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Conformity of Medical Device Regulation in Health Technology Company

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Medical devices are regulated in Europe by a new law from 26.5.2017 onwards. The name of the law is Medical Device Regulation (EU) 2017/745, MDR for short. The goal of this Master's thesis was to provide the case company with recommendations on the actions that have to be taken to comply with the requirements set forth in the law, so that sales in Europe can continue when the transition period of the previous directive ends.

The research was carried out by analysing the current state of the company; what had already been done for MDR. After this, recommendations were created for fulfilling the requirements that still required actions. The recommendations were evaluated by 12 specialists working in the company, and they were updated based on these evaluations.

The theory section of this thesis is a comprehensive information package on the new regulation. It provides information about its effects on different stages of the approval process, for example quality management, risk management, incident reporting, UDI, and post-market surveillance systems. In addition, the new requirement on the person responsible for regulatory compliance and the new European electronic database (Eudamed) are described. The recommendations and their evaluation are described in the practical section.

The actions taken based on the evaluated recommendations, which are the final results of this research will eventually be audited by a notified body. This may affect the recommendations by making them even more comprehensive. However, the recommendations presented in this thesis are a good basis for fulfilling the requirements set forth in the new regulation. Because of the new law, fulfilling the requirements will be more time-consuming than before, and the need for documentation will increase. Special emphasis is given on the increased requirements for the risk management system and clinical evaluations throughout the life cycle of the product.

The Commission's goal for the regulation is to remove the room for interpretation from the legislation, meet the challenges of developing technology, exclude problems that had occurred in use, improve safety and people's health and support the functioning of the internal market while also maintaining the spirit of innovation. With the help of the recommendations, the case company can for their part help the Commission to reach this goal.

Keywords	medical device regulation, 2017/745, MDR, health technology

Contents

List of Abbreviations and Terms

AR	Authorized Representative
CAMD	Competent Authorities for Medical Devices
CAPA	Corrective and Preventive Action
CEN	European Committee for Standardization
CENELEC	European Committee for Electrotechnical Standardization
CER	Clinical Evaluation Report
COCIR	The European Coordination Committee of the Radiological, Electromedical and Healthcare IT Industry
DoC	Declaration of Conformity
Eudamed	European Database on Medical Devices
FDA	Food and Drug Administration (USA)
DoA	Date of Application
Fimea	Finnish Medicines Agency
FSC	Free Sales Certificate
FSCA	Field Safety Corrective Actions
GSPR	General Safety and Performance Requirements
HRI	Human Readable Interpretation
IMDRF	International Medical Devices Regulators Forum
IN-VITRO / IVD	Diagnostics of samples taken from the human body (Regulation 2017/746)
MAUDE	Manufacturer and User Facility Device Experience (FDA)
MD	Medical Device
MDD	Medical Device Directive
MDR	Medical Device Regulation
MEDDEV	Guidance Documents to Assist Stakeholders in Implementing Directives Related to Medical Devices
NANDO	New Approach Notified and Designated Organizations, Database of Notified Bodies
NB	Notified Body
NEN	The Royal Netherlands Standardization Institute
OEM	Original Equipment Manufacturer
OJEU	Official Journal of the European Union
PMCF	Post-Market Clinical Follow-Up
PMS	Post-Market Surveillance
PRRC	Person Responsible for Regulatory Compliance

PSUR	Periodic Safety Update Report
QMS	Quality Management System
SFS	Finnish Standards Association
SOP	Standard Operating Procedure
SRN	Single Registration Number
STED	Summary of Technical Documentation
TDA	Technical Documentation Assessment
UDI-DI	Unique Device Identification - Device Identifier

1 Introduction

1.1 Background of Medical Device Legislation

The development of legislation is often lagging behind, and this is the situation also in the case of medical devices. In the US, the regulation of such devices began in 1938 when the FFDCA regulation (Device regulation under the federal food, drug, and cosmetic act [1]) became effective. In Europe, each country had its own legislation until the European Union was formed and medical device directives [2] that bind all countries in the EU were created (*Medical Device Directive* (MDD) 93/42/EEC, *Active Implantable Medical Device* (AIMD) 90/385/EEC, *In Vitro Diagnostic Device* (IVD), 98/79/EC). From the beginning of the 1990s, each country applied these directives as a part of their own legislation.

However, it has been known for several years that the medical device directives need updating. The interpretation and application of the regulations in different countries caused differences of interpretation even between authorities, the technology used in the devices develops all the time, and the problems with the use of medical devices (such as the breast implant scandal in France that gained international attention in 2010) required that the requirements be checked and tightened. Therefore, two regulations based on the earlier directives were published in 2017 (the Medical Device Regulation (MDR) and the In Vitro Diagnostic Regulation (IVDR)), with transition periods of 3 and 5 years. The new regulations have to be taken into use in each member country as such, so they are no longer open to interpretation. The Commission's additional goal for the regulations is to improve safety and health, and support the functioning of the internal market while maintaining the spirit of innovation.

1.2 Current Challenges in Europe

If a company wants to sell medical devices in Europe, the entire life cycle of the product (including design and manufacturing and the lifetime expectancy) has to comply with the current EU legislation for medical devices. During this research the transition period is ongoing in Europe, and two separate legislations are effective at the same time. In May

2020, the period of validity of the current regulation ends, and then, at the latest (in theory, it is already possible) the companies that want to continue operating in the field have to start operating in compliance with the requirements set forth in the new regulation (MDR), and to get an approval for their declaration of conformity from an external notified body, depending on the risk class, like has been done before with MDD. MDR will thus replace the current directive and national legislation as such.

The current status of the notified bodies is problematic. In autumn 2017, guidelines were published regarding what is required from these bodies in the future concerning the regulation that became effective in spring 2017 (MDR). Because many of the currently MDD compliant notified bodies want to achieve MDR compliance as well, the submitted compliance applications have piled up for the EU authority that approves the notified bodies. Because of this, there are no notified bodies in Finland, and not many elsewhere in the world, either, that are approved to operate as a notified body according to the new regulation (situation in April 2020). The earlier implications that these notified bodies would get their approval six months before the end of the transition period have not, for the most part, actualised, and the pressure that these bodies will have a massive amount of companies trying to get approval for their declarations of conformity within the set time limit grows all the time.

In addition to the current lack of MDR compliant notified bodies there are also other challenges in the transition to MDR. The harmonised standards approved in the directive are not MDR approved yet, and the Eudamed database, which will be used to save information about economic operators, notified bodies, certificates, unique device identifiers (UDI), serious incidents, clinical evaluations, and post-market surveillance, is not in use.

Originally the regulation was planned to be effective on 26.5.2020 (Date of Application, DoA), but now the deadline will probably be delayed by a year till May 2021. The requirements set forth in the new regulation and the incomplete structures in relation to its tight schedule are a big challenge to European authorities and notified bodies, as well as to economic operators.

1.3 Transition from legislation to another as a company level

The case company (founded in the 1970s) designs, manufactures, and markets medical devices for dentistry in Herttoniemi, Helsinki. The main market area for the company is Europe, but the products are exported all over the world. The company has a valid MDD certificate, which certifies that the operations comply with European legislation. Thus, the products can be marked with a CE mark at the moment (situation in April 2020). However, this certificate will expire eventually, and it cannot be renewed anymore in accordance with the MDD. In order the business operations can continue in Europe and also in several other countries where EU approval is used fully or in part to achieve marketing authorization, some activities have to be updated or modified to comply with the new regulation. Because of this, the company has ordered this research to identify and adopt the new obligations. As a result of this research, the company is provided with recommendations on how the requirements set forth in the regulation are to be implemented, which will contribute to making it possible to continue business operations in Europe and globally.

1.4 Scope

The topic of this research is the new European legislation for medical devices: Medical Device Regulation (EU) 2017/745, MDR in short. The research is thus limited in accordance with the regulation to medical devices only, excluding in vitro devices, which have a separate regulation (Regulation on in vitro diagnostic medical devices (EU) 2017/746). The regulation defines medical device as any device, instrument, or software intended by the manufacturer to be used for human beings for medical purposes, such as diagnosis or treatment of disease or injury or investigation of a physiological state.

Considering the case company's role in the market and its product portfolio, there are several limits set for the research to concentrate on for example mass-produced and its current risk class devices which have been manufactured in Europe. Table 1 (below) lists the contents of this research, and also what has been left out.

Table 1: Contents and exclusion criterias of the research

Contents of the research	Not included in this research
Medical devices	In vitro devices
Manufacturer obligations	The obligations of importer, distributor, and authorised representative (AR)
Products manufactured in Europe	Products manufactured outside Europe
Mass-produced devices	Custom-made devices
Risk class I, Im, IIa and IIb devices	Risk class III devices
Conformity assessment method based on quality management system and the evaluation of technical documents	Conformity assessment method based on type examination
Non-sterile devices	Sterile devices
Devices currently in the market	New devices

2 Medical Device Regulation (MDR)

The first purpose of this Master's thesis is to give an overall idea of what obligations the new regulation determines. The expiring MDD directive (93/42/EEC) and the new MDR regulation (2017/745) contain mostly the same basic requirements for manufacturers and products. The number of old requirements has not decreased, but new requirements have been added.

Because the new MDR has over 20 articles that bind the manufacturer, and more than 10 applicable annexes, the content is limited to the parts that are the most relevant for the case company. They address the other goal of this thesis – provide the case company with recommendations on actions to be taken to comply with the requirements set forth in the regulation.

2.1 Definitions and Scope

The notification drawn up by the Union, Factsheet for Manufacturers of Medical Devices [3], describes how the definitions have slightly changed when moving from the directive to the regulation. To ensure shared understanding at the EU level, 57 new definitions for terms have been added to the regulation. Some of the main examples of these new definitions are Unique Device Identifier (chapter 2.2.9), Clinical Data (chapter 2.3), Clinical Evidence (chapter 2.3) and Serious Incident (chapter 2.4.2), all of them are explained more in the chapters listed after definitions.

The scope of Medical Device Regulation follows basically the same lines as the current directive MDD. Regulation [4] says: "Regulation lays down rules concerning the placing on the market, making available on the market or putting into service of medical devices for human use and accessories for such devices in the Union." There are still some extensions in MDR, which shall be taken into the consideration when determining, if the device fall in the scope of regulation.

The first example is, as Emergo, a company specialising on international consulting, writes in their notification Understanding Europe's New Medical Devices Regulation [5], that the new regulation will place requirements also on some devices that do not have a

medical purpose. One example of this kind of products is contact lenses. Another example is described in the Commission's instructions Factsheet for Manufacturers [3]: "Software, which have medical purpose, whether embedded or not, falls within the scope of MDR." Previously this kind of software were mostly non-medical devices. Third example are the devices for cleaning, disinfection or the sterilization of devices, which will now be considered as medical devices, whereas before they were only accessories to medical devices, says Petri Pommelin, former Finnish competent authority (1992-2006), in his book *Survival Guide to EU Medical Device Regulations* [6].

2.2 General Obligations for Manufacturers

The new regulation lists several different obligations and recommendations for manufacturers throughout the life cycle of the device. The most essential ones are explained below. Clinical compliance (chapter 2.3) and post-market surveillance (chapter 2.4) are separated into sub-chapters because of their extensive content.

2.2.1 Person Responsible for Regulatory Compliance (PRRC)

One of the new requirements of the regulation is that the manufacturer has to have in their organisation permanently (midsize and large companies) or continuously available (micro and small companies) at least one person responsible for regulatory compliance (PRRC). If there are more than one person, the division of responsibilities has to be defined in a written form. The person must be formally qualified for the task. The qualification is attained either through an appropriate university degree and one year of work experience, or by four years of work experience about regulatory affairs related to medical devices or quality management systems. The person has to be registered in Eudamed (when available). In addition, it has been defined that the person must not be legally in weaker position within the organisation because he or she is performing the duties. In Finland, health technology, including PRRC, is supervised by Fimea (Finnish Medicines Agency).

PRRC is responsible, for example, for making sure that product conformity is assessed appropriately before the device is placed in the market, technical documents and declaration of conformities (DoC) are drawn up and kept up to date, post-market surveillance obligations are fulfilled, and authorities and, depending on the device, the notified body

and partners in the target country (economic operators) are informed and the necessary notifications are given. COCIR (European coordination committee of the radiological, electromedical and healthcare IT industry) recommends limiting the person's liability with an agreement between the person and the company. In addition, they recommend that the responsible person takes a personal liability insurance for possible legal consequences [7].

2.2.2 Classification of Devices

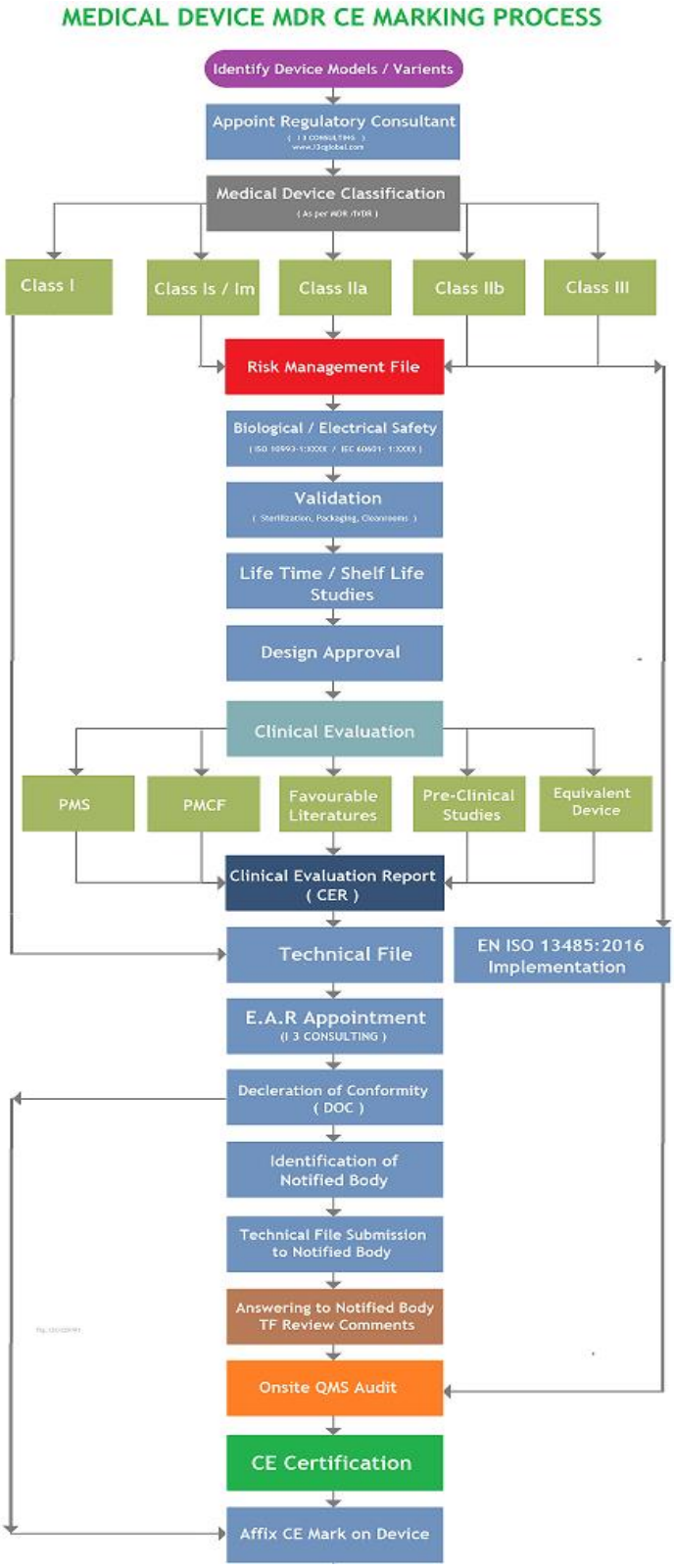
The classification of medical devices into different risk classes is already used in the expiring directive. The new regulation does not bring significant changes to this. The classes (I, IIa, IIb and III) stay the same, and devices are still placed in the classes based on their purpose of use and typical risks. However, noteworthy changes are the new rules 9 for nanomaterials and 11 for software programs, which elevate them to medical devices. The guidance document on the classification of medical devices "MEDDEV 2.4" [8] is still a very useful document according to Petri Pommelin [6] when the manufacturer analyses the classification of their products. The notified body and the Competent Authorities for Medical Devices (CAMD) in a European manufacturing country help with the classification if needed.

The case company's devices will probably stay in their current classes (I, Im, IIa and IIb), with the elaboration that the situation of software has to be re-evaluated because of the adoption of MDR. The product range of the company in question does not include nanomaterials or products that contain them.

2.2.3 Conformity Assessment Procedures

The conformity assessment procedure in the Union depends on the risk class of the device both in the current directive and in the new regulation. The case company's products are currently in risk classes I, Im, IIa, and IIb, and the assumption is that this will not change, so the focus in this chapter is on the assessment procedures of these classes. For the company's current devices, the directive-compliant approval is based on the quality system (93/42/EEC Annex II, Excluding Section 4), and the plan is to continue using it, as applicable, even after the new regulation becomes effective. In the regulation, the selected route is called "Conformity assessment based on a quality management

system and on assessment of technical documentation" (Annex IX). There are several, risk class depending stages in the approval process, depicted in picture 1.



Picture 1: Medical Device MDR CE Marking Process [9]

When a device, for which an application for EU approval is planned, has been identified, its risk class is determined. There are specific classification rules for this purpose in the regulation. For devices in the lower risk class (class I), it is enough in the future if they have a technical file and a declaration of conformity. For devices in higher risk classes, the use of a notified body, the existence of a quality system, and more specific post-market surveillance are required. The approval requirements of the regulation by risk class are presented in table 2 below.

Table 2: Requirements for risk classes

	TDA	PMS	DoC	NB	QMS	PSUR
Class I	X	X	X			
Class Im	X	X	X	X	X	
Class IIa	X	X	X	X	X	X
Class IIb	X	X	X	X	X	X

TDA = Technical Documentation Assessment
PMS = Post Market Surveillance
DoC = Declaration of Conformity
NB = Notified Body
QMS = Quality Management System
PSUR = Periodic Safety Update Report

The presence of the notified body in the conformity assessment procedure will continue as it is now: it is obligatory for class Im, IIa, and IIb devices. The case company will probably continue cooperation with the current notified body, assuming that it gets the MDR qualification it has applied for.

The case company has many devices approved for the European market according to the current directive. The adoption of the regulation brings about the following changes:

- The device approvals compliant with the directive are valid until 26.5.2024 at the most, if significant changes are not made to them, after which they expire automatically. The validity requires MDD compliant yearly follow-up audits.
- After 26.5.2020 it is not possible to apply for an MDD approval anymore, and therefore only MDR approvals are possible from that date onward (if there is an MDR-approved notified body then).

In practice, this means that if an MDD approval expires between May 2020 and May 2024, an MDR approval has to be applied for the device if the company wants to continue selling it. If major changes are made to the product after May 2020, an MDR approval

has to be applied for it. There is a need for MDR approval in 2024 the latest. It is, of course, possible to prune the current product portfolio, in which case the approvals will expire and the marketing authorizations cease on their own. If possible, it is recommended to already apply for MDR-compliant approvals for new devices, so that the eventual reapproval process will be easier.

2.2.4 Harmonized Standards

The Finnish Standards Association (SFS) summarises the definition of a standard as follows [10]: A standard is a shared procedure for repeated actions. Standards are recommendations by nature, but authorities may require that they be used. A standard is a written publication, and it is approved by an authority, organization, or other recognized body that is responsible for standardization. In order to make the manufacturing of regulation-compliant devices easier, the EU requests European organizations of standardization to draw up detailed standards to expand on directives and regulations. They are given an official status as additions to directives by mentioning them in the Official Journal of the European Union (OJEU). Standards retain their voluntary nature, but the products that fulfil the requirements of the standards are deemed to fulfil the requirements of the regulations insofar as they concern things in essential requirements.

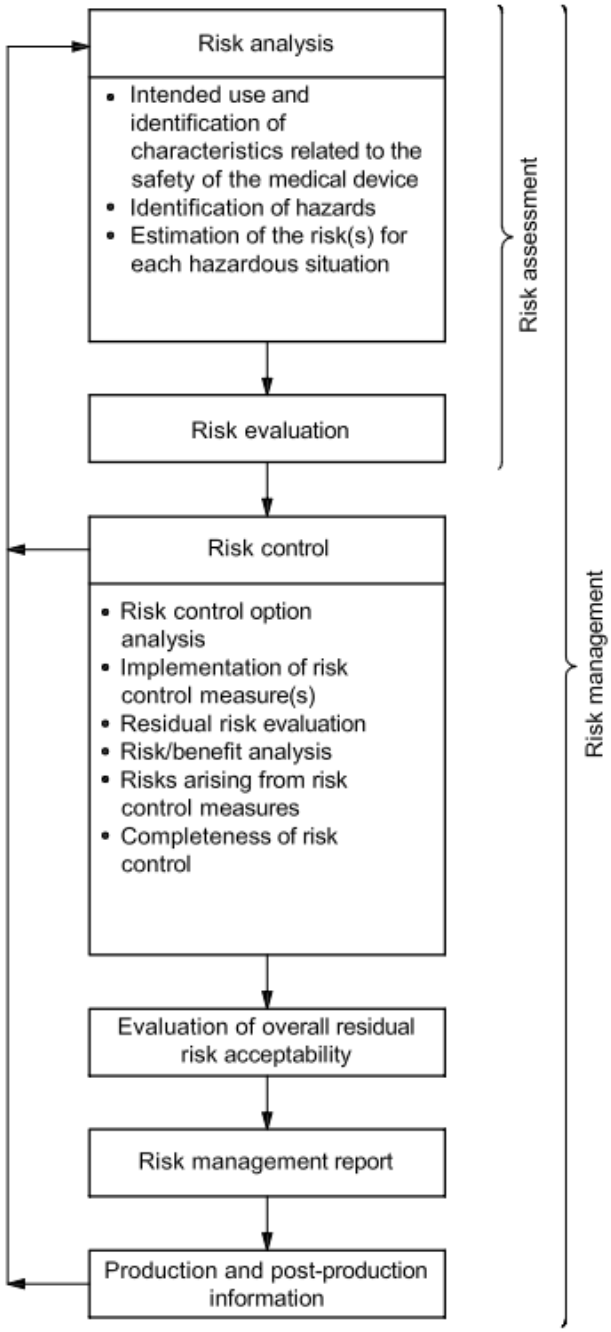
Standards that acquire an official status are called harmonised standards in the European Union. Manufacturers and other operators are thus free to use standards or choose some other technical solution to show compliance with obligatory legal requirements. However, the use of standards makes it easier to demonstrate conformity to authorities in different countries, because their requirements are known to everybody.

The expiring directive is associated with several harmonized standards. A similar list of harmonised standards for MDR has not been published yet. There is, however, a draft version of such list [11], which implies that there is a future for the familiar standards, and it is probably a good idea for manufacturers to continue using them until they are made official, in other words published in the Official Journal. For example, the quality system (ISO 13485) and risk management system (ISO 14971), also mentioned in the regulation, both have their own standards and are included in the draft list mentioned above.

2.2.5 Risk Management System

The manufacturer of medical devices has to set up, document, implement, and maintain a risk management system. Risk management is a repeating process, and it has to be updated regularly and systematically. MDR brings about some special considerations to risk management: ”In carrying out risk management, manufacturers shall … evaluate the impact of information … , in particular, from the post-market surveillance system, on hazards and the frequency of occurrence thereof, on estimates of their associated risks, as well as on the overall risk, benefit-risk ratio and risk acceptability.” [4]

The case company already uses a risk management tool: *ISO 14971 - Medical devices -- Application of risk management to medical devices* [12], which is also listed in the MDR draft of the harmonized standards [11], so it seems that its use will continue in the same way as before. Picture 2 illustrates the risk management process from the point of view of the ISO 14971 standard.



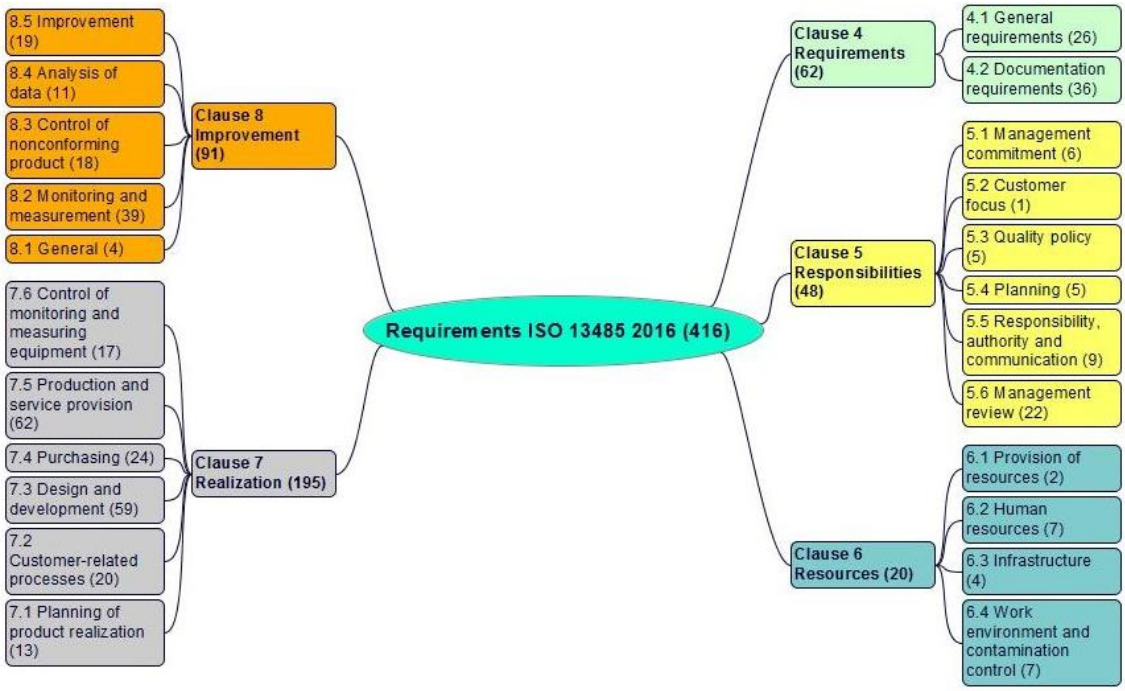
Picture 2: A schematic presentation of the risk management process [12]

The risk management system contains risk analysis and the risk management section. The analysis considers the risks, and the management attempts to remove or minimize them. Because it is not possible to remove all risks, a decision has to be made on accepting residual risks in relation to the benefits the device produces. Therefore, the expression “benefit-risk analysis” is often used. Risk management covers the entire life cycle of the product, from the beginning of design to the time when sales have ended.

Risk analysis has to be maintained and updated actively based on feedback from different sources. Such sources include, for example, the manufacturer's own observations and PMS, as well as trend follow-up.

2.2.6 Quality Management System (QMS)

The manufacturer has to set up, document, implement, and maintain a quality management system. The case company already has certified a harmonised standard ISO 13485 - Medical devices -- Quality management systems -- Requirements for regulatory purposes [13], which has been approved in the directive. There are grounds for continuing to use and certify it, because it is already included in the draft list of harmonised standards for MDR, and because the case company wants to continue to get approvals for their devices in the method based on the quality system. Picture 3 is a comprehensive presentation of the requirements of the newest standard version.



Picture 3: Requirements, clauses and sub-clauses of the standard ISO 13485 v 2016 [14]

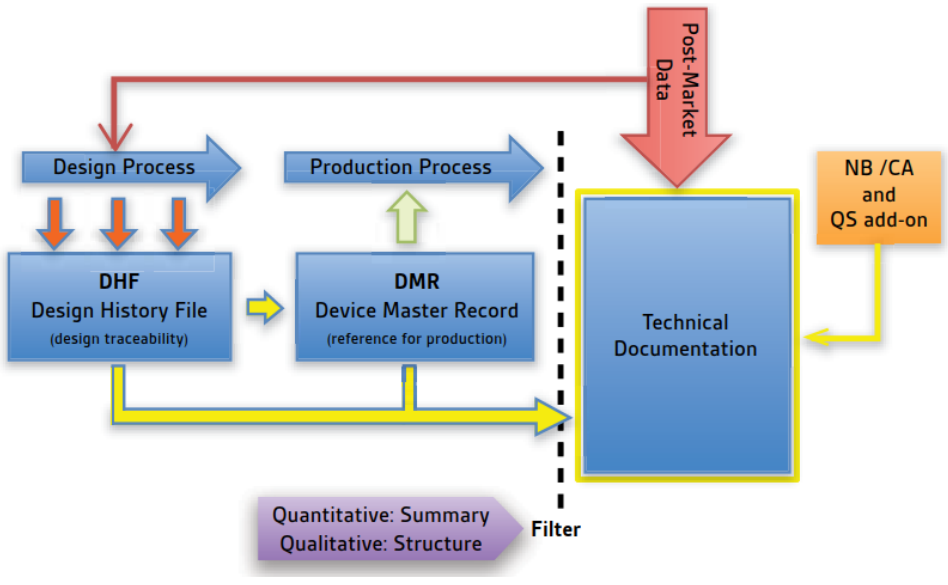
A quality management system, like the one in picture 3, is a management system whose purpose is to fulfil the clients' requirements and attempt to exceed customer expectations. With the help of the system, management is able to reach its goals, people are

fully involved, the operations follow processes and it is possible improve them, decision-making is based on evidence and managing the relationships with interest groups brings about continuous success. A quality system that follows ISO 13485 gives instructions for the whole life cycle of the product. There are obligations for company management, product design, and manufacturing, but documentation and customer deliveries are not forgotten, either. The commission has attempted to keep the regulation consistent with the quality standard for medical devices when creating the MDR regulation.

2.2.7 Technical File

The manufacturer has to create a technical file of the documents of its medical devices and keep it up to date. The technical documents have to be sufficient for the regulation's conformity assessment. The content of the file is depicted in picture 4, and for example the following topics have to be found:

- Description and specification of the device, including variants and accessories
- Information provided by the manufacturer
- Design and manufacturing information
- General safety and performace requirements
- Benefit-risk analysis and risk management
- Product verification and validation

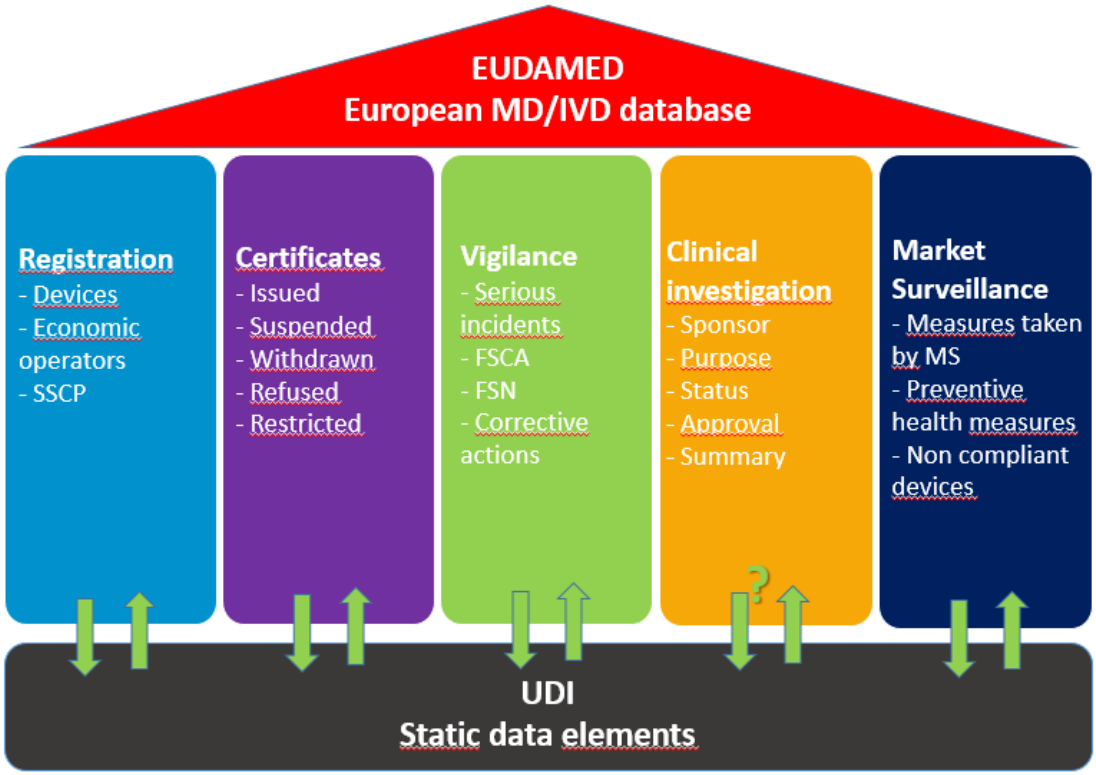


Picture 4: Subsets of Technical Documentation [15]

Thus, the file consists of documents from the design phase (Design History File), produced by manufacturing (Device Master Record), and post-market documents, complemented with content from the quality system (QMS). The summary of the technical file is called STED (Summary of Technical Documentation). The manufacturer has to keep the technical documents of the device for the whole life cycle of the product and 10 years after the end of its sales. The file or its summary has to be provided to the competent authority if requested.

2.2.8 European Database (Eudamed)

The Commission sets up, maintains, and administers the European database on medical devices called Eudamed. The goal is to increase visibility and the availability of information on medical devices. In the future, the registered economic operators and devices with their approvals and identifiers, incidents, post-market surveillance, and clinical evaluations, for example, can be found in the system. Picture 5 (below) depicts the division of Eudamed into different sections.



Picture 5: Eudamed's structure [16]

Some parts of the system will be open to everyone (e.g. devices in the market and economic operators), while others can only be viewed by certain operators. This is presented in picture 5 with rectangulars of different colours. All information is available to the Commission and the competent authorities. Eudamed is free of charge to the users.

The regulation obligates economic operators to save a lot of different kinds of information to Eudamed. Anu Lehtonen writes in her thesis EU:n asetus lääkinnällisistä laitteista (MDR) (The European Union's regulation on medical devices (MDR)) [17] that the manufacturer can choose whether they want to provide the information manually, using XML download or M2M technology. Each option has its own challenges. The manual method requires instructions for use, in XML downloading the data has to be EC compatible, and M2M requires a system based on AS4 protocol, so that the data can be transferred directly from the manufacturer to the database. The Guidelines for Member States on the use of Data Exchange solutions [18], created by the Union, helps to get more information on this.

The database has not been published yet (situation in April 2020). The regulation estimates that it will be in use by the time the transition period ends in May 2020, but the possible postponement is already taken into account in the regulation. It was mentioned in the Regulatory & Compliance Summit Conference in February 2020 that Eudamed is not expected to be ready until Q2/2022 [19]. Economic operators are therefore recommended to follow the Commission's notifications regarding the adoption of Eudamed.

2.2.9 Unique Device Identification (UDI)

The identification and traceability requirements of devices will expand in Europe because of the new regulation. To make managing them easier, the regulation requires that a unique device identification, UDI system, is taken into use. For those manufacturers that currently export products to the USA, this requirement is already quite familiar from the UDI by Food and Drug Administration (FDA).

UDI is formed from UDI-DI, device-group-specific identifier (the approved issuing entities provide the information), and UDI-PI, device-specific identifier such as serial number. The way UDI is formed is presented in more detail in the picture 6 (below).

UDI regulatory requirements	GS1 Standards
Basic UDI-DI « New » level of identification in the EU	**GMN** (Global Model Number) *No Application Identifier (AI) for regulated medical devices*
UDI-DI * Device Identifier (DI)	**GTIN** * Global Trade Item Number
UDI-PI * Production Identifier (PI) *(if applicable)*	**AI** * Application Identifier (AI) • Expiration date AI(17) - e.g. 141120 • Batch – lot AI(10) - e.g. 1234AB • Serial number AI(21) - e.g. 12345XYZ • Manufacture date AI(11) - e.g. 250717
Production Identifier data will vary by medical device type and manufacturer current practice.	
UDI-DI + UDI-PI = UDI	**GTIN or GTIN + AI(s) = UDI**

Picture 6: Terms of UDI [20]

According to the regulation, the UDI system has to be applied to all medical devices placed in the market, except for custom-made devices. To fulfil the requirements, the manufacturers have to

- produce the UDI-DI part (picture 6) needed for the UDI code, using the issuing entities approved by the Commission: GS1 AISBL, Health Industry Business Communications Council (HIBCC), International Council for Commonality in Blood Banking, Automation (ICCBBA), Informationsstelle für Arzneispezialitäten (IFA) Gmb [21]
- publish the UDI in the Eudamed database
- place the UDI identifier (human readable interpretation (HRI) and barcode) in the product and/or package
- use the UDI when reporting serious incidents and field safety corrective actions
- mark the UDI-DI in the declaration of conformity (DoC)
- keep an up-to-date list of all the UDI devices the manufacturer has named as a part of the technical documentation.

The UDI information has to be saved in the UDI database (Eudamed) by 26 November 2021 (if Eudamed is working). The UDI has to be marked in the product or package by 26 May 2023 (class IIa and IIb devices) and 26 May 2025 (class I devices).

2.2.10 Labeling

The regulation defines the minimum amount of information the manufacturer has to provide in their customer documents that are supplied with the device. The information has to be provided in the Union's official language or official languages, defined by the member country where the device will be placed available to users or patients. The information included in the label has to be permanent, easily readable, and clearly understandable for the intended user or patient. The requirements set forth in the directive will stay as they are, and as a new requirement the unique device identifier UDI (chapter 2.2.9) will be added to customer documents.

2.2.11 Declaration of Conformity (DoC)

The EU Declaration of Conformity is a document, in which the manufacturer declares that the product conforms to the requirements. The EU Declaration of Conformity is a part of the conformity assessment procedure in accordance with the EU product legislation, writes The Finnish Safety and Chemicals Agency Tukes on their website [22]. The manufacturer has to draw up a DoC before the product is placed on the market, and it has to be translated into one of Union's official languages or into the language(s) which the member countries require. For each device there can be only one DoC, which shows all the Union's regulations that are applied to the device, was told in the SGS Academy seminar in 2018 [23].

A DoC that has been updated to be MDR compliant contains everything the directive requires, and also:

- the registration number of the company (when Eudamed is working)
- unique UDI-DI identifier (when in use)
- the intended use of the device
- MDD conformity updated to MDR conformity
- as applicable, the number of the certificate issued by the notified body.

2.2.12 Certificate of Free Sale (FSC)

The certificate of free sale is a familiar document already from the directive's time. It is issued upon manufacturer's request for export, for CE-marked devices that are sold in the Union. In Finland, it is issued by Fimea. One of the new requirements is to supplement it with a part of the device identifier, the so-called Basic UDI-DI (chapter 2.2.9), and the number of the certificate issued by the notified body, if it exists.

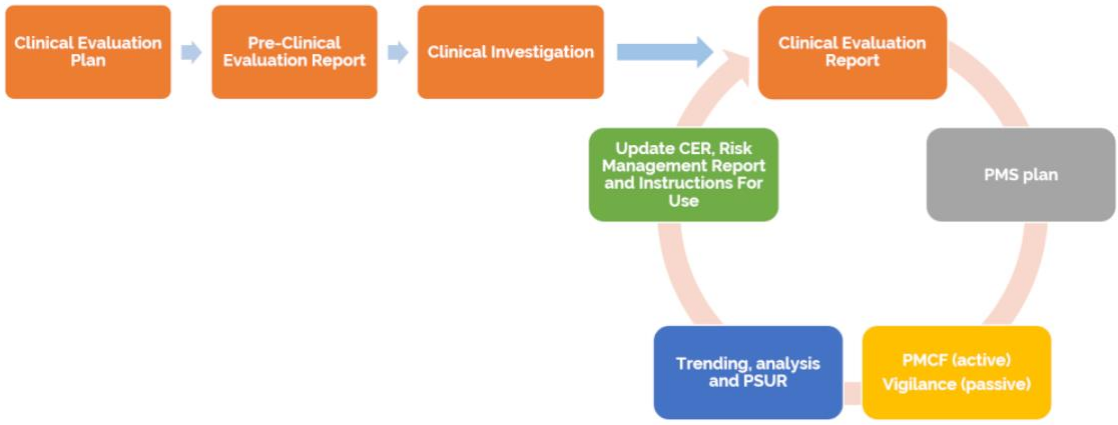
2.2.13 Identification within the Supply Chain

The identification requirements within the supply chain expand because of the new regulation. According to the regulation, economic operators, such as the manufacturer and distributors, have to be able to identify and, if requested, deliver to the competent authority the information about where they got the device and to whom they have delivered it. Importers and distributors are obligated to collaborate more closely with the manufacturer to ensure appropriate identification for 10 years. The UDI system (2.2.9) helps to manage this requirement.

2.3 Clinical Compliance

Patient safety and the performance of the device are the essential requirements of a medical device. As a part of the approval process, devices are tested based on harmonised safety standards, but in the legislation there are also requirements for tests carried out in authentic environments of use, called clinical tests.

With MDR, the requirement for clinical evaluations and investigations is further highlighted, new ways of working are adopted, and they are expanded to cover devices in more risk classes than before. The process, which covers the whole life cycle of the product, is presented in picture 7 below.



Picture 7: Clinical evaluation process [24]

The evaluation and investigation of clinical safety are divided, as depicted in picture 7, into time before placing the device in the market (orange boxes) and after placing the device in the market (other boxes). Before placing the device in the market, a clinical evaluation and investigations, taking into account the risk class, are carried out for the device, and these result is the Clinical Evaluation Report (CER), which is a part of the technical file of the device. Post-market actions (described in more detail in chapter 2.4) include, as described in the process description presented above, the PMS plan, Post-Market Clinical Follow-Up (PMCF), incident monitoring, and PSUR, which all have to be used as sources of information for updating the CER during the life cycle of the product. In the following sub-chapters, the requirements of clinical evaluation and investigation are described in more detail.

2.3.1 Clinical Evaluation

The regulation defines clinical evaluation as a systematic and planned process carried out by the manufacturer, whereby the safety and performance of the device in its intended purpose of use, including clinical benefits, is continuously produced, collected, analysed, and evaluated. The clinical evaluation starts with the clinical evaluation plan. In the plan, the manufacturer has to specify and justify the level of clinical evidence which is needed to demonstrate compliance with the relevant general safety and performance requirements. This level has to be appropriate considering the features of the device and its intended use.

After the plan, a clinical evaluation is carried out, based on literature and existing information. It has to be documented. The evaluation has to be a thorough and objective review of the current state, which takes into account both favourable and unfavourable information. It is recommended to use the instruction MEDDEV 2.7/1: Clinical Evaluation [25], from the time of the directive, in the evaluation process.

2.3.2 Clinical Investigations

A clinical investigation is defined in the regulation as a systematic research, which involves one or more people to be studied, and the purpose of which is to evaluate the safety and performance of the investigated device. During the directive, just a clinical evaluation (chapter 2.3.1) was often sufficient clinical evidence, in other words, a literature review by comparing with other similar devices. Now this method option has been limited in the regulation. Based on this, it can be said that clinical investigation can in many cases be considered as a new requirement.

To avoid performing a clinical investigation, the manufacturer can use the clinical investigation of a similar device that is already in the market, if both manufacturers have a valid agreement based on which the manufacturer of the other device grants full and continuous access to their technical documents. In addition, it is required that the original clinical evaluation has been carried out in accordance with the requirements, and the manufacturer of the other device provides clear evidence of that to the notified body.

If the procedure of using clinical investigation of a similar device is not possible, the manufacturer has to commission an investigation. The clinical investigation is made easier by the fact that in the future, a unified standard for clinical investigations ISO 14155 - Clinical investigation of medical devices for human subjects -- Good clinical practice [26], will probably be made official, because it is already mentioned in the draft list of harmonized standards [11]. In addition, it is recommended to take into account the guidelines that were approved in the directive's time, MEDDEV 2.7/4: Guidelines on Clinical Investigation [27], which gives important information on the matter. The manufacturer of risk class IIb devices can hear a panel of specialists appointed by the Union before the clinical investigation to specify the clinical development strategy of the plan and recommendations of the clinical research, the regulation states.

Clinical investigations have to be planned, approved, performed, recorded and reported when they are carried out for conformity assessment. The investigation has to:

- ensure that the device is designed, manufactured, and packed so that it is appropriate for the special uses listed in the regulation and it reaches the performance defined by the manufacturer
- analyse and check the clinical benefits of the device defined by the manufacturer
- ensure the clinical safety of the device and define the possible unwanted side effects in the normal environments of use, and assess if they form acceptable risks, taking into account the benefits of the device.

A permission has to be obtained from the Commission for performing a clinical investigation. The regulation instructs the sponsor of the investigation to supply the application documents to the member country/countries where the clinical investigation is planned to be carried out. The application is submitted in Eudamed (when available), which gives the clinical investigation a union-wide unique identification number that is used in all communication related to the clinical investigation. The member country in question has to inform the sponsor in 10 days after receiving the application whether the clinical investigation is in the scope of this regulation and whether the application document is complete. For the devices in the risk classes of the case company, the clinical investigation can usually be started right after getting the confirmation from the member country.

The regulation lists the following general obligations for performing clinical investigations:

- The party who commissions the investigation (the sponsor) and the investigator have to ensure that the clinical investigation is carried out according to the accepted clinical investigation plan.
- The sponsor has to ensure that the rights, safety, and well-being of the research subjects are secured, that the provided information is reliable and the research to be carried out is compliant with the requirements set forth in the regulation. In addition, the sponsor has to ensure sufficient surveillance for the investigation.
- The sponsor and the investigator have to save, modify, handle, and keep all the information pertaining to the clinical trial in such manner that they can be communicated in detail, interpreted and verified while maintaining the confidentiality of the documents and the personal information of the research subjects.
- The sponsor has to create a process for emergencies, which makes it possible to immediately identify the devices used in the investigation, and if necessary, recall them.

2.4 Post-Market Surveillance System

2.4.1 Post-Market Surveillance (PMS)

Nowadays the life cycle of a product is thought to expand beyond the time the product is for sale. The life cycle is considered to start from the beginning of design, and end 10 years after the product is discontinued. The MDR has expanded obligations also for the time after the product is taken into use.

The manufacturer has to plan, draw up, document, carry out, maintain, and update a post-market surveillance system (plans and reports) for each device, proportionate to the risk class and in a way suitable for the device type. The PMS has to be an integrated part of the manufacturer's quality system, says Petri Pommelin [6]. This is carried out by, for example, creating a standard operating procedure about it that belongs to the quality system. The PMS system is divided into parts and described in detail below. Picture 8 illustrates the reporting obligations.

PMS activities	MDR articles	Purpose	Device class	Connection with other QMS processes	Frequency of update
PMS plan	Art.84	Define a proactive and systemic process to collect the PMS data to: • characterize the device performance • compare the device performance with similar devices on the market	All	• Technical documentation • Customer feedback (including complaints) • Vigilance • FSCA • PSUR • Trend reporting • CER • Risk management file • QMS's PMS procedures • CAPA • PMCF plan or rationale	When necessary
PMS report	Art.85	Summary of results and conclusions resulting from PMSP including the description of CAPA taken	Class I		When necessary (frequency to justify)
PSUR	Art.86	Summary of results and conclusions resulting from PMSP including: • the description of CAPA taken • conclusion of B/R • PMCF findings • Sales • Number of patient (estimate) • Usage frequency (if applicable) • Patient characteristics	Class IIa		Every two years
			Class IIb		Every year
			Class III		Every year

Picture 8: Post-Market Surveillance Activities [28]

The manufacturer has to have a PMS system, based on the PMS plan. The plan shows how information is collected (e.g. vigilance, feedbacks, post-market clinical follow-up), analysed (CAPA), and reported (Eudamed) in the way required by the risk class of the device, and what the information is used for:

- developing and improving risk management
- updating design and manufacturing information and customer documents
- updating the clinical evaluation
- identifying the need for preventive, corrective, or field safety corrective actions
- identifying the improvement possibilities of usability, performance, and safety
- the contribution of the post-market surveillance of other devices and trend observation and reporting (as applicable).

The reports that are drawn up based on the plan are different, and different requirements concern them, depending on the risk class of the device. The different report types are presented next.

Post-Market Surveillance Report for class I devices

The manufacturer has to draw up a post-market surveillance report, which presents a summary of the results of post-market surveillance analysis and conclusions, as well as grounds for and description of all preventive and corrective actions. The report is updated when necessary and made available to a competent authority if requested.

Periodic Safety Update Report (PSUR) for class IIa and IIb devices

The manufacturer has to draw up a periodic safety update report for a device or a device group which presents a summary of the post-market surveillance analysis and conclusions, as well as grounds for and description of possible preventive and corrective actions. The lifelong PSUR has to present:

- conclusions of the risk analysis
- main findings of PMCF
- the sales volume of the device and estimated size of the population using the device and other features and, if possible, the frequency of use of the device.

For class IIa devices, the manufacturers have to update safety reports when necessary, and at least every two years. For class IIb devices, the PSUR has to be updated every year.

2.4.2 Serious Incidents and Field Safety Corrective Actions

The current directive already requires the manufacturer to inform competent authorities of suspected incidents and need for field safety corrective actions. A new requirement brought by the regulation is that this information has to be delivered through Eudamed (2.2.8), and the notified body has to be informed as well (as applicable) of non-conformity and possible corrective actions.

The manufacturers have to deliver, upon the request of competent authority, all information and documents that are needed to demonstrate conformity of the device in the union's official language defined by the concerned member state. The competent authority of the member country where the manufacturer has a registered place of business may require the manufacturer to deliver samples of the device free of charge, or if that is not possible in practice, to grant permission to use the device. Manufacturers have to work in cooperation with the competent authority upon its request in all corrective actions that are carried out to remove risks caused by placing the device in the market or taking the device into use, or if that is not possible, to decrease them.

A manufacturer that believes or has a reason to suspect that the device placed in the market is not compliant with the MDR has to immediately take the necessary corrective actions to make the device compliant or to remove it from the market. The manufacturer has to inform the device distributors about this, says the regulation.

Natural persons or legal persons can claim compensation for damage caused by a faulty device according to the applicable legislation of the union or national legislation. According to the regulation, the manufacturers must have defined actions in proportion to the risk class, device type and the size of the business that ensure sufficient funds for their possible responsibility in accordance with the directive 85/374/ETY.

Manufacturers must have a system for recording and reporting incidents and field safety corrective actions. MEDDEV 2.12: Guidelines on a Medical Devices Vigilance System

[29], approved as official instructions during the directive's time, helps in creating and maintaining the system. According to the regulation, analysing serious incidents and field safety corrective actions are the manufacturer's responsibility as follows:

- notification obligation to authority/notified body, distributor, etc.
- necessary investigations carried out without delay for serious incidents and the devices in question
- cooperation with authority and notified body during the investigations
- final report with conclusions and possible corrective actions to authority through Eudamed.

According to the regulation, the manufacturer has to make sure that the users of the device in question are immediately informed about field safety corrective actions that have been taken by a safety notification. The notification has to be delivered in the union's official language or languages, defined by the member country where the field safety corrective actions are taken. Except for urgent cases, the content of the safety notification draft has to be delivered to the competent authority so that they can comment on it if necessary.

The device or devices and the manufacturer that carried out the field safety corrective action have to be appropriately identifiable based on the safety notification. This is accomplished by, for example, including the unique UDI-DI identifier of the device and the manufacturer's registration number in the notification. The notification has to describe the reasons for the field safety corrective action clearly and without belittling the risk level by referring to the malfunctioning of the device and the risks for patients, users, and other people. In addition, it has to list clearly all actions the users have to take. The manufacturer has to save the safety notification in Eudamed (chapter 2.2.8), through which it is made available to the general public, the regulation says.

2.4.3 Trend Reporting

MDR adds a new requirement to complement the requirements on serious incidents and field safety corrective actions, the requirement of trend follow-up. In the future, the manufacturer has to follow and report statistically significant increases in the frequency or severity of side effects that could have a significant effect on benefit-risk analysis and

that have caused or could cause, in proportion with the benefits, unacceptable risks for the health or safety of patients, users or other people. A significant increase means an increase in the frequency or severity of the foreseeable side effects in a particular time period defined in the technical file.

The manufacturer has to define a process that is followed to observe statistically significant increases and the frequency of the observation periods. In the future, trend reporting will be carried out through Eudamed (when available).

2.5 Notified Bodies

A notified body is an organisation which an EU member country has named to assess the conformity of particular products before they are placed in the market. These bodies carry out the tasks pertaining to the conformity assessment procedures confirmed in the applicable legislation, when a third party is required. This is told on the European Union's website [30]. The European Commission publishes a list of approved notified bodies in a database called Nando [31].

National authorities are responsible for the notified bodies. This is the same practice as with the earlier directive. In Finland, the authority is Fimea. The difference is that the MDR has a lot of new requirements for these bodies, especially as regards clinical qualification. Therefore, granting the MDR authorization and later monitoring takes the bodies significantly more time than before. At the moment (situation in April 2020) there are no MDR-qualified notified bodies in Finland. For a couple of notified bodies, the approval process is ongoing.

The manufacturer is recommended to follow whether the notified body they already have cooperation with is named on the basis of the new regulation, and whether its area of responsibility covers the company's products. It is recommended to start cooperation with the notified body in planning the timing of the verification of the product portfolio immediately after the notified body is qualified, taking into account the availability of the notified body, need for additional information about the devices, and the transitional provision of the new regulation, because the MDR will soon become effective in full.

2.6 Summary of MDR

The new regulation for medical devices became effective in May 2017. A transition period of three years was set for it, after which the current directive will expire. The Union's goal for the new regulation is to remove the room for interpretation from the legislation, meet the challenges of developing technology, exclude problems that have occurred in use, improve safety and people's health and support the functioning of the internal market while also maintaining the spirit of innovation. The patient safety of the devices will certainly improve because of the new regulation, but the goal of innovativeness is challenging, because the regulation's requirements are strenuous, and the ability to understand and fulfil them, especially in start-up companies, will eliminate companies operating in the field and attempting to get there, Ben-Menahem and colleagues write in their scientific article *How the new European regulation on medical devices will affect innovation* [32].

The regulation contains the same requirements as the directive, but it will also bring additions and entirely new requirements. With the regulation, many software programs used with medical devices will become medical devices themselves. Picture 1, CE Marking Process, presents the regulation's requirements that depend on the risk class of the device.

For devices in a lower risk class (class I), a technical file which contains, for example, risk management, safety tests, clinical evaluation, post-market surveillance, and the declaration of conformity (DoC) will be required. For devices in a higher risk class (Im, IIa, and IIb), in addition to the requirements above, also the participation of a notified body in the approval process, quality system (QMS), and a more detailed clinical evaluation/research and reporting are required. A new requirement for all medical devices is the unique device identification (UDI) and the obligation to report several matters in the new information system, Eudamed. In the future, the large manufacturers of medical devices must have a person responsible for regulatory compliance employed by the company.

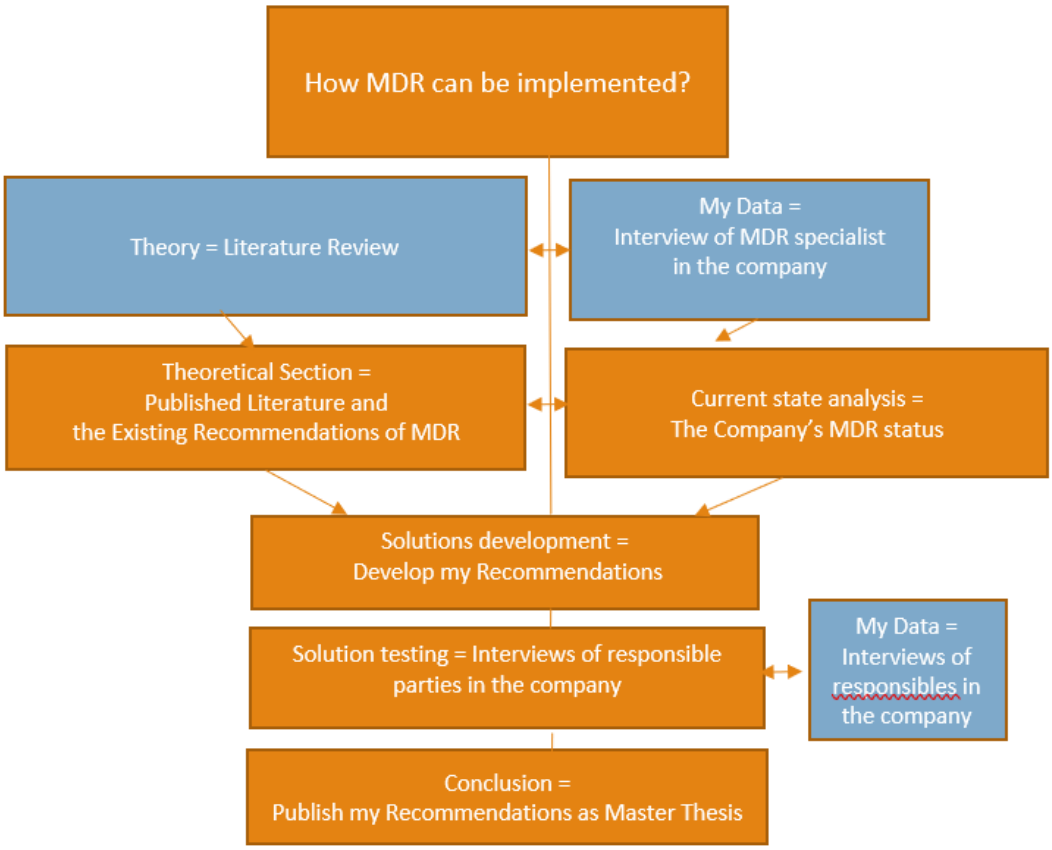
3 Materials and Methods

3.1 Research Approach

The purpose of this research was to draw up recommendations for the case company on how to comply with the requirements set forth in the new European law. The transition period of the regulation is approaching its end (26.5.2020), so the topic of this research is very current, and there is a lot of new information about it especially in the Internet. In addition, some of the company's personnel had already familiarised themselves with the theme, for example by participating in MDR trainings, so there was existing expertise on the topic within the company. This made it easier to analyse the current state and to evaluate the recommendations.

3.2 Research Design and Project Plan

The problem with the case company is that it is not entirely known how the MDR should be implemented, because there are some things that have not been instructed yet. The goal of this research is to provide the missing recommendations that make the implementation easier. Several steps have been taken to create the recommendations (picture 9 below).



Picture 9: Research Design

First, information about the ongoing change and different research methods has been collected. There is plenty of new material on the MDR regulation, because the topic is very current. Chapter 2 (Medical Device Regulation) is about the existing information about obligations and the change. The selected research methods are described in chapter 3 (Materials and Methods).

The current state of the case company is analysed in chapter 4 (Current State Analysis), focusing especially on the parts of the legislation that will change the most, insofar as the actions for meeting them have not been carried out yet. After this, it was possible to outline recommendations regarding what the implementation of MDR still requires (chapter 5: Recommendations for Implementation of MDR). So the result – the recommendations for meeting the requirements – would be as comprehensive as possible and would fulfil the needs accurately, it had to be evaluated before publishing. This was done by interviewing key people working at the company (chapter 6: Evaluation of Recommendations). After this, it was still possible to update the recommendations, based on the findings from the interviews.

The last chapter (chapter 7: Conclusions and Discussion) includes the conclusions about the change and its influences on the company that sells medical devices in Europe. Finally, the recommendations are published as a Master's Thesis both in the company and in Theseus, the shared database for theses from Finnish Universities of Applied Sciences [33].

3.3 Data Collection and Analysis

The research method selected for this research was qualitative research and content analysis. The content was collected from twelve interviews (see the following chapters), so the result is in the qualitative category because of its volume. The content analysis was carried out according to the instructions given by Tuomi and Sarajärvi in their book *Laadullinen tutkimus ja sisältöanalyysi* [34]. First, the decision was made on which topics of the data were interesting, and others were separated and excluded from the research. The remaining data was divided into separate themes. Finally, a summary was written about the remaining data.

The current state of the company (situation in February 2020) was analysed by interviewing the company's MDR specialist about what has already been done for the regulation (chapter 4). The interview was conducted as a semi-structured personal interview. This means that parts of the MDR that may change compared to the expiring directive were collected in advance. The interview progressed part by part, and the questions for each part were the same – are changes needed when transitioning from the directive to the regulation, and if yes, has something been done already and are the actions already taken enough to fulfil the requirements set forth in the regulation.

Based on the current state analysis interview, it was possible to identify the parts that still require actions to comply with the regulations. Recommendations about the necessary actions, schedules, and resources were drawn up for them. The recommendations are based on the suggestions that came up during the interview and the facts discussed in the theory chapter (chapter 5, Recommendations for Implementation of MDR). The SMART criteria [35] were taken into account when creating the recommendations: The goal was to make them – if possible – Specific, Measurable, Achievable (who is responsible for implementation), Relevant, and Time-bound.

In order to make the result of the research as reliable as possible and also consistent with the needs of the company, the result was evaluated by interviewing 12 key people working at the company. The interviewees were selected based on their long experience (several years) of activities complying with the directive, and the upcoming changes will directly affect their area of work. An additional criterion for the selection was an attempt to cover the company's different lines of business as extensively as possible, to enhance the preparation for the information about the upcoming change throughout the whole company.

The evaluation interviews for the recommendations were conducted as semi-structured personal or pair interviews. In their book about research interviews, Hirsjärvi and Hurme [36] use the term theme interview for semi-structured interviews. They describe that the questions in this interview type are the same for everybody, but the interviewees can answer in their own words; the answers are not limited by the given options, like in structured interview. A theme interview follows certain central themes, and there is no need to connect it exclusively to either qualitative or quantitative methods. This makes the interview more free from the researcher's point of view, and gives more prominence to the voices, interpretations, and meanings of the interviewees.

The theme interviews for evaluating the recommendations in this research were carried out by going through all recommendations one by one and by asking if the recommendation is necessary and comprehensive, and if the interviewee has anything to add as regards the actions that are needed to meet the requirements set forth in the regulation.

The interviewees were unanimous on the correctness and necessity of the recommendations. There were also some good additional observations, so the recommendations were modified based on these, and a couple of new recommendations were added as well (chapter 6, Evaluation of Recommendations).

4 Current State Analysis

4.1 Current State Analysis

The case company has a long history in the European medical device market, because its first EC certificate dates back to 1995. However, the new regulation brings about new requirements and additions to old requirements. In order to start preparing for the changes, several people from different departments have acquainted themselves with the changes, some have participated in external trainings, and some changes have already been made in the company. Now there is a need for a current state analysis to evaluate what has already been done and what still needs to be done so that the company is ready to work in compliance with the MDR requirements.

A specialist interview was chosen as the method by which to get information on the current state. The interview was conducted and recorded on 15.1.2020 as a semi-structured personal interview, and its topic was the current state of the MDR requirements, with emphasis on quality. The interviewed specialist was a Process Development Manager, who works at the target company and whose education is Bachelor of Engineering in Information and Communications Technology. The specialist had learned about the MDR by trainings and self-education, and by attending working groups organized by Healthtech Finland.

4.2 Specialist Interview

Topic: The current state of the MDR requirements in the target company

Time and place: 2020-01-15 in target company premises, in Helsinki

Interviewee: Process Development Manager

The interview was conducted by presenting the interviewee with the possible targets of changes title by title, selected from the regulation in advance. The questions for each were: Does the item require actions in order to meet the requirements in the regulation, and if it does, what is the status of these actions in the company. The items that the interviewee commented are presented below.

Distance sales

According to current understanding, the company's range does not include products or services that are delivered or used as intended in the article about distance sales.

Use of harmonised standards

The situation is open. The directive had a group of harmonised standards as an attachment, and it included up to two or three hundred standards. Now this is completely open as regards the MDR, there have not been expressions of opinion on what is the group of standards that needs to be followed to fulfil the requirements set in the regulation. The common policy is to continue operations according to them, but they do not have a legal role in the world of MDR for the time being. The situation is interesting. For now, there are no other options to be seen but to continue using the current standards.

General obligations for manufacturers

The quality system obligation will apply to manufacturer, distributor, and some other functions. The old way of working focused mostly on the manufacturing point of view, but now it expands to distribution and maintenance actions. The company should surely check what kind of guidelines it has for maintenance actions. The company trains the distributors, and they carry out maintenance in the field. He had also seen such policies and some companies interpret that the companies operating in distribution and maintenance have to have a quality system. The company as a manufacturer has a quality system.

The risk management system has been a part of the quality system. What will change is that the quality system should be built from risk management point of view; risks in different areas of operation should be assessed. The practical implementation is in accordance with ISO 13485:2016. The standard operating procedure for product development risk management [37] has been renewed and complies with ISO 14971:2019. It is ready for MDR.

Technical documents are a major challenge. The work instruction for the technical file has been made, and it takes a stand on different markets and their differences on the

global level. The basic structure is the structure of the MDR technical file. The work instruction describes the technical file at a conceptual level. Work is still in progress as regards the output/document of the case company, i.e. what corresponds to each section of the technical file. The challenge is that the company has different divisions that work in slightly different ways at the moment, and additional instructions are needed on what is the document template in the case company and what corresponds to each section of the technical file. A working group is now working on this as a part of the product process management project. The amount of work is tremendous. The schedule is uncertain.

Customer documentation, such as labels and manuals: The guidelines will change as regards the software, he did not know about other changes. The MDR states explicitly the recommended location of the CE mark in the software. In the future, the CE mark must be in the first view the user sees. This change has already been taken into account in our upcoming software update.

The Essential Requirements will change to General Safety and Performance Requirements, and he has created a new EU MDR Safety and Performance checklist for it. It collects new requirements (such as nano materials) and replaces the old ones. The list has been converted to checklist format, and it covers all elements and areas in sufficient detail. When the company develops something in the future, the list can be used to check that each area is covered in some way. It is a general-purpose checklist, suitable for all departments and products as it is. The checklist has not been released yet, but an announcement could be made to inform everyone about it.

There is an existing working group in the Usability department. They are in charge of their entities, they are trained in MDR, and their operations have been updated. This is in a good shape considering MDR, efforts from the quality department have not been needed.

UDI system requirements in EU will be new to the company.

Person responsible for regulatory compliance

This is a new requirement. Qualification requirements are defined, and the responsibilities of this person are also described. The current quality director has announced avail-

ability, but the job description has not been updated yet. There has been some discussion in HealthTech Finland groups about the need for some kind of an insurance for the person in such role, personal-level protection.

Declaration of Conformity

There are new requirements in the content of the Declaration of Conformity, for example the UDI information and the intended use of the medical device have been added. The current Declaration of Conformity is based on the old standard, and the declarations sent recently to the notified body are already very close to the MDR requirement.

Identification within the supply chain

The roles will be defined in more detail (manufacturer, distributor, importer etc). The identification of the device in the supply chain will probably happen through the forthcoming UDI system. Actors are obligated to identify and keep the information about the other actors to whom they have delivered the device or who have delivered the device to them for 10 years (15 years for implantable devices).

UDI system/UDI database

Seems to be still open/in open issue. According to the latest information, there will be an Italian UDI type, which is different from the FDA-UDI. There is a separate transition time for the European UDI, but this will naturally influence the way the company marks the products. The Commission has to provide information about the contents of the UDI. The products of the company are for the most part class IIa or IIb devices, and for them the UDI obligation will become effective on 26.5.2023.

Registration of devices

The notified body system will stay as it is. The use of possible national databases may be discontinued. The company will keep the same approval path based on the quality system. When the company modifies a product after May 2020, it has to be done in accordance with the MDR. After 2024 the delivery of a product is not allowed anymore if

it has not been registered in accordance with the MDR. He does not know about decisions to leave some products without MDR registration.

Notified bodies

The company do not know when its current notified body will be MDR-designated. Therefore, the company cannot yet apply for an approval in accordance with the MDR, even if that was otherwise possible. At the time of the interview, there are only 9 MDR-designated notified bodies in the European Union, and none of them is in Finland. According to the Commission's notification from last autumn, the goal was to have about 20 notified bodies designated by the end of 2019, but clearly this schedule has not held.

Classification of devices

The company's current products will probably stay in their current risk classes, maybe except for software. Some software that is currently not medical device may rise to class I, which means that a declaration is needed. These software products that are unclassified according to MDD and rise to class I because of MDR have to be classified and comply with the conformity requirements by May 26, 2020.

Clinical evaluation and clinical investigations

The Commission has emphasised in their communication that the notified bodies now really have to inspect the clinical investigations. A clinical evaluation is needed for each device, and at a minimum it means a comprehensive literature review. A large amount of work instructions [38] and document templates have been prepared. They have been released and are ready to be used. The instructions are ready for the MDR. Additional resource has also been hired, but it could be good to allocate more as regards updating the yearly report.

For predicate devices the practice will change. The MDR says that it is possible to base on a product that has been released already, like with MDD, but a technical file is needed for the product to ensure sufficient similarity between the products. Because competitors probably will not give their technical files for us to use, this path is not possible.

The regular proactive follow-up after placing the clinical evaluation on the market and the report that is based on it, and depends on the product's risk class, requires new skills. This procedure is related to the general follow-up after placing on the market.

Post-Market Surveillance

An essential change is that the PMS actions have to be proactive in the future, and in stead of passive collection of data they have to be based on preventive actions. The manufacturer is also required to set up a system for post-market surveillance. A good question is how this kind of action is proved. A way is to follow the incident reports in the archives of other countries to show that the company follows similar cases and considers if they could be like our own. However, this requires more detailed instructions at the company level. In the future, manufacturers have to provide a periodic device-specific safety review. In addition, a clinical follow-up report has to be saved to Eudamed, but in which format and when is not yet decided by the Commission.

Reporting of serious incidents and field safety corrective actions

A new requirement is a notification procedure through Eudamed, as soon as it is ready to be used and the Commission has given instructions on how to use it. The MDR lists requirements at a detailed level regarding the reporting of serious incidents and field safety corrective actions, but the actions themselves will probably stay as they are for the most part.

Trends

Statistical analysis is carried out and trends are followed already at the moment as a part of the quality system, for example in management reviews. Reports on trends are required to be given through Eudamed, but its adoption seems to be delayed from the Commission's side. The related instructions have not been made yet.

4.3 Summary of the current state

The MDR came into effect in 2017, so the company has already had time to do several things to comply with the new regulations. Because there are no MDR-qualified notified

bodies in Finland at the moment and the Eudamed is not yet in use, it has not been possible for the company to do everything yet. Based on the specialist interview presented in section 4.2, the MDR readiness of the following areas can be deemed unnecessary or ready enough to be left out of the focus of this research, excluding the recommendation to follow trends and the adoption of Eudamed, which applies to most of the following:

- Distance sales
- Use of harmonised standards
- Quality system of the case company
- Risk management system
- Technical documents
- General safety and performance requirements (GSPR)
- Usability requirements
- Notified bodies
- Clinical evaluation and clinical investigations
- Reporting of serious incidents and field safety corrective actions.

The interview focusing on the current state revealed the following areas on which changes are needed but not yet done and will benefit from the recommendations provided by this research:

- Notification/surveillance of the obligations of other economic operators than the manufacturer (e.g. possible quality system obligation and the identification of the product within the supply chain)
- Person responsible for regulatory compliance
- Declaration of Conformity
- UDI
- Classification of devices
- Post-Market Surveillance
- Trends.

5 Recommendations for Implementation of MDR

Based on the current state analysis done in chapter 4, recommendations were created in order the company meets the requirements of the regulation. The recommendations are suggestions on how to update the current standard operating procedures in the quality system, or if they do not exist, how to create new ones to meet the needs of the company. Because it is not necessary to give instructions on all actions at an operating procedure level, some of the recommendations are requests to do some separate action.

5.1 Person Responsible for Regulatory Compliance (PRRC)

Recommendation: A PRRC is appointed by 26.5.2020 by company management

One of the new requirements of the regulation is that the manufacturer has to have permanently (large companies) at least one person responsible for regulatory compliance in their organisation. If there are more than one person, the division of responsibilities has to be defined in writing. The person must be formally qualified for the task. The qualification is attained either by an appropriate university degree and one year of work experience, or by four years of work experience about regulations related to medical devices or quality management systems. In addition, it has been defined that the person must not be legally in weaker position within the organisation because he or she is performing the duties. The requirements are described in more detail in chapter 2.2.1.

The Finnish Enterpreneurs (in Finnish: Suomen Yrittäjät), classifies companies that employ at least 250 people as large companies [39]. Thus, the case company is a large company (it employs about 700 people in Helsinki), and it has to have at least one person responsible for regulatory compliance in the organization.

The recommendation is to appoint a qualified person for the task or divide the responsibility between several people, and make a written agreement about this by, for example, updating the job description. The appointment has to be done by the end of the transition time, and the person has to be registered in Eudamed as soon as it is possible.
Taking into account the level of responsibility associated with the task, it is recommended that the person is a member of the Executive Board. Furthermore, it is recommended that the responsibility of the responsible person is limited in an agreement between the

company and the responsible person. In addition, the responsible person is advised to consider taking a personal liability insurance.

5.2 Product Classification

Recommendation: The conformity of software products that are sold for ready to use is ensured by 26.5.2020 by product managers

The case company is responsible for class I, Im, IIa, and IIb devices and non-medical devices. As the specialist's interview indicated, the classifications will probably stay as they are, except the currently non-medical software. However, it is worthwhile to follow the Commission’s notifications, because it is possible that qualifications on the classifications are made at a later time.

The MDR adds a new risk class classification rule (no 11) to the conformity assessment for software that is intended to provide information used in diagnostic or therapeutic decision-making. In the future, such software will probably belong to risk class IIa with minor exceptions, and other software to class I.

The recommendation is to evaluate the software that the case company is responsible for and that are sold after 26.5.2020. Because none of the current non-medical software is manufactured by the company, the recommendation is to send a letter to the manufacturers and ask them to confirm the risk class classification and be responsible for its requirements. The requirement for class I devices is the technical file and DoC. For class IIa devices it is required that the notified body and PMS are used. In addition, it may be necessary to update supplier contracts, taking into account MDR conformity.

5.3 General Safety and Performance Requirements

Recommendation: The existing instructions are released as soon as possible (on 26.5.2020 the latest) by the process development manager

In order to meet the new MDR requirements, an EU MDF Safety and Performance checklist has been created for the company. It collects new requirements together and replaces the old ones. However, this checklist has not been released yet within the company (situation in February 2020), so the recommendation is to release it immediately. If that is done, any MDD compliant actions are not in jeopardy, but all upcoming changes would already be as compliant with the MDR as possible.

5.4 Registration of Economic Operators

Recommendation: The company is registered into Eudamed by the quality department

The manufacturers of mass-produced devices have to register in Eudamed (when it is available) before placing the devices on the market. If the conformity assessment procedure requires the participation of the notified body (devices in risk classes Im, IIa, and IIb), the manufacturer has to save the requested information in the electronic system before the registration request is presented to the notified body. After this, a competent authority acquires the manufacturer's single registration number (SRN) and sends it to the manufacturer and the notified body. The manufacturer has to use the registration number when requesting for the conformity assessment from the notified body and to get into Eudamed to fulfil its other obligations. To conclude, it is recommended that the case company is registered in Eudamed as soon as possible.

5.5 Unique Device Identifiers (UDI)

Recommendation: The devices are registered in the UDI database by 26.11.2020 and introduced within the UDI schedule by the FDA-UDI responsible persons

There is a new requirement in the regulation about the unique identification of devices. The purpose of the actions is to improve device traceability, make recalls easier, prevent forgeries and improve patient safety.

A corresponding requirement is already in force and in use in the case company in the form of an American UDI (there is no official standard operating procedure). However, the European UDI is probably different from its counterpart in some respects, although they are both based on The International Guidance on a Unique Device Identification

(UDI) System for Medical Devices (2013) [21], created by the International Medical Device Regulators Forum (IMDRF). Therefore, revising and updating the implementation to comply with the MDR is needed. The UDI requirement applies to all medical devices in Europe (except for custom-made devices). The UDI marking belongs to manufacturer's responsibilities, and the schedule varies between risk classes.

Recommendations for meeting the UDI requirements are the following:

- The company should be registered as a manufacturer in the Eudamed database (when available)
- UDI-DI is recommended to be formed through the Commission-approved GS1 AISBL issuing entity, because it is already used in the company
- The devices should be registered into the UDI database (when available) by 26 November 2021 (also software as a medical device)
- Devices belonging to the risk classes IIa and IIb should be marked with the UDI identifiers by 26 May 2023
- Devices belonging to the risk class I should be marked with the UDI identifiers by 26 May 2025
- UDI-DI has to be used at least in the following documents: User manuals, certificates, DoC, and the technical file.

Further information can be found in the European Union publication Unique Device Identification (UDI) System – FAQs [21] and in the instructions by GS1 Be ready for UDI in the EU! [20].

5.6 Declaration of Conformity (DoC)

Recommendation: The declarations of conformities should be updated to comply with the regulation in conjunction with the device-specific MDR approvals by the quality director

The case company has created and updated declarations of conformities that comply with the expiring directive for all its medical devices, so there is already experience with the process. There are no instructions on the process, but because the responsibility will

probably stay with the current quality director (upcoming PRRC), there is no need for one-person-instruction.

As stated in the current state interview (chapter 4), the DoC has already been slightly updated towards MDR as requested by the notified body. The current DoC mentions, for example, the name and address of the company, the official name of the product, notification about MDD conformity, standards the product meets, the risk class of the product, declaration that the DoC is issued under the sole responsibility of the manufacturer, and the date and place of issue, name of the responsible person, title, signature, and information about on behalf of or in the name of whom the person signs the declaration of conformity. As applicable, also the name and identification number of the notified body and a description of the conformity assessment procedure are given.

The new additional DoC requirements to the information presented earlier are:

- the registration number of the company (when Eudamed is available for use)
- the unique UDI-DI identifier (when available)
- the intended use of the device
- updating the MDD compliance notification to MDR compliance
- as applicable, the number of the certificate issued by the notified body.

The recommendation is that these information should be updated to the current declarations of conformities.

5.7 Regulation's Requirements for Economic Operators

Recommendation: The distribution agreements should be updated by 26.5.2020 by the export department

The regulation defines the manufacturer, authorised representative, importer, distributors and persons responsible for regulatory compliance as economic operators. The company's operations regarding manufacturer's responsibilities are already compliant, excluding the UDI markings (chapter 5.5) and PRRC (chapter 5.1). The company is lo-

cated in the European Union area, in Helsinki, so an authorised representative and importer for Europe are not needed. Taking these into account, the changes and updates for requirements for economics operators can be focused concerning only distributor responsibilities.

It is recommended that the distribution agreements are checked and updated if needed concerning distributor's obligations. If the agreements have not been updated recently, it may be necessary to inform the distributors about their responsibilities and schedule that the regulation sets out for them in written form. The distribution agreements or the notification should include the following points:

- The distributor must check with a sampling method that the device has a CE mark and a MRD-DoC has been created for it, that the labels drawn up by the manufacturer and the instructions for use are supplied with the product, and the device has the UDI identifier.
- The distributor has to make sure that the storage and shipping conditions meet the manufacturer's requirements.
- If the distributor suspects that the device is non-compliant, they cannot place the device on the market before compliance is achieved and the distributor has fulfilled its notification obligation to the manufacturer, and in case of serious injury or suspected forgery, also to the competent authority.
- Complaints and incident reports received by the distributor have to be forwarded to the manufacturer without delay. The distributor has to keep a register of complaints, non-compliant products and product recalls, and withdrawals from market. The distributor has to keep the manufacturer up to date about such monitoring and provide the information if requested.
- The distributors have to work in cooperation with authorities, which means that they have to provide the available information to demonstrate conformity, help with actions to remove the risks of devices placed on the market, and provide samples free of charge or the opportunity to access the device.
- The requirements set forth in the regulation will become effective product by product depending on when they are registered as MDR compliant by the manufacturer, but on 27.5.2024 at the latest. At the moment (situation in February 2020) none of the case company's products are MDR compliant. From 26.5.2020 onwards, new products placed on the market or old products with significant changes have to be MDR compliant.

5.8 Post-Market Surveillance (PMS)

Recommendation: A new SOP is created as soon as possible (on 26.5.2020 the latest) by the process development manager

A new requirement in the regulation is that the manufacturer has to have a post-market surveillance (PMS) system. The quality system already in use in the company consists of standard operating procedures (SOP), so the PMS system requirement is fulfilled when an SOP is created for it and it is included in the quality system. At the moment (situation in February 2020) the case company does not have such an SOP.

The recommendation is to create an SOP for post-market surveillance for the company. It has to be designed, set up, documented, developed, maintained, and updated actively and systematically. The collected data has to be analysed from the points of view of quality, safety, and performance. The actions have to cover the entire lifecycle of the product, and the provided data has to be sufficient for making conclusions to define, develop, and oversee corrective and preventive actions (CAPA). To help the practical work, it is recommended to use the relevant technical report published by the International Organization for Standardization (ISO): ISO/PRF TR 20416 Medical devices - Post-market surveillance for manufacturers [40].

PMS is based on the plan on post-market surveillance (part of the technical file). The plan's follow-up actions depend on the risk class of the device. The standard operating procedure has to include instructions for each risk class as follows:

Risk class I devices and the PMS report

> Based on the PMS plan, the manufacturer has to draw up a PMS report for class I devices. The report summarises the results and the collected conclusions of the PMS data analysis together with the CAPA information. The report has to be updated as necessary and provided to the NB and the authorities if requested.

Risk class IIa and IIb devices and a period safety update report (PSUR)

> For risk class IIa and IIb devices or device groups, the manufacturer has to draw up a PSUR (a part of the technical file) based on the PMS plan. The report summarises the results and the collected conclusions of the PMS data analysis together with the CAPA information. The class IIa report has to be updated as necessary and at least once every two years. The class

IIb report has to be updated at least yearly. The reports have to be provided to the NB and the authorities if requested.

The collected information should be used, for example, in the following:

- benefit-risk determination and the improvement of risk management
- to improve design and manufacturing instructions, user manuals, and device labels
- to update the clinical assessment and safety and clinical performance summary
- to define the need for preventive or corrective actions, or field safety corrective actions
- to define the development potential of usability or the safety and performance of the device
- to expand the PMS of other similar devices as applicable
- to prevent and report of trends.

Post-Market Clinical Follow-up (PMCF), which is also a post-market obligation, is included in the existing instructions on clinical assessment at the case company (chapter 4.2).

5.9 Monitoring and reporting of trends

Recommendation: A new SOP should be created as soon as possible by the process development manager

The monitoring and reporting of trends is a new requirement that will become effective with the MDR. The company has followed the development of the field at some level, for example by monitoring competitors' product ranges, by analysing the changing requirements of customer needs, and by reviewing the received customer feedback, but this monitoring has to be deepened and expanded due to the new regulation, and it has to be reported in a new way.

The new regulations regarding trends concern significant increases of unacceptable side effects. A significant increase is defined in relation to the foreseeable frequency or severity of the side effect of the device in question during a particular period of time, as defined in technical documents and product information. The reporting has to be done through the electronic system (Eudamed). It is worth noting that this requirement does not apply to serious incidents (chapter 5.10).

The recommendation is that in order to comply with the regulation, the company should create a new standard operating procedure for trend follow-up and reporting or include the requirement in an existing SOP (for example PMS, chapter 5.8) as a new chapter. The follow-up can be, for example, active monitoring of received customer feedback and existing incident databases, such as MAUDE/FDA [41] and Eudamed/EU (upcoming). To comply the requirement easier, it may be necessary to utilise statistical methods. The reporting has to be done through Eudamed, as soon as it is available.

It would be good to mention in the SOP that the current actions have to be assessed based on the observations made in trend follow-up e.g. at the following levels:

- benefit-risk determination and improvement of risk management
- the improvement of design and manufacturing instructions, user manuals, and device labels
- the improvement of the clinical assessment and safety and clinical performance summary
- defining the need for preventive or corrective actions, or field safety corrective actions
- defining the development potential of usability or safety and performance
- expanding the PMS of other similar devices as applicable.

5.10 Serious Incidents and Field Safety Corrective Actions (FSCA)

Recommendation: SOPs of Vigilance and Creating and Delivering Technical Bulletins should be updated regarding Eudamed oblication by 26.5.2020 by the quality director

The company's procedure of reporting serious incidents is already compliant with the regulation. There are separate SOPs on creating incident reports, and they are analysed

according to the CAPA guidelines. However, the regulation adds a new requirement in the form of an electronic database, Eudamed.

The recommendation on updating the SOPs Vigilance (in Finnish: Toimitetun laitteen aiheuttama vaaratilanne) [42] and Creating and Delivering Technical Bulletins (in Finnish: Teknisen tiedotteiden laatiminen ja jakelu) [43] is needed because of these new obligations related to the reporting process. In the future, both serious incidents and field safety corrective actions have to be reported in Eudamed (when available).

6 Evaluation of Recommendations

6.1 Interviews

The goal of this thesis is to provide the case company with comprehensive and timely recommendations on how to comply with the requirements set forth in the MDR regulation when the transition period ends in May 2020. Some changes required by the new regulation had already been done when the current state interview (chapter 4) was conducted in January 2020. Based on that interview, recommendations were created (chapter 5) to complement the actions that had already been taken and to meet the requirements that were not met yet. To make sure that the recommendations are of the correct kind and sufficient, an evaluation of the recommendations was carried out as internal interviews in the company.

To evaluate the recommendations, a total of 12 people were interviewed from different areas of responsibility and departments. The interviewees were from the regulatory affairs quality department (3 people), operative quality department (2 people), different divisions of product development (2+2 people), legal department (1 person), production (1 person), and technical support of the customer service (1 person). One thing all interviewees had in common was that they had a long work history at the case company or some other company that designs and manufactures medical devices. Therefore, they are familiar with the way of working that is compliant with the current directive as regards their own tasks. In addition, the recommendations will have an effect on their areas of responsibility. For some of the interviewees the topic was already partly familiar, for example through an external course, but for others the contents of the regulation seemed to be new.

The interviews were conducted as pair or personal interviews in the case company's premises, and with remote workers as Microsoft Teams meetings during 26.2. – 17.3.2020. They were recorded. The interviews followed the theme interview method in that the questions were based on the theme selected before the interview and they were the same for all, but the discussion was not limited except by the time reserved for the interview.

At the beginning the interviewees were told about the degree this thesis is part of. Next, the approval process was gone through at a general level (picture 1) with the interviewees, to help them gain an overall understanding and to make it easier to understand specific requirements. The interviews were valuable not only because the recommendations were evaluated, but also because during the interviews were presented a summary of the actions that had already been taken for the regulation and provided information about the upcoming actions that comply with the recommendations. The interviewees got the overall picture of the MDR requirements, and they commended its comprehensiveness.

The recommendations were evaluated one by one, and the question about each was whether the recommendation is necessary and sufficient. At the end, the interviewees were asked to say if they know about something else to recommend related to the topic, and they were asked to arrange the recommendations in order of importance. Almost all interviewees said that deciding on the order of importance was difficult, because all recommendations are required by the law. It was only possible to find differences between them based on the schedule or the interviewee's own area of responsibility.

In the next chapter, the clarifications, changes, and additions that were made on the recommendations based on the interviews are described in more detail. The final recommendations, in the order of importance based on the interviews, are in chapter 6.3.

6.2 Changes of Recommendations

The purpose of the recommendation evaluation interviews was to analyse whether the recommendations are sufficient and timely to meet the requirements set forth in the upcoming regulation. The recommendations were updated based on the findings from the interviews. Recommendation 5.3 (chapter 5) about General Safety and Performance Requirement was removed, because the recommended actions had already been taken. Two new recommendations were added. The schedule (26.5.2020) for many of the recommendations was updated to ”by the end of the transition period”. Table 3 (below) provides a brief comparison of the differences between the final and original recommendations.

Table 3: Changes of recommendations

Final recommendation	Change compared to earlier (chapter 5)
Recommendation 1: A new SOP should be created for Post-Market Surveillance by the end of the transition period of the regulation by the process development manager	Added: Cyber and data security
Recommendation 2: A Person Responsible for Regulatory Compliance (PRRC) should be named by the end of the transition period of the law by company management	Added: In addition to the responsibilities, it would be good to agree on the authorisations in writing
Recommendation 2: A Person Responsible for Regulatory Compliance (PRRC) should be named by the end of the transition period of the law by the company management	Added: Insuring the person primarily by the company
Recommendation 3: The conformity of software products sold to customers as ready to use should be ensured and the supplier contracts of OEM products should be updated by the end of the transition period by the product managers	Added: Updating the supplier contracts of OEM products with MDR conformity and the case company's new distributor responsibilities related to these
Recommendation 4: The declarations of conformities (DoC) should be updated to comply with the requirements set forth in the regulation in conjunction with the device-specific MDR approvals by who signs the declaration	Added to the DoC content requirement list: "all standards and requirements that the product fulfils…"
Recommendation 4: The declarations of conformities (DoC) should be updated to comply with the requirements set forth in the regulation in conjunction with the device-specific MDR approvals by who signs the declaration	Changed responsible person: Quality director -> Person who signs the declarations
Recommendation 5: SOPs of Vigilance and Creating and Delivering Technical Bulletins should be updated regarding the Eudamed obligation by the end of the transition period by the persons responsible for the SOPs	Changed responsible person: Quality director -> Persons responsible for the SOPs
Recommendation 6: The company is registered into Eudamed by the quality department.	No changes
Recommendation 7: The devices are registered in the UDI database by 26.11.2020 and introduced within the UDI schedule by the FDA-UDI responsible persons	No changes
Recommendation 8: The distribution agreements should be updated with the distributors' new MDR responsibilities by the end of the transition period by the export department	No changes

Recommendation 9: A new SOP should be created for trend follow-up by the end of the transition period by the process development manager	No changes
Recommendation 10: All SOPs (as applicable) should be updated as soon as possible by the persons responsible for them	New recommendation
Recommendation 11: The Medical Device symbol should be added to the type labels and manuals by the end of the transition period by the product managers	New recommendation

6.3 Final Recommendation

According to current knowledge, the new regulation for medical devices sold in Europe will become effective in full on 26.5.2020. However, it is possible that the schedule will change. On 25.3.2020, the European Commission released an announcement [44] saying that because patient health and safety are their guiding principles, they propose that the implementation of the MDR regulation (2017/245) is postponed by a year. The Commission's goal is to submit their proposal about the postponement at the beginning of April, so that the parliament and the council can approve it by the end of May. A year of extra time would be warmly welcomed and needed by the Commission, the notified bodies, and economic operators, considering both the MDR challenges and the current challenges caused by the coronavirus (COVID-19).

In this thesis, recommendations have been created for the case company on how to meet the requirements of the upcoming regulation and continue manufacturing and sales in Europe. The recommendations cover the areas and activities for which the necessary changes had not been made yet in January 2020. The recommendations evaluated and deemed necessary by specialists and the new recommendations that came up in the interviews are listed below.

Recommendation 1: A new SOP should be created for Post-Market Surveillance (PMS) by the end of the transition period of the regulation by the process development manager

The recommendation is to create an SOP for post-market surveillance for the company, because it is a new requirement set forth in the regulation. It has to be designed, set up,

documented, developed, maintained, and updated actively and systematically. The collected data has to be analysed from the points of view of quality, safety, and performance. The procedure has to cover the entire lifecycle of the product, and the provided data has to be sufficient for drawing conclusions to define, develop, and oversee corrective and preventive actions. The SOP has to contain separate instructions for each risk class as follows:

- Risk class I devices: PMS plan and report (updated as necessary)
- Risk class IIa devices/device groups: PMS plan and a Period Safety Update Report (PSUR) (updated every two years)
- Risk class IIb devices/device groups: PMS plan and a Period Safety Update Report (PSUR) (updated yearly).

To help creating the SOP, it is recommended to use the technical report published by the International Organization for Standardization (ISO): ISO/PRF TR 20416 Medical devices - Post-market surveillance for manufacturers [40]. An additional recommendation is to collect data related to cyber and data security, because the requirements and threats related to these increase all the time.

Recommendation 2: A Person Responsible for Regulatory Compliance (PRRC) should be named by the end of the transition period of the law by the company management

One of the new requirements of the regulation is that the manufacturer has to have permanently at least one person responsible for regulatory compliance in their organisation. The law stipulates that the person must not be legally in weaker position within the organisation because he or she performs these duties. The recommendation is to appoint a qualified person for the task or divide the responsibility between several qualified persons. It is recommended to create a written agreement on the responsibilities and authoritisations, for example by updating the job description. The naming has to be done by the end of the transition period of the regulation, and the person(s) have to be registered in Eudamed when it is available.

Taking into account the level of responsibility associated with the task, it is recommended that the person is a member of the Executive Board. It is also recommended that the company arranges a liability insurance for the responsible person, but otherwise the responsible person is advised to consider taking a personal insurance.

Recommendation 3: The conformity of software products sold to customers as ready to use should be ensured and the supplier contracts of OEM products should be updated by the end of the transition period by the product managers

The MDR adds a new risk class classification rule (no 11) to the conformity assessment for software. The recommendation is to evaluate the software that the case company is responsible for and that is sold after the transition period ends. Because none of the sold currently non-medical software is manufactured by the company, the recommendation is to send a letter to the manufacturers and ask them to confirm the risk class classification and be responsible for its requirements.

The company also has other products (currently medical devices) that are bought ready and sold forward, either under the company's own or the original manufacturer's responsibility. They are called original equipment manufacturer products (OEM). Updating the supplier contracts for both the software mentioned above and the other OEM products taking into account MDR conformity would be necessary. Another noteworthy thing are new distributor responsibilities (recommendation 8 below), which concern some of the OEM products in the case company.

Recommendation 4: The declarations of conformities (DoC) should be updated to comply with the requirements set forth in the regulation in conjunction with the device-specific MDR approvals by who signs the declarations

In order to comply with the requirement set forth in the regulation, the recommendation is that the information below is updated to the current declarations of conformities:

- the registration number of the company (when Eudamed is available for use)
- the unique UDI-DI identifier (when available)
- the intended use of the device
- updating the MDD compliance notification to MDR compliance
- as applicable, the number of the certificate issued by the notified body
- all standards and requirements that the product fulfils, because there can be only one DoC for each product.

Recommendation 5: SOPs of Vigilance and Creating and Delivering Technical Bulletins should be updated regarding the Eudamed obligation by the end of the transition period by the persons responsible for the SOPs

In order to meet the new reporting obligations for Serious Incidents ja Field Safety Corrective Actions (FSCA), the recommendation is to update the SOPs Vigilance (in Finnish: Toimitetun laitteen aiheuttama vaaratilanne) [42] and Creating and Delivering Technical Bulletins (in Finnish: Teknisen tiedotteiden laatiminen ja jakelu) [43] regarding the Eudamed reporting obligation.

Recommendation 6: The company is registered into Eudamed by the quality department

The manufacturers of mass-produced devices have to register in Eudamed (when it is available) before placing the devices on the market. If the conformity assessment procedure requires the participation of the notified body (devices in risk classes Im, IIa, and IIb), the manufacturer has to save the required information in the electronic system before the registration request is presented to the notified body. After this, a competent authority acquires the manufacturer's single registration number (SRN) and sends it to the manufacturer and the notified body. The manufacturer has to use the registration number when requesting for the conformity assessment from the notified body and to get into Eudamed to fulfil its other obligations. So, the recommendation is that the case company is registered in Eudamed as soon as possible.

Recommendation 7: The devices are registered in the UDI database by 26.11.2020 and introduced within the UDI schedule by the FDA-UDI responsible persons

There is a new requirement in the regulation about the unique identification of devices. Recommendations for meeting the UDI requirements are the following:

- The company should be registered as a manufacturer in the Eudamed database (when available)
- UDI-DI (chapter 2.2.9, picture 6) is recommended to be formed through the Commission-approved GS1 AISBL issuing entity, because the company already uses it
- The devices should be registered into the UDI database (if available) by 26 November 2021 (also software as a medical device)
- Devices belonging to the risk classes IIa and IIb should be marked with the UDI identifiers by 26 May 2023
- Devices belonging to the risk class I should be marked with the UDI identifiers by 26 May 2025

- UDI-DI has to be used at least in the following documents: User manuals, certificates, DoC, and the technical file

Further information can be found in the European Union publication Unique Device Identification (UDI) System – FAQs [21] and in the instructions by GS1 Be ready for UDI in the EU! [20].

Recommendation 8: The distribution agreements should be updated with the distributors' new MDR responsibilities by the end of the transition period by the export department

The regulation defines new responsibilities for distributors. So that the responsibilities between the case company and its distributors are clear, it is recommended that the distribution agreements are updated with the distributors' new MDR responsibilities. In the future, the distributor responsibilities include the following, for example:

- The distributor must ensure with a sampling method that the device has a CE mark and a MRD-DoC has been created for it, that the labels drawn up by the manufacturer and the instructions for use are supplied with the product, and the device has the UDI identifier
- The distributor has to make sure that the storage and shipping conditions meet the manufacturer's requirements
- If the distributor suspects that the device is non-compliant, they cannot place the device on the market before compliance is achieved and the distributor has fulfilled its notification obligation to the manufacturer, and in case of serious injury or suspected forgery, also to the competent authority
- Complaints and incident reports received by the distributor have to be forwarded to the manufacturer without delay. The distributor has to keep a register of complaints, non-compliant products and product recalls, and withdrawals from market. The distributor has to keep the manufacturer up to date about such monitoring and provide the information if requested.
- The distributors have to work in cooperation with authorities, which means that they have to provide the available information to demonstrate conformity, help with actions to remove the risks of devices placed on the market, and provide samples free of charge or the opportunity to access the device.

Recommendation 9: A new SOP should be created for trend follow-up by the end of the transition period by the process development manager

The new regulations regarding trends concern significant increases of unacceptable side effects. A significant increase is defined in relation to the foreseeable frequency or severity of the side effect of the device in question during a particular period of time, as defined in technical documents and product information.

The recommendation is that in order to comply with the regulation, the company should create a new SOP for trend follow-up and reporting or include the requirement in an existing SOP (for example PMS, recommendation 1 above) as a new chapter. The follow-up can be, for example, active monitoring of received customer feedback and existing incident databases (MAUDE/FDA active [41], Eudamed/EU upcoming). To comply the requirement easier, it may be necessary to utilise statistical methods. The reporting has to be done through Eudamed, as soon as it is available.

Recommendation 10: All SOPs (as applicable) should be updated as soon as possible by the persons responsible for them

The recommendation is to evaluate the current SOPs, and if necessary, make the following changes to them:

- Valvira is mentioned in some of the company's current standard operating procedures. Because the responsibility for medical devices was transferred from Valvira to Fimea [45], the recommendation is to update the SOPs by removing Valvira and replacing it with *the competent authority*.
- In the current SOPs, there are references to the current directive. Because over the next few years the company will have both MDD and MDR compliant devices, the SOPs should be updated to include references to both of them.

Recommendation 11: The Medical Device symbol should be added to the type labels and manuals by the end of the transition period by the product managers

A new requirement in the regulation is that the manufacturer has to mark its products with a Medical Device symbol. A sample symbol was found on the MedTech Europe website (in the picture 10 below).

Picture 10: Medical Device Symbol [46]

The recommendation is to monitor the harmonization of the standard ISO 15223-1 Medical devices — Symbols to be used with medical device labels, labelling and information to be supplied — Part 1: General requirements [47] and take it into account when selecting the symbol. This makes it possible to use the same symbol not only in Europe but in

almost all countries. The symbol has to be added to the type labels and manuals of medical devices by the end of the transition period.

Common recommendations

As different specialists mentioned in the interviews, by acting on these recommendations the company complies with the requirements set forth in the regulation. However, it is still recommended that the company actively monitors the notifications issued by the Union, because the requirements may still be supplemented, the end of the transition period may change, and currently open issues (such as harmonized standards, MDR approvals of notified bodies, and the availability of Eudamed) may be solved.

7 Conclusion and Discussion

The manufacturers of medical devices faced a big challenge when the Union replaced the MD directive that had been in use for about three decades with the new MD regulation that became effective in 2017. The Union's goal was to remove the room for interpretation from the legislation, meet the challenges of developing technology, exclude problems that had occurred in use, improve safety and people's health and support the functioning of the internal market while also maintaining the spirit of innovation. According to current knowledge, the transition period of the regulation probably ends in May 2021, so the topic is very current.

The case company for which this thesis was made has operated in the European market for several decades, designing and manufacturing medical devices. Because Europe is the main market area for the company, it is crucial that the company is able to meet the challenge brought by the MDR and fulfil its requirements, which are prerequisites for continuing operations in Europe.

The theory section of this thesis provides a comprehensive information package on the new regulation. The MDR requirements affect different stages of the approval process, and therefore the theory section describes, for example, the increased requirements of quality management, risk management, and incident report system. New requirements are described in more detail, and they have their own sub-chapters (below).

There has long been a requirement in the pharmaceutical industry regarding a person responsible for pharmacovigilance. Now a similar requirement is introduced for medical devices: person responsible for regulatory compliance. The qualification requirements and responsibilities of such person, for example, are described in the theory section.

The requirement for unique device identification (UDI) will become effective also in the European market area, like it already is in the US. With the help of UDI, it is possible to guarantee the traceability of medical devices and ensure that they comply with the patient safety requirements of the European Union. The goal is to prevent incidents such as the breast implant scandal from happening again.

In order to further improve patient safety, the regulation brings a requirement for post-market surveillance system. In the future, information has to be collected from both the

company's own (PMS) and other companies' (Trends) devices. After analysis, actions are required, for example, on informing patients and risk management updates.

The new European electronic information system (Eudamed) will be opened in 2022, according to current knowledge. The information system will collect information about, for example, device approvals, UDIs, notified bodies, economic operators, clinical investigations and incident reports. Because the system is so comprehensive, there will be much more information than before, but for manufacturers, for example, this means increased documentation obligation.

In the practical section of the Master's thesis, the current state of the company was analysed, and based on that, recommendations were drawn up on how to meet the new requirements of the regulation. The resulting recommendations on fulfilling the requirements were created to make the challenge easier for the case company. The recommendations were created specifically for those parts of the regulation for which the actions were still incomplete or not taken in January 2020. To make the recommendations as comprehensive and well-targeted as possible, they were evaluated with the help of specialists. The company's specialists believe that by meeting these updated recommendations the case company will comply with the requirements set forth in the regulation. In addition, one of the specialists suggested that the recommendations created in this thesis could be used as the quality targets for the next five years at the case company.

The actions taken based on the final recommendations will eventually be audited by a notified body. This will provide valuable information about their interpretation, and the actions can be updated to comply even better with their and the authorities' requirements.

Considering that the previous directive was effective for decades, it is to be expected that also the new MDR will be effective for a long time. Therefore, with the help of these recommendations the case company can continue and further expand operations in Europe now and during the coming decades.

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