently satisfy user and regulatory requirements. This internationally agreed standard was first introduced in 2003, and its most recent version was released in 2016. A company that meets this standard may be engaged in several lifecycle phases, such as design and development, manufacture, storage and transportation, installation, and support of MD provision or related activities. ISO 13485 can also be applied by suppliers or third parties that supply products, including QMS-related services, to such entities [41]. All ISO standards are evaluated every five years to determine whether a revision is necessary to keep it updated and suitable for the current marketplace [42].

2.2.2 Quality Management System according to ISO 13485

Regulatory standards are becoming stricter at all stages of a product's lifecycle. Companies in the market must develop and provide their QMS and guarantee best practices in every task they perform. In the MD industry, ISO 13485 specifies the requirements for a QMS that every organization in this field must follow. Its purpose is to provide general requirements for a QMS that companies may use in the design, manufacturing, setup, and servicing of MD and associated operations. This standard is also suitable to assist internal and external parties, such as certification bodies, with auditing processes. ISO

³ Research date: 10/05/2024

13485 helps companies develop a QMS, demonstrating a solid commitment to continuous improvement and offering customers trust in the ability to deliver reliable and efficient devices to market [43].

Regulations differ significantly from country to country. Hence, ISO 13485 does not specify exact guidelines but requests a MD company to identify and incorporate legal requirements relevant to its specific circumstances and include them in its QMS. The certification of ISO 13485, like other ISO management system standards, is optional, and companies may profit significantly from implementing the standard without engaging in the certification process. However, whenever an organization intends to sell a device in the European market, it must comply with the standard [42].

A company must adopt several processes to demonstrate conformity with ISO 13485. Like any ISO certification, MD companies interested in being certified with this standard should first familiarize themselves with the ISO 13485 requirements and then develop a tailored management system consistent with them. This standard provides several viewpoints on different areas crucial for the certification and for a manufacturer to implement good practices within a company (**Figure 7**). ISO 13485 outlines that management responsibilities are critical for setting priorities throughout a company's different sectors and departments, assigning duties to the proper employees, and understanding how the organization can grow in response to market needs. Resources are also necessary within a company and can be divided into two categories: infrastructure resources, which are responsible for understanding the type of work environment required for the production of a certain MD, the requirements that must be fulfilled to comply with the regulation and how to adopt best practices; and human resources, which assist in determining the most qualified people to work in the production of the MD, as well as the qualities and skills that are most suited for the company's team. Depending on the type of MD and their risk to patients, the supplier's assessment may also be crucial when developing a device since the company might have to comply with several legal requirements and standards. Therefore, understanding how the product or service is offered and delivered may be critical to avoiding non-conformities. QMS are built on continuous improvement, which should be used to certify an MD and guarantee the company's overall organization and progress. Keeping track of complaints and receiving feedback is crucial for improving the company's systems and procedures, improving communication, and adapting the MD to the client's preferences. The Post-Market Surveillance and Vigilance process works in parallel with continuous improvement. It must consist of a proactive and reactive strategy for when a device is already on the market to understand if the product is operating as anticipated. Finally, the Design, Development, and Production step is the most significant stage of developing MD's QMS, as it ensures that the device functions and performs most reliably according to the safety and environmental requirements established by the regulation. It is crucial to highlight that there are several approaches to implementing a QMS. Therefore, this process should be adapted to each company's specific goals, needs, size, and industry [41].



Figure 7. Main focus areas of ISO 13485 (based on [41]).

2.2.2.1 Documentation Requirements

The current regulation requires documenting the design control process inside the QMS for developed MD, as described in ISO 13485. The QMS's documentation hierarchy can be divided into three categories, as displayed in **Figure 8**. The primary document is the Quality Manual (QM) (Level A), followed by all essential documents, which are frequently much more complex and may be separated into two other levels: documented procedures (Level B) and document records (Level C). The QM is considered the primary source of information since it describes the organization's targets, processes, and methods for its design and manufacturing procedures in line with the standard's requirements. This document can be created internally by the company's team or by an external, qualified consulting company. The QMS procedures, or standard operating procedures (SOP), define the methods, procedures, policies, and requirements that must be followed. They contain both technical and clinical information and follow a standard structure, using flow charts and diagrams when relevant. The quality manual usually refers to the relevant SOPs. Lastly, document records and forms provide evidence of a previous event, documenting the outcomes or actions that occurred. Records generated during the development of a new product include laboratory notebooks, device specifications, functional features, risk management reports, validation and verification protocols, packaging and sterilization, and manufacturing processes. The records, specifications, and reports will be utilized to complete the MD's design history. They will also act as proof to establish the implementation of the design control process and the development of a secure and trustworthy solution. After all procedures have been specified and documented in the QM, the organization may request an external assessment by an accredited certification body. If all requirements are implemented and fulfilled, ISO 13584 certification can be granted [44], [45].

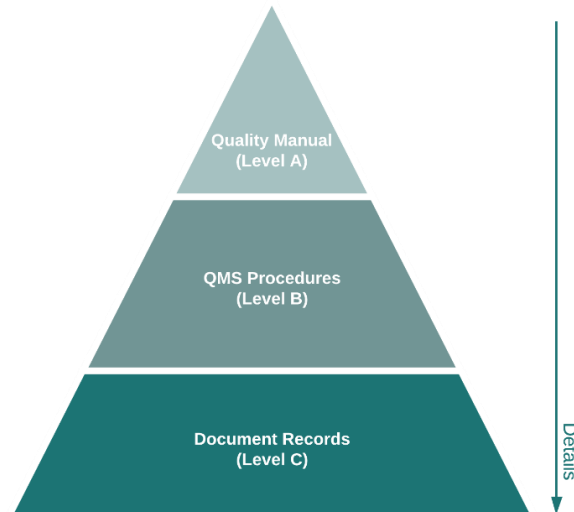


Figure 8. QMS documentation hierarchy within the QMS (adapted from [44]).

The extent of the QMS's documentation varies according to the company. However, the ISO 13485 standard states that it must contain documented statements of a quality policy and objectives, a QM, documented procedures and records demanded by the standard, as well as documents, including records, established by the company to guarantee the successful planning, functioning, and supervision of their processes [44].

2.3 Requirements for Technical Documentation according to MDR

A technical documentation (TD), that may also be referred to as technical file, consists of a set of documents that an MD manufacturer must provide to the proper authorities before placing it on the market. Submitting a technical documentation is necessary to accomplish the conformity assessment or approval procedure. It contains information on the device's design, production, and function and must include all the required data to establish the product's conformity with the applicable requirements [46]. The TD, as the QMS, is subject to assessments. Auditors determine whether the regulation's basic requirements have been met and whether the company followed the processes outlined in the QMS. Therefore, a technical documentation must be developed during the device's design and development process and maintained throughout its entire life cycle [47].

The TD comprises the entirety of the documents defining a device. Therefore, it must be written in a clear, structured, easily accessible, and straightforward way and incorporate the device description and specifications, including variants and accessories, information to be supplied by the manufacturer, design and manufacturing information, GSPR, benefit-risk analysis and risk management, and product verification and validation, including clinical and performance validation [48]. Furthermore, the MDR now demands a closed-loop procedure, executed using data from the Post-Market Surveillance (PMS) or device use, to guarantee that early warnings are recorded, GSPRs are met, and patient benefits always outnumber the risks [49]. **Figure 9** illustrates all the details that must be included in each specified area of the technical file.

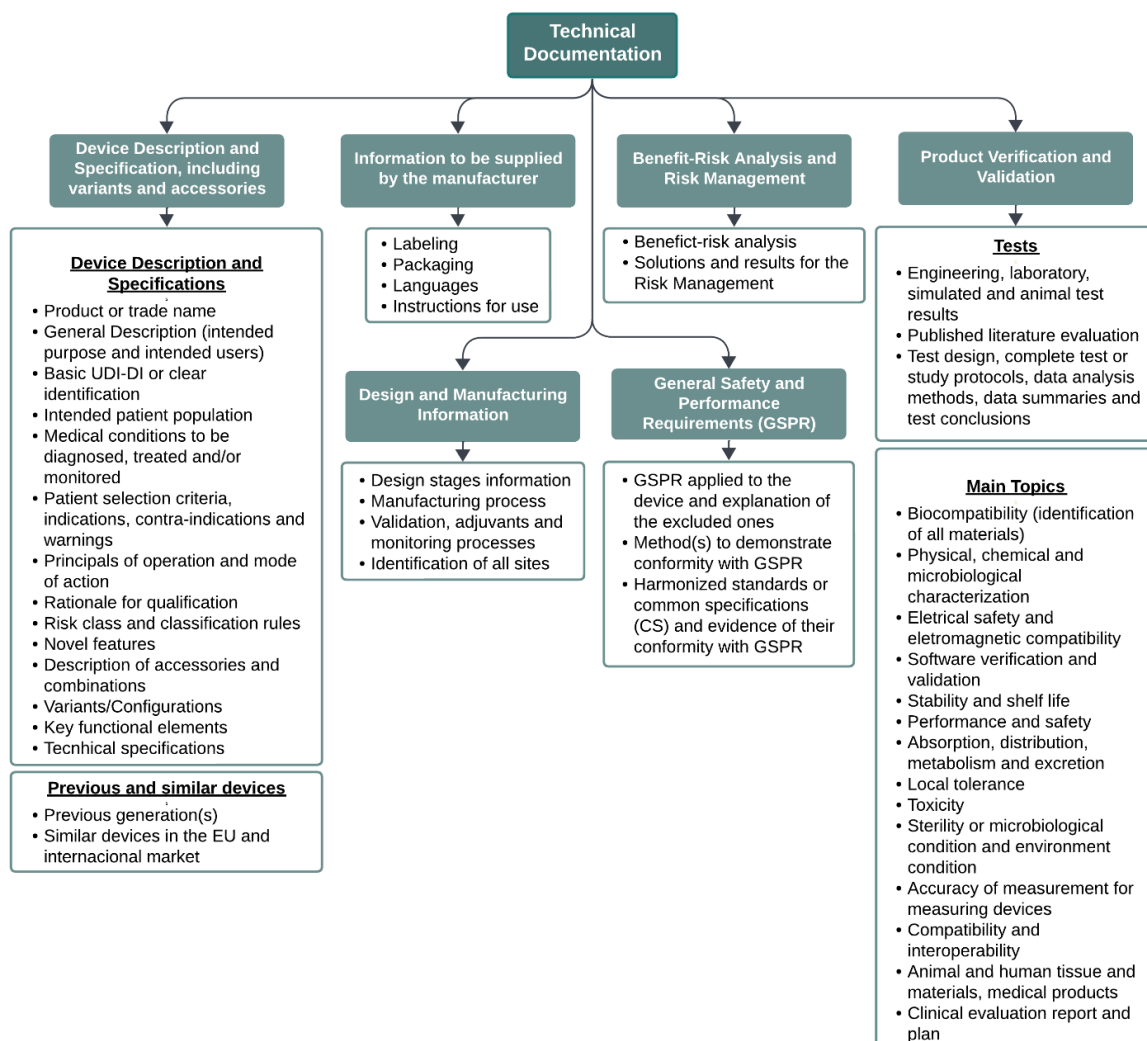


Figure 9. Technical Documentation Requirements according to the EU 2017/745 (information from [17]).

3 Accepted Methods

Healthcare organizations are vital in the operation and progress of any country, considering their effect on public health and well-being. Today's healthcare firms confront unique challenges that require operational excellence and effective resource management. Unlike other sectors, healthcare leaves limited space for error since mistakes can directly influence human health. As a result, society places great expectations on healthcare professionals and institutions to implement and maintain quality standards [50]. This has sparked greater interest in QMS among researchers from various fields, as these systems play an important role in assuring the efficiency and effectiveness of an organization's operations while identifying opportunities for improvement. Researchers have applied a number of scientific methodologies to explore the QMS, each with advantages and limitations. Qualitative and quantitative research approaches provide valuable insights into the QMS development processes and implementation within healthcare and other industries [51]. This chapter assesses several qualitative and quantitative methods to determine the best research methodologies for this dissertation.

3.1 Qualitative Methods

Qualitative methods are research approaches that generate insights without relying on quantitative measurements or statistical analyses. These research procedures include various strategies for collecting and analyzing data on individuals' and groups' perspectives, attitudes, perceptions, and comprehension in several contexts. Qualitative methodologies vary depending on the methods used for data gathering and analysis. These strategies can be used in healthcare research to develop successful treatment solutions, understand a patient's perspective, or assist professionals in daily work. Additionally, it may improve organizational management by analyzing the complex relationships between, for example, the healthcare facility and its surrounding environment [52].

Standard qualitative research techniques encompass individual and focus group interviews, framework development, case studies, and other methodologies. Although qualitative approaches remain commonly employed in different sectors, like social sciences, their significance in health research is progressively acknowledged, with growing support for their use in healthcare studies [52].

3.1.1 Literature Review

Every research subject requires an analysis and review of relevant existing literature. Researchers from all disciplines generally begin by reviewing prior studies to describe the research landscape and justify the study's goals and assumptions. This technique, commonly known as a literature review, involves gathering and synthesizing previous research to identify current understanding and specific research gaps. To gather considerable evidence for literature, multiple database searches using specified keywords to collect significant evidence are frequently required. The search criteria for inclusion may vary based on the research question(s), ranging from limited to much broader, allowing for a variety of research approaches and evidence sources. Researchers may use several strategies, criteria, and particular guidelines depending on the study's purpose while conducting literature reviews [53], [54].

A literature review may be the most effective technique for answering specific research questions in some instances. This approach is helpful in examining hypotheses or evidence in a particular subject or determining the validity of competing theories. Literature reviews can be narrowly focused on correlations between individual variables or broad in scope, assessing the evidence base in a specific study issue. Furthermore, these reviews help summarize information on a particular topic, which may aid in establishing research goals, identifying gaps in the literature, or providing a complete discussion on a subject. When the goal is theoretical engagement, literature reviews can lay the foundation for

developing new conceptual frameworks or mapping the evolution of a research field. However, it's essential to recognize that the literature review methodology is adaptable and should be chosen based on the study's intended purpose [53].

When pursuing a study about the implementation of a QMS or the development of a TD, a literature review is frequently a vital and indispensable element researchers use. The literature review presents an overview of existing QMS frameworks and their implementations in various industries, particularly in highly regulated sectors such as healthcare. Examining prior studies can assist researchers in identifying practical QMS methodologies, implementation challenges, and critical success factors contributing to a favorable outcome. This is particularly valuable in learning how QMS frameworks have been adapted to meet industry-specific requirements such as those outlined in ISO 13485. A literature review also reveals best practices for developing a TD, including the structure, content, and necessary progress and maintenance to ensure, for instance, regulatory compliance and product lifecycle management. Moreover, the literature review helps identify gaps in current research related to both QMS and TD, which is essential for researchers since they can tailor their study to address unresolved questions or areas that require further assessment [55].

3.1.2 Case Studies

Case studies are often employed as a qualitative research methodology. They are characterized by an in-depth examination focusing on a particular individual, group, or unit to derive more general findings that may be applied to comparable units. Case studies are frequently used to achieve several research goals as they are particularly efficient for theory-building [51]. A case study may also be characterized as a thorough examination of systems analyzed from a complete perspective using one or several approaches. The case study technique does not focus on studying examples but instead serves as a practical approach to defining cases and exploring a particular context to gain a deeper understanding [56].

Despite its widespread use, the qualitative case study approach remains incompletely comprehended. Conflicting epistemological ideas and the complexity inherent in qualitative case studies make it challenging to establish scientific rigor and evaluate the ensuing findings. Case studies typically serve a dual purpose, functioning as studies of individual units and a broader group of units. A case study might have either an illustrative or affirmative result. The design of a case study is impacted by these concerns, which will continue to produce uncertainty due to their fundamental nature inside the organization. The qualitative case study technique requires instruments that enable scientists to examine a comprehensive perspective within specific situations. When implemented correctly, this technique may provide significant benefits for studying science, evaluating programs, and developing theories and engagements [56].

Within the context of QMS, the characteristics of case studies are intricately linked to their contexts. They are not susceptible to manipulation for investigation, and the research is centered explicitly around current events. The research entails analyzing complex systems to identify solutions for specific problems that can be best addressed through comprehensive and extensive data analysis. Multiple studies have examined the occurrence of regulatory decoupling and the fundamental processes of ISO 9001 or ISO 13485 operations in different firms. However, employing an exploratory case study approach is essential to offer a theoretical explanation [57].

3.1.3 Interviews and Focus Groups

In recent years, focus groups have become extensively employed in health research to investigate the viewpoints of patients and other groups within the healthcare system. Incorporating them into mixed-methods research is a common practice to enhance understanding of questionnaire construction and result interpretation. The group method facilitates identifying and clarifying

individuals' perspectives, which is a fundamental benefit of focus groups in contrast to individual interviews. The group fosters cohesion and spontaneity by urging participants to engage in comments, explanations, disagreements, and the sharing of their perspectives. This enables the growth of group experiences and ideas that may not be uncovered through individual interviews [57].

Focus groups allow participants to freely express themselves and select discussion subjects, but they also adhere to a specific degree of organization. Researchers have a vital role in creating questions that direct the conversation, and the level of organization depends on how flexible the research question(s) are. Conducting focus groups requires a substantial commitment of time and effort compared to individual interviews. Nevertheless, this investment justifies the possibility of creating more ideas and acquiring more profound insights into the subject being studied [57].

Focus groups, originally used for market research, have now been utilized for healthcare research. However, there is a lack of specific methodological standards for this subject. Researchers mainly depend on broad guidance from the social sciences. Despite the widespread use of focus groups in several health research domains, such as patient treatments, community health studies, and developing novel diagnostic or therapeutic approaches, their application in health research is never critically examined [57].

Multiple research papers examine the importance of individual in-depth interviews and focus groups in analyzing evaluation methodologies. Both strategies utilize open-ended inquiry with inductive probing of responses, but they vary in terms of structure and strengths. Individual in-depth interviews involve direct communication, while focus groups often include a moderator, an assistant, and a group of participants. These systems' logistics differ in schedule, location, and time. Focus groups are particularly suitable for collecting information about group norms, dynamics, or brainstorming sessions. Conversely, in-depth interviews are more effective in obtaining personal narratives or facilitating talks on delicate subjects. Each technique can provide equally substantial information to achieve an evaluation objective, depending on the particular research topic or practical constraints [58].

3.1.4 Framework Development

Frameworks frequently arise by integrating several sources and cannot be directly copied from pre-existing literature. Although current theories can be used as a basis by offering important concepts and structure, they typically constitute the complete framework. They serve as tools or collections of tools that enhance comprehension of a topic's complexity. Their efficacy is maximized when they include complementary ideas encompassing various aspects of the topic. This approach recognizes the need to integrate many viewpoints and understand that each position has its own benefits and drawbacks. Combining these multiple approaches frequently results in enhanced insights and a deeper understanding than depending on one theory or method [59].

Conceptual frameworks are not simply a combination of unrelated and theoretical ideas. They possess coherence, which connects the different components and allows them to serve as persuasive arguments that support the study. This does not necessarily indicate precise, logical coherence, as frameworks can integrate various or contradictory concepts. Nevertheless, it is essential to clearly express the connections between the multiple components, emphasizing the crucial parts of the subject that are most important for the research. It is necessary to clearly explain how these components combine and influence the study targets and methodological choices [59].

Frameworks are dynamic structures that do not remain unchanged from the beginning of the research. They should adapt to novel concepts and data acquired during the study procedure. Therefore, frequent adjustments or enhancements to the framework are necessary. A framework is a visual or verbal representation of ideas and a clear expression of the concepts and principles that influence and direct the research. It may need continuous consideration to adequately understand its importance throughout the study [59].

3.2 Quantitative Methods

Quantitative research is a systematic approach to studying events that involve gathering and evaluating statistical or numerical data. This technique includes the measurement process and assumes that the researched phenomena can be measured. Quantitative research seeks to find patterns, establish correlations, and assess data reliability. Quantitative research enhances QMS development by measuring policy efficacy and identifying patterns in quality metrics [60], [61].

Quantitative research distinguishes itself from other approaches owing to its logical approach. It starts with theoretical frameworks or hypotheses and then develops specific conclusions from them. Quantitative research is the careful investigation of concepts using theories and statistical methods. This technique allows researchers to get reliable and experimentally validated understandings of a wide range of phenomena, including those related to quality management systems [60].

3.2.1 Surveys and Questionnaires

An effectively constructed questionnaire is crucial for gathering accurate and practical data. Achieving success relies on implementing concepts, selecting appropriate metrics, and formulating accurate questions based on known literature. It is essential to validate the questionnaire by pilot testing with the intended respondents. While survey design guidelines provide instructions for these procedures, they are often not adhered to or reported accurately. Surveys that involve several cultures and languages have extra difficulties related to translation and cultural disparities that need to be acknowledged and documented [62].

Surveys play a crucial role in several fields, each having its own set of standards for optimal methods, although they may not always be consistent. A typical guide on survey research provides a systematic process for designing surveys, focusing on distinguishing between the target population, the sampling frame, the invited sample, and the realized sample. Researchers employ varying definitions and methodologies to determine and compute response rates, necessitating clarification [54].

The method of survey administration, such as phone, internet, mail, in-person, or a combination, impacts the design considerations. Every technique has distinct advantages and disadvantages, relying upon the specific study inquiry and the intended group of subjects. Nowadays, internet surveys have become increasingly popular since they are cost-effective and adaptable [54].

3.2.2 Benchmarking

Benchmarking is widely recognized as an ongoing process of discovering and evaluating best practices through comparison and assessment. The process involves assessing an organization's products, services, and practices in contrast to those of high-performing businesses, identifying crucial factors for success, and applying successful solutions from either internal or external sources. Organizations can recognize their operational advantages and deficiencies through this approach, establish goals, and improve their overall performance [63].

Benchmarking, as a tool for management, aids in closing performance gaps and facilitates ongoing improvement, enhancing competition. It allows firms to strategically position themselves for success by benchmarking their operations against industry leaders, discovering competitive strengths, and implementing appropriate adjustments [63].

Integrating benchmarking methods is essential in the QMS framework as it facilitates growth by enabling firms to get insights and information from industry leaders. It offers a systematic approach for conducting external comparisons, assisting companies in collecting data, establishing performance goals, and improving their operations. Gaining information about their position concerning competitors enables organizations to make informed decisions to enhance their performance and maintain their competitive advantage [63].

Benchmarking often centers around three primary domains: quality, productivity, and time. Continuous improvement is essential in several areas, including pharmaceuticals and healthcare, based on quality management principles. Benchmarking is crucial for enhancing QMS, enabling firms to assess the disparity between their current and optimal practices. Companies can modify strategies, which can improve their overall success [63].

3.3 Proposed Research Methodology for the Implementation of QMS and Technical Documentation

This master's dissertation employs different research methodologies since multiple studies have demonstrated that combining research techniques provides numerous benefits. By integrating various methods, researchers may obtain diverse perspectives on the study issues, enhance the reliability of collected data, lead to more accurate analysis, and expand the scope of the research by introducing new viewpoints. Moreover, the combined approach helps reduce the drawbacks of relying on one research technique while amplifying its benefits.

This dissertation employs three primary qualitative research approaches: case study, literature review, and framework development. The case study method was chosen to explore the specific circumstances under which the QMS and TD were implemented and developed. Two distinct case studies will be undertaken: one concerning the development of a TD for MDSW and the other focusing on implementing a QMS for the design and development of an IVD. The purpose of these case studies is to offer practical insights into the challenges arising from these procedures. Additionally, they have been created to act as an intermediary between theoretical and practical knowledge. Ethical issues were prioritized when collaborating with the actual companies. Two established research questions will guide the research and address the highlighted concerns during the case studies. In addition, a detailed literature review will be conducted to address these concerns, offering a theoretical foundation and addressing any gaps in current understanding. The literature review will focus on TD development for software development projects and QMS implementation. It will clarify the QMS requirements and examine the impact of businesses' maturity on the different stages of MD development. Ultimately, a framework will be developed to implement a QMS, particularly for the design and development of an MD. This framework will be evaluated in the two companies identified in the case studies. This framework will be tailored to align with the ISO 13485 requirements and function as a proficient tool for guiding the implementation of the QMS. Learning and deductions will be obtained from it.

Although relevant to this topic, the other research methodologies mentioned in the previous chapters were not selected for several reasons. Focus groups and interviews can provide valuable insights. However, they were not used in this research since they did not benefit the purpose of this dissertation. The study focused on developing technical documentation, implementing a QMS, and including digitalization in both these processes. Therefore, the complexity of this dissertation further necessitated a focus on literature analysis and real-world testing rather than exploratory discussions. Additionally, this research did not employ surveys and questionnaires due to their limited applicability to the study's focus on technical documentation, QMS, and regulatory compliance. It required a more detailed analysis rather than broad quantitative data collection. Additionally, this work's focus made it challenging to design a survey yielding relevant and accurate insights from a target population. Finally, this research did not employ the benchmarking methodology. Although comparisons were drawn between the two organizations in the case studies, the primary purpose was to evaluate the framework's performance, not to compare the companies regarding top competitors. Benchmarking typically focuses on identifying best practices across the industry. Therefore, it was not necessary for this purpose, as the goal was to assess how well the framework could be adapted to different levels of a company's maturity and stage.

4 Case Studies

4.1 Case Study 1: Developing Technical Documentation for Medical Device Software for CE Mark Submission

This case study explores the development of a TD for the CE Mark Submission of a medical device software developed by a healthcare consulting firm.

4.1.1 Background

The consulting firm was founded in the late '90s, and it aims to become a leading organization in the healthcare industry. Over the years, the company has worked with both public and private healthcare facilities, focusing on Management Systems, Logistics, and Information Systems. As part of its growth, the firm expanded its services by acquiring another firm in the mid-2000s. It later became the exclusive representative of several technology products and employed specialists with extensive expertise in hospital engineering. At the time of writing this dissertation, the company is in the process of certifying several digital products and IT solutions as a medical device aimed at improving healthcare quality and safety and enhancing the efficiency of healthcare professionals. Their products are designed to provide accuracy and safety in patient care delivery.

4.1.2 Device Description

The device is a mobile software application that supports and tracks clinical procedures. It was specifically designed to ensure compliance with best practices across specific medical processes, from the initial stages of the procedure to the completion of a patient's treatment. It includes an app for managing pre-analytical information, reducing errors made by nursing staff. The device allows nurses to handle patient and sample data, ensuring the correct components match during a specific medical procedure. It additionally offers features to monitor vital signs variants that help alert other healthcare professionals to potential issues that may not be identifiable by the supervising nurses, improving patient safety.

The device is incorporated into a broader platform that combines several nursing activities into a single mobile device for increased mobility and productivity.

4.1.3 Device Classification

According to Annex VIII of Regulation (EU) 2017/745 on medical devices, the device is considered an active medical device, classified as a product Class IIa. This classification is due to Rule 11 and is based on the defined medical purpose of detecting variations in the vital signs of the patients receiving a specific medical procedure. The software is intended to provide information to make decisions, but only when the procedure occurs. Therefore, it cannot be used for remote monitoring. Given the patient's state, the device will not have an impact that can cause death or an irreversible deterioration of a person's state of health, nor a serious deterioration of a person's state of health or surgical intervention, as being used within the existing standard of care. Thus, the device is classified under Rule 11 as Class IIa.

4.1.4 Developed work

Over several months, I prepared part of the TD required for the CE Mark Submission of the medical device software produced for the consulting company.

My primary contributions included creating detailed and extensive documentation in several critical areas required by the MDR. First, I defined the device's Intended Use, which entails its specific

purpose, structure, and function. Moreover, I identified the target population, intended users, and context of use. I also specified contraindications, exclusions, as well as potential foreseeable misuse of the device. Additionally, I highlighted previous generations of the device in both the EU and US markets.

In the Medical Device Classification document, I classified the device using the classification rules outlined in Annex VIII of the MDR. This involved a comprehensive justification based on the device's medical purpose and possible impact on patient safety.

For Stakeholder Requirements, I selected relevant stakeholder groups based on the specified user profiles outlined in the Intended Use document. I described the characteristics, qualifications, and major responsibilities expected from these stakeholders. I also defined the stakeholder requirements, taking into account the use requirements for product functionalities, safety, and performance to ensure that the device serves its intended purpose, requirements derived from hazard-related use scenarios to be tested during usability testing, and all applicable regulatory requirements. The System Test Protocol document entailed creating and documenting tests for these specific stakeholder requirements, including information on input data, expected and actual results, and the tests' default outcomes.

I also evaluated the device's compliance with the GSPR required by the MDR, noting where each requirement was recorded or met.

In the Software Description document, I described the device's purpose and role, as well as its user interface characteristics. This included graphic representations of several screens and processes to help provide a clear understanding of how the software works. I also included a brief description of the technical runtime environment of the key elements, such as the CPU, RAM, and operating system, along with their minimum requirements.

For the Software Safety Classification, I assessed the device and each component's software safety classification according to the IEC 62304:2006 + A1:2015 standard. This evaluation was crucial in determining the scope of the documentation to be prepared. I also created a flowchart to link and classify components based on their medical purpose and data processing type. Ultimately, the device's software safety classification was determined to be Class B.

Finally, in the Software Architecture document, I described the architecture of the medical device software for the technical implementation of software requirements. This document was designed to provide developers with a technical framework for implementing the operating system, to offer new project members a quick overview of the software structure, and to give the test team sufficient information on how software components are successively assembled and tested during integration tests. Throughout the document, I described the system context requirements, programming guidelines, the architecture overview (including platforms and operating systems), top-level components and their interconnections, the database schema and its architecture, as well as data encryption and other relevant security measures.

The framework presented in **Section 7** allowed to determine the templates required for the company and MD presented in this case study. Following every stage of the framework made it easy to map all the documents, verify, and create missing templates. Although the company is in a later stage of the MD development process, there was still a lack of some parts of the technical documentation required in previous phases. The framework helped map these missing documents, allowing the company to correctly complete some phases of the MD development and comply with the requirements associated with each one of those stages.

4.2 Case Study 2: Implementing a Quality Management System for the Design and Development of an IVD Medical Device

This case study addresses the implementation of a QMS for the design and development of an IVD of a healthcare startup.

4.2.1 Background

The company is associated with the digital health sector by developing an innovative platform to speed up the future of personalized drug discovery and development. It combines contemporary technological tools to gather biological data to provide patients with faster, life-saving, tailored treatments. The company is recognized by several industry publications and institutions for its healthcare business. It is backed by leading global organizations and prestigious academic institutions and is considered a rising leader in areas such as AI-driven medical research, health screening, and data analytics.

4.2.2 Device Description and Classification

The company is focused on creating innovative technologies for analyzing biological samples using contemporary methods such as photonics and AI. These technologies seek to identify specific biomarkers, allowing customized patient or disease profiles. The start-up's devices are not yet on the market but are in the advanced research and development phase. They use sensors to extract indicators from biological samples, which are then processed by AI algorithms to identify several health conditions and diseases.

The classification of one of the company's IVD is expected to fall under Class A, while the algorithm used for disease detection may be classified between Class B and D, depending on the target disease to be diagnosed.

4.2.3 Developed work

Over several months, I followed the implementation and certification of the QMS of the IVD developed by the company presented in this case study.

Before developing and implementing the QMS, it was crucial to plan the project and identify all essential steps and timelines for this implementation. It was vital to assign responsibilities to the relevant personnel, identify all involved departments, and discuss the importance of implementing a quality culture among all team members.

After planning the project, the first documents that began to be developed were the Quality Manual and the procedure on document control. This last one was essential for traceability, as it defined the different coding used for all company areas or internal documentation. These templates of documentation were used and adapted throughout the entire development project and updated according to the changes implemented within the organization.

Then, the documents related to management, human resources, infrastructure, suppliers, and purchasing were developed since the company already had some knowledge in these areas and had implemented specific procedures. The templates for the management review report and procedure management review were created. For human resources, an organizational chart was developed with all departments and team members of the organization, the procedure for human resources, a training plan for the team, and an updated document with all relevant job descriptions were designed. For this purpose, training records were also developed. Related to infrastructure, the template procedure control and monitoring of work environment was created. Finally, a list of suppliers was developed and later transposed to the software tool Notion, and a purchasing procedure was made.

During several weeks, the organization's quality policies and objectives were defined, and all procedures related to the design and development of its IVD were established. The business process was also mapped, and all inputs, outputs, and tools used for all relevant areas of the QMS implementation were defined. All documentation started to be stored in a Google Drive for easy team collaboration, and the developed software, data information, and test repositories were saved in GitHub.

After this, several documents and procedures related to corrective and preventive actions and complaints management were created.

During several weeks, the different phases related to the development of the IVD were defined, and all documentation pertaining to this development started to be created. The project was divided into general QMS implementation, which refers to resources and infrastructure, among others, and design and development activities, where the framework presented in Section 7 was essential.

The first documents developed for the design and development activities were the stakeholder requirements, the traceability matrix, the intended use, the product/software requirements specifications, the product design specifications, the software architecture, and the software safety classification. These were worked on for several months.

The templates related to post-market surveillance and vigilance procedures were also developed, and other documents, such as the post-market surveillance report and plan, were also created. Documents about regulatory updates, such as the procedure regulatory update and list of monitored regulations and standards, were also developed, along with sales and data analysis templates.

Related to risk management, the procedure risk management, the risk management file, plan, and report were also developed. Related to usability, the usability engineering procedure, file, and plan were also created.

Some essential documents related to monitoring and measuring equipment were developed, such as the procedure computer software validation.

For the QMS certification, additional procedures, such as the procedure for product/software development, production and service provision, and nonconforming products, were also defined, along with several templates. These included the product/software development plan, system test protocol, software verification and validation report, production run sheet, and servicing and provision templates.

Timelines for the internal and external audits were also defined, and documents such as the audit action plan, program, and report were created.

5 Research Questions

Two research questions were formulated to address some challenges identified during the case studies.

5.1.1 RQ1: How to create an always updated Technical Documentation for a Medical Device Software

Developing and maintaining the TD for MDSW is critical to ensure regulatory compliance with the current regulation. MD manufacturers, particularly small and medium-sized enterprises, face significant problems in navigating the complexity of the regulatory landscape while meeting rigorous requirements for the TD [64].

The TD must be developed during a device's design and development process and maintained throughout its entire life cycle [65]. However, modifications to the device are not always clearly documented in TD records, resulting in compliance gaps. Several challenges were faced during the development of the TD for the first case study. These challenges highlighted a critical issue related to the lack of integrated digital tools for managing changes and supporting ongoing TD updates. The absence of tools resulted in difficulties in maintaining records updated.

Successful integration of digital tools may streamline the development of the documentation process, reduce errors, and contribute to demonstrating regulatory compliance. Such tools also aid in the efficient management of updates, ensuring that all changes are correctly documented and traceable [66].

The primary research question arises from the challenges previously discussed and can be articulated as follows: “How to create an always updated Technical Documentation for a Medical Device Software?”.

5.1.2 RQ2: How to adapt the implementation of a QMS to the different stages and maturity of a company

As companies proceed through the different stages of the QMS implementation, they face a number of challenges and encounter strict regulatory and technical requirements that must be met. One of the most significant obstacles often arises from tailoring the specific requirements of particular procedures or the TD to each company's level and maturity. Small organizations still in the early phases of device development, such as the company from the second case study, must prioritize establishing core processes and procedures and aligning their initial goals with regulatory expectations. Contrariwise, companies ready for submission, such as the company from case study one, must ensure all documentation is complete, compliant, and prepared for regulatory certification [67].

Mastering the challenge of adapting and implementing the QMS to the company's maturity is a strategic decision that must be taken by organizations that can help improve its overall performance and provide a good foundation for development projects and initiatives [68]. Evaluating an organization's maturity level allows for a complete understanding of its system's operation. If performed correctly, this assessment can help detect weaknesses in a QMS and provide suggestions for improvement [69].

The second research question stems from the challenges related to the QMS development and implementation and can be articulated as follows: “How to adapt the implementation of a QMS to the different stages and maturity of a company”.

A literature review, presented in the following section, will address both research questions. The review offers a theoretical foundation and addresses any gaps in current understanding.

6 Literature Review

6.1 Literature Review Protocol

The main goal of this literature review was to identify, analyze, and synthesize current research and information on the development, management, and regulatory compliance of MDSW in the EU. The literature primarily focused on addressing all TD requirements for MDSW in new development projects that followed particular standards, such as the IEC 62304. The literature review also emphasized development approaches such as Agile and Scrum, digital tools for project management and documentation, QMS requirements at every stage of MDSW development, and the challenges MDSW manufacturing organizations encounter when implementing digital tools.

The literature review was guided by the research questions mentioned in the preceding section and presented as follows: RQ1: How to create an always updated Technical Documentation for a Medical Device Software; RQ2: How to adapt the implementation of a QMS to the different stages and maturity of a company.

For this literature review, inclusion criteria were considered. These include papers related to the development of MDSW, mentioning the IEC 62304 standard, studies discussing development models such as Agile and Scrum in the context of MDSW, articles on project management digital tools like Jira, Confluence, Polarion ALM, and Greenlight Guru used for MDSW projects, literature on QMS stages in MD development projects and the impact of companies maturity on its implementation, and recent articles, published after 2014, to ensure updated information was used and current practices and standards considered. The exclusion criteria included research that did not address current issues in digital tools for MDSW development and articles written in languages other than Portuguese or English.

The literature search was carried out using the following databases and sources: *PubMed*, *ScienceDirect*, *Google Scholar*, and *Medline* for academic and industry research papers. International standards were consulted to collect information on IEC 62304 and QMS development stages and frameworks. Additionally, relevant industry white papers and technical reports from organizations specializing in MDSW were included. All research was performed using the following combination of keywords or phrases: “IEC 62304”, “MDSW”, “Agile in MDSW”, “Scrum in MDSW”, “Jira in MDSW development projects”, “Digital tools in MDSW development projects”, “QMS requirements for MDSW”, “QMS stages in MDSW development projects”, “company maturity and impact on QMS”, “digital tools in MDSW”, and “challenges in implementing digital tools in MDSW”.

Relevant articles and EU standards were identified by analyzing the title and abstract. Full-text versions were reviewed based on their relevance to the specific sections of this literature review. Data extraction focused on key themes, such as “regulatory guidance” focusing on the crucial aspects of IEC 62304 and software safety classification, “software development methodologies” describing traditional and more recent approaches, such as Agile and Scrum in MDSW development, and certification, “project management digital tools”, containing relevant information on tools such as Jira, Confluence and others, “QMS frameworks” regarding the evolution of several QMS frameworks following the ISO 13485, and the influence of company maturity on QMS implementation, and “challenges”, documenting barriers faced by organizations in adopting digital tools for MDSW development.

The data that was extracted was categorized and included in the following sections. Each section integrates regulatory, methodological, or technical perspectives to find standard and best practices.

This literature review may be limited by the absence of studies on the application of Agile methodologies in MDSW development projects, potential publication bias, where companies are more likely to share successful case studies rather than failures in adopting digital tools, and the lack of consistency in the development activities of QMS stages.

6.2 Documentation of Medical Device Software Development Projects

MDSW is crucial in contemporary healthcare as it improves diagnostic and therapeutic procedures. Hence, the top priority is to ensure the quality and safety of the device since any error might result in severe and perhaps lethal outcomes. In addition, the device's development process is guided by strict regulations and supported by detailed TD. Proper documentation ensures that the device meets all regulatory requirements and performs as intended, avoiding unnecessary difficulties. Some standards, such as IEC 62304, are focused on the MDSW development and provide guidelines on how to successfully manage the software lifecycle [70].

6.2.1 Regulatory Framework: IEC 62304 for MDSW Development

6.2.1.1 Overview of IEC 62304

The IEC 62304 standard establishes the software lifecycle requirements for MDSW. It provides instructions on how to design, develop, and maintain such software by defining a uniform framework of processes, activities, and tasks. This standard is applicable when the software is either an MD itself or when it is an embedded or integrated component of the final MD [71].

The IEC 62304 standard hierarchy consists of nine chapters: Scope, Normative references, Terms and definitions, General requirements, Software development process, Software maintenance progress, Software risk management process, Software configuration management process, and Software problem resolution process. This process comprises the decomposition of sub-processes into different activities and tasks. Although the standard outlines the software lifecycle processes for MDSW, it does not include a process model or particular software engineering methodologies to meet the normative requirements [71].

From this standard, it is expected that MDSW is developed and maintained within a QMS and a risk management system. The International Standard ISO 14971 defines a complete risk management process, which IEC 62304 uses as a normative reference [72].

IEC 62304, first issued in 2006 and later revised in 2015, addresses the software's safe design and maintenance to ensure product safety from the beginning of its development. While the certification is not required, organizations that comply with the standard are more likely to have an easier process in obtaining regulatory approval. As a result, it is strongly recommended that MDSW manufacturers comply with IEC 62304 requirements. This guarantees high safety and conforms with the expectations of several regulatory organizations involved in formulating these standards [72].

In addition, the MDR and IVDR clearly specify that harmonized standards such as IEC 62304 enable manufacturers to prove conformity with the overall safety and performance requirements. While using harmonized standards is voluntary, it provides manufacturers with a substantial advantage in proving their compliance with mandatory legal requirements [71].

6.2.1.2 Software Safety Classification

IEC 62304 requires the identification of safety-related processes and the classification of software into three distinct classes: Class A, when there is no possibility of damage or harm to health; Class B, when the injury is possible but not severe; and Class C, when there is the possibility of death or serious injury. The manufacturer is required to categorize each software system based on its safety classification, taking into account the potential harm it may cause to patients, operators, or other individuals in the event of a hazardous situation. This classification is outlined in **Figure 10**. This significantly influences the entire software development life cycle, affecting several aspects, such as the requirements, coding to release, level of detail of the TD, testing, and maintenance [71], [72].

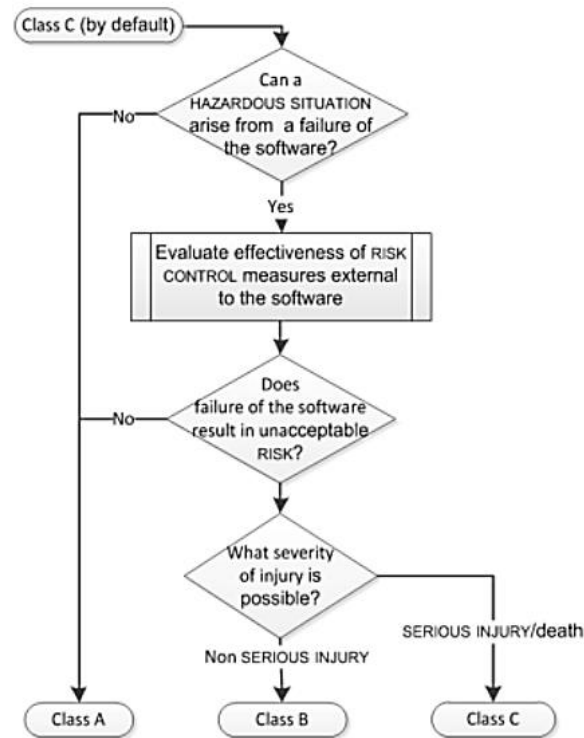


Figure 10. Software Safety Classification according to IEC 62304:2006 + A1:2015 (extracted from [20]).

For software systems that are initially classified as software safety class B or C, the manufacturer is required to include additional risk control measures that are separate from the software system. This includes modifying the system architecture that contains the software system and then assigning a new software safety classification to the system [72].

The software safety class of each software system must be documented in the risk management file, which contains records of all risk management activities, including all documents, files, and records generated during the risk management process [72].

6.2.2 Software Development Models for MDSW

The IVDR, MDR, and specific MDSW standards and guidance documents do not include explicit instructions on how to use any particular software development model. The requirements of IEC 62304 for software development may be misconstrued as being aligned with the waterfall-oriented model and thus might be comparatively challenging to apply in a contemporary software development environment. In addition, IEC 62304 acknowledges the presence of waterfall, incremental, and evolutionary development approaches. The manufacturer is advised to select the suitable approach for the project, ensuring that the three core requirements of the standard are met: It is necessary to provide consistent maintenance of all process outputs, which entails updating every document and software item whenever a connected item changes; All process outputs must be readily accessible as inputs as required, indicating that certain stages of the process cannot start until others have been completed; Before the release, it is imperative that all process outputs align with each other and that all dependencies, whether expressly or implicitly specified by the standard, are adhered to [72], [73].

6.2.2.1 Agile in MDSW development

Self-organizing teams employ agile software development to quickly and regularly provide valuable software to customers. The software development process follows an incremental lifecycle,

strongly emphasizing tight cooperation among the software development team, the customer, and other stakeholders. The program is flexible, prioritizing the necessity to modify the principles and methods to suit the specific context and environment in which it is being developed [74].

The Agile model is more suitable for projects with rapidly changing requirements or increased competition in the product field because of its enhanced flexibility in implementing customer requirements and frequent product releases [75]. Agile development prioritizes delivering the most valuable outcomes to the customer by using short, time-limited iterations, receiving and providing immediate feedback, collaborating with stakeholders, using self-organizing teams, embracing changes in requirements, balancing upfront and just-in-time work, and favoring adaptive and exploratory development methods [74].

An essential goal of the agile approach is to fulfill the customer's needs by promptly and consistently providing valuable software. An agile methodology has several advantages, including enhanced quality, sustainable development, consistent focus on technical excellence, and the ability to use this technique even in later stages of development. Implementing agile methodologies enhances the efficiency of bringing devices to market, facilitating the achievement of a competitive edge in the industry [74].

Despite the advantages of agile outlined above, scientific research suggests that documentation is a major barrier when it comes to using agile approaches in safety-critical situations [76]. The regulatory agencies responsible for managing MDSW inspection do not support reducing software requirements and design documentation. This is because it becomes challenging to evaluate the quality of systems without adequate documentation [76].

Medical device projects require a basis of evidence to guarantee the reliability and security of the device. The crucial stages of the software development process are documented in a manner that allows for easy traceability from the beginning to the final release. The agile manifesto prioritizes the development of functional software over the creation of extensive documentation, which may not adequately assist in obtaining regulatory approval. Nevertheless, Agile software development methodologies do not diminish the need for essential documentation. Indeed, effectively managing artifacts using tailored approaches and software tools helps overcome documentation and traceability issues in agile projects [74].

The integration of verification processes and the high effort associated with testing provide substantial challenges to implementing agile methodologies in safety-critical situations. While test-driven development is frequently used in the agile community, testing is usually carried out only in the later phases of safety-critical software development. Moreover, several regulations mandate that the testers are responsible for defining the test. Therefore, developers and testers must be different and independent persons. This contrasts with test-driven development, where developers may be tasked with writing the requirements or the actual tests, although they are verified and reviewed by different persons. The literature contains recorded cases where safety-critical software development has successfully included test-first methodologies. This mitigates the risk associated with requirement changes that arise from untestable requirements [76].

6.2.2.2 Scrum

The Scrum methodology is a variant of the Agile approach that facilitates the quick execution of new client requirements. It is essentially a management model for software development that may be used for MDSW. In Scrum, the product backlog is a fundamental idea that comprises a set of high-level requirements. The backlog is used as a foundation for developing a sprint backlog, a prioritized list of software items that must be accomplished to fulfill the high-level requirements outlined in the product backlog. Sprints, with an ideal duration of two to four weeks, yield a potentially deliverable product

increment, also known as a prototype. It is advisable to have daily meetings, and the successful completion of each sprint results in a concrete outcome [77].

While the Scrum model is acknowledged as a project management approach that aids at every stage of the MDSW process, its developers did not propose any technical guidelines for implementation. Alternatively, the technique relies on the core concept of using process control theory in software development to improve versatility, adaptability, and efficiency. Scrum emphasizes the need for regular feedback, exploiting and maximizing variability, being adaptable, and finding a balance between upfront and just-in-time work. It promotes continuous learning by offering practical solutions such as clearly defined roles, assignments, and guidelines [78].

A Scrum Team comprises multiple positions, such as the Product Owner, the Scrum Master, and the Development Team. Scrum teams exhibit self-organization and cross-functionality, indicating they carry out their work independently without external guidance. Notable events in Scrum are intentionally structured to provide a regular timetable, minimize unnecessary meetings, and adhere to a predetermined timeframe [78].

6.2.3 Project Management and Documentation Tools in MDSW Development

Since the 1980s, researchers and practitioners have discussed the challenges associated with using project management methodologies in software development. This search for answers has led to the creation of development process tools for the software industry and the widespread distribution of management guidelines for this sector. These were created to improve development, ensure supervision, and project reliability [79].

However, despite all the efforts, the complexity of software development activities and the quick changes in organizations during the 1990s have led to circumstances where projects continuously alter their scope. These variables contribute to long modifications, major risks, and significant expenses, resulting in project failures, financial losses, and damage to an organization's reputation [79].

Contemporary enterprises need to efficiently handle their surrounding environment's unique characteristics and initiatives while being very flexible to fulfill innovation requirements. Consequently, several companies combine traditional and modern project management technologies to create a technique that may efficiently suit their needs [79].

6.2.3.1 Jira and Confluence

MDSW development is regulated by many standards and support papers, including IEC 62304, which emphasizes the importance of traceability across the whole software development process. Traceability is essential for demonstrating that following defined protocols has developed reliable and secure software since it establishes clear links between software requirements, design, implementation, and verification activities [80].

Jira, a software project management platform, is suggested for improving the traceability and implementation of software requirements [81]. This tool provides a flexible solution for software teams to oversee and control issues, tasks, and requirements. It also facilitates bug tracking and streamlines approval processes. Non-technical teams commonly use this tool for many activities, including change requests and general work management. Jira is also compatible with Scrum's agile methodologies [66].

Confluence is a sophisticated knowledge management system designed for enterprises. It allows users to easily maintain extensive TD using wikis' user-friendly nature, a web-based cooperative tool that enables users to save, produce, and edit data in a structured and organized way [66].

6.2.3.2 Polarion and Greenlight Guru

Polarion is a lifecycle management application tool first developed to fulfill the requirements of regulated sectors and processes, such as healthcare and MD certification. Indeed, MD manufacturers

provided input in the early stages to shape its fundamental concepts and essential features. Software and device development teams use it to manage requirements, specify a device's architecture, mitigate risks, manage tests, handle changes, manage configurations, oversee projects, and manage agile work [66].

Polarion is frequently recognized for its extensive process coverage in planning, management, and documentation. There is no need for additional plugins or maintenance to comply with the regulatory requirements. Polarion provides crucial functions that make it suitable for areas subject to strict regulations. The Polarion solution consolidates all processes in one platform, facilitating effortless traceability and transparency. It provides online documents with trackable objects for efficient document management, including a complete history and versioning of documents and their associated objects. The tool also offers an audit trail, configurable workflows with automation for actions and conditions, and the ability to freeze content and workflows for seamless interactions with third-party tools, making it a very effective and crucial tool for MD TD development and maintenance [66].

Greenlight Guru Clinical is a digital platform that assists in collecting clinical data for both post-market clinical follow-up and pre-market MD trials. The platform serves several purposes, such as facilitating the extraction and management of data from other interconnected devices or software [82].

6.2.3.3 Next Generation Digital Tools

The application of MDSW is increasing significantly. It may be employed across several technological platforms, and there is an increasing demand for more advanced features that facilitate intricate, flexible, and compliant operations. This results in enhanced project management, leading to increased productivity and creativity.

Artificial intelligence (AI) and machine learning (ML) are being widely used in software development processes. This connection offers significant prospects for automating repetitive tasks, improving decision-making, and ensuring compliance with regulatory requirements. As part of MDSW, there is continuous progress in creating AI tools that assist with managing requirements, conducting testing and validation, and assessing risks. AI and ML technologies can potentially revolutionize the healthcare industry by using the immense daily data generated while providing healthcare services. An important advantage of AI/ML in software is its ability to gain knowledge from real-world usage and experience, enhancing its performance [83].

6.3 QMS Requirements: Stages and Maturity Impact

Implementing an effective QMS is critical for organizational success, ensuring consistent quality, compliance with industry standards, and constant improvement. Nowadays, companies of all sizes, types of enterprises, and industries seek to adopt ISO 9001 since it serves as a vital starting point for quality improvement. ISO 9001 standard defines the requirements for the implementation of a QMS by all types of organizations that intend to improve their system's quality and increase their efficacy [84].

In the MD industry, implementing and maintaining a QMS is crucial in obtaining MD certification. This process requires a complex, well-structured, and accurate QMS to guarantee the consistent application of methods for controlling quality and complying with regulatory and technical requirements, such as ISO 13485. As previously mentioned, unlike general standards, ISO 13485 is specific for MD. It acts as a reference for device design, development, and manufacturing and is widely accepted as a global standard for quality management in the EU [85].

6.3.1 QMS frameworks

During the last decades, product innovation and effective new product development management have been at the core of both academic research and administrative concerns. The basis of these

initiatives encompasses understanding the elements that contribute to new product success and the goal of driving new devices from concept to market promptly and with fewer flaws [1].

Among the most significant contributions has been the development and application of product development stage-gate processes. These processes acknowledge that product innovation and development can be managed and comprise conceptual and operational tools to reach the market. A stage-gate approach separates the development process into anticipated and organized phases, each separated by a set of requirements that must be fulfilled before the device progresses. Furthermore, each phase comprises several predefined activities that are often connected and occur concurrently. These stages typically encompass a preliminary evaluation, a thorough investigation, a development process, verification and validation, and the manufacturing and commercialization of a new product. The stage-gate process facilitates formal descriptions, task documentation, traceability, and decision-making. They are frequently summarized in standard operating procedures and plans to aid development [1].

While formal development processes and equivalent methods have been defined for many industry sectors, no clear and unanimous model has been regularized for new product development in the MD field. Several researchers, including Rochford and Rudelius, in [86] have defined various phases and milestones for MD development but have not offered a detailed analysis of all actions and decisions required. Furthermore, Kaplan et al., in [87] identified various core product development activities ranging from concept to approval but did not present a model of the device development process [1].

A variety of graphical representations have been developed to illustrate multiple aspects of the MD development process. They range from representations of product definition processes to representations of models of design control that have suffered several modifications over the past years. The design input and product definition process representation (shown in **Figure 11**) summarizes the product definition process. It illustrates the progression from specifications to available technologies and subsequent options to define applications, platforms, and enhancements based on the defined technology concept [1].

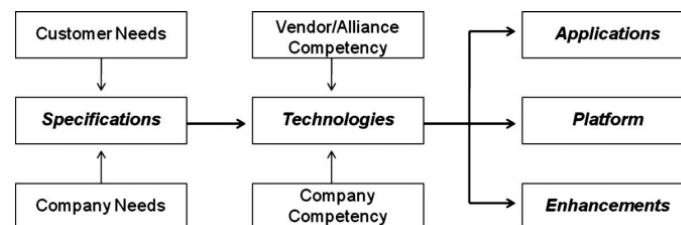


Figure 11. Product Definition Process (based on Ref. [1]).

The design control process representation is frequently represented as simple waterfall diagrams connecting user needs through design inputs, processes, and outputs to the completed MD (shown in **Figure 12**). The conventional methodology of the waterfall model starts with the conceptual investigation, namely the examination of requirements. The model sets out specific and unambiguous criteria and requirements that must be followed prior to beginning the project's design and development. This enables the execution of a thoughtful and systematic sequence of steps, guaranteeing a strong basis and strategy for the project. The primary drawback of the waterfall approach is its inability to adapt to fast modifications to stakeholders' requirements until the project is fully or almost finished. Thus, it is better suited for projects that have generally consistent or unchanging requirements over a long period. Several researchers state that the waterfall model requires each phase to be completed before the next one can begin. This poses a high risk of errors from the previous phase being carried over to the next phase, as verification takes place at the end of the software development process or near the end phase. This approach follows a conventional management structure, in which requirements flow from top-level management to basis management and then to employees. There is limited or no interaction between

development teams and customers or other stakeholders. Requirements are typically communicated indirectly through members of an organization [75].

While this model helps to understand the interaction of multiple development stages, it lacks some essential details, such as procedures, processes, and documentation requirements, that are crucial to the successful development of a QMS and subsequent MD regulatory approval and market launch [1].

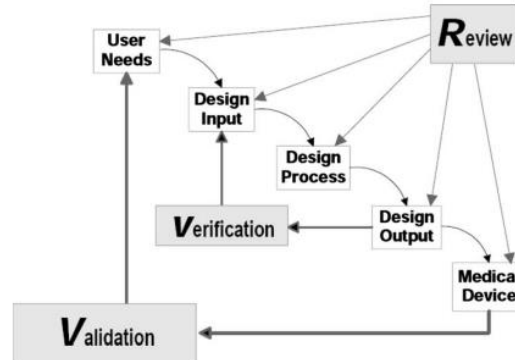


Figure 12. Application of design controls to the waterfall design process (based on Ref. [1]).

Another stage-gate process model developed was the linear model, presented by Pietzsch et al. in [1]. **Figure A.1.**, from **Appendix A**, shows that the model identifies five primary phases of development activities separated by four decision gates. Predevelopment activities occur before Gate 1, development is conducted between Gates 1 and 3, and product launch and post-market evaluation occur after Gate 4. The model lists upper-level activities for each function in boxes inside each phase. Milestones can happen at different points in the development process based on the type of MD. The five major phases and decision gates are Phase 1/Gate 1, which is concerned with initiation, opportunity, and risk analysis; Phase 2/Gate 2, related to formulation, concept, and feasibility; Phase 3/Gate 3, which is concerned with design and development, and verification and validation activities; Phase 4/Gate 4 regarding ultimate validation, and product launch planning; and Phase 5 related to product launch into market and post-market evaluation. Deliveries for each phase and decisions made at the four decision gates for this model are described in **Figure A.2.**, from **Appendix A** [1].

More recent research introduced a for MDSW and other general software development (**Figure A.3.**). As per this workflow, the software development process starts with requirements gathering, involving interviews with key stakeholders, administering surveys, and user observation. The obtained data determines the intended purpose and classifies the MDSW. These tasks are necessary since the requirements will vary based on the established safety class. Subsequent procedures encompass system functionality and graphical user interface design. According to this diagram, it is crucial to carefully prioritize the usability of the graphical user interface to mitigate potential risks. Furthermore, it is crucial to incorporate IEC 62304 standards throughout the whole process of implementing and validating the system. Throughout the analysis, design, development, and testing phases, TD must be generated to assess the device's compliance with crucial requirements [88].

Although several models and frameworks exist for developing MDSW, sufficient guidelines are still lacking to assist developers successfully throughout the process. Existing frameworks frequently lack the specificity or flexibility needed to implement a QMS effectively in MDSW development [67]. This creates an opportunity for future enhancement and development of frameworks and guidelines in this domain.

6.3.2 Stages of an MD Development

MD development is a complex and multi-staged process covering several critical QMS areas. It is highly regulated to ensure the safety of patients and healthcare professionals. As a result, MD

manufacturers must establish an effective QMS and demonstrate regulatory compliance with current regulations to ensure that the entire design process is managed and planned in a systematic and repeatable manner and that devices reach the intended market without complications [89].

Early in the development process, it is essential to fully understand user perspectives and needs, determine how the finished product will be used, research supporting technologies, and mitigate all critical risks connected to the device. Doing this thoroughly in an early development stage can help avoid nonconformities, significant time and money spent, and delays in the MD certification process. To achieve this, it is crucial to define the MD development process clearly before moving into the device production and market launch [90]. These different phases may vary in what they include, are called, or even be divided according to different methodologies or interpretations. The phases below were selected based on the various frameworks/standards and the methods applied to the case studies, especially case study 2.

6.3.2.1 Concept Phase

The first stage, or phase 0, is commonly seen as a predevelopment stage, in which ideas begin with a need to benefit patients' health. It is typically a research and strategy phase to understand key elements, intended users, and MD needs. It also aims to clarify the use, user and business motivations, and potential contexts in which the device may be employed. The primary goal of phase 0 is to define a prospective device and assess the project's feasibility. It additionally provides a first draft of the customer's needs, including everything a customer and/or clinician requires from a device or supporting services [90].

6.3.2.2 Planning Phase

Phase 1, or the Planning phase, intends to demonstrate further the technical feasibility of the system and its components and create a detailed product development plan. This plan defines all development and post-market activities required in the following phases to guarantee the safe manufacturing and use of the product. It is used, for instance, to define clinical goals, perform risk analysis, and allocate the necessary resources [90].

Early in the concept or planning phase, a manufacturer must identify the GSPRs specified by EU MDR Annex I, to which the product and manufacturer's processes must conform based on the device's intended use [91].

Design control also begins in the planning phase, with the development of a plan that meets all QMS requirements. The plan is a means of interaction designed to guarantee that a company understands the device and how it will be developed. It must describe the organizational responsibilities for tasks and their execution, often drawn from the quality manual required by the QMS. This plan must also specify important tasks and deliverables for each task, review points, and estimate the required resources and timeline for implementation. The information needed and its level of detail varies depending on the organization's size and the device's complexity. Complex projects may necessitate the contributions of several sources to the device's design process. When this occurs, interrelationships and interfaces must be defined, planned, and managed. A task breakdown within the plan is also necessary to determine what resources are needed to accomplish the intended outcome, as well as a projected completion time. Tasks that produce evidence of conformity with rules, standards, and regulations are recommended. Many plans define antecedent and successor links between tasks and identify milestones for management assessment of activities. This plan should be reviewed and modified regularly as new information becomes available to guarantee that management can make correct and sound decisions regarding the device's performance, patient safety, and resource allocation [92].

The planning process should also include a risk management plan containing specific methods for mitigating and controlling the potential risks, particularly the ones associated with user misuse to guarantee patient safety [90].

An essential step within the planning phase additionally involves defining and documenting user stakeholder/user needs and requirements. During this stage, stakeholder requirements are translated into a specific product specification(s) regarding the product's design, functioning, or performance to meet user needs. Product design specifications or design requirements are also essential as they define precisely what is expected of the design and allow each design stage to be evaluated. Although the project's initial steps highlight some of the technical requirements, it is crucial to follow a process to guarantee that all functional performance needs are understood as early in the design process as possible [89].

6.3.2.3 Design and Development Phase

The design and development phase defines all activities and outputs related to the device's development. It takes all initial draft prototypes from previous phases and adjusts them to create a final design for manufacturing. This stage usually involves third-party suppliers or manufacturers to ensure regulatory and technical requirements. It specifies the final device function, performance, and safety requirements and defines all regulatory, commercial, and clinical activities. Once this stage is completed, the device has reached design freeze, and any future design changes are subject to formal change control [45].

During this phase, the main activity involves translating design inputs or user needs into detailed product requirements specifications, including packaging and labeling specifications, and then achieving a design freeze. Functional prototypes are produced at this stage before the approval of the design freeze [45].

6.3.2.4 Design Verification Phase

Design verification intends to prove that the device meets all design requirements. Although the verification phase happens later in the development project, it is crucial to consider it early in the design and development process. Ideally, when a design requirement is created and thought of, a method for verifying it should also be developed [45], [89]. During the design iteration process, approaches for design verification may include both simulated and physical testing on prototypes. However, formal design verification for clinical or regulatory approval must be conducted on devices as close to final manufacturing as possible. This allows the manufacturer to demonstrate that the verified prototype is equivalent in material, functionality, and performance to the final product that will be released to the market. Biocompatibility, functional and sterility testing, packaging, and shipping studies are all possible testing criteria for verification [45].

Design verification is accomplished by developing records demonstrating that previously specified requirements have been met. Like other stages of the QMS process, design verification activities, including testing, inspection, and analysis, must adhere to written procedures. Design verification of design outputs involves documenting who, what, when, and how each design element was assessed. For many device manufacturers and complex devices, verification is often divided into planning, writing protocols, executing protocols, data analysis, and results reporting, all of which are always subject to a design review. It's important to note that all design verification activities must be traceable [92].

6.3.2.5 Design Validation Phase

The design validation phase focuses on producing objective proof that the device specifications comply with the user requirements and intended use. It follows several design verification activities and

is conducted on initial production batches or equivalents under predefined operating conditions. The device's design validation is performed under actual or simulated conditions of use. Validations on devices that meet these requirements include all predicted variations in components, materials, manufacturing processes, and the use environment [92].

Conducting a design validation, similar to a verification activity, requires meticulous planning. User needs and intended uses identified throughout the requirements definition process are now traced to corresponding tests described in previous plans and protocols that detail the timeline, necessary resources, techniques, and acceptance criteria [92].

6.3.2.6 Design Transfer to Production Phase

Before a design is transferred to production, it is necessary to ensure that all documents and device training are well-established. Design transfer activities aim to follow procedures to guarantee that the device design is accurately converted into manufacturing instructions. This ensures that devices are produced consistently and safely within the product and process capacities resulting in devices that meet all requirements. Design transfer may include concluding the instructions for use, finalizing the labeling and packaging, total cost bill of materials, completing inspections of all development files and plans, and compiling all information related to the medical device or Technical Documentation if already developed [92].

This stage is an integral part of the design and development process, as it ensures that proper controls are defined within the manufacturer or supplier's operations [92].

6.3.2.7 Design Review

A design review is required at the end of each phase of the design and development process to document and examine the device's design formally. The review intends to evaluate the adequacy of design requirements and the capacity to meet them. It also aims to identify potential device issues to mitigate and manage them as early as possible. The scope of the design review varies according to the development phase and can cover concerns about manufacturability or how effectively a design meets the user's or patient's needs.

6.3.3 Impact of Company Maturity on QMS Implementation

Start-ups are newly established firms that aim to create and promote a distinctive product or service to revolutionize sectors and have an extensive effect worldwide. Unfortunately, the failure rate for start-ups is 90%. The factors contributing to failure encompass but are not restricted to, inadequate management, insufficient financial resources, absence of market demand, lack of expertise, intense competition, and more [93].

Researchers are increasingly interested in studying the correlation between maturity levels and organizational success. Insufficiently developed quality systems in many firms, especially smaller or less mature organizations like start-ups, result in inefficient implementation of QMS. Obstacles to successfully implementing ISO requirements in these organizations include employee resistance, lack of awareness, insufficient knowledge and expertise of ISO requirements, and limited time and resources. These firms require skilled staff to create a favorable environment for adopting a QMS. This involves increasing awareness, clarifying the value and advantages of QMS, and carrying out smaller projects like pilot studies. Small businesses and start-ups encounter substantial challenges, such as inadequate support from top management, commitment to carrying out and sustaining projects, and access to training materials. These companies frequently face challenges while implementing QMS due to budgetary constraints, limited human resources, and inadequate time dedicated to QMS design and implementation [67].

6.4 Challenges in the Adoption of Digital Tools in Digital Development

The overwhelming availability of digital technology does not ensure its use in organizations. Although digital technologies like the Internet of Things (IoT), artificial intelligence (AI), cloud computing, and cyber-physical systems (CPS) are becoming increasingly accessible, many companies are finding it challenging to integrate these improvements owing to various challenges.

One of the most significant barriers is the financial expense associated with digital transformation. Incorporating digital tools requires an upfront investment in infrastructure, technology, and qualified personnel. Small companies generally struggle with this, limiting their ability to operate digitally fully.

Data privacy and security concerns are additional significant challenges. Digital transformation usually includes managing and integrating large amounts of sensitive data, increasing the risk of breaches and illegal data use. These risks may be unacceptable for MD manufacturing companies since patient safety is a top concern. Compliance with regulatory requirements adds complexity, as companies must guarantee that their digital systems fulfill rigorous data protection standards.

Furthermore, data collection and integration remain significant challenges. The availability and quality of real-time data significantly impact digital technology's performance. Nevertheless, several enterprises have difficulties acquiring, integrating, and ensuring uniformity in data across their systems. This is especially relevant for firms that depend on obsolete systems that are not easily compatible with contemporary digital technologies, creating further barriers to adopting advanced tools like AI and IoT.

Another significant barrier is the lack of standardized protocols and demonstrated credibility of digital technology. Due to the fast development of digital and smart technologies, there is sometimes a gap between the speed at which technical advancements occur and organizations' ability to adopt them. MD manufacturers can choose not to invest in new digital technologies until they have reached an extensive agreement on industry requirements and conducted extensive testing to ensure stability. A significant barrier is the lack of standardization since companies are cautious about using technology that may fail to meet future regulatory requirements.

Before fully integrating digital technology, organizations must overcome significant technological, financial, and organizational challenges, particularly in MD development.

7 Implementation of a Framework for Implementation of a QMS and Development of Technical Documentation

7.1 Framework Overview

The current chapter presents an overview of the developed framework for the implementation of a QMS and the development of the TD for an MD (**Figure 13** and **Figure 14**). The framework specifies all documents, procedures, and information required for the design and development of an MD, which will be divided and explained into six different phases in the following sections. The framework is also divided into three main areas related to product development, which will be represented as number 1; risk management, expressed as number 2; and usability engineering, associated with number 3, which are crucial requirements for an MD's certification.

Documents that appear with several layers represent a compilation of several documents. This may occur due to the latest version of a document not always being the sole relevant version, as each phase of the device's development may require a different version, all of which are crucial. Also, numerous research studies might be highly relevant to the concept and manufacture of a device. Several protocols or tests may apply to different device components or be tested in multiple ways. These may be associated with various documents/records crucial for understanding the risks and feasibility of the device. All templates mentioned in the framework are described in **Appendix B**.

Each of the six phases incrementally develops upon previous ones. Although they follow a logical sequence, the framework is flexible, allowing constant reviews between phases to address potential issues, updates, and any additional relevant changes.

The framework is intended to be tailored to different types of MDs, allowing it to be adapted to a wide range of projects. Depending on the complexity of the MD, certain phases or documents may require more detailed information or attention. This framework's purpose is to help all types of companies, from smaller to more mature ones, get an overview of the procedures and documents needed to develop and implement their QMS and meet all regulatory requirements outlined by ISO 13485 and additional supporting standards like ISO 15288 related to product development.

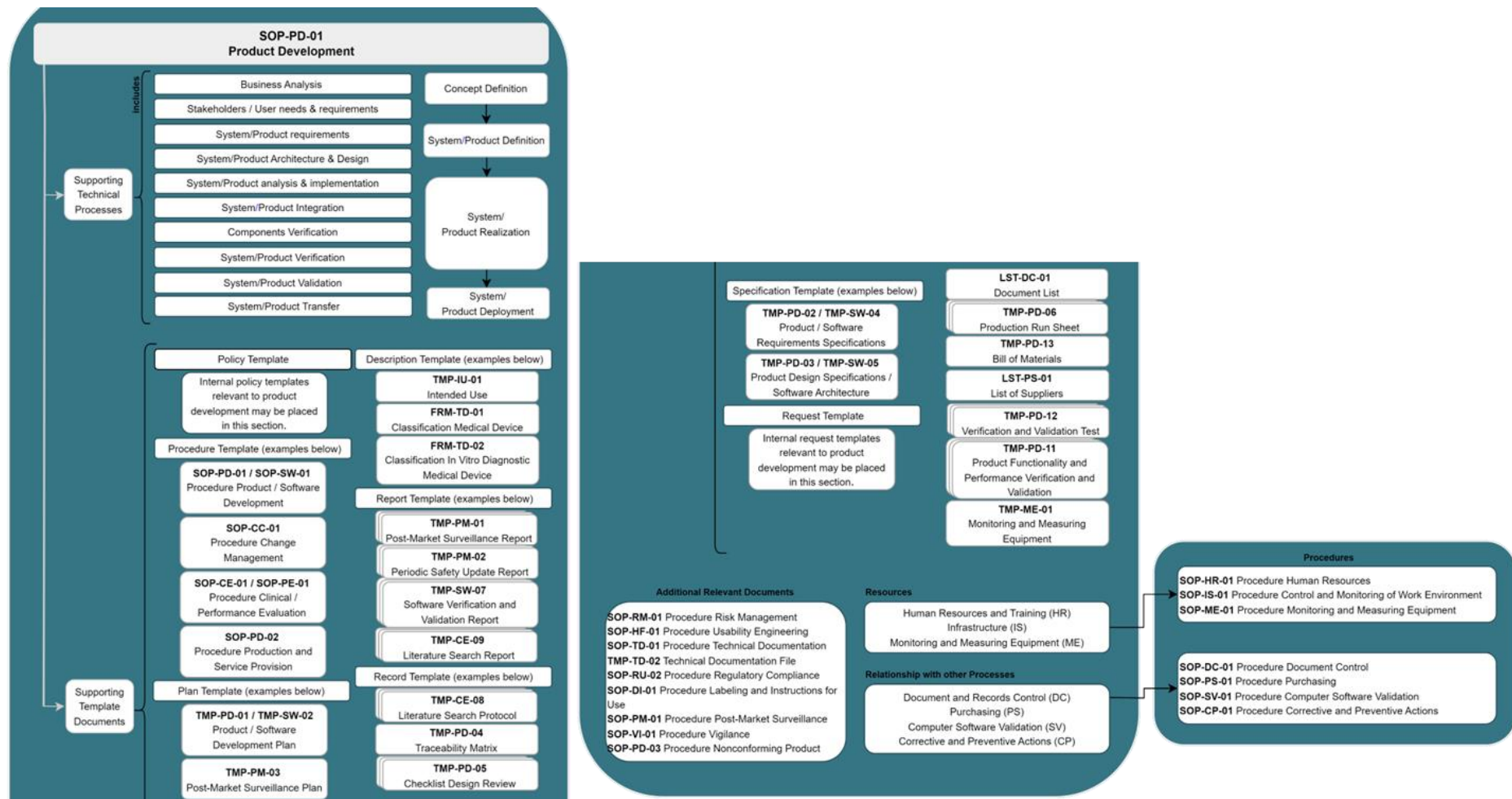


Figure 13. Framework Overview of the Templates Related to Product Development.

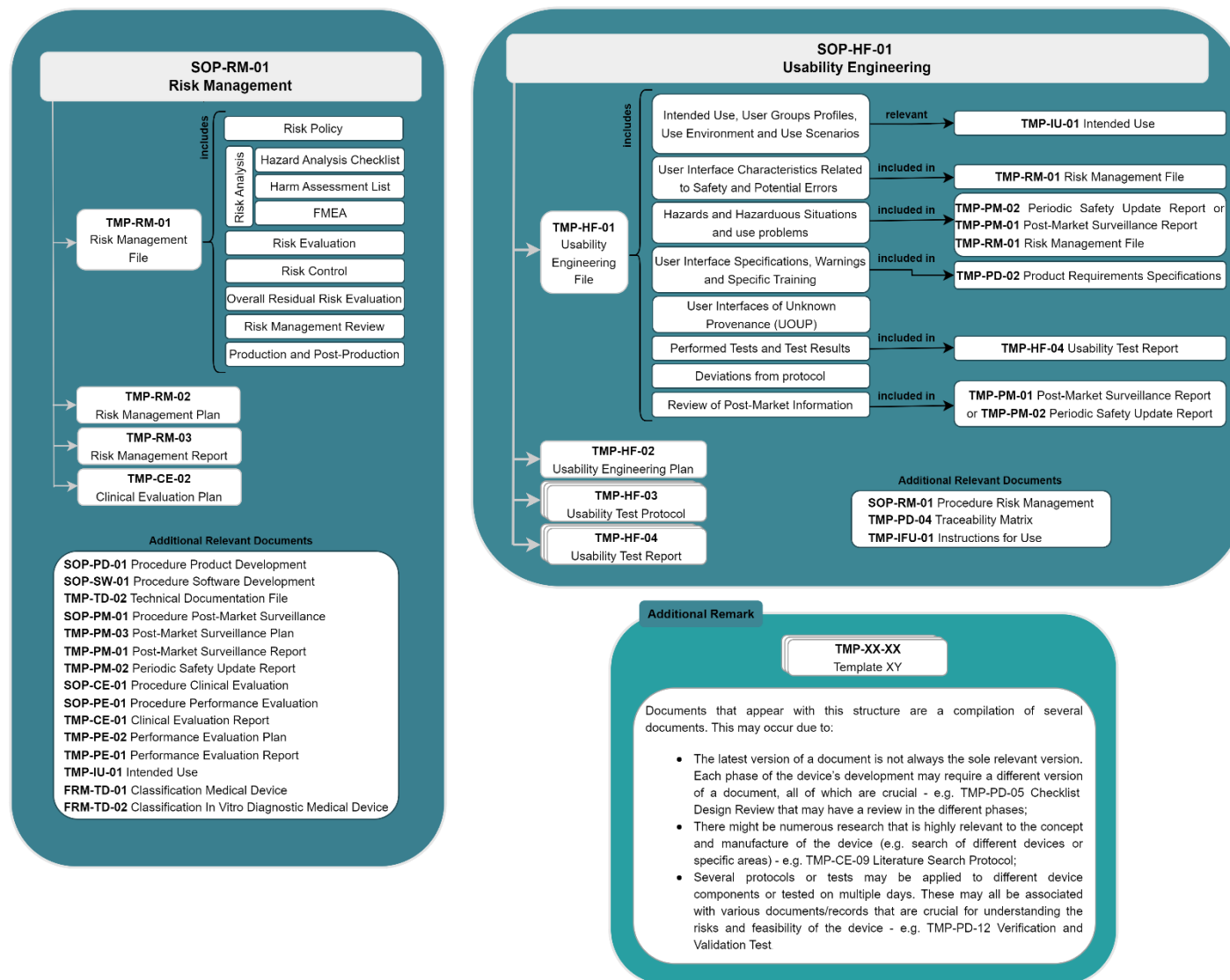


Figure 14. Framework Overview of the Templates Related to Risk Management and Usability Engineering.

7.2 Mapping Organization Development Projects

Each year, a substantial number of medical technologies are developed, with billions invested in their advancement to meet the growing demand for innovation in the field. Developing a new MD is critical for the growth and prosperity of any manufacturer or organization. However, despite the increasing amount of novel medical technologies, only a few devices and resources have successfully entered the market. This often occurs due to the perception of the MD development process as risky and expensive, which is driven by the rising complexity and stringency of regulatory requirements, standards, and guidance documents. These evolving demands highlight the value of gaining an early and full understanding of essential requirements to avoid non-compliance and considerable delays in device development [94].

To ensure secure product development and demonstrate conformity with regulatory and normative requirements, it is critical to design a process that complies with the MDR, IVDR, ISO 13485, ISO 14971, and IEC 62366-1, and in the case of MDSW IEC 62304. This process is heavily reliant on adopting precise methods that enable developers to optimally stage concept, planning, development, testing, verification, validation, and market release. As a result, the MD development process is typically divided into multiple phases (**Figure 15**). This phased approach promotes effective project management, resource allocation, and compliance with all requirements and was determined based on the literature review performed in **Section 6.3.2**.



Figure 15. Phases of the development process of a medical device.

7.3 QMS Implementation and Technical Documentation Development

7.3.1 Concept Phase (Phase 0)

In the initial stage of a project, feasibility is assessed and used to guide preliminary research and concept development. During this phase, concepts are quickly developed without comprehensive design change control or traceability, and draft versions of design control documents and procedures, including development plans, are created.

The first step in assessing the project's feasibility is to evaluate if the product qualifies as MD or IVD under the company's defined Procedure Regulatory Compliance (which under the documents templates is coded as SOP-RU-02 Procedure Regulatory Compliance). Furthermore, determining the device's intended use (TMP-IU-01 Intended Use) is crucial since it significantly influences its classification and future development. A preliminary hazard analysis (PHA) should also be performed and documented in the company's Risk Management File (TMP-RM-01 Risk Management File).

7.3.1.1 Framework

For the concept phase, **Figure 16** mentions the templates related to Product Development and Risk Management Procedures, and **Figure 17** mentions the ones related to Usability Engineering.

In the framework, the templates appearing in white are referred to as the documents to be created in the current phase, and the ones in grey are referred to as the documents already developed in previous phases. Each phase includes corresponding inputs and outputs, the first for templates, procedures, data, or information developed in the previous phase and required in the current one, and the second for results achieved by completing the phase in question. Outputs often arise from updating the required inputs. Whenever a template created in a prior phase needs to be updated or worked on, it is marked with a "Rev. x" symbol, indicating the revision required.

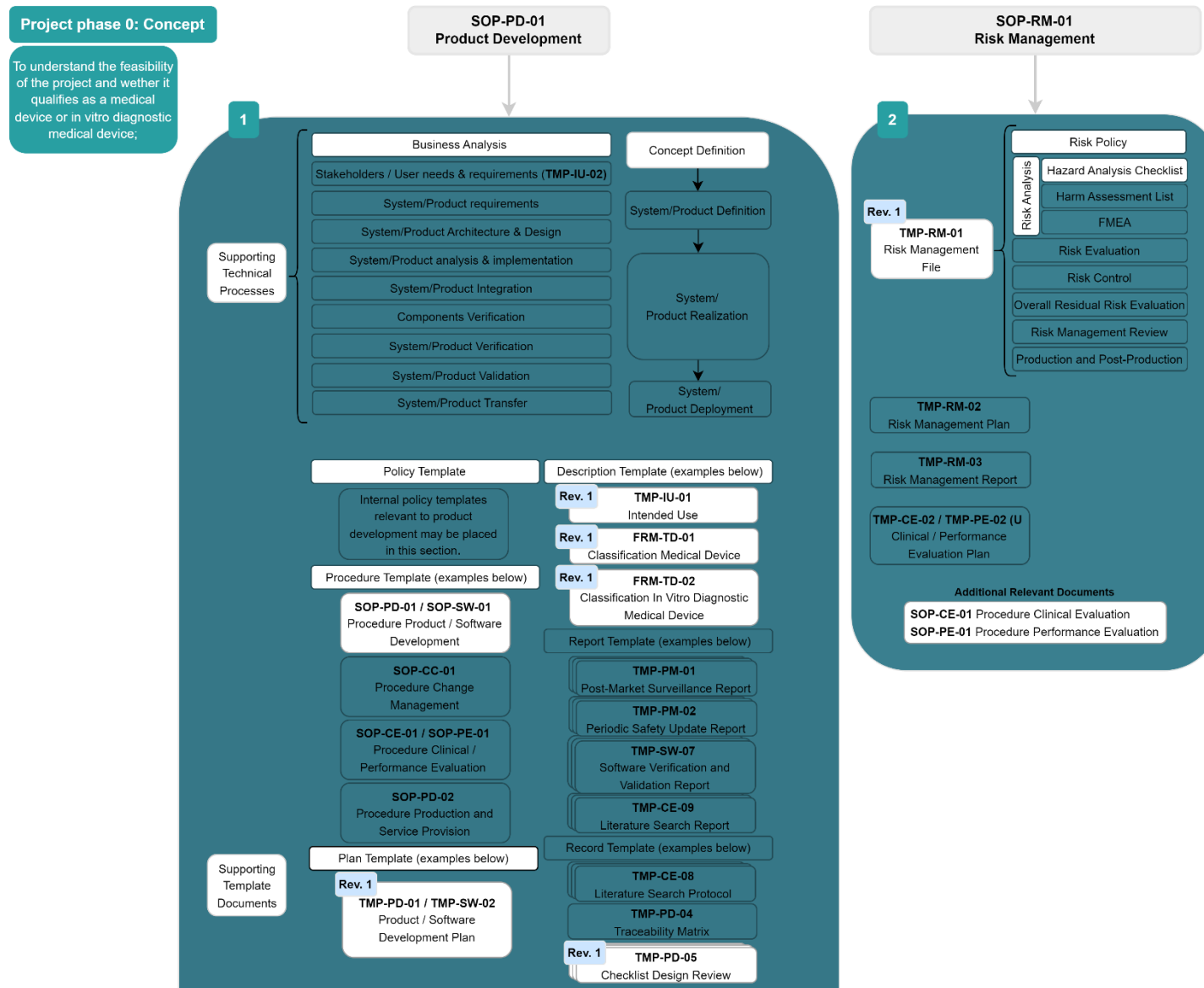


Figure 16. Templates related to (1) Product Development and (2) Risk Management Procedures required for the Concept Phase (Phase 0).

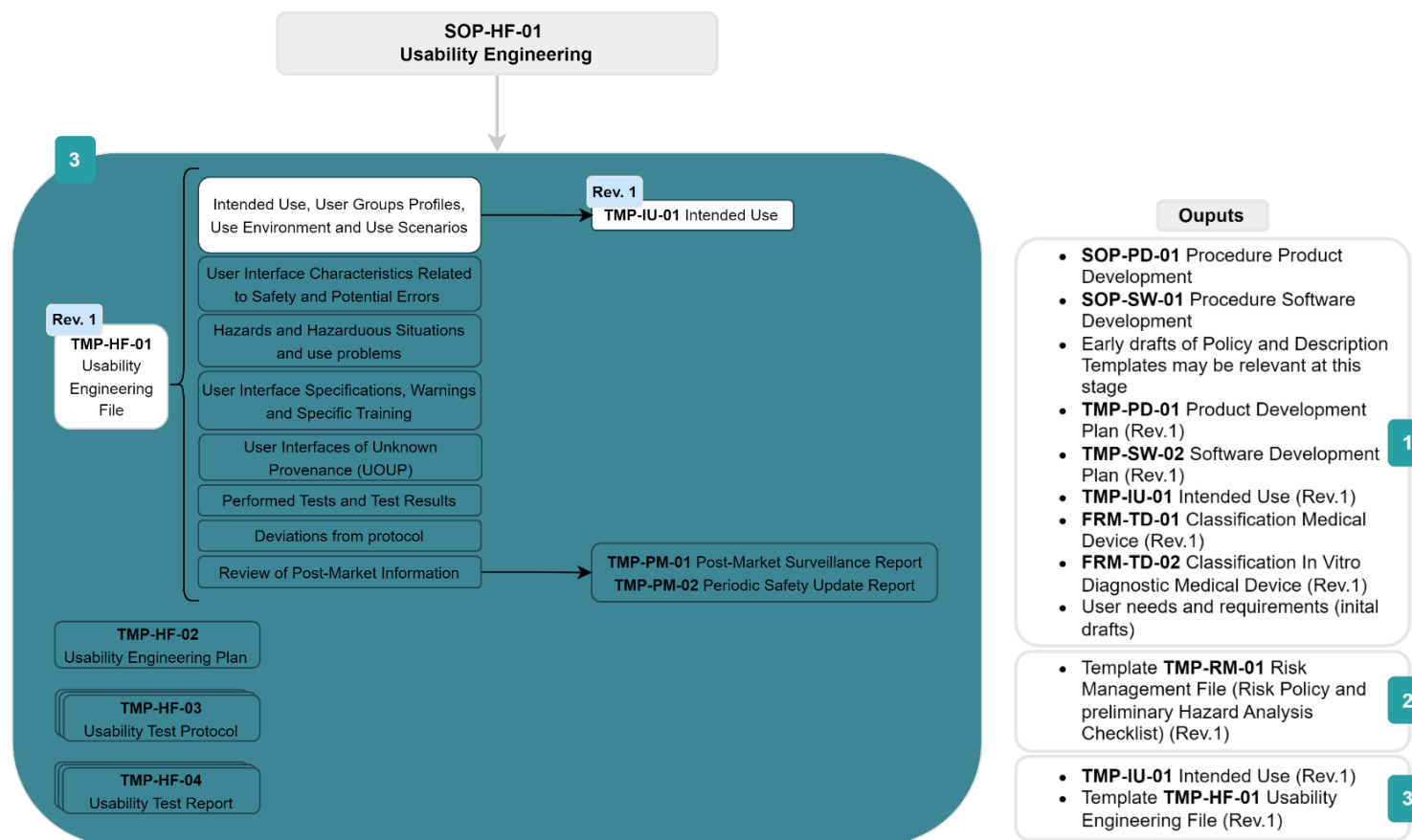


Figure 17. Templates related to the Usability Engineering Procedure required for the Concept Phase (Phase 0).

7.3.2 Planning Phase (Phase 1)

In the planning phase, stakeholder requirements must be identified and well-defined, as they are essential for the device development and for defining the product's requirements and specifications. These requirements include those specified by the customer, covering delivery and post-delivery activities, as well as unstated needs essential for determining the device's intended use. They also encompass applicable regulatory requirements, essential user training to ensure the device's performance and safety, and any additional requirements relevant to the design and manufacturing processes. These requirements should be documented in the TMP-IU-02 Stakeholder Requirements template. Identifying stakeholder requirements involves recognizing relevant stakeholders and creating user groups, as described in the TMP-HF-01 Usability Engineering File. This process includes outlining fundamental activities using, for instance, context interviews and identifying requirements into user, regulatory, market, and organizational categories. Stakeholder requirements must be regularly reviewed, with assessment results and actions documented in the TMP-PD-05 Checklist Design Review.

When developing a new device, it is crucial to consider its intended use, even as a preliminary one. At the start of the planning phase, a development plan must be established, documented in the TMP-PD-01 Product Development Plan (or TMP-SW-02 Software Development Plan, for software-specific), and updated regularly. This plan must cover all aspects of the product development process, such as the planned development stages, verification, validation, transfer activities, and design and development reviews for the system or sub-system in question. It must outline all activities for each phase, such as deadlines, design reviews, and the necessary technical and organizational interfaces to facilitate development activities. It should also provide details of any additions or changes to procedures and processes, e.g., risk management, usability information, change management, product coordination, and component development procedures. The product development plan should also document and allocate all necessary human resources, specifying roles, responsibilities, and competencies, and provide a description of all tools used for documentation.

The development and integration of individual components of complex devices that incorporate, for instance, mechanical, electronic, or software parts, can be divided into specific plans for each type of component, as they may have different technical, regulatory, or business requirements. For instance, software components may follow different procedures, such as SOP-SW-01 Procedure Software Development, that aim to meet software-specific regulatory requirements, including IEC 62304. Additional development processes may be necessary for the development or qualification of MD or IVD components. However, components already available in the market and compliant with all relevant requirements may be deemed qualified. For this reason, depending on their intended application and function within the device, their functionality should be analyzed separately during either analytical or clinical performance evaluations.

During the device development planning phase, the SOA should be considered as part of the Clinical Evaluation Plan (TMP-CE-02 Clinical Evaluation Plan) or, if a prior device exists, the Clinical Evaluation Report (TMP-CE-01 Clinical Evaluation Report). Similarly, for IVD, the SOA should appear in both the Performance Evaluation Plan (TMP-PE-02 Performance Evaluation Plan) and the Performance Evaluation Report (TMP-PE-01 Performance Evaluation Report). The SOA must comprise several key aspects, including the identification of relevant medical fields and conditions, methods for collecting or retrieving information, applicable standards, and guidance documents. It must additionally include a description of alternative and similar devices, as well as their safety and performance profiles based on clinical data, side effects management, identified risks and competitive therapeutic options on the market.

Another significant aspect of the planning phase is defining the product requirements, which must be recorded in the TMP-PD-02 Product Requirements Specification. These requirements should be

included in the TMP-SW-04 Software Requirements Specification for software components. The requirements must be thorough, consistent, accurate, and traceable to the stakeholder requirements. In the context of IVD, the description of the device under development must cover all pre-analytical steps, such as specimen collection, sample preparation, quality control, qualification, and data and results analysis. The device should be examined within the risk analysis framework, as described in SOP-RM-01 Procedure for Risk Management. Use scenarios and user interfaces must additionally be specified according to the SOP-HF-01 Procedure for Usability Engineering and the draft of TMP-HF-01 Usability Engineering. Once documented, the product requirements specifications are reviewed to verify if they are consistent with the stakeholder requirements.

Individual product components and interfaces are developed and identified based on the product requirements. At this stage, the TMP-PD-03 Product Design Specification should be created by the development team to document the specifications for designing, producing, or acquiring all individual components. To guarantee traceability, each component must be granted a unique ID, which should be mapped in the TMP-PD-04 Traceability Matrix. The specifications must be measurable and converted into corresponding test cases for component verification. Following this, the risk manager and the development team must conduct a risk analysis according to the procedure risk management. Finally, the head of product development is responsible for reviewing the design specifications to verify that they are complete and precise enough to generate test cases for verification and integration.

If verification and validation plans for testing specific device components were not established during the preparation of the product requirements, they should be developed at this stage. Each product requirement must be assigned at least one design verification test to demonstrate that the design meets the requirement. Similarly, each stakeholder requirement must be linked to at least one design validation test to provide supporting evidence that the requirement has been satisfied. Additionally, equipment and facilities intended for verification and validation must be qualified, and methods must be validated. All plans should encompass or reference the methods to be used, acceptance criteria, and, if applicable, statistical techniques, including a rationale for the chosen sample size.

Before a company commits to supplying devices to clients, a thorough analysis of the requirements must be performed. This assessment involves verifying that all product requirements are established and recorded, including those provided by the customer and those linked to delivery, post-delivery activities, and any unstated requirements necessary for determining the device's intended use. The review also ensures that any contract or order requirements differing from those previously expressed are handled, applicable regulatory requirements are met, and user training needs are considered to guarantee that the MD performs as stated and is used safely. Additionally, the organization must ensure that it fulfills the established requirements. Records of the review results and subsequent actions must be kept. Along with this evaluation, the technical implementation of the proposed solutions must be verified to confirm their viability as indicated in the product requirements specifications. It is crucial to note that when product requirements change, the company must ensure that all essential documentation is updated and that appropriate employees are notified of these changes.

7.3.2.1 Framework

Figure 18 provides the inputs for the planning phase and the revisions and documentation related to product development required for this stage. Additionally, **Figure 19** presents all additional information related to product development and the one concerning the risk management procedure. Finally, **Figure 20** provides all templates related to the usability engineering procedure and the outputs for this phase.

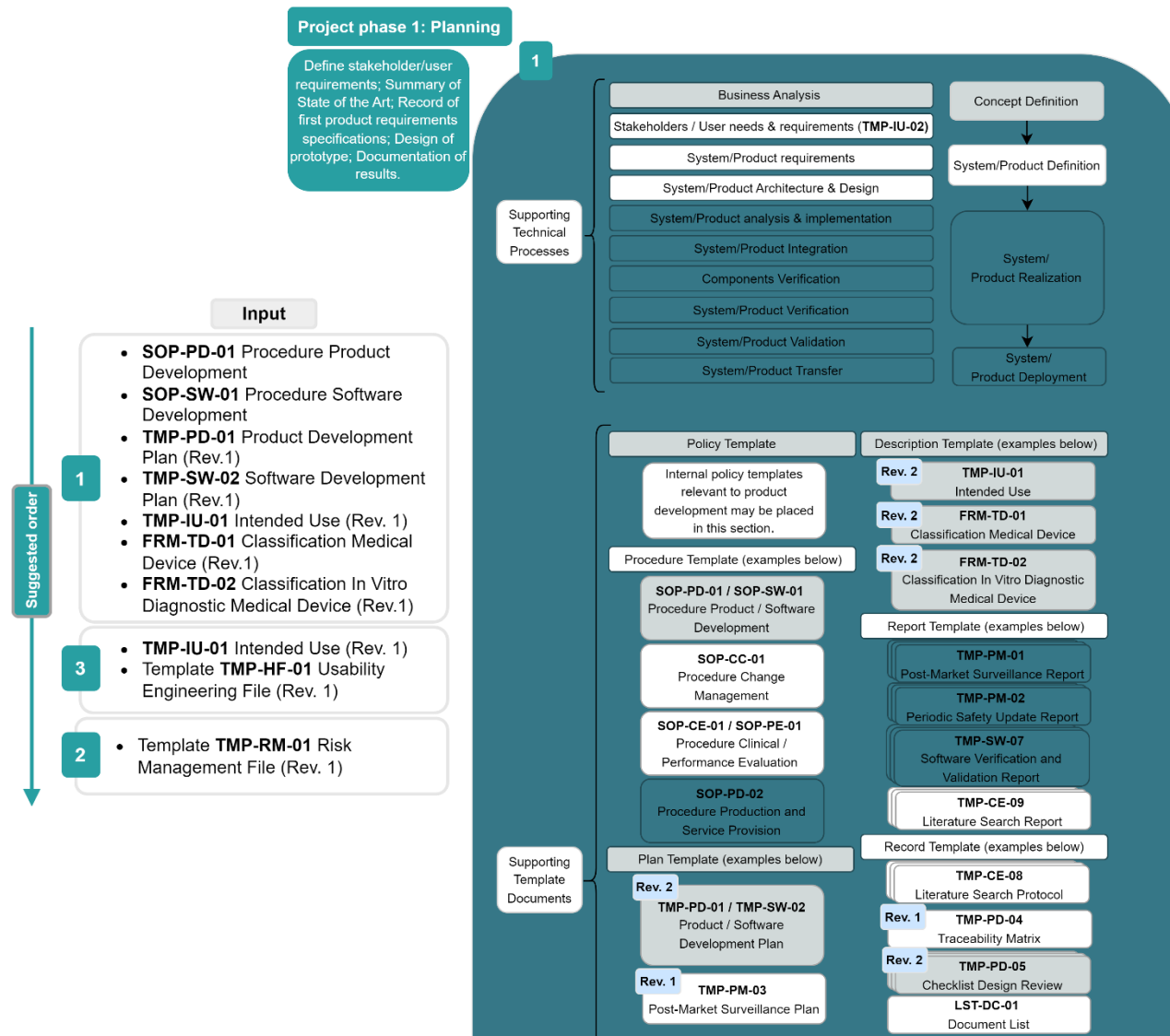


Figure 18. Inputs of the Planning Phase (Phase 1) and templates related to Product Development.

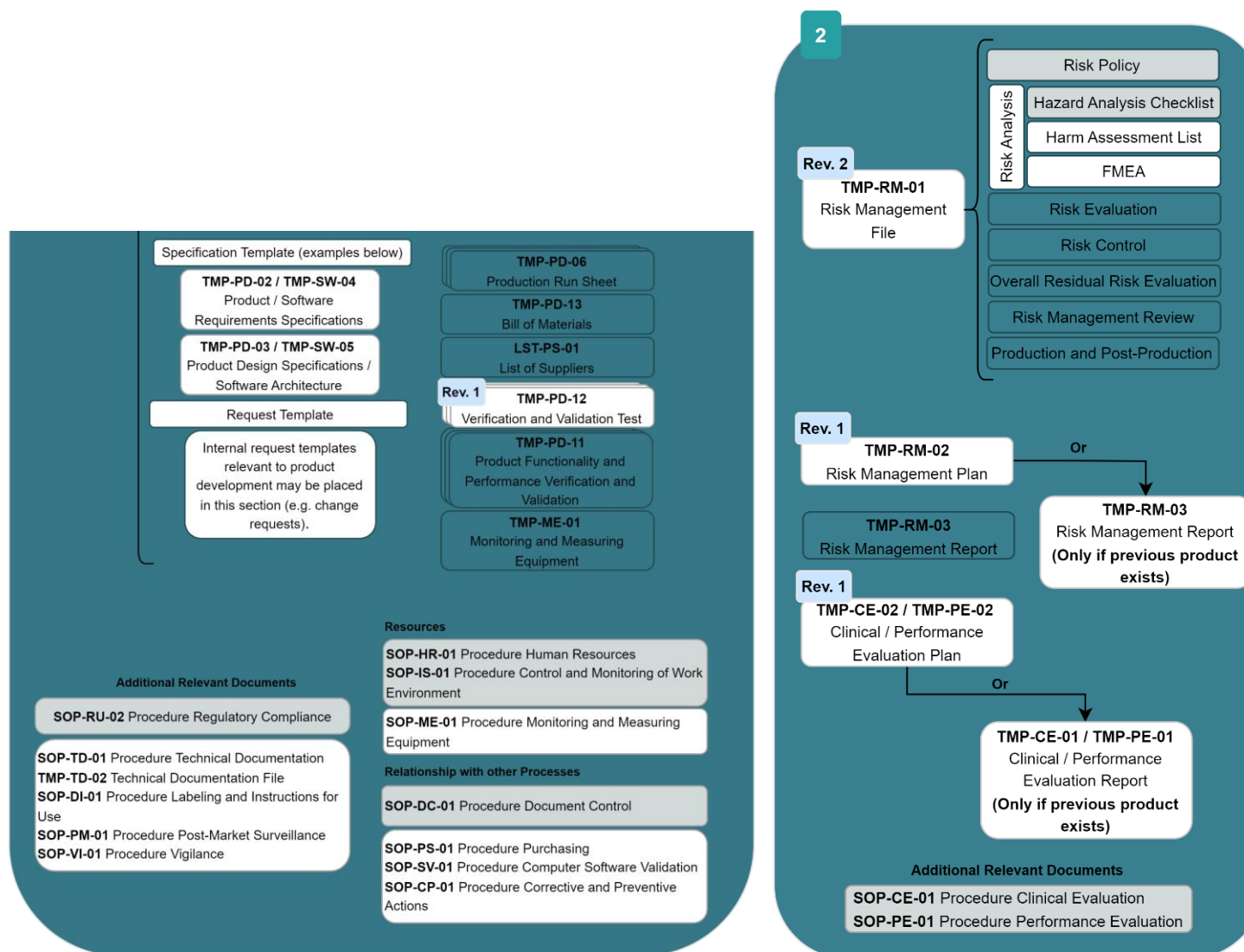


Figure 19. Additional templates related to the Product Development Procedure (on the left) and the Risk Management Procedure (on the right) for the Planning Phase (Phase 1).

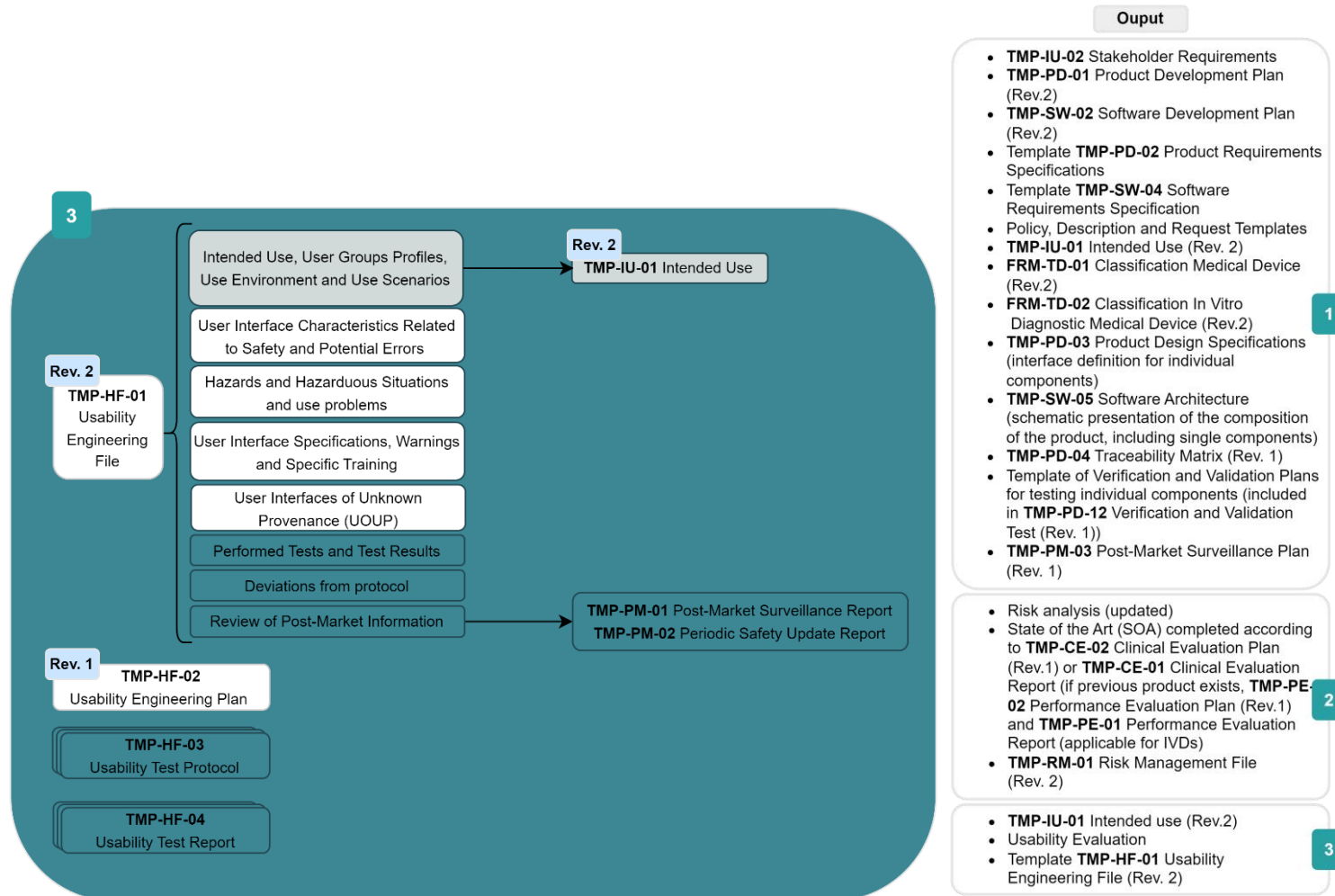


Figure 20. Templates related to the Usability Engineering Procedure and outputs required for the Planning Phase (Phase 1).

7.3.3 Design and Development (Phase 2)

The Design and Development Phase is vital in the MD development process, building on the foundation established during the concept and planning phases. It focuses on the design's precise implementation, which involves rigorous planning, full design controls, and engineering testing to guarantee the product fulfills all relevant technical and regulatory requirements.

During this stage, the head of product development and the development team, including external partners, are responsible for developing the device according to the applicable procedures and plans created in the preceding phases. All previously initiated documentation must be updated with new revisions of the planning documents as necessary.

Key activities during the MD's development include establishing development records, outlining the components' design, documenting the implementation of product design specifications, defining quality control measures, and generating all essential documentation for the design implementation. Schematics, design drawings, lists of components and critical parts, a bill of materials (TMP-PD-13 Bill of Materials), material specifications with procurement and manufacturing information, acceptance criteria or quality control requirements, a list of suppliers (LST-PS-01 List of Suppliers), packaging descriptions, and product specifications for components, raw materials, sub-assemblies, finished devices are all possible additional information that can be provided. Furthermore, product labels, instructions for use and packaging, software information such as source codes, build instructions, libraries and executables, procedures and work instructions, sampling plans, test methods, and their acceptance criteria must also be documented.

By the end of this phase, drafts of the verification and validation plans for testing the specific device components must be updated to reflect the most recent information.

7.3.3.1 Framework

Figure 21 provides the inputs required for the design and development phase. **Figure 22** mentions all documentation and revisions related to the product development procedure. Additionally, **Figure 23** provides all templates associated with the risk management and usability engineering procedures, and **Figure 24** shows the outputs intended to be accomplished in the current stage.

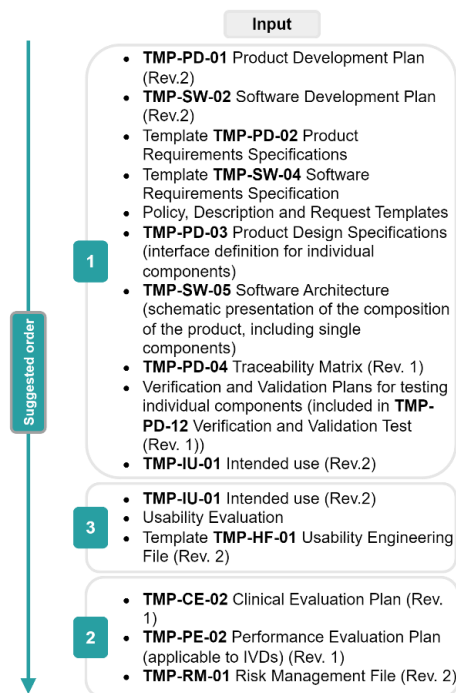


Figure 21. Inputs of the Design and Development Phase (Phase 2)

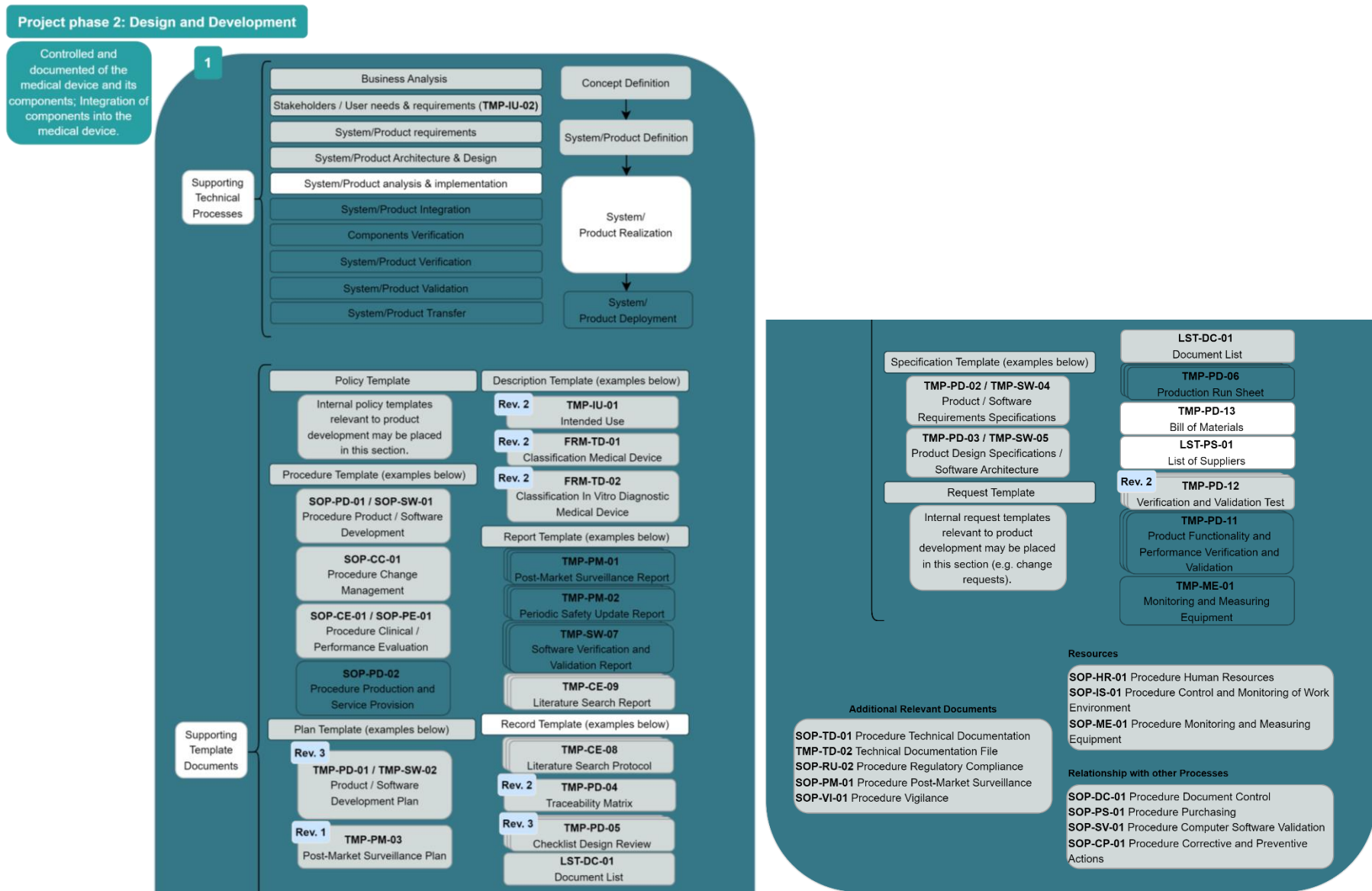


Figure 22. Templates related to the Product Development Procedure for the Design and Development Phase (Phase 2).

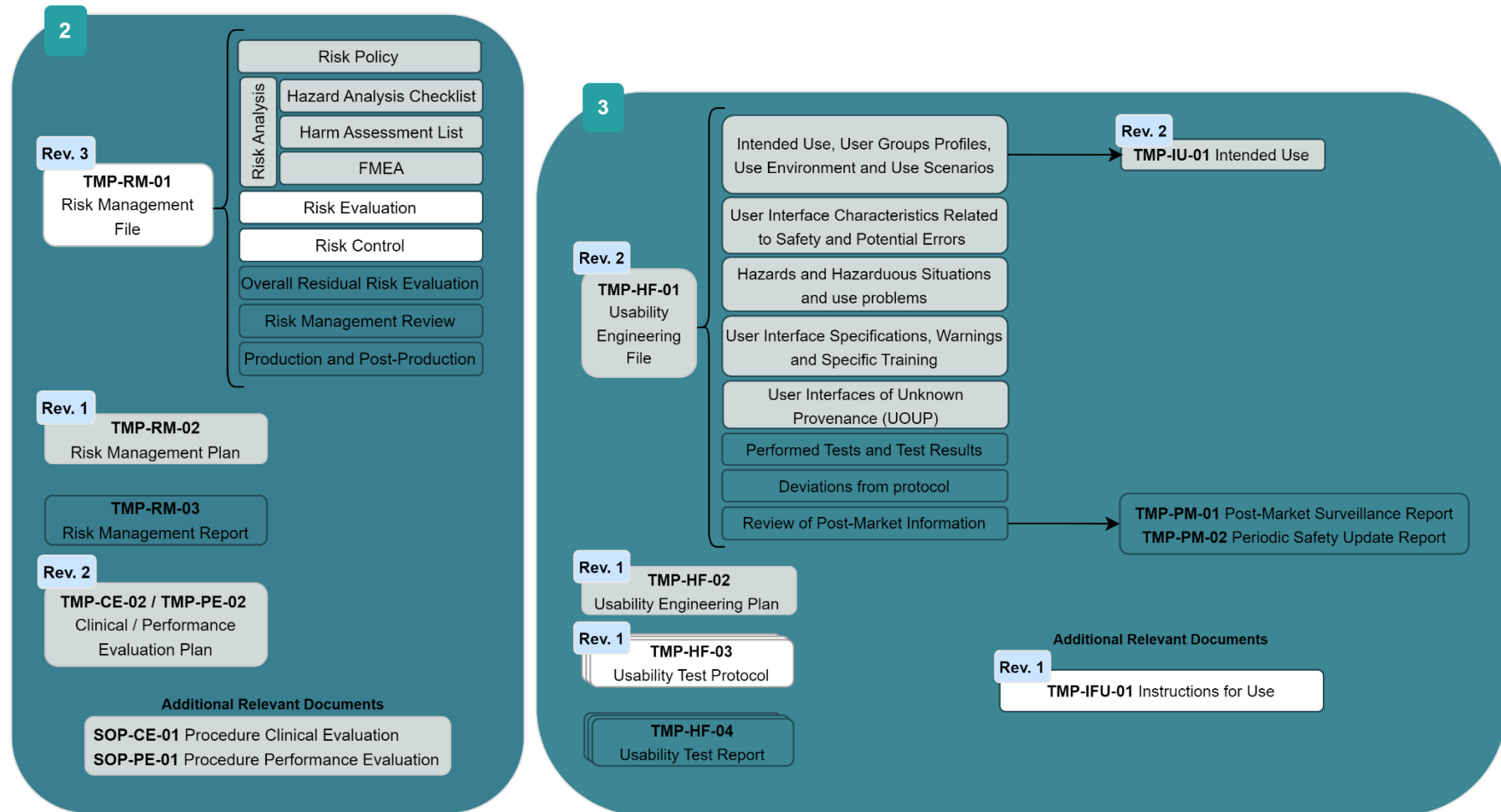


Figure 23. Templates related to the Risk Management (on the left) and the Usability Engineering Procedure (on the right) for the Design and Development Phase (Phase 2).

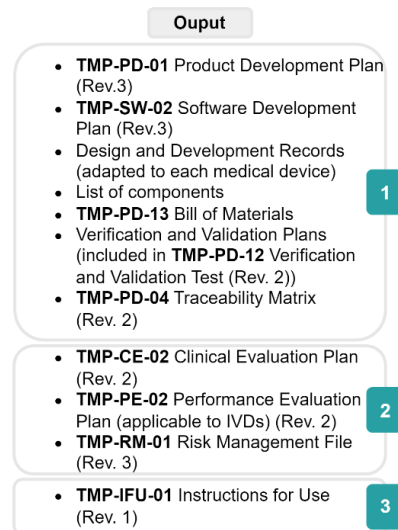


Figure 24. Outputs of the Design and Development Phase (Phase 2)

7.3.4 Design Verification (Phase 3)

In the design verification stage, design output is verified based on design input at the level of each component and the overall system.

Verification activities must be conducted at all stages and levels of the device's design. Any strategy that demonstrates conformity with the design input requirements is considered a valid design verification method and must be included in the design verification plan, along with any stability testing required to verify the design inputs.

During the verification of design components, testers may modify the verification plans as necessary. Verification plans may only be released after a successful assessment. These plans outline the testing procedures for individual product components and detail the quality assurance actions to be taken during production, which are then documented in verification protocols. The performance and outcomes of the tests are detailed in verification reports. If external parties are involved in the development and testing, they are responsible for verifying the relevant product components and documenting the implementation and results in a verification report. The verification of individual components should always be mapped in the Traceability Matrix and detailed in specific procedures or plans, such as the Procedure for Software Development, for software components.

If the verification of a component fails, the responsible development team must return to the beginning of Phase 1 and redefine the product designs. Changes to the development inputs must be managed following a Procedure Change Management.

A design freeze suspends any design changes, enabling the performance of a stable design iteration to be recorded and verified. Following the results of such testing, a technical or phase design review must be followed to document those outcomes. The components of the product design subject to the design freeze are identified and reported by the project manager and head of product development. This process may be applied to all components at once or successively to individual components. All team members must be aware that the frozen components, entire product, or system are no longer subject to modifications. If the verification testing reveals any design flaws, the design can be unfrozen and adjusted under design change control, with any following changes handled according to the Procedure Change Management.

Final design verification is conducted on the design intended for regulatory submission and planned for manufacturing, launch, and distribution. Under design controls, traceable records of verification plans, test protocols, test reports, and test materials are required. Design samples undergoing

testing must be subjected to a design freeze, and any design modifications should be mentioned in the test report.

According to the Product Development Plan, testers conduct tests using approved test plans and protocols on the final product, which comprises all specified and verified components. The verification protocols keep track of all results, including raw data. The responsible tester collects and summarizes these outcomes in the verification report(s).

If the product verification fails, the development team must return to Phase 1 to redefine the product requirements. Contrariwise, the verified product can move forward to the validation phase if the verification is successful.

Technical Reviews can be made anytime during this phase. They can record design status at planned project milestones within the Phase or be called ad hoc to address specific design and development issues that require cross-functional or management involvement. This phase review is a critical review of the product design and quality management, conducted to solicit consensus agreement that design verification results are satisfactory and that the project can move into phase for design validation. Phase review is documented using the TMP-PD-05 Checklist Design Review.

7.3.4.1 Framework (Components)

The framework is divided into two sub-phases for the verification phase: verification of components and verification of the system. Both these sub-phases present different documentation requirements and document revisions. **Figure 29** presents the decision-making required between these two sub-phases, which do not allow a transition from one phase to another without meeting specific requirements. **Figure 29** figure guides how to proceed if specific issues occur during this stage, and **Figure 33** shows the decision-making after the verification stage is completed.

Figure 25 provides the inputs required for the component's verification phase. **Figure 26** mentions all documentation and revisions related to the product development procedure associated with the component's verification. Additionally, **Figure 27** provides all the templates related to the risk management and usability engineering procedures. **Figure 28** shows the outputs intended to be accomplished in the design verification of components phase.

Regarding the overall system verification phase, **Figure 30** provides the inputs required for the phase in question. **Figure 31** mentions all documentation and revisions related to the product development and risk management procedures. **Figure 32** provides all the templates associated with the usability engineering procedure and shows the outputs intended to be accomplished in the design verification of the overall system phase.

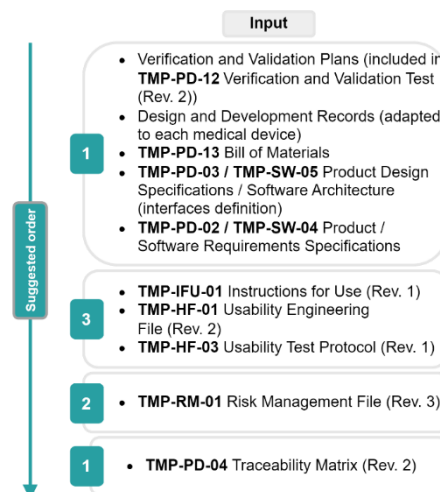


Figure 25. Inputs of the Design Verification of Components Phase (Phase 3.1)

Project phase 3.1: Design Verification (Components)

To demonstrate the design outputs of each component meets the design inputs.

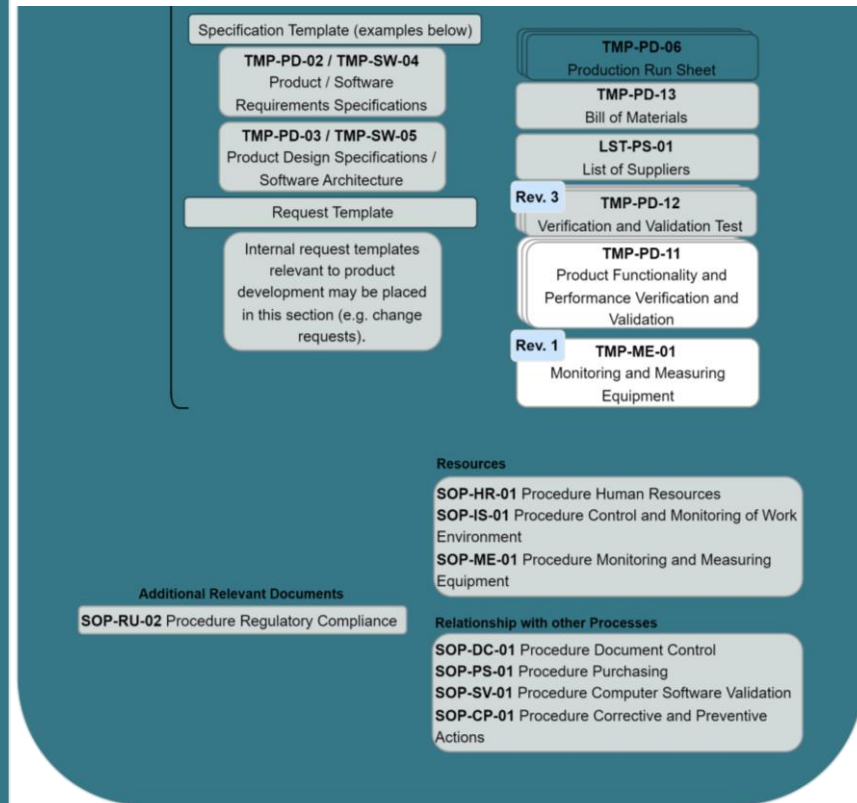
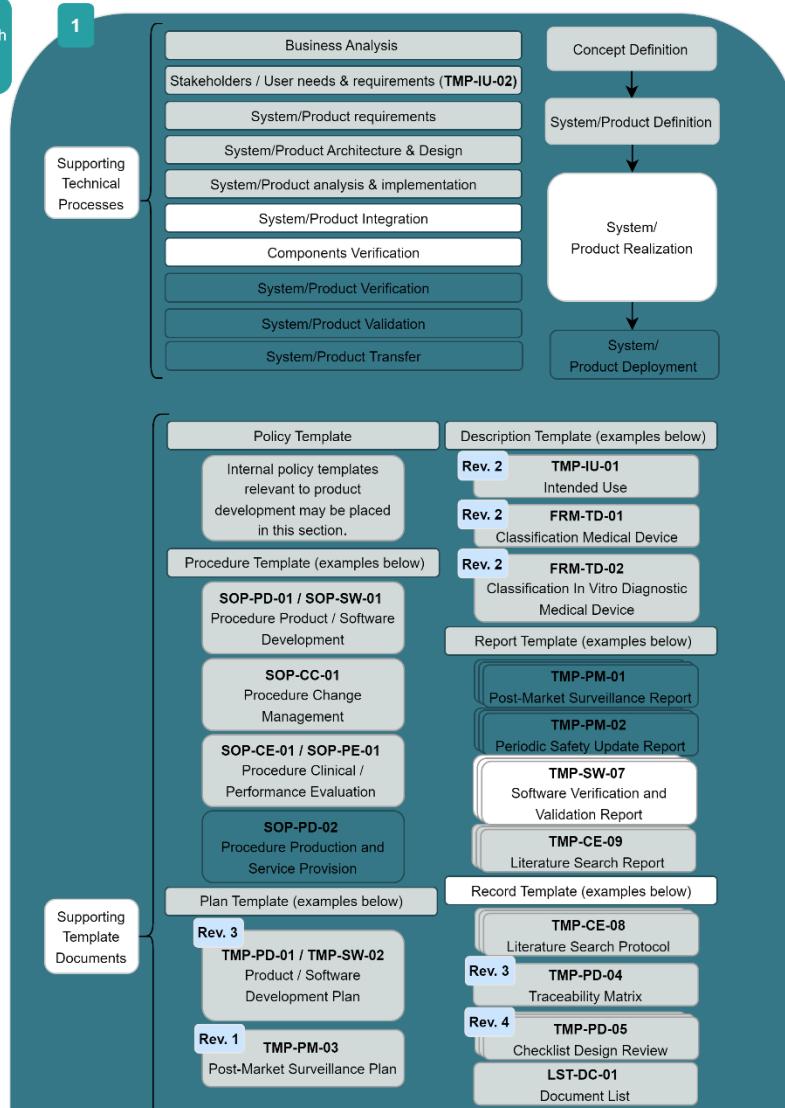


Figure 26. Templates related to the Product Development Procedure of the Design Verification of Components Phase (Phase 3.1)

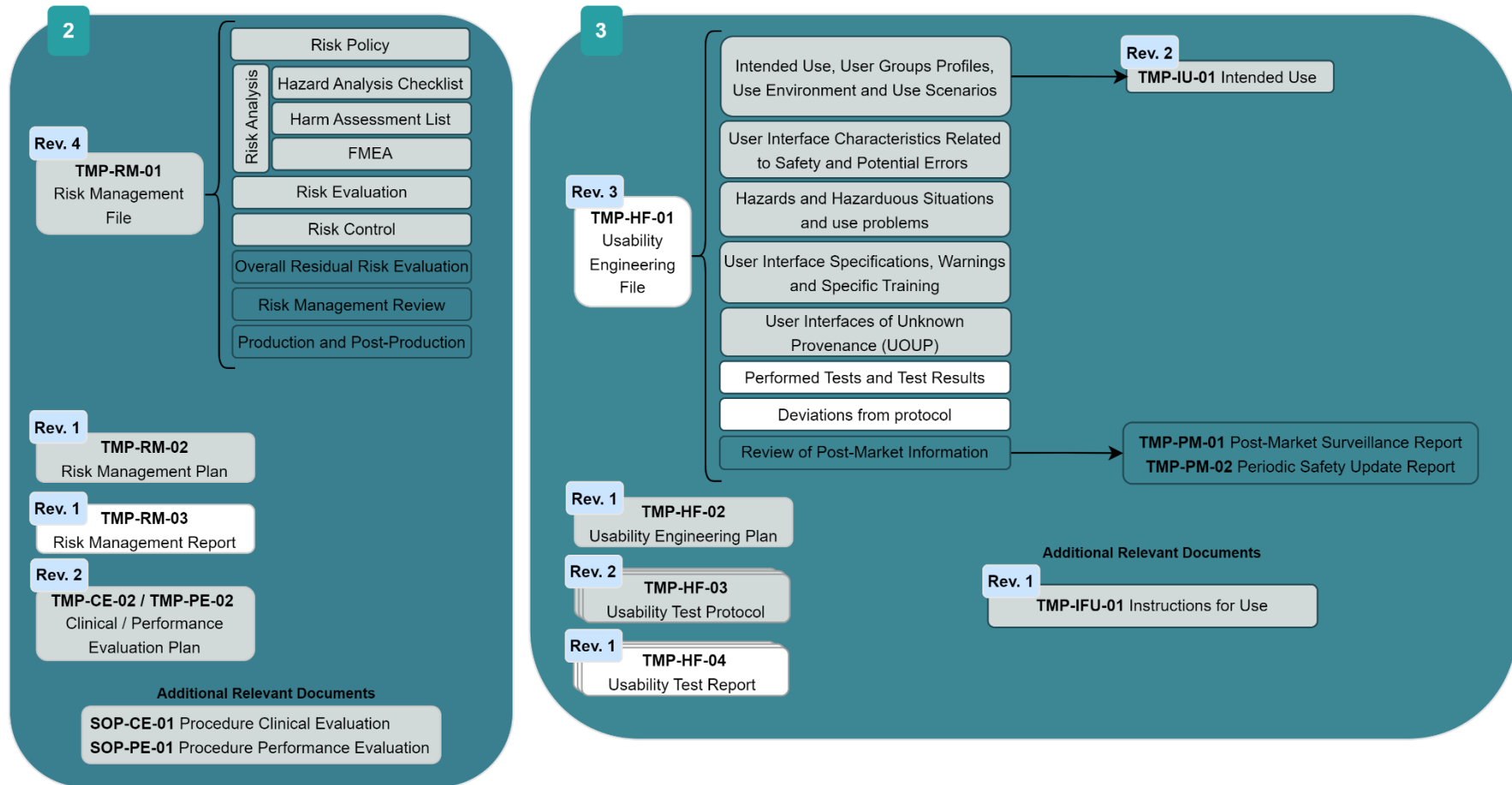


Figure 27. Templates related to the Risk Management (on the left) and Usability Engineering Procedures (on the right) of the Design Verification of Components Phase (Phase 3.1)

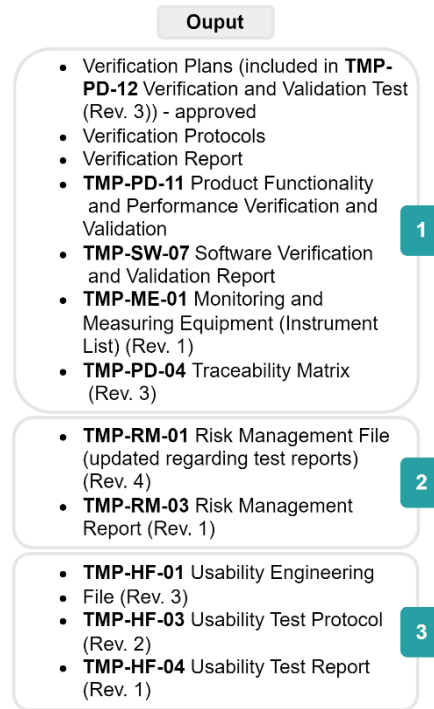


Figure 28. Outputs of the Design Verification of Components Phase (Phase 3.1)

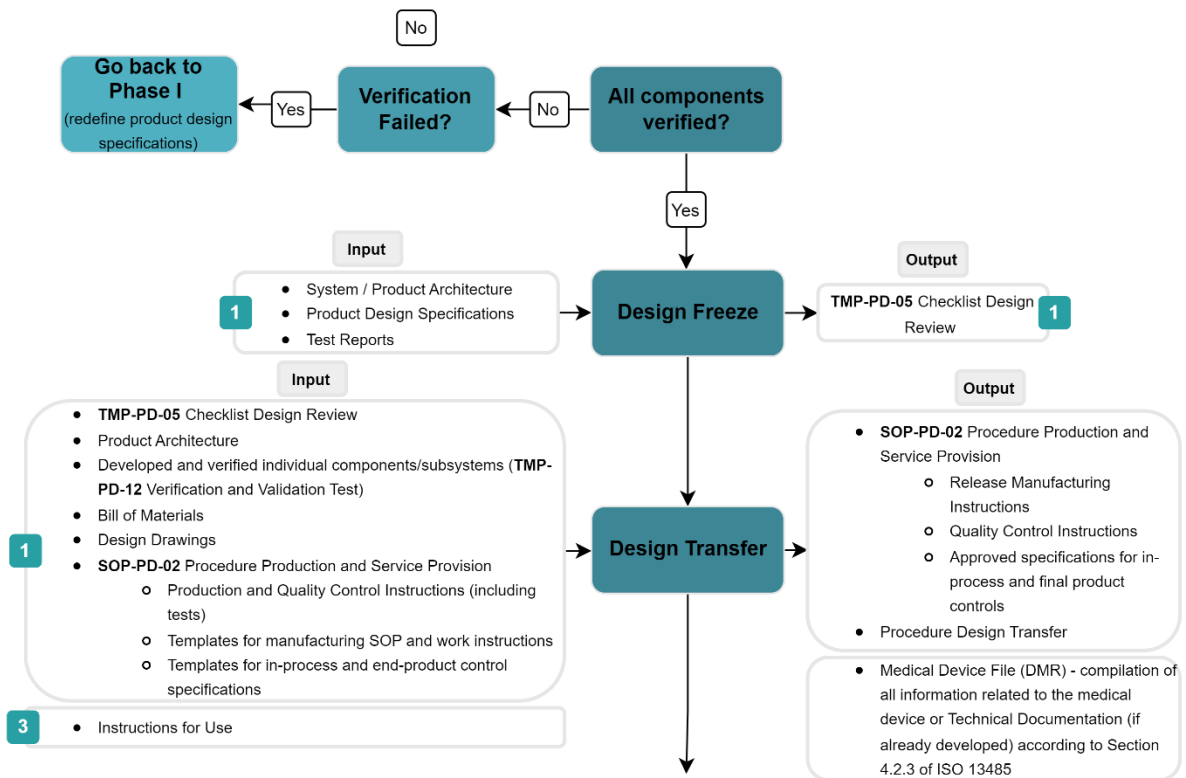


Figure 29. Decision-making after the Design Verification of Components Phase and additional templates required.

7.3.4.2 Framework (Overall system)

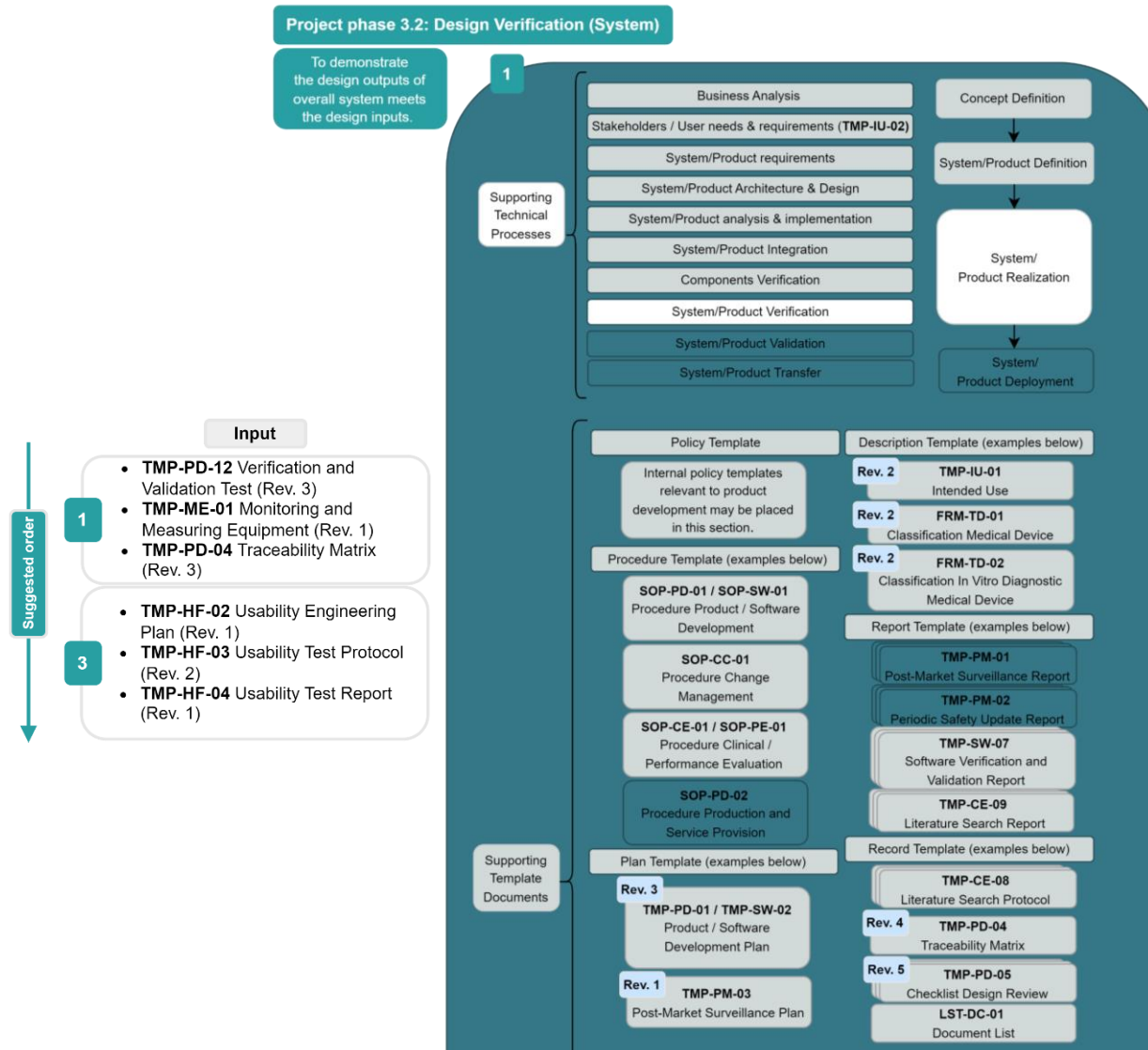


Figure 30. Inputs (on the left) of the Design Verification of the System Phase (Phase 3.2) and templates related to the Product Development Procedure (on the right).

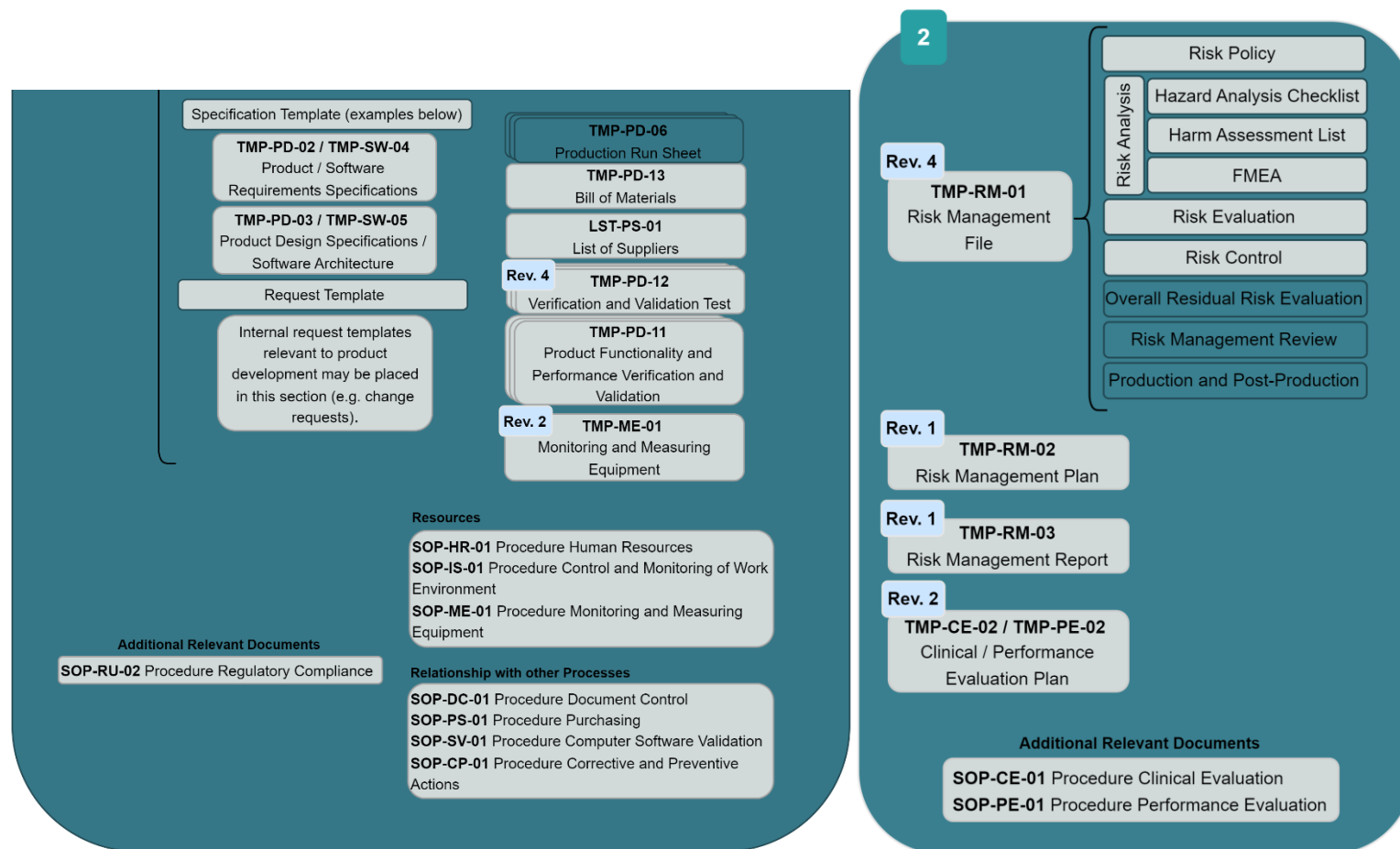


Figure 31. Additional templates related to the Product Development (on the left) and the Risk Management Procedures (on the right) related to the Design Verification of the System (Phase 3.2).

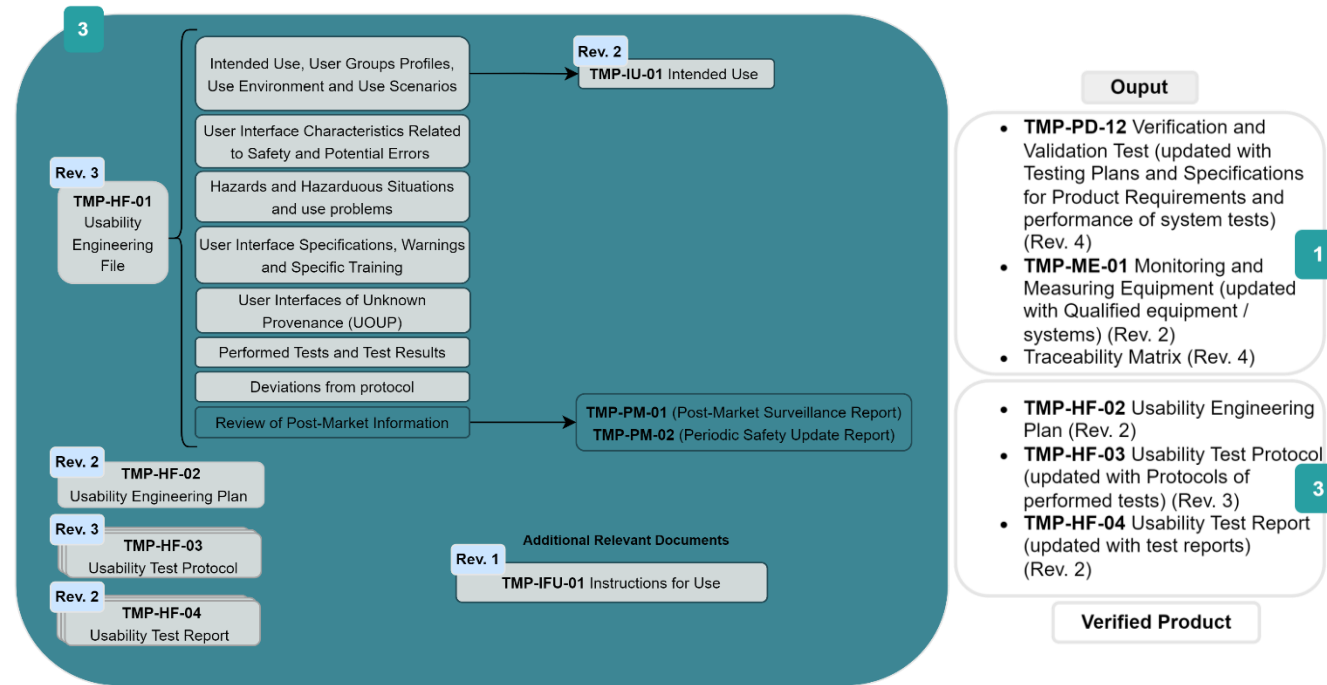


Figure 32. Templates related to the Usability Engineering Procedure (on the left) and outputs (on the right) related to the Design Verification of the System Phase (Phase 3.2).

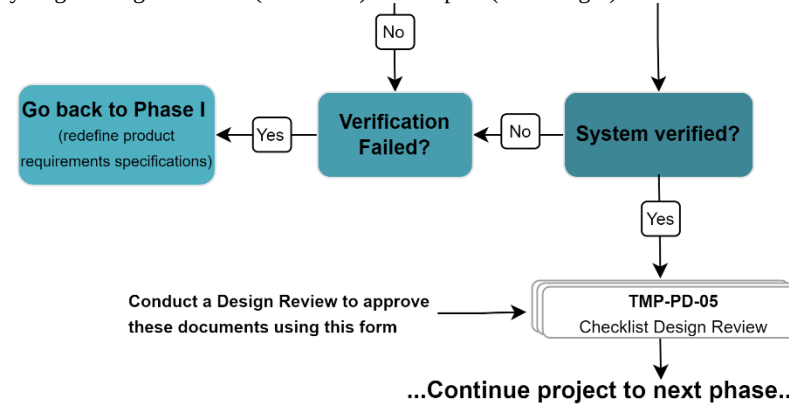


Figure 33. Decision Making after the Design Verification of the System Phase (Phase 3.2).

7.3.5 Design Validation (Phase 4)

The primary purpose of design validation is to guarantee that the product design meets the requirements for its specified intended purpose. Design validation should be performed under established operating conditions, either through actual or simulated use, on initial production units, lots, batches, or their equivalents. When the unit under test is connected or interfaced with another MD, confirmation that the requirements for the specified application or intended purpose have been met is required. During design validation, the usability of the product or system is assessed as outlined in the Usability Engineering File, derived from the Usability Engineering Plan. Clinical/Performance evaluation is also conducted as part of the validation phase. This is a continuous process by which data is assessed and analyzed, as described in SOP-CE-01 Procedure Clinical Evaluation and SOP-PE-01 Procedure Performance Evaluation (for MD or IVDs respectively), including an assessment of whether the product requirements are appropriate. This stage also includes validating design performance concerning user needs under actual or simulated use circumstances and concerning hazard-related use scenarios. Under design controls, it is essential to maintain traceable records of validation plans, test protocols, test reports, and materials. Design samples under test must be subjected to a design freeze, with any design modifications documented in the test report. All validation activities should be recorded in the Traceability Matrix to ensure traceability.

During this stage, the risk manager completes the risk analysis by identifying new risks and connecting validation results to the appropriate risk control measures. The outcomes of design validation can demonstrate the effectiveness of risk control measures in the context of risk assessments. Here, risk analysis is completed with any new risks identified, and the validation results are linked to the appropriate risk control measures. Furthermore, the risk management report is prepared, reviewing whether an overall residual risk has been evaluated and classified as acceptable. Additional instructions must be referenced in the Risk Management Procedure (SOP-RM-01 Procedure Risk Management).

If the product's validation is unsuccessful, the development team must return to Phase 0 to redefine the stakeholder requirements.

Validation of design performance regarding the aging and shelf-life of components is crucial. During this phase, stability studies must be accomplished, and the results documented in a stability studies report. The device's lifetime should be explicitly defined and considered in relation to other product design, development, and evaluation aspects. In general, product lifetime is defined as the time from the device's initial use until it no longer serves its intended purpose. The overall product lifetime should be calculated using the shortest lifespan of its individual components or, if applicable, the lifespan of the entire product if shorter than any component. This assessment and management of the product's lifetime must adhere to specific market requirements, as outlined in the Product Development Plan. For software components, the lifetime must be established according to the Procedure Software Development (SOP-SW-01 Procedure Software Development). Before the product's development cycle ends, all existing information, including testing results, should be gathered and the product's lifetime determined. The manufacturer should incorporate this data into the product information materials according to each market's requirements.

The final evaluation, also known as the design review, represents the end of a product's development cycle. This review incorporates vital participants, such as the General Management, the Project Manager, the Head of Product Development, developers, and the Validation and Verification Team, among others. Their responsibilities include ensuring that all artifacts, such as documents, records, and outcomes required by the Procedure Product Development (SOP-PD-01 Procedure Product Development) and/or Procedure Software Development (SOP-SW-01 Procedure Software Development) and the product-specific development plan, are present and properly controlled. They

must also guarantee that all risks have been identified, all risk mitigation strategies have been adopted and tested, and that the product or system can be produced in series as specified.

If design reviews significantly impact design decisions, they must be documented in the Checklist Design Review (TMP-PD-05 Checklist Design Review). For standalone software products, the output of the design review replaces the overall design review, as specified in the Procedure Software Development (SOP-SW-01 Procedure Software Development).

7.3.5.1 Framework

Figure 34 provides the inputs for the design validation phase and the revisions and documentation related to product development required for this stage. Additionally, **Figure 35** presents all additional information related to product development and the one concerning the risk management procedure. Finally, **Figure 36** provides all templates related to the usability engineering procedure and the outputs for this phase. **Figure 37** shows the decision-making after the validation stage is completed.

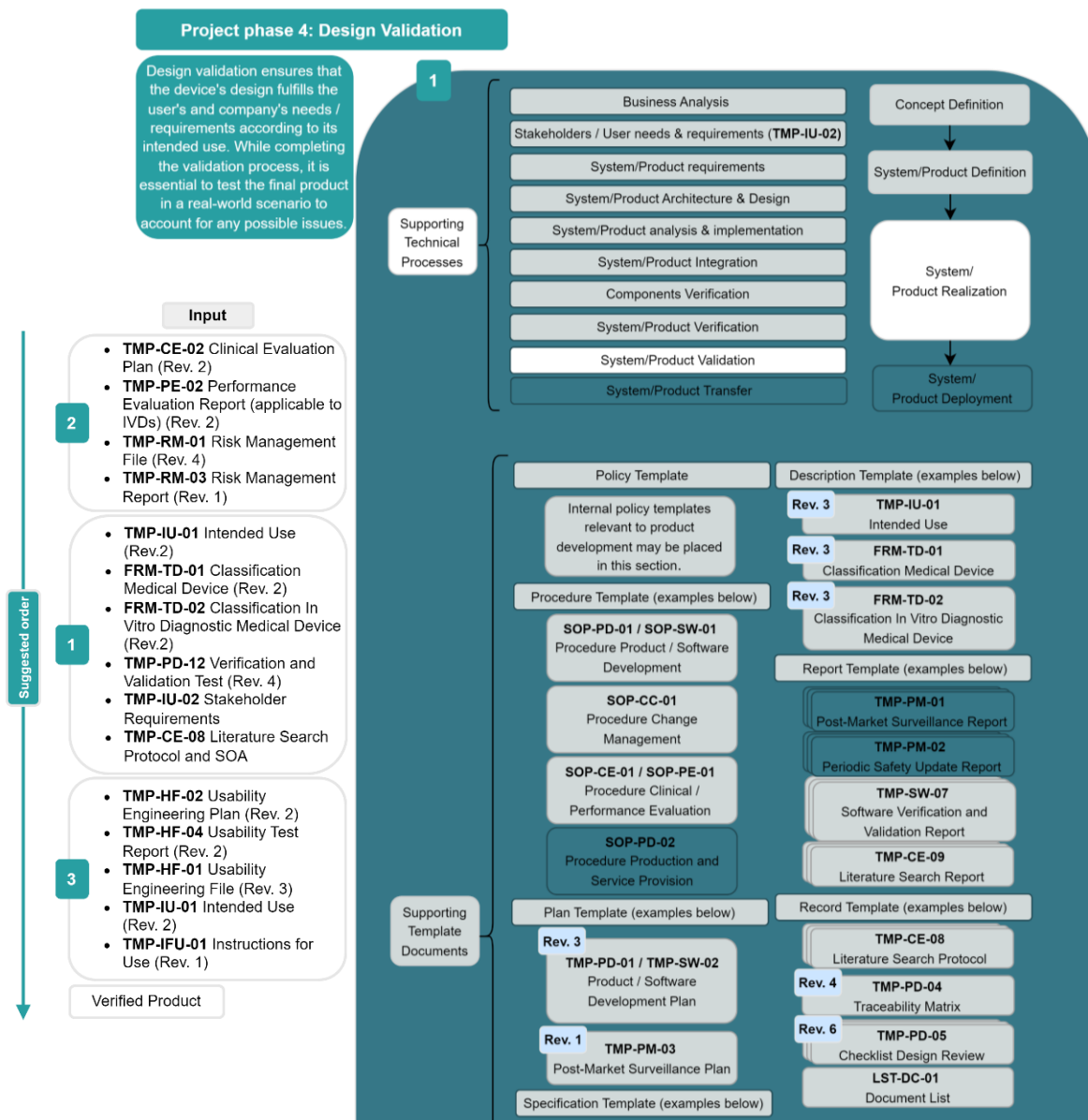


Figure 34. Inputs (on the left) and templates related to the Product Development Procedure (on the right) of the Design Validation Phase (Phase 4).

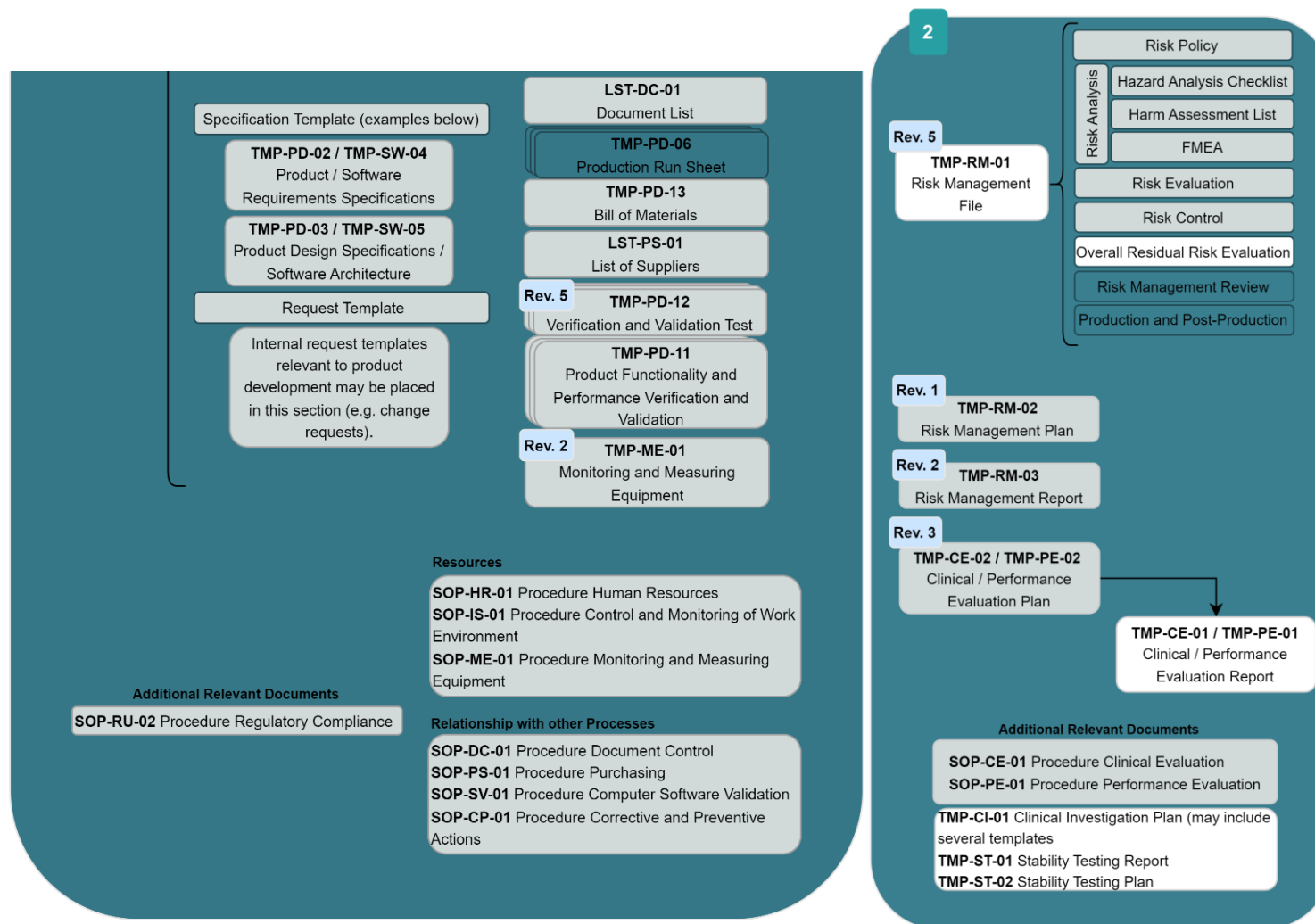


Figure 35. Additional templates related to the Product Development (on the left) and the Risk Management Procedures (on the right) of the Design Validation Phase (Phase 4).

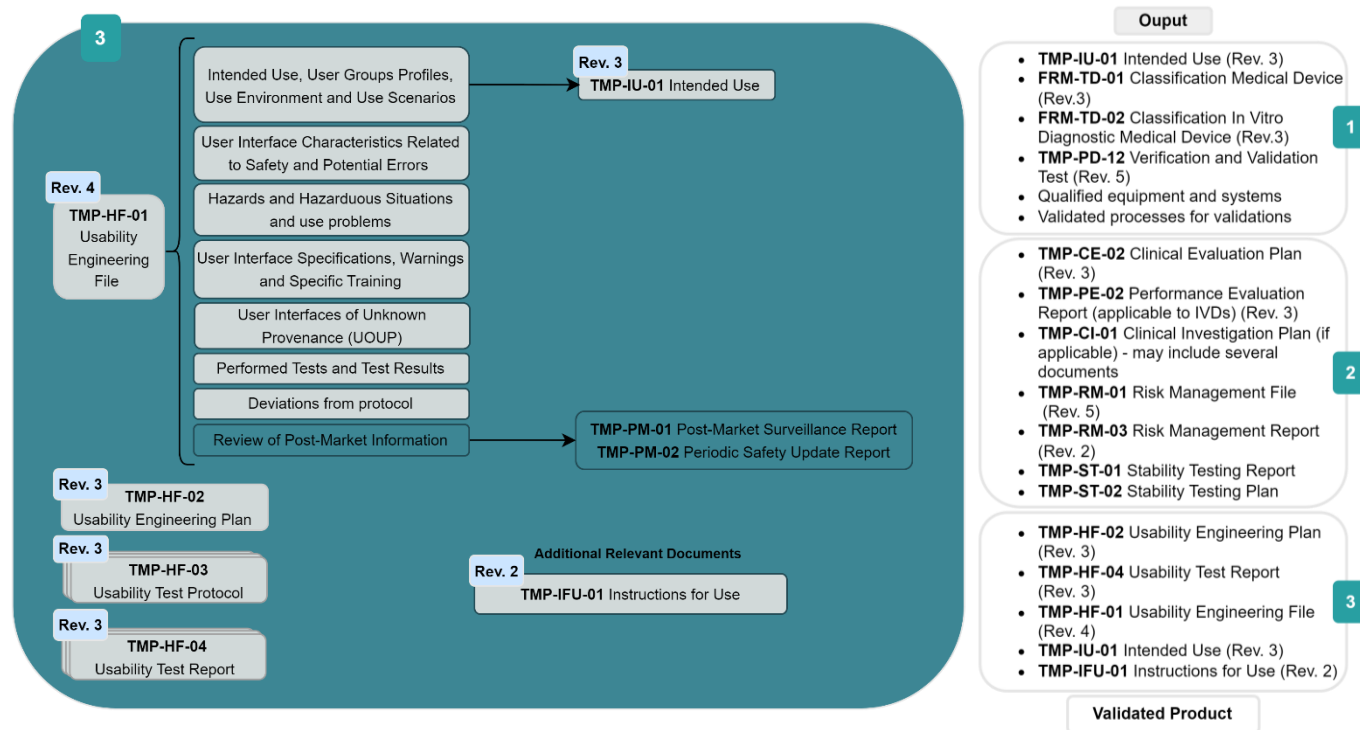


Figure 36. Templates related to the Usability Engineering Procedure (on the left) and outputs (on the right) of the Design Validation Phase (Phase 4).

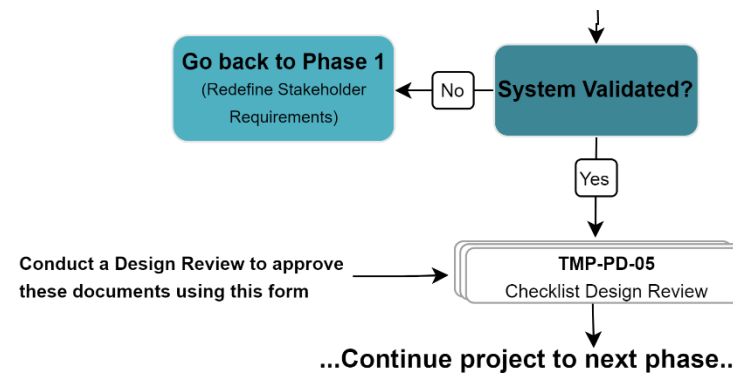


Figure 37. Decision Making after the Design Validation Phase (Phase 4).

7.3.6 Design Transfer to Production (Phase 5)

Design transfer ensures that the proper versions of final production specifications are suitable for manufacturing and that the manufacturing processes have the capacity to produce the launch volumes of a product. While it is preferred to conduct design validation with products from the final manufacturing process, employing products manufactured in similar processes is acceptable.

Involving the production team early in the development process ensures an effortless transition from product development to manufacturing. The Head of Production and Product Development and the Project Manager, or someone with a similar position, collaborate to complete the design transfer according to the Product Development Plan by submitting a production request.

The production team is responsible for drafting product-specific manufacturing instructions, including inspection stages. Specifications for in-process and end-product inspections are derived from the product requirements and design specifications and are documented in a Production Run Sheet (TMP-PD-06 Production Run Sheet), as described in the Procedure for Production and Service Provision (SOP-PD-02 Procedure Production and Service Provision). The production team, in collaboration with the Risk Manager, or someone with those responsibilities, conducts a risk assessment following the Procedure for Risk Management (SOP-RM-01 Procedure Risk Management) to identify critical steps in the production process and determine the appropriate risk control measures. The quality control team then prepares the necessary test instructions for in-process and end-product controls, validating each test method.

Successful design transfer ensures that all manufacturing processes and equipment, including packaging and labeling, are qualified for producing the finished device. It also guarantees that manufacturing output consistently meets the specified versions approved for the launch device, that quality control acceptance criteria are fully defined, that design and associated documentation are under full change control, and that necessary quality audits and agreements are completed. Additionally, it establishes the supply chain, identifies backup or alternative suppliers, and validates all test fixtures for production use.

Documentation describing the manufacturing and quality control testing procedures and materials is transferred and controlled. A formal record of the design transfer is maintained and subjected to document control, ensuring that all necessary documents for the complete medical device record are compiled.

7.3.6.1 Framework

Figure 38 provides the inputs for the design transfer to production stage and the revisions and documentation related to product development required for this stage. Additionally, **Figure 39** presents all additional information related to product development and the one concerning the risk management procedure. Finally, **Figure 40** provides all templates related to the usability engineering procedure and the outputs for this phase.

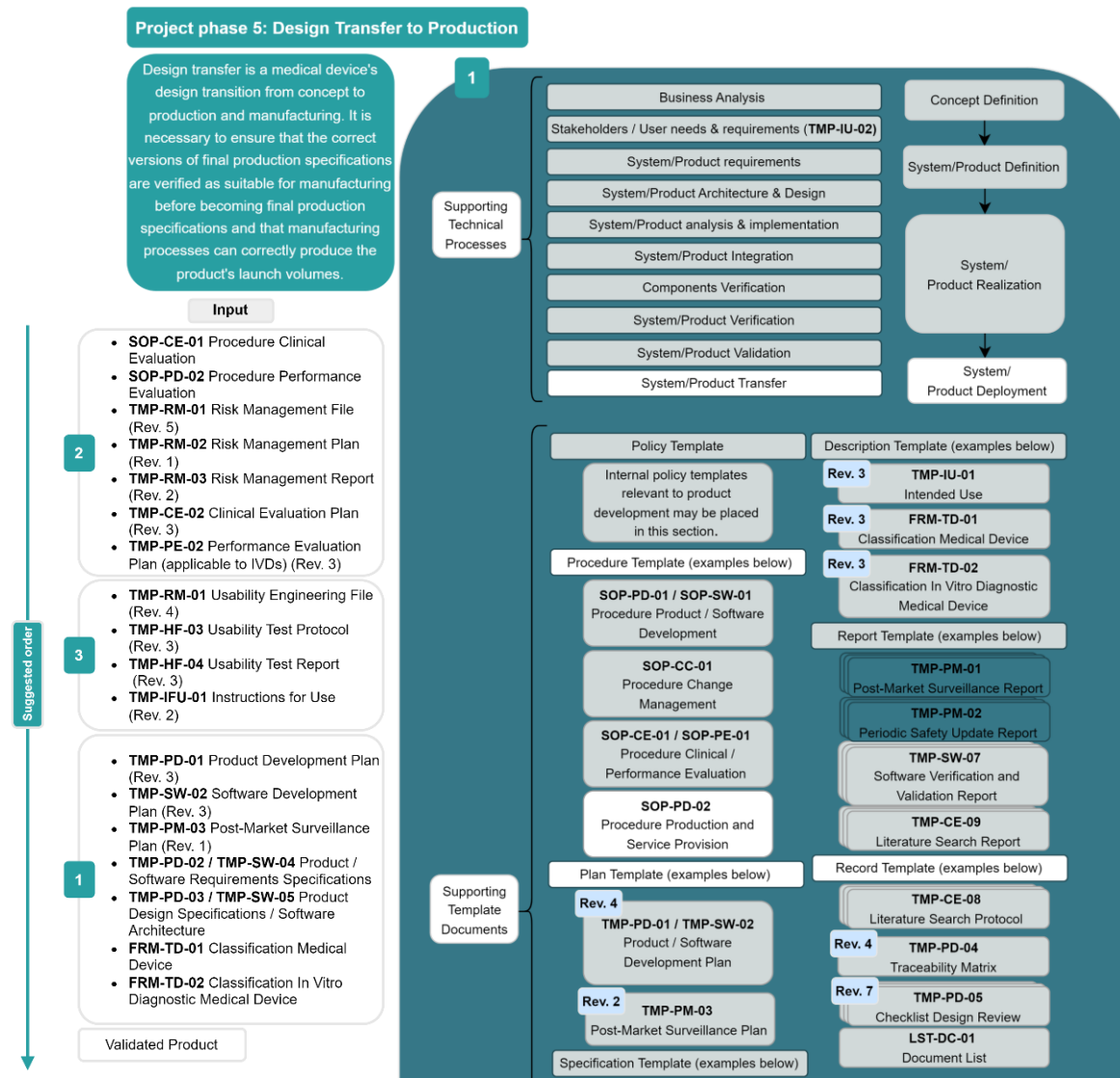


Figure 38. Inputs (on the left) and templates related to the Product Development Procedure (on the right) of the Design Transfer to Production Phase (Phase 5).

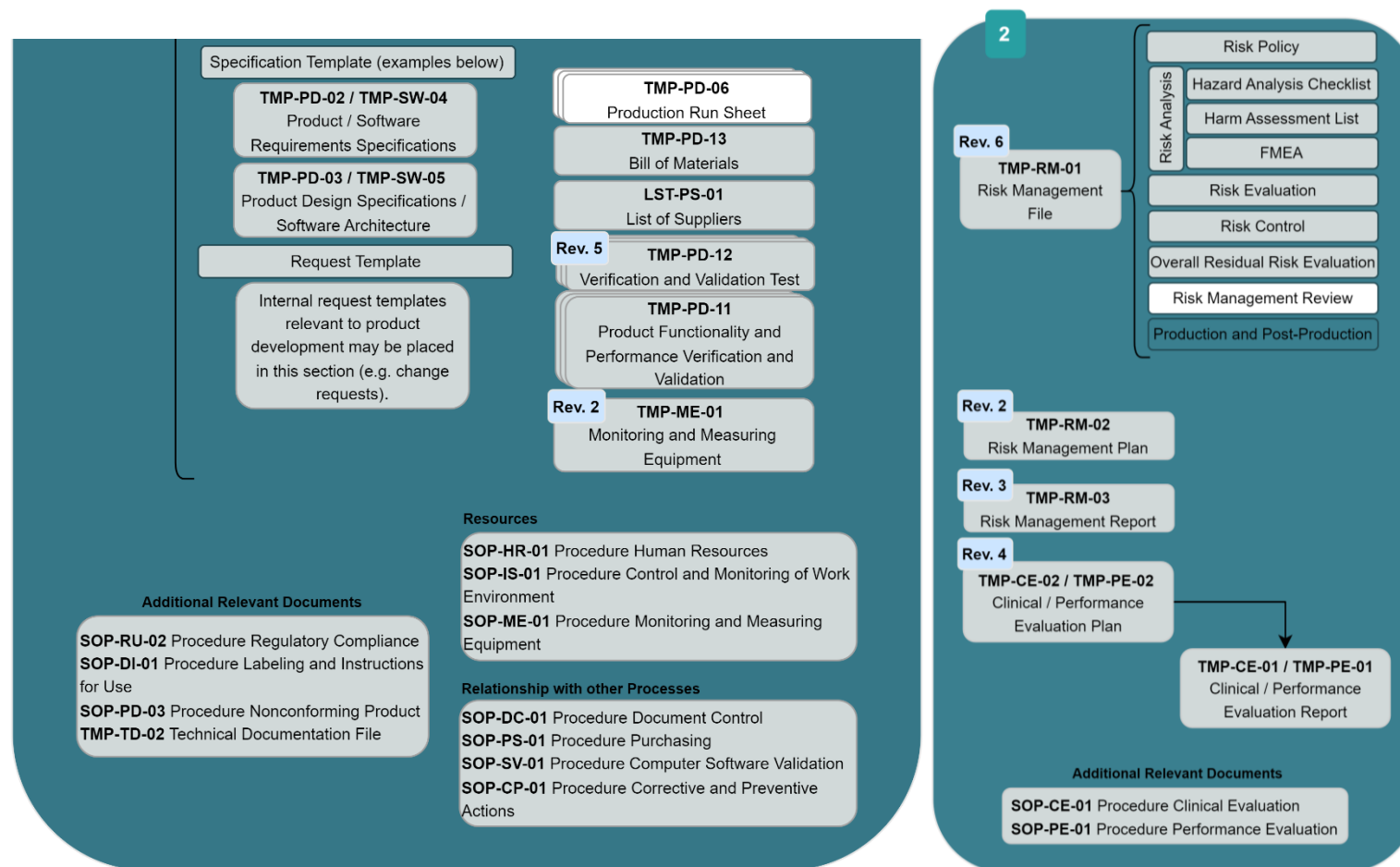


Figure 39. Additional templates related to the Product Development (on the left) and the Risk Management Procedures (on the right) of the Design Transfer to Production Phase (Phase 5).

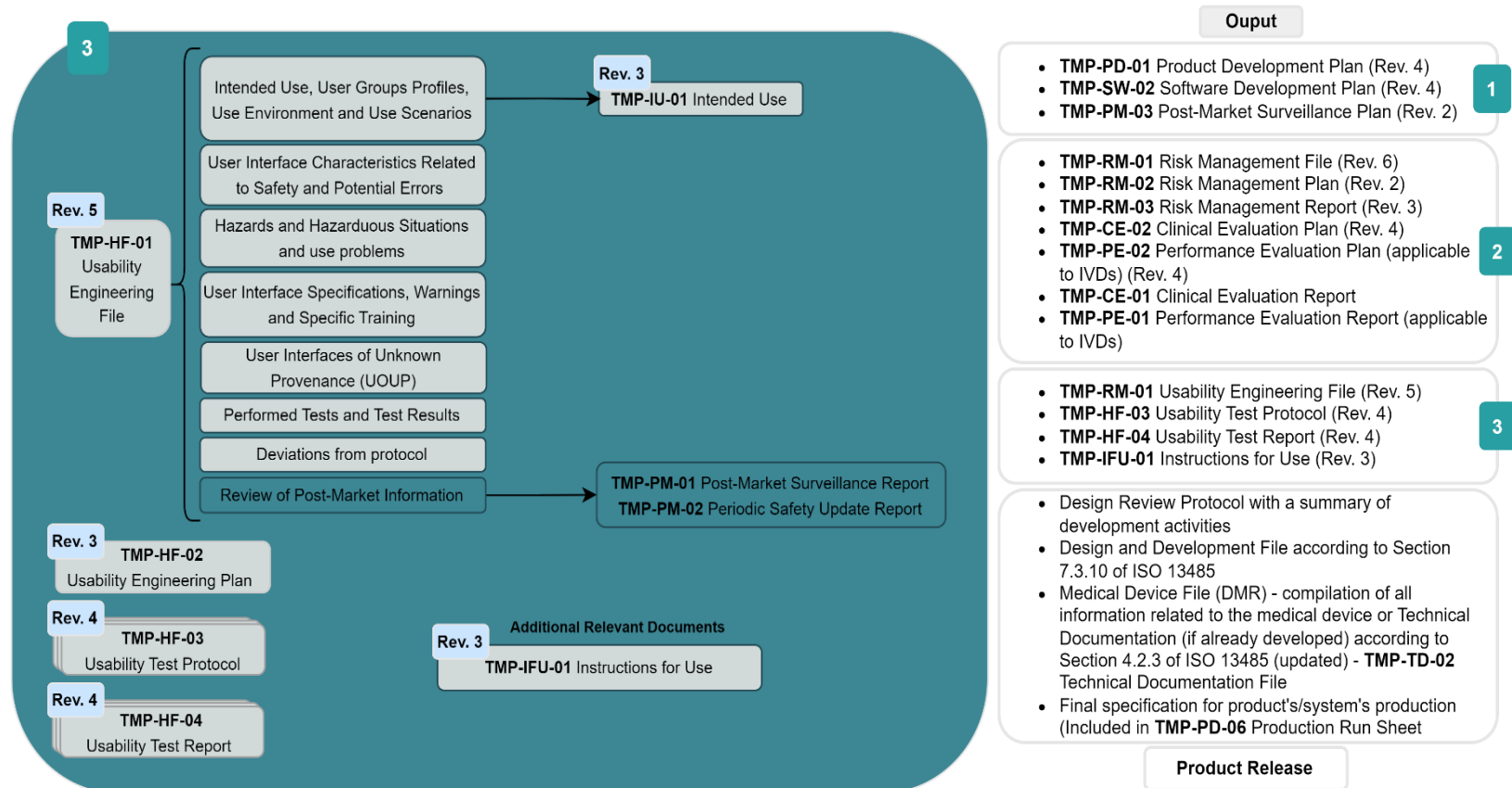


Figure 40. Templates related to the Usability Engineering Procedure (on the left) and outputs (on the right) of the Design Transfer to Production Phase (Phase 5).

7.4 Digitalization Options in the Case Studies

While using the framework for QMS implementation and TD development, the two companies mentioned in the case studies used several digital tools and platforms to manage the required documentation for each phase of the MD development. These were used to facilitate real-time collaboration, manage documents, and for traceability purposes.

7.4.1 Case Study 1

In the first case study, most templates and SOPs were managed and created using Microsoft Sharepoint and the company's internal cloud. This platform allowed real-time collaboration on documents such as the intended use, software architecture, and technical documentation files. The team could keep track of all modifications made to the documents and clarify possible doubts.

Jira was used for traceability purposes, such as developing the traceability matrix template and defining software requirements specifications. It was also employed to track the progress of document creation and approval. SoftComply (a Jira add-on) was used for risk management activities and related documentation, such as the Risk Management File.

Finally, the digital tool Confluence was used to manage the entire MDSW developed by the company.

7.4.2 Case Study 2

In the second case study, Google Drive was the primary digital tool and platform used for TD management. All documents were maintained in Google Docs format to allow multiple team members to work on them simultaneously and guarantee quick feedback and revisions.

All suppliers for the MD development were managed in Notion to keep track of all the relevant information related to the suppliers in case any issues were detected during the development and verification of the MD.

All software developed by the company was managed and saved in GitHub. This digital platform was essential for software version control to track changes and review software-related documentation efficiently.

7.5 Challenges and Learnings from Case Studies

7.5.1 Case Study 1

The first case study highlighted substantial obstacles in developing the TD and implementing the QMS for MD certification.

The organization's primary challenges were time management and project prioritization. Despite the company's prior healthcare experience, its workload and projects periodically impacted QMS adoption and TD development, causing delays in both processes. In more mature organizations, such as the one in this case study, leadership often prioritizes long-term strategic objectives, such as profitability or market growth, and not the specific procedures necessary for regulatory compliance. The company had challenges in obtaining an ongoing commitment to QMS and TD development, as leadership frequently perceived these procedures as burdensome rather than integral elements of MD certification. This often resulted in insufficient priority and urgency in adhering to specific deadlines.

The organization had previous expertise in other QMS implementations, having obtained ISO 9001 certification. This indicated that essential quality procedures and policies were already established inside the company, promoting a clear understanding that quality should be embedded across all departments rather than being just the responsibility of the quality department. The key challenge, however, was adjusting the present procedures to meet the ISO 13485 standard's requirements for MD

certification. Although both standards focus on QMS, ISO 13485 defines more detailed and specific requirements due to its influence on patient safety. The shift to ISO 13485 required that the firm alter its current processes to meet different demand levels for the standard certification.

The company also faced some organizational challenges due to relevant personnel leaving the organization. Several key team members who were more involved with the QMS and TD development left the company, creating delays in the process. Furthermore, despite the company's prior implementation of ISO 9001, this adoption lacked a digital approach and was not executed with streamlined automation. This caused several challenges in transmitting knowledge to their replacements. Many had different mindsets or were unfamiliar with the company's policies.

Additionally, the company resisted change. These more mature companies often develop strict organizational policies and processes over time. This can provide stability and make adapting to new procedures and rules more challenging. Older systems and established practices might be challenging to overcome, making it more difficult to comply with increasingly demanding requirements, such as those stated in ISO 13485. In this case study, despite the company's long record of successful projects, many employees were used to procedures that did not comply with MD certification. Despite the organization's well-established quality practices, implementing MD-specific standards posed a considerable operational modification. A more organized change management strategy, good communication, and leadership focused on the long-term advantages of these procedures would have facilitated the transition.

These challenges highlighted that even if a company has been in the market for an extended period, it may struggle to adapt to new procedures. Staff turnover, difficulties transferring knowledge, and aversion to change can all negatively impact the company's success. Proper prioritizing and effective change management can assist in overcoming these issues.

7.5.2 Case Study 2

The second case study faced substantial obstacles, which brought attention to common issues that startups or less mature organizations sometimes suffer, particularly when implementing a QMS and developing a TD for MDSW certification.

A significant obstacle they faced was insufficient documentation from the beginning of the QMS implementation and a lack of management tools. Crucial data regarding, for instance, testing, purchasing, suppliers, or other procedures must be kept available in an easily accessible form since the beginning of developing such a product given it is crucial for the certification process. The lack of records resulted in communication gaps across several departments and required last-minute measures to comply with all requirements for the certification. Detailed information was also restricted to some departments or kept on paper, impacting the flow of information. These issues could have been mitigated if digital tools or platforms had been used and applied to the company's procedures and TD to avoid communication and documentation issues.

Another major challenge was related to the poor engagement of other departments in quality management. The quality-related responsibilities of this organization were limited to the quality department, leading to a segregated approach that might limit the effective administration of quality measures. Quality should not be limited to a specific department. Instead, it should be integrated across the entire organization. In my opinion, the quality department has a vital role in establishing and outlining quality policies and procedures. For that, it needs top management support, which must be made a priority for the entire company. Nevertheless, the effective execution of these initiatives relies on their incorporation into the day-to-day activities of every department inside the organization. This issue might be alleviated by offering further training to all staff members within the company as well as implementing procedures to ensure that every employee takes responsibility for the quality of their work.

When quality becomes embedded in the company's culture, people naturally prioritize quality in every activity they do.

One of the most critical barriers was the limited time required to implement and certify the QMS. The start-up had no previous knowledge or adoption of the ISO 9001 standard, which could have been beneficial in implementing ISO 13485. Ideally, the company would have been certified for ISO 9001 to understand and enforce the general management of an organization. Once that was embedded within the company, they could have tried implementing ISO 13485 specifically for their IVD. More general procedures related to the company's policies, procedures, and environment would have been already implemented that way. Also, an extended deadline would result in a more reliable QMS implementation.

Finally, the lack of skilled personnel for MD certification had a tremendous impact on implementing and certifying the company's QMS. This highlighted the necessity for focused recruiting or training to address these organizational drawbacks and gaps.

8 Final Remarks

8.1 A Framework to Guide Medical Device Development at Different Stages

The developed framework was designed to guide companies of various sizes and maturity levels through all phases of the MD development, focusing on the QMS procedures and templates and all required TD. It was developed to fulfill all requirements mandated by ISO 13485, ISO 14971, the MDR and IVDR, and additional standards like IEC 15288. The framework was built with a structured approach, yet it was intended to be adaptable to each type of MD and company.

The framework was structured around six phases of MD development: concept (phase 0), planning (phase 1), design and development (phase 2), design verification (phase 3), design validation (phase 4), and design transfer to production (phase 6). Each phase was built on the preceding one, allowing for iterative activities between phases to conduct constant reviews, resolve issues, and update documents. The framework also included methods for change management to help handle all changes successfully. If verification or validation steps failed, the framework guaranteed that all modifications were managed according to pre-established change control procedures, with the possibility of returning to previous stages. This phased approach was established to assist companies with allocating resources and managing timelines.

The framework was centered on three essential fields: product development, risk management, and usability engineering. The product development section covered the entire MD concept and design. This included defining stakeholder requirements, product/software specifications, product design specifications, software architecture, and traceability documentation, such as the Traceability Matrix. It also covered documentation on verification and validation tests, such as the product functionality and performance verification and validation template, as well as documents related to the required equipment and purchasing, like monitoring and measuring equipment, bill of materials, and list of suppliers templates. The framework was also focused on the risk management procedure and related activities to guarantee proper documentation, identify and mitigate risks throughout the entire MD lifecycle, and comply with all requirements mandated by ISO 14971. The framework was finally focused on usability engineering to guarantee the proper use of the MD before and after market launch and to guarantee it complied with IEC 62366-1.

This framework was designed to be adaptable and ensure that all MDs and companies can apply it. In certain phases, simpler devices may require less description or detail. In more complex MDs, additional verification and validation activities, additional usability testing, or more detailed documentation might be necessary to comply with all requirements. This guarantees significant adjustability and suitability for a variety of MDs.

This project is essential for MD development and forthcoming certification. The framework encompasses all policies, procedures, and documentation pertinent to QMS implementation, consolidating all operations associated with device development, risk management, and usability engineering, which are essential for acquiring the CE marking. Due to the lack of studies on this subject, this framework was established to assist organizations without expertise in producing high-quality and compliant MD efficiently, simplifying the process as much as possible.

8.2 A Guide for the Implementation of Digital Tools for Medical Devices Software Manufacturers

Digital technologies have become essential in MDSW development, as they facilitate demonstrating and maintaining compliance with several regulatory requirements.

Nowadays, digital tools are essential for managing documentation, ensuring traceability, and complying with standards like IEC 62304 for MDSW development. Agile approaches like Scrum and digital platforms such as Jira, Confluence, Polarion, and Greenlight Guru have been recognized as essential for enhancing project management and TD procedures. However, several technologies provide significant obstacles, especially when substantial customization is necessary.

While software development is typically quick, the development of a medical device, given the requirements, may take a toll on organizations. Therefore, the development of MDSW is sometimes hard, especially for smaller organizations. It comprises many strictly regulated procedures to guarantee the safety and efficacy of MDs. Companies face an increasing array of regulatory requirements, particularly in the health sector. Guidance documents and regulations like MDR and IVDR, GDPR, the AI Act, and various cybersecurity and environmental requirements add challenging complexity, especially for smaller organizations. To guarantee compliance with these requirements, companies often need the implementation of digital tools or guided support. Consequently, methodologies such as Agile may benefit MDSW development due to their flexibility, emphasis on brief iterations, rapid feedback, stakeholder collaboration, and adaptable strategies. It is appropriate for projects characterized by rapidly changing requirements or increased competition in the product domain. Agile approaches provide benefits, including improved quality, sustainable development, technical proficiency, and applicability in later stages of development. Nevertheless, documentation poses a substantial obstacle to implementing agile methodologies in safety-critical contexts. MD projects require documentation to ensure reliability and security, and the agile approach prioritizes functional software development over extensive documentation. A variant of Agile is the Scrum model, which relies on process control theory in software development to improve versatility, adaptability, and efficiency. It offers consistent feedback and balances preliminary and just-in-time tasks.

When addressing challenges related to TD, Jira and Confluence tools can be essential, as, for instance, traceability is crucial in MDSW development and documentation management. Jira is suggested to improve traceability and the implementation of software requirements. It aids software teams in controlling issues, tasks, and requirements, facilitates bug tracking, and facilitates approval processes. Confluence is a knowledge management system designed for companies that allow users to maintain extensive TD, structured data storage, production, and editing.

Greenlight Guru and Polarion are among the top tools for MDSW development. Polarion is a lifecycle management application tool mainly utilized in regulated industries such as healthcare and MD development. It enables teams to manage requirements, architecture, risks, tests, revisions, configurations, and versatile projects. Polarion consolidates all processes in one platform, facilitating traceability and transparency. It offers online documents with trackable objects, audit trails, configurable workflows, and the ability to freeze content and workflows for seamless interactions with third-party tools. Greenlight Guru Clinical is a digital platform that collects clinical data for post-market clinical follow-up and pre-market MD trials, facilitating data extraction and management from interconnected devices or software.

Nowadays, digital tools are becoming more innovative, incorporating AI and ML features. They have been frequently used for software development to automate repetitive processes, enhance decision-making, and guarantee regulatory compliance. They include features to track requirements, conduct tests, validate, and evaluate risks. AI can help make predictions, recommendations, or decisions for a defined set of objectives, influencing how documents are written, and processes are implemented. ML

can train AI algorithms to improve tasks based on the received data. This can help in automating repetitive actions or information. In TD development, AI or ML features can provide complete device descriptions based on documents already performed for other MDs, saving much time. One of the most crucial benefits of integrating AI and ML features into digital tools is its impact on making learning more accessible. For instance, it provides translation tools, chatbots, and error-detection features that could easily help reduce errors.

The Complear platform is among these innovative solutions, and it facilitates product classification, regulatory knowledge management, and compliance. It further provides automated electronic TD (eTD) submission preparation and an electronic QMS (eQMS). The classification feature aids users in identifying the regulatory requirements applicable to their products. The platform uses AI to provide response recommendations based on a sequence of inquiries, justifying each response. The platform enhances cooperation in design and development by allowing team members to work on various product variation scenarios. The training module provides context-specific training to aid users in comprehending the documentation required at different phases of the product lifecycle, hence enhancing compliance. The AI Copilot tool suggests content for product items, recognizes relationships among them and advises on completing certain parts. The AI also identifies potential risks, highlights absent tests, and maintains consistency across documents, assisting users in producing complete and precise records. Complear's eQMS solution facilitates the development of eTD through automated workflows and procedures, guaranteeing consistency and precision. The eTD module offers version control and approval processes, ensuring accurate document management across the device lifecycle.

Despite the regular use of digital technology, several organizational obstacles remain. The significant obstacles include financial expenses, data privacy issues, security concerns, data gathering and integration challenges, and the absence of standardized protocols. Small companies usually struggle to allocate infrastructure, technology, and qualified employee resources. Also, the increasing complexity of regulatory requirements can overwhelm smaller organizations that lack digital tools and proper support. On the other hand, more mature organizations are affected mainly by data breaches and illicit data utilization. When discussing outdated systems, data gathering and integration pose significant challenges. Standardization is also a concern, as companies are cautious about acquiring technology that may not comply with future regulatory requirements and standards. Creating new digital tools to overcome these main concerns would benefit all businesses. New tools could focus on reducing costs, offering diverse plans suitable for both small and large companies, and providing explicit guidelines for use. Additionally, one of the most critical advancements would be delineating the primary benefits and applicable features that could enhance the specific characteristics of a company and its MD. This would significantly improve the compliance process and motivate organizations to adhere to these solutions.

9 Conclusion

9.1 General Conclusion

This work aimed to present an in-depth overview of MDSW certification within the EU, following the MD and IVD regulations and other relevant guidance documents and standards, like MDCG guides and IEC 62304. The focus was on several essential requirements for certification, including implementing a QMS and developing a TD centered on MDSW. It provided insights into contemporary digital tools and platforms to improve and simplify these operations.

The case studies helped understand most MD manufacturers' difficulties when implementing a QMS and TD, particularly within smaller and less mature organizations. These processes may frequently be affected by organizational issues, insufficient financial and technological resourcing, or a lack of expertise in the field. Fortunately, digital tools can help minimize these challenges by efficiently managing documentation, ensuring traceability, and improving internal communication. Several tools like Jira, Confluence, and Polarion were highlighted for their role in MD certification.

Additionally, digital tools now integrate AI and ML features to automate repetitive tasks, enhance decision-making, and ensure compliance. For instance, platforms like Compear facilitate product classification, regulatory knowledge management, and automated document submission through AI features. These tools also assist in risk assessment, content generation, and document consistency, significantly reducing manual effort and enhancing precision. AI and ML features can predict risks, improve document management, and ensure consistency across the product lifecycle.

However, despite these advantages, there are still significant challenges related to these technologies' customization, integration, and adaptability in highly regulated sectors like MD development. The technologies may offer benefits in managing documentation and ensuring traceability, although adapting them to fulfill specific requirements is not always a simple process. Smaller companies usually struggle with the need for customization to meet all regulatory requirements, often lacking resources for this adaptation. Furthermore, integrating digital solutions requires considerable effort, especially in companies with long-established processes and policies. An additional challenge is the high cost of employing this digital technology. Offering different plans so all types of companies can use these tools would benefit and ease their employment. There are also a lot of concerns related to data security and compliance with data protection in bigger organizations that deal daily with sensitive information. Another concern is the lack of clear procedures and guidance for implementing these tools. The missing recommendations cause concerns among companies who are hesitant to invest in solutions that may later fail to comply with updated regulations or standards. All these challenges still need to be overcome before digitalization becomes an integral part of an organization.

One of the most considerable contributions of this work was developing and testing a framework for implementing a QMS and TD in MDSW development projects. This framework was tested in real-world scenarios on the companies stated in the case studies. This work specified all documentation, procedures, and information required to design and develop an MD. For better understanding, the framework was divided into six main phases: concept, planning, design and development, design validation, design verification, and design transfer to production. The focus was on three essential procedures: product development, risk management, and usability engineering. This staged methodology intends to assist and guide companies during the entire QMS implementation and MD development process, which is frequently demanding. This work was designed to accommodate different types of MDs, allowing high flexibility to fulfill a wide range of projects.

In conclusion, one of the key purposes of this work was to provide all of the resources needed for developing a TD and implementing a QMS for MDSW certification. To address the previously raised research questions, developing an always-updated Technical Documentation for MDSW entails

incorporating an effective document management system that allows for real-time updates, integrates automated data, and assures traceability. Incorporating digital technologies can help with documentation, allowing for periodic assessments and modifications as needed. To address the second research question, adapting the implementation of a QMS to a company's various phases and maturity levels demands a tailored approach that considers the specific challenges that organizations encounter. Start-ups and smaller companies may benefit from developing frameworks appropriate for their resources and capabilities, while more mature organizations can use sophisticated approaches to optimize their QMS processes. Ensuring that QMS implementation is flexible and iterative will assist in accommodating different maturity levels and enable continual development. However, significant obstacles must be overcome before fully recognizing the advantages of digitization in this field. The section on future work discusses options for further growth, improvement, and study.

9.2 Future Work

This research helped better understand how digital tools and appropriate guidance, such as frameworks, may help with compliance and promote innovation in digital health and MD development. Integrating AI and ML into future-developed digital tools will become increasingly important as the regulatory landscape evolves and requirements become more complex.

During this study, some limitations were encountered, providing opportunities for future research. The developed framework was evaluated in a limited number of case studies. Applying it to different types of MDs and organizations may reveal additional challenges in the certification process. Future studies could look at the use of this framework in additional highly regulated projects to understand its impact further.

For future work, handling financial costs, data privacy issues, and security concerns with new digital tools adapted to different companies is critical. New digital tools that are tailored to the demands of organizations and adaptable to various project types are also necessary. It would be helpful to investigate how these technologies may help companies, particularly less mature ones, overcome some of the challenges related to MD certification. Developing established protocols for using digital tools within organizations could also help overcome data collection and regulatory compliance issues.

Another area of research could involve creating tools that include AI and ML features to assist companies in understanding and implementing a QMS and TD for MD or MDSW. These might give specific guidance, helping organizations navigate the complexities of the certification process, particularly those with less maturity and less qualified personnel.

All of these topics are open to further investigation.

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Appendix

A. Appendix A



Figure A.1. Linear medical device development model (based on Ref. [1]).

Phase I					Phase II		Phase III		Phase IV	
Deliverables	Marketing – needs assessment & validation, competitive analysis, SWOT, overview of business opportunity	Identification of core team members	Part / component drawings, assembly drawings, and packaging drawings generated	Design Validation completed						
	Financial – forecast, preliminary cannibalization analysis	Approval of general project timeline	Material specifications defined	Assure design outputs satisfy inputs						
	R&D – early stage technical risk assessment and design inputs	Design inputs approval / Identification of target specifications	Design risk assessment (dFMEA) updated with action items	Process risk analysis and process plan completed						
	Legal – preliminary IP landscape review	Project concept documentation	Verification and validation (V&V) test matrix created	Design risk analysis updated and reviewed						
	Regulatory – regulatory plan and clinical path	Proposed concept evaluation (bench top, animal testing, physical evaluation)	Verification protocols approved, testing performed, reports written	Risk management plan reviewed to ensure risk is at acceptable level						
	Reimbursement – early stage reimbursement strategy	Preliminary legal review to verify the right to use a proposed device	Quality and process validation plan created	Product branding, catalog numbers assigned						
	Business Plan for the device	Initial regulatory plan established	Clinical investigation plan created	Legal clearance obtained						
		Initial design risk assessment (dFMEA)	Regulatory submission completed	Manufacturing and operations launch preparation						
		Design for manufacturing (dFM) initiated	Manufacturing strategy further developed	Sales and marketing team launch preparation						
		Comprehensive concept definition		Supplier qualification						
				Reimbursement strategy finalized						
Phase I					Phase II		Phase III		Phase IV	
Decisions at Gates	There is a market opportunity	Product development is ready to begin, based on user needs and design inputs	Design Outputs satisfy requirements from Design Inputs	Validation testing shows that the device conforms to user needs & requirements						
	The market impact is determined (i.e., breakthrough, line extension, etc.)	The products offer customer value. It is a viable and sustainable product.	Device has an acceptable design risk level	Verification testing shows that design outputs satisfy design inputs						
	Project risk from a regulatory and IP perspective is acceptable	The device's technical feasibility is proven and optimized.	Device can be developed from an IP perspective; there are no IP violations	Device is ready and cleared for launch, from an IP and Regulatory perspective						
	The device has an intended regulatory class (Class I, II or III)	Manufacturing and value chain confidence has been assessed.	Design is frozen	Design transfer complete - design prints to manufacturing specifications						
	Device is ready to transfer from concept to active project status		Device is ready for regulatory submission	Process and Design Risk are acceptable (DFMEA, PFMEA)						
	Device fits company strategy			Sales reps are equipped to sell the product to physicians; acceptable LMR sites have been established						
				Inventory levels are acceptable.						
				Launch quantities are available						

Figure A.2. Deliverables and decisions at gates for Phases 1 to 4 of a product development process ([1]).

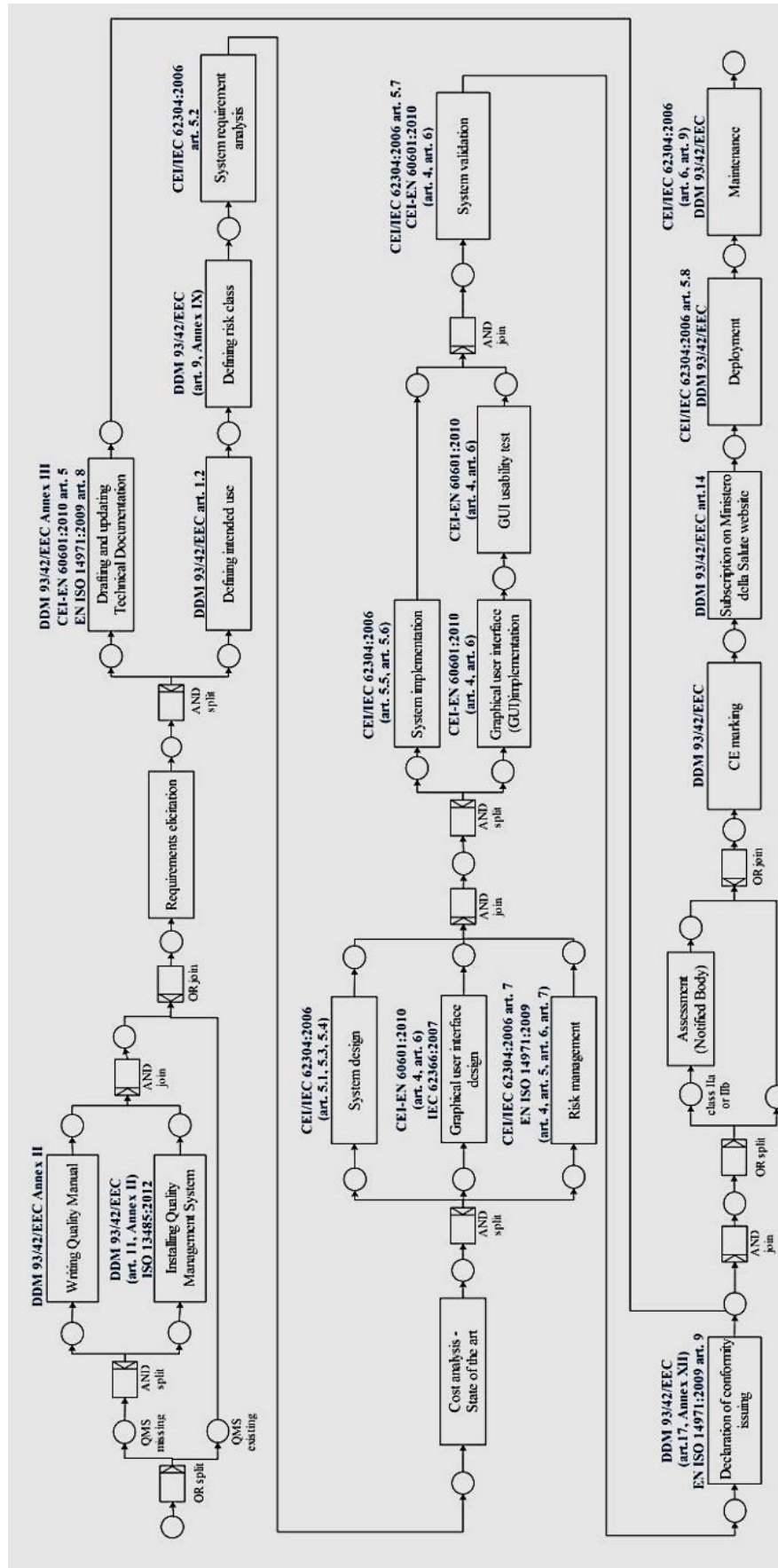


Figure A.3. Diagram showing activities needed for the development of MDSW. It also includes activities related to developing generic software that were not used for the dissertation. For each activity, the reference regulations are specified (adapted from [1]).

B. Appendix B

Table B.1. Description of the templates presented in the framework for QMS implementation.

Name of Template	Purpose and Scope
SOP-RU-02 Procedure Regulatory Compliance	To understand the applicable regulatory requirements and ensure their compliance. Applicable when a company's management intends to introduce a new or updated MD to the market or a new market and communication with the regulatory entities.
SOP-CC-01 Procedure Change Management	Description of methods for planning and handling modifications on the devices and/or services of the company and their design development after they have been released, as well as for handling relevant changes to the QMS that may impair the performance and/or conformity of the company processes, such as outsourcing a process to an external service provider, changing a critical supplier, or changing the scope of the QMS. It applies to all changes in the QMS, the company's product development, production, and services, except changes in documents and templates already covered by SOP-DC-01 Procedure Document Control.
SOP-PD-01 Procedure Product Development	Description of product design and development methods that enable the secure development of the specified quality in conformity with regulatory and normative requirements. It applies to all MD development activities, whether in the initial development phase or maintenance stage of existing products.
SOP-PD-02 Procedure Production and Service Provision	Description of MD's production and service provision process, ensuring adherence to demanded quantity, deadlines, and product quality as requested by customers.
TMP-PD-01 Product Development Plan	Description of the development plan for an MD to be certified. It specifies or transfers the product development requirements described in the SOP-PD-01 Procedure Product Development.
TMP-PD-02 Product Requirements Specifications	Description of the requirements for a product. It functions as an input for the device's developer team to understand what technically needs to be performed and provides information for the product testers to develop test specifications.
TMP-PD-03 Product Design Specifications	Description of the design and development outputs of the MD to be developed. It defines responsibilities and provides the device's components view, as well as the overall product view and their functions.
TMP-PD-04 Traceability Matrix	To track and link all activities related to the design and development process, such as stakeholder requirements, product requirements, product requirements specifications, and design verification and validation.
TMP-PD-05 Checklist Design Review	To verify the device's design review at each phase of the design and development process. It outlines the activities, the company's responsibilities, and the personnel accountable for the review.
TMP-PD-06 Production Run Sheet	Verify that documentation and activities are completed before a new device version is released. It clearly identifies the device and provides information regarding the production preparation, manufacture and deviations, label checking, the final inspection, and the product release.
TMP-PD-11 Product Functionality and	Summary of the product functionality and performance verification and validation activities, as described in SOP-PD-01 Procedure Product Development and specified in the TMP-PD-01 Product Development Plan. It includes testing protocols and reports with evidence of compliance with design requirements, including

Performance Verification and Validation	measurement accuracy and range, outputs generated, and stability, among others, integration and system testing, electrical safety and electromagnetic compatibility testing, measuring function testing, and stability testing.
TMP-PD-12 Verification and Validation Test	To document all performed tests related to the product's verification and validation stages, as described in SOP-PD-01 Procedure Product Development. It outlines the component or device to be tested, the execution data, the tester's name, tests, acceptance criteria, recorded evidence, expected and actual results, and applicable standards.
TMP-PD-13 Bill of Materials	Description of the bill of materials for all components related to the MD. It includes the components' manufacturer, serial or lot number, description, purchase quantity, and type.
SOP-SW-01 Procedure Software Development	Description of software design and development methods that enable the secure development of the specified quality in conformity with regulatory and normative requirements, avoiding unnecessary interactions, rework, non-conformities, and communication efforts. It applies to all software development activities for software that qualifies as an MD or components of a product that qualifies as an MD, whether in the initial development or maintenance of existing products.
TMP-SW-02 Software Development Plan	Description of the development plan for software qualified as an MD or software component of an MD to be certified. It specifies or transfers the software development requirements described in the SOP-SW-01 Procedure Software Development.
TMP-SW-04 Software Requirements Specifications	Description of the requirements for software. It functions as input for the device's developer team to understand what technically needs to be performed and provides information for the software testers to develop test specifications.
TMP-SW-05 Software Architecture	Description of the software's architecture for the technical implementation of the software requirements. It aims to serve as input for the developers or programmers to technically realize the device, give future project members a quick overview of the structure of the software system, and provide the test team with sufficient information on how the software components are successfully assembled and tested during integration tests.
TMP-SW-07 Software Verification and Validation Report	Summary of the software verification and validation activities, as described in SOP-SW-01 Procedure Software Development and specified in the TMP-SW-02 Software Development Plan. It includes code reviews, unit testing, software integration and system testing, penetration testing and vulnerability scanning, AI algorithm validations, and usability testing.
TMP-RM-01 Risk Management File	It provides initial guidance on identifying hazards and risks based on standards, guidelines, questions, and/or examples. It also provides an initial top-down analysis of all harms a user, property, or environment can get when using, manufacturing, and disposing of the product. The risk management file additionally provides an initial bottom-up of all the failures that can lead to a hazard and a compilation of the hazards identified through different methodologies, information mandatory by ISO 14971, and information that should be assessed according to the complexity of the device and the risk management process implemented.
TMP-RM-02 Risk Management Plan	It is a plan concerning risk management that encompasses the entire lifecycle of the MD, from development to disposal. It includes clear identification of the device, a defined risk management process, delineation of responsibilities, establishment of risk acceptance criteria, documentation requirements, integration with the QMS, post-market surveillance procedures, risk related to interoperability, risk communication strategies, periodic review and updating, compliance with regulatory requirements, change management procedures, and contingency planning.

TMP-RM-03 Risk Management Report	It reports from following the risk management plan. It includes clear identification of the device, delineation of responsibilities, risk management activities and deviations from procedure risk management, risk analysis, and evaluation, risk control, verification of risk control measures, assessment of single and overall residual risk, risk management review, and information regarding production and post-production phases.
TMP-HF-01 Usability Engineering File	It consists of a report summary of usability engineering, which includes all performed tests and their outcomes related to the usability engineering process, user interface characteristics related to safety and potential errors, hazards and hazardous situations, warnings, and interface specifications. This template additionally provides post-market information.
TMP-HF-02 Usability Engineering Plan	Description of the usability evaluation plan (in conformity with IEC 62366-1:2015+AMD1:2020) to evaluate the effectiveness, efficacy, and user satisfaction of the MD's user interfaces in the intended use environment and to assess and mitigate risks associated with the incorrect use of the device's interfaces.
TMP-HF-03 Usability Test Protocol	Protocol for specific usability tests, including test scenarios and acceptance criteria. Its primary focus is to assess the device's safety and effectiveness to improve overall usability.
TMP-HF-04 Usability Test Report	It consists of a report for specific usability tests that includes relevant details of usability test performance and the tests' results. The primary focus of this evaluation is to define how safe and effective the device is when used while aiming to improve overall usability.
SOP-TD-01 Procedure Technical Documentation	Description of all the information that must be included in the TD, such as the device's description and specifications, GSPRs, benefit-risk analysis, among others, the TD structure, and maintenance. It applies to all MD technical files regardless of their class, either for one or a group of MDs.
TMP-TD-02 Technical Documentation File	It consists of a compilation of all relevant documents/information about an MD. It provides a complete device description, including the trade name, principles of operation and/or mode of action, technical specifications, materials, and key functional elements, the intended use, medical purpose and intended purpose of the device, the MD qualification and risk class classification, the device identification, novel features, market history, and similar devices. It also includes information supplied by the manufacturer, such as the declaration of conformity, EU target countries, and user information. The technical documentation file also refers to design and development information, such as the different stages, product design specifications, and manufacturing information, the GSPRs, benefit-risk analysis and risk management, device verification and validation activities, such as biocompatibility, electric safety and electromagnetic compatibility, software verification and validation, stability, and performance and safety. It additionally provides information regarding the clinical evaluation, post-market surveillance and clinical follow-up, packaging and transport testing, and sterilization.
FRM-TD-01 Classification Medical Device	To classify the device according to Annex VIII of the MDR. It provides specific definitions and descriptions of each classification rule defined in the MDR so that the manufacturer can justify why particular rules don't apply to their MD and find the one that does.
FRM-TD-02 Classification In Vitro Diagnostic Medical Device	To classify the device according to Annex VIII of the IVDR. It provides specific definitions and descriptions of each classification rule defined in the IVDR so that the manufacturer can justify why particular rules don't apply to their MD and find the one that does.

SOP-HR-01 Procedure Human Resources	Description of the procedure to ensure employees are sufficiently qualified and competent concerning their skills and training to ensure the QMS's efficacy and the MD's development. It applies to all employees who impact the quality of the products and services.
SOP-IS-01 Procedure Control and Monitoring or Work Environment	Description of the procedure for monitoring and controlling the work environment to ensure product and service conformance when work environment conditions adversely affect product quality. It additionally identifies the infrastructure elements, their needs, and related activities. This procedure applies to all processes related to product development, as well as production, storage, and shipping.
SOP-DC-01 Procedure Document Control	To establish the methodology for managing internal and external documentation related to the QMS and to ensure the adequacy, access, and availability of documentation and information to support QMS compliance. It covers all QMS documents and records, including internal, external, physical, and digital documents.
LST-DC-01 Document List	To keep track of all information related to existing documentation within a company, such as the documents' title, status, type, ID, area, version, author, and requirements compliance.
TMP-IU-01 Intended Use	Description of the manufacturers' perspective of each device's purpose, process, or service. It defines how a product's specification, instruction, information, or procedure must be followed to guarantee that the device serves its purpose.
TMP-IU-02 Stakeholder Requirements	Description of customer, user, and other stakeholder requirements, including requirements regarding delivery and post-delivery activities, applicable regulatory requirements, user training specifications for the MD's safe performance, and additional requirements relevant to the device's development.
TMP-IFU-01 Instructions for Use	It consists of a user guide with instructions for use (IFU) in the languages accepted in the Member States where the device is envisaged to be sold. It contains information about the device's intended purpose, indications, contra-indications, and other safety-related information, such as side effects and warnings aligned with the risk management, clinical evaluation, usability, and pre-clinical performance data. It may include how users can report malfunctions, clinical incidents, lost passwords, or potential security breaches and a description of algorithms, e.g., for machine-learning-based MD. It must be complemented by a user manual, installation, surgical technique, and service manuals if applicable. The IFU must contain all information specified within the MDR Annex I GSPR 23.
SOP-CE-01 Procedure Clinical Evaluation	To provide instruction for performing a clinical evaluation of the MD developed by a company to demonstrate MD safety, performance, and clinical benefits according to the requirements outlined in the MDR. It applies to all personnel involved in the clinical evaluation process, including clinical researchers, regulatory affairs, and quality assurance.
SOP-CE-02 Procedure Post-Market Clinical Follow-Up	To define the post-market surveillance activities involved in continuously gathering, appraisal, and assessing the clinical data after the MD has been placed on the market. Its purpose is to update the manufacturer about the device's performance and identify potential issues that may arise in the post-market phase. It applies to all personnel involved in the clinical evaluation process, including but not limited to clinical researchers, regulatory affairs, and quality assurance.
TMP-CE-01 Clinical Evaluation Report	It documents the clinical evaluation and implementation of an MD's clinical strategy. Based on data considered appropriate to the strategy, it aims to demonstrate the device's safety, performance, and clinical benefit requirements. The clinical evaluation report follows the TMP-CE-02 Clinical Evaluation Plan.

TMP-CE-02 Clinical Evaluation Plan	It is used to plan a device's clinical evaluation and clinical strategy. It aims to specify the MD's clinical safety and performance characteristics and describe the procedure and criteria for providing clinical evidence to comply with the safety, performance, and clinical benefit requirements for the MD. The clinical evaluation plan should be continuously updated, considering the state of the art and any new information about the MD.
TMP-CE-05 Post-Market Clinical Follow-Up Plan	It is compiled along with concluding the clinical evaluation and is based on the TMP-CE-01 Clinical Evaluation Report. It specifies the methods used to collect and evaluate clinical data to confirm the safety and performance of the device, including the clinical benefit, if applicable, throughout its expected lifetime, identify and monitor previously unknown side-effects and contraindications, identify and analyze emergent risks based on factual evidence, ensure the continued acceptability of the benefit-risk ratio referred in Annex I of the MDR, and identify possible systematic misuse or off-label use of the device, to verify that the intended purpose is correct. The scope of the post-market clinical follow-up plan is limited until the end of the lifecycle of the device or generic device group.
TMP-CE-08 Literature Search Protocol	To document literature search and identify all relevant available published data to demonstrate, for instance, clinical performance, safety, or state of the art for an MD.
TMP-CE-09 Literature Search Report	To document literature search and identify all relevant published data to demonstrate, for instance, clinical performance, safety, or state of the art for an MD, according to TMP-CE-08 Literature Search Protocol.
TMP-CI-01 Clinical Investigation Plan	Plan of investigation reflecting the latest scientific and technical knowledge to confirm or refute the manufacturer's claims regarding the safety, performance, and aspects relating to the benefit-risk determination of MD. It sets out the rationale, objectives, design methodology, monitoring, conduct, record-keeping, and method of analysis for the clinical investigation.
SOP-PE-01 Procedure Performance Evaluation	To provide instruction for performing a performance evaluation of the IVD developed by a company to demonstrate device safety, performance, and clinical benefits according to the requirements outlined in the IVDR. It applies to all personnel involved in the clinical evaluation process, including clinical researchers, regulatory affairs, and quality assurance.
TMP-PE-01 Performance Evaluation Report	It demonstrates the clinical evidence for an IVD and is an essential element of the conformity assessment with the GSPRs according to the IVDR. It aims to summarize the results of evaluating scientific validity and safety and the IVD's analytical and clinical performance. It also aims to demonstrate that the device is safe and achieves the intended clinical benefits when used as intended. The performance evaluation report includes the scientific validity report, the analytical performance report, and the clinical performance report. It also comprises a qualified assessment of the resulting data to demonstrate the clinical benefit and safety of IVDs by weighing benefits against risk considering state of the art.
TMP-PE-02 Performance Evaluation Plan	It is used to continuously plan, conduct, and document the performance evaluation of an IVD. It aims to specify the IVD's characteristics and performance, describe the process and criteria to generate the necessary clinical evidence, and demonstrate the device's safety. The performance evaluation plan should be continuously updated, considering the state of the art and any new information about the IVD.
SOP-PM-01 Procedure Post- Market Surveillance	Description of the Post-Market Surveillance process. It ensures that new information about safety and performance is proactively collected and can be used as input for risk management, clinical/performance evaluation, and device development. The procedure applies to all MDs placed on the market.

TMP-PM-01 Post-Market Surveillance Report	To report device/device-family-specific post-market surveillance activities (as defined in the TMP-PM-03 Post-Market Surveillance Plan) to assess the device's safety, quality, and performance throughout its life cycle. It highlights the safety and performance issues of the device that were identified by the post-market surveillance activities, including background information related to the risk-benefit profile and information on the intended benefit. This report also clarifies if the benefit-risk ratio changed negatively or positively based on the summarized results of the report and includes significant changes identified in previous reports, such as new risks.
TMP-PM-02 Periodic Safety Update Report	To report a summary of device/device-family-specific post-market surveillance activities to assess the device's safety, quality, and performance throughout its life cycle. Its goal is to identify and evaluate changes in the benefit-risk profile and provide information on Corrective or Preventive Actions.
TMP-PM-03 Post-Market Surveillance Plan	Plan device-specific post-market surveillance activities to assess the device's safety, quality, and performance throughout its life cycle. It includes information regarding the MD type or MD family, including accessories, regulatory classification, the jurisdiction where the device is available, the expected lifetime of the MD, expected number of uses or usage frequency, intended use, available data related to the MD's safety and performance, including clinical data, and lifecycle stage regarding product and technology maturity concerning the state of the art.
SOP-DI-01 Procedure Labeling and Instructions for Use	Description of the procedure for assignment and labeling, as UDI, labeling according to MDR/IVDR Annex I, and traceability of devices during production. It also helps understand the information needed in the instructions for use.
SOP-VI-01 Procedure Vigilance	Description of methods for processing and reporting incidents and field safety corrective actions. It applies to all MD's incidents and required field safety corrective actions that occurred in the EEA.
SOP-ME-01 Procedure Monitoring and Measuring Equipment	To guarantee precise measurements and proper monitoring of MD and related processes to ensure valid results with sufficient accuracy, precision, stability, and analytical performance for their intended purpose. It applies to all monitoring and measuring equipment influencing the device's QMS quality.
TMP-ME-01 Monitoring and Measuring Equipment	Description of all monitoring and measuring equipment influencing the device's quality. It includes all equipment's ID, description, version, manufacturer, location, responsible person and their competencies, date of acquisition, purpose, maintenance required, calibration information, and use status.
SOP-PS-01 Procedure Purchasing	Description of the products and services purchased. It includes supplier evaluation, budget approval, and continuous supplier surveillance. This procedure applies to all products and services that may impact the quality of the MD and/or QMS.
LST-PS-01 List of Suppliers	Identification of the critical MD's suppliers, including the supplier's name, purchase description, status, criticality, certification, evaluation, impact on the device, possible issues or nonconforming purchases, terms of payment, and other relevant information regarding the supplier. It also includes all purchases, their QMS and minimum requirements, acceptance criteria, required quantity, date of supply, and additional observations.
SOP-SV-01 Procedure Computer Software Validation	To ensure that the software/computer systems used and the safety and performance of the MD throughout their lifetime are validated. It applies to all software/computer systems relevant to the QMS, software used in production and service provision, and/or software used for monitoring and measuring requirements concerning the MD.

TMP-ST-01 Stability Testing Report	To report the results and conclusions of stability testing regarding the device's lifetime, including shelf life, in-use stability, and recommended shipping conditions as defined in the TMP-ST-02 Stability Testing Plan. It includes the protocol followed for testing, the batch(es) involved, all results obtained, data analysis, acceptance criteria with pass/fail determination, and conclusions regarding stability.
TMP-ST-02 Stability Testing Plan	It aims to evaluate an MD's ability to maintain its physical, chemical, and functional properties over time under specified storage conditions. The primary objective is to ensure the device remains safe and effective throughout its intended shelf life, in-use, and shipping stability according to MDR and IVDR. Stability testing is crucial for verifying the safety and efficacy throughout an MD's lifecycle during the verification and validation phase. It assesses how a device performs under various environmental conditions and validates its lifetime, considering design input during development.
SOP-CM-01 Procedure Feedback and Complaints Management	To describe the entire feedback and complaints handling procedure. It applies to all feedback and complaints that affect the MD and services under the QMS.
SOP-CP-01 Procedure Corrective and Preventive Actions	To describe the methods for analyzing the cause of problems and nonconformities, planning, conducting, and documenting resulting corrective and preventive actions (CAPAs), and reviewing the effective implementation. It applies to all processes and fields of the QMS.
SOP-IA-01 Procedure Internal Audit	Description of how internal audits are planned, performed, and documented and how to manage audits in general, including supplier audits and audits by NB, Designated Authorities, and other entities. Its goal is to determine and improve the effective implementation and ensure compliance of the QMS and its process with relevant regulations and standards. It applies to all QMS processes and procedures.
SOP-MR-01 Procedure Management Review	Description of the management review procedure to improve the adequacy, suitability, and efficacy of the QMS, guarantee compliance of processes with the quality policy, evaluate the achievement and suitability of quality objectives, prove compliance with customer and regulatory requirements, assess opportunities for improvement or changes to the QMS and assess the need for further resources to ensure the QMS efficacy through periodic management review. It applies to all QMS processes and procedures.
SOP-MR-02 Procedure Data Analysis	Description of the methods to analyze data to determine and improve the suitability, adequacy, and effectiveness of the QMS. It also defines the use of statistical techniques for establishing, controlling, and verifying the acceptability of process capability and product characteristics. This procedure applies to all analyzed data, including the one generated by measurements and monitoring activities.