

A photograph of a surgical team in an operating room, wearing blue scrubs and masks, illuminated by large overhead surgical lights. The scene is dimly lit, with the primary light source being the circular surgical lamps.

# EUROPEAN MEDICAL DEVICE REGULATIONS MDR & IVDR

A Guide to Market

**BUSINESS  
FINLAND**

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## BUSINESS FINLAND – A PATH TO THE GLOBAL MARKETS

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# BUSINESS FINLAND

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## PROLOGUE


Modern medicine would be helpless without medical devices. These devices enable the diagnostics, prevention and monitoring of diseases, as well as their treatment and alleviation. They enable the investigation of human anatomy and physiology with a wide range of technologies. Solutions for replacing or modifying the anatomy or a physiological process of a human being come in many shapes and forms: from dental equipment and X-rays to MRI, patient monitors and patient beds; from surgical instruments to biodegradable implants; and from in vitro diagnostics and reagents to diagnostic artificial intelligence software. Altogether, there are many hundreds of thousands of different types of medical devices globally and the above are just a scratch on the surface of the variety produced by the constantly growing Finnish health tech sector. Research and development in the sector is booming due to many advancements in medical sciences and information technology. With the ever-increasing capacity of harnessing knowledge and bytes, we barely realise that the science fiction of the past is already here. Yet we cannot even comprehend the advancements we will see in the near future.

No matter what the novelties are, their time to market could be dramatically faster if they laid their foundation on robust know-how regarding the international regulatory requirements. A great magnitude of the experience on producing safe and efficient medical devices, gathered throughout the decades by the industry, is printed in international legal acts and standards. These writings should therefore be studied in detail by every new innovator if they are to excel in medical technology and its commercialisation. Even more so, when the manufacturer understands that the legislators and the authorities are concerned about the health and safety of local citizens, and that they will not let you distribute products without complying with the absolute minimum of requirements.

The value of the Finnish health tech exports in 2019 raised to a new record of 2,4 billion euros. The growth of exports in the field during the past 20 years has been 5,7 % on the average. Finland is one of the few countries in the world that exports considerably more medical technology than it imports. The foreign trade balance surplus on medical technology in 2019 was 1,1 billion euros. The Ministry of Economic Affairs and Employment in Finland has set a national growth strategy for research and innovation in the health sector. The strategy focuses on systematically developing the sector's operating environment and ensuring its competitiveness, boosting investments and achieving further economic growth. Strengthening the know-how on regulations and standards in the sector is one of the key measures of the strategy. Because only the tiny minority of medical devices produced by the Finnish health tech industry remain in Finland, we must focus on international market access. This, in combination with the highly-educated and capable workforce in Finland, a digitized society, advanced health legislation, and a small society of well-connected people willing to work together, providing a platform of opportunities for great innovations.

The first edition of this book was published in 2015 in Finnish and focused on the medical device directives, which are to be replaced by the new EU regulations, with Tom Ståhlberg as the author. It guided many medical device manufacturers on their path to the European and global markets. During the transition time to the new EU regulations, the first edition still holds value. However, there was a great need to rewrite the book to cover the new regulations that will replace the directives. The current edition focuses on the new Medical Device Regulation (MDR) and the In Vitro Diagnostic Medical Device Regulation (IVDR). By following the European regulations, the manufacturer, in most cases, comes to fulfil the majority of global safety and performance requirements for their medical devices. Nevertheless, there are differences in regulations globally, and only some related to the US FDA requirements are mentioned in this book. It is, therefore, a matter of educating yourself on the many mechanisms of market entry globally. The language of this edition is English due to the high number of international health tech innovators finding homes for their business and life in Finland, and the fact that business in this field is increasingly global.

It goes without saying that a guidance book can only help one in getting started with the regulatory knowledge. But all the more important, it may open the eyes of the newcomer to pay enough attention to a topic that is one of the foundations in business. A medical device manufacturer must invest substantially to learn more and to move beyond the regulatory basics to gain all the know-how that is vital for reaching and remaining on the market. Experience is a key winning factor, and where regulatory or quality expertise is not available within the innovator team, it must be outsourced.



We welcome feedback from all stakeholders regarding the contents and interpretations in this book. Engaging in dialogue with all stakeholders and knowledgeable parties, including medical device manufacturers, researchers, authorities, legislators, and investors, will make it possible to make the message all the more valuable and accomplish the strategy of the Finnish Ministry of Economic Affairs and Employment. The health tech sector requires dedication from its stakeholders, but as long as health remains one of the basic needs of humanity, this sector will grow and evolve.

Our team of authors would like to thank everyone who has currently or in the past supported the publishing of this book. The first edition would not have seen the light of day without the strong support of Business Finland, Healthtech Finland, and many individuals in their ranks. It is thanks to Business Finland that there is a continuum in providing this baseline of knowledge for the Finnish health tech sector. And it is the great privilege of the Lean Entries team, Ilona Santavaara, Leena Raunio, and Heikki Pitkänen to contribute to the invaluable and devoted groundwork by Tom Ståhlberg. There is great power in collaboration!

Thanks to our loved ones for the support and encouragement to write this book!

Heikki Pitkänen, Leena Raunio, Ilona Santavaara & Tom Ståhlberg

Tampere and Nagu, 17 December 2020

## ABSTRACT

The aim of this book is to provide guidance to the Finnish medical device manufacturers regarding the new European regulatory requirements brought by the Medical Device Regulation (MDR) and the In Vitro Diagnostic Medical Device Regulation (IVDR). Business Finland has found it necessary to provide this guidance as there is an obvious hurdle and potential market barrier for companies in the health tech sector if regulatory requirements are not sufficiently acknowledged. A health tech innovation will never become a CE marked medical device unless regulatory aspects are taken into account efficiently from Day One.

The bottom line in medical device regulations and in this book is that devices placed on the European Union market must be safe and effective. All relevant safety and performance requirements must therefore be fulfilled and the device must be suitable for its intended purpose. In order to meet the most stringent safety and performance requirements, the manufacturer takes two complementary approaches: first, the device must meet all related requirements and hold a complete Technical Documentation, and second, the manufacturer must meet all Quality Management System (QMS) requirements. By running an efficient QMS, the manufacturer comes to control its processes to create highly performing medical devices and to manage their commercial activities throughout the life cycle of the device. Fortunately, this is nothing separate or different from the other key activities of the company, but creates the baseline for a successful business.

The manufacturer's journey starts from their marketing and regulatory strategy, how the innovation is turned into a medical device that is eventually placed on the market. To craft the strategy, the first step is to define whether or not the product is regulated as a medical device, and the answer is not always as easy as it may seem. The intended purpose of the device, as defined by the manufacturer, is decisive when solving this problem. The risk classification and the type of the device define the extent of the conformity assessment and the amount of work ahead prior to placing the device on the market. From collecting the design inputs, through to design verification and validation, clinical evaluation, and risk management, as well as proper design reviews, the design reaches a point where the manufacturer can declare conformity to the regulations and CE mark the device. This, however, is not the end of the manufacturer's compliance activities, but only the beginning. Compliance runs throughout the entire life cycle of the device, from the innovative idea to taking care of all post-market responsibilities.

This book provides the reader with an overview of the European medical device regulatory landscape, yet remains on a general level to keep the contents to a minimum. Please note that the European Commission is working on many guidance documents as well as delegated and implementing acts that may influence the interpretations provided in this book. The intention of the book is to give valuable insights on topics that are not easy to comprehend for the newcomer and which require experience to master. This may save months of time by turning confusion into the first strings of clarity. In the end, it is the manufacturer that holds full responsibility to ensure awareness and adherence to every relevant regulatory requirement applicable to their devices and organisation. By doing it right the first time, the medical device manufacturers hold a great competitive advantage.

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A female healthcare professional with dark hair, wearing blue scrubs and a stethoscope, is looking down at a tablet computer she is holding. The background is a blurred clinical setting with soft bokeh lights.

# **1. INTRODUCTION TO MEDICAL DEVICE LEGISLATION IN THE EUROPEAN UNION (EU)**


The European Union (EU) medical device legislation is undergoing a major transformation from the former medical device directives to the new regulations, the Medical Device Regulation (MDR) 2017/745 and the In Vitro Diagnostic Medical Device Regulation (IVDR) 2017/746. The original directives, the Medical Device Directive (MDD) 93/42/EEC, the Active Implantable Medical Device Directive (AIMDD) 90/385/EEC, and the In Vitro Diagnostic Medical Device Directive (IVDD) 98/79/EC were all published in the 1990s. As these directives were adopted into the national legislation of the EU Member States, each member state provided some differences in the interpretations and practices in relation to the directives. To add on the variety of requirements, the directives had been complemented by many more pieces of legislation, guidance documents and recommendations by the European Commission (EC), partly due to the speed of innovation in the medical device sector. After publishing the most extensive amendment to the medical device directives in 2007, concerns nevertheless arose, for instance, regarding the performance of software in medical use and too many severe incidents which took place with implantable medical devices. Clear shortcomings were observed, most notably in the processes of some medical device manufacturers and of some Notified Bodies. These examples provide some highlights of the pressure that mounted especially as the EU medical device directives were no longer in line with the development and harmonization of legislation in other countries. As a consequence, an enhanced and more harmonised medical device legislation was found obligatory, and the MDR and the IVDR were eventually published in May 2017. EU regulations, contrary to the directives, are adopted to national legislation as they are with little room for deviations. The date of application for the MDR was originally 26 May 2020 but was extended to 26 May 2021. The date of application for the IVDR is 26 May 2022.

The most significant changes brought by the new medical device regulations are:

- Reclassification of some devices into a higher class, resulting in an increase in requirements and oversight, especially for software as a medical device and for devices containing software, as well as for in vitro diagnostic (IVD) devices with a completely renewed classification.
- Emphasis on clinical evaluation, risk management, and benefit-risk analysis throughout the product life cycle.
- Stricter control of the entire supply chain, starting from vendors and ending at increased requirements for importers and distributors all the way into post-market activities.
- More emphasis on post-market surveillance activities in general.
- More stringent requirements on clinical evaluation for all classes and especially on the oversight of the highest device class.
- A mandatory Quality Management System (QMS) also for manufacturers with products in the lowest risk class.
- Bringing specific products that do not have an intended medical purpose but which bear a similar risk profile to medical devices, under the medical device regulations (See Annex XVI of the MDR).
- Establishing the European database on medical devices (EUDAMED) and defining responsibilities related to the database for the economic operators in the supply chain.
- Deployment of the Unique Device Identifier (UDI) for medical devices and connecting the identifiers with EUDAMED to enhance transparency and the follow-up on vigilance activities.
- More stringent requirements on the Notified Bodies, for example, regarding their clinical and technical know-how and conformity assessment processes, starting from the manufacturer's application for certification.
- More defined and increased responsibilities of the EU Member State competent authorities.
- In summary, substantially more requirements and contents to become familiar with.

Many business decisions in the health tech sector are dependent on or affected by regulations, making regulatory compliance one of the foundations of a successful business. At first, it may feel counterintuitive to consider regulations or related standards as enablers due to their grim outlook, but winning medical device manufacturers recognise the great value of their teachings for their business and apply regulations and standards efficiently in their processes.

Timing is of the essence, as one would not want to miss crucial regulatory inputs and repeat the development cycles. Therefore, it is advisable to become acquainted with the definition of a medical device or an in vitro diagnostic (IVD) medical device early on. It is the intended purpose and technical properties of the product that define whether or not the product qualifies as a



medical device and how heavily the manufacturer is then affected by the regulatory requirements. However, among the hundreds of thousands of different types of medical devices sold in Europe and worldwide and new technological milestones reached, it is not always evident what qualifies as a medical device and what does not. For instance, it may be a daunting process to define whether a software or its modules qualify as medical devices according to either the MDR or the IVDR, making it worthwhile to ask for experienced support. If a product fulfils the definition of medical device or an IVD device, the manufacturer must comply with the MDR or the IVDR. If not, the product cannot be CE marked or placed on the market as a medical device. It is also important to remember that a medical device manufacturer may need to comply with several other European legislations aside the MDR or the IVDR. Further chapters go into more detail of CE marking and EU legislation in general.

It is a requirement in the MDR and the IVDR that a manufacturer creates a regulatory strategy for the device. Not only is this good business practice, but it should also address the manufacturer's plans and means to enter other international markets. The regulatory strategy should identify opportunities and threats related to those markets and align with the company's marketing strategy. It is necessary to know the global regulatory requirements to find the most efficient path from product development to market.


When a product or software qualifies as a medical device, it is essential to classify the device at the early stages of product development, if not before any design activities. Both qualification and classification can be complicated tasks, but false interpretations may bring dramatic consequences for the business. Further chapters provide an overview on qualification and classification of devices and what guidance to look for. The manufacturer might also need to take into account the intended combined use of products, the definition of an 'accessory' to medical devices, many European and international guidelines, or even the EU case law.

A medical device that is not CE marked cannot be placed on the EU market, not even by distributing it free of charge. It is under the responsibility of the manufacturer that the product is appropriately CE marked. The concept of a "sales approval" does not exist in the EU, as it does for drugs, for example. The manufacturer must provide safe medical devices that are appropriate for their intended purpose and in compliance with their performance requirements. When the risk class of the device is higher than class I, a Notified Body performs an assessment on the conformity of the device and on the manufacturer's Quality Management System (QMS), and issues an EU certificate of compliance. However, printing the CE mark on the packaging label of the device remains the responsibility of the manufacturer.

The General Safety and Performance Requirements (GSPR, in Annex I of the MDR and the IVDR) applicable to a specific medical device need to be identified by the manufacturer. To comply with the general requirements, manufacturers mainly utilise international state of the art standards (harmonised to the EU medical device legislation or not) and guidelines. When a manufacturer is convinced of having all required activities performed and documented, and a Notified Body has provided the EU certification (where applicable), the manufacturer signs the Declaration of Conformity (DoC) and prints the CE mark on the device label. A European-wide database named EUDAMED is the register to which the manufacturer then uploads this information together with other device information. Thereafter, the device may be placed on the European market and put into service for end users.

Most EU countries will pose certain additional obligations to the manufacturers, such as requirements for national languages available for the device user in the instructions for use, in other labelling, and on the device interface. To initiate clinical investigations for the medical device, or performance studies for the IVDs, the manufacturer needs to seek approval from the competent authority and becomes exposed to their surveillance. Then, after registering the device to EUDAMED, the manufacturer also becomes subject to the market surveillance activities of the EU competent authorities

An overview on the path to CE marking is presented in Chapter 4.2. It must be remembered that the responsibility over the device is carried by the manufacturer throughout the life cycle of the device. The post-market and vigilance requirements for device manufacturers are described in Chapter 7. Now that a Quality Management System (QMS) is a requirement also for



devices in class I, the international ISO 13485 Quality Management System (QMS) standard is relevant for all manufacturers. The QMS requirements are discussed in Chapter 8.



## 2. LEGISLATION IN THE EU



## 2.1. EU LEGISLATION IN A NUTSHELL

EU legislation is divided into primary and secondary. The treaties (primary legislation) are the basis or ground rules for all EU action. Secondary legislation, which comes in the form of multiple different legal acts including regulations and directives, are derived from the principles and objectives set out in the treaties.

EU legislation concerning product rules is mainly composed of 'directives' and 'regulations'. The difference between these two is significant. Regulations are binding legislative acts which must be applied in their entirety across the EU from their date of application. Directives, on the other hand, are legislative acts that set out rules that all EU countries must achieve. However, it is up to the individual EU Member State to transpose these rules into their own national legislation. Directives set a deadline by which member states must have adopted the directive into their national legislation.

- Other legal acts of the European Commission (EC) include 'decisions', 'recommendations', 'opinions', 'delegated acts', and 'implementing acts'.
- A 'decision' is binding on those to whom it is addressed (e.g., an EU country or an individual company) and is directly applicable. An example of a decision related to medical devices is the *Implementing Decision (EU) 2017/1445 of 8 August 2017 on the group of products whose principal intended action, depending on proanthocyanidins (PAC) present in cranberry (Vaccinium macrocarpon), is to prevent or treat cystitis*.
- A 'recommendation' is not binding. A recommendation allows the institutions to make their views known and to suggest a line of action without imposing any legal obligation on those to whom it is addressed. Despite their status as recommendations, it is advisable to apply them with the same rigour as one applies the guidance documents published by the EC (e.g., the MDCGs). An example of a recommendation related to the MDD, AIMDD, and IVDD is the *2013/473/EU Commission Recommendation on the audits and assessments performed by notified bodies in the field of medical devices*.
- An 'opinion' is not binding either. It is an instrument that allows the EU institutions to make statements in a non-binding fashion, in other words without imposing any legal obligation on those to whom it is addressed.
- A 'delegated act' is a legally binding act that enables the EC to supplement or amend non-essential parts of EU legislative acts, for example, in order to define detailed measures. The MDR and the IVDR refer frequently to the power of the EC to adopt delegated acts, for instance, to amend the Annexes II and III regarding the requirements for Technical Documentation, or to amend the definition of nanomaterials in the light of technical and scientific progress, or to amend the minimum contents of the Declaration of Conformity (DoC) or certificates provided by Notified Bodies.
- An 'implementing act' is a legally binding act that enables the EC – under the supervision of committees consisting of EU countries' representatives, such as the MDCG – to set conditions that ensure that EU laws are applied uniformly. The MDR and the IVDR refer frequently to the power of the EC to adopt implementing acts through consulting the MDCG and following an examination procedure defined in EU law. Examples of implementing acts could be to determine whether or not a specific product (or category or group of products) falls within the definition of 'medical device' or 'accessory for a medical device', or the adoption of common specifications (CS) in respect of the requirements in the several annexes of the MDR and the IVDR.

At the time of publishing this book, the medical device industry waits for several delegated and implementing acts as there are obvious needs to complement the original MDR and IVDR in order to bring clarity to a number of articles within the regulations.

Directives and regulations need to be updated over time. This is done by the means of 'corrigenda' and 'amendments'. If there is an error in the original publication that needs to be corrected, a 'corrigendum' is released. If the legislation is altered or supplemented, this can be done by publishing an 'amendment'. In practice the difference between these two can sometimes be quite vague.

Many legal texts published in the Official Journal of the European Union are also available as a ‘consolidated’ version in EUR-Lex. All changes applied by the successive amendments and corrigenda of a legal act have been integrated in the text of the consolidated version. This provides more transparency and is usually easier to read compared to reading the legal act and its amendments and corrigenda separately. It should also be noted that if a corrigendum provides only a minor change, it might not be consolidated before the next major change (another corrigendum or amending act) takes place. The EU institutions do not assume any liability for the content of the consolidated versions, and state that these texts have no legal value. The original texts published in the Official Journal are the only legally valid version. However, since consolidated versions provide a much easier read and give a better understanding of the rules that are currently in force, this book provides links to consolidated versions. The same advice regarding consolidated texts is repeated when discussing the utilisation of standards.

EU legislation is available in all official member state languages. If one is reading the legislation in their own language and if interpretations are challenging, it may be worthwhile checking the English original version. If these two seem contradictory, the English original version is the safer version to follow.

Chapter 2.5.3 discusses the Finnish national law in relation to medical devices.

## 2.2. THE EFFECT OF EU LEGISLATION ON EUROPEAN AND OTHER COUNTRIES

### 2.2.1. EU Member States

The European Union was established in 1957, after which the number of member states has grown from six to 28, to be reduced to 27 by Brexit. Currently, five more countries are considered candidates and they are in the process of ‘transposing’ (or integrating) EU legislation into national law.

The EU regulations, directives, and related guidance apply directly to all member states (Table 1), but also to the candidate countries (Table 2) and potential candidates (Bosnia and Herzegovina, Kosovo). Negotiations between EU and Turkey have been stalled for years.

Table 1 EU Member States

Austria	Denmark	Hungary	Malta	Slovenia
Belgium	Estonia	Ireland	Netherlands	Spain
Bulgaria	Finland	Italy	Poland	Sweden
Croatia	France	Latvia	Portugal	
Republic of Cyprus	Germany	Lithuania	Romania	
Czech Republic	Greece	Luxembourg	Slovakia	

Table 2 EU Member Candidates

Albania	Montenegro	North Macedonia	Serbia	Turkey
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### 2.2.2. EFTA and EEA Countries

The EU medical device regulations (MDR and IVDR) can be considered to be in force also in those European Economic Area (EEA) countries that are not EU members (Iceland, Liechtenstein, Norway). Switzerland is not part of the EEA, but as a member of the European Free Trade Association (EFTA), it, together with the three EEA countries, continues to align its medical device

legislation with EU regulations. Some national deviations to EU law may exist in these countries and should be verified prior to placing devices on their markets.

### 2.2.3. United Kingdom and Brexit

The guidance from the Medicines & Healthcare products Regulatory Agency (MHRA) of the United Kingdom (UK) defines how medical devices are regulated and how manufacturers register in the UK from 1 January 2021, as the transition period following Brexit comes to an end. At the time of publishing this book, the new UK medical device legislation is under development, and therefore the below guidance leans on the anticipated legal regime. This guidance will be updated by the MHRA if anything changes:

- MHRA Guidance (as updated 7 Dec 2020): [Regulating medical devices from 1 January 2021](#)
- MHRA Guidance (as updated 8 Dec 2020): [Register as a manufacturer to sell medical devices from 1 January 2021](#)

The guidance is divided into sections on the different rules that will apply in Great Britain (England, Wales, and Scotland), Northern Ireland and the EU.

This is a summary of the key requirements for placing a device on the Great Britain market:

- Until 30 June 2023
  - CE marking according to the MDD, AIMDD, and IVDD as well as the MDR and IVDR will continue to be recognised.
  - Certificates issued by EU-recognised Notified Bodies will continue to be valid.
- From 1 January 2021
  - The EU will no longer recognise UK Notified Bodies.
  - UK Notified Bodies will not be able to issue EU certificates (other than for the purposes of the “CE UKNI” marking which will be valid in Northern Ireland) - and will become UK Approved Bodies.
  - A new route to market and product marking will be available for manufacturers wishing to place a device on the Great Britain market.
  - All medical devices, including IVDs, placed on the UK market will need to be registered with the MHRA. There will be a grace period for registering:
    - Class IIIs and Class IIb implantables, all active implantable medical devices, and IVD List A products must be registered by 1 May 2021.
    - Other Class IIb, all Class IIa devices, IVD List B products, and Self-Test IVDs must be registered by 1 September 2021.
    - Class I devices, custom-made devices and general IVDs (that do not currently need to be registered) must be registered by 1 January 2022.
  - Manufacturers of Class I devices, custom-made devices, and general IVDs that are currently required to register their devices with the MHRA must continue to register their devices on the same basis as they do now until the new registration requirements start to apply to those devices.
  - If you are a manufacturer based outside the UK and wish to place a device on the Great Britain market, you will need to appoint a single UK Responsible Person who will take responsibility for the product in the UK. Further details on the UK Responsible Person are set out in the guidance.

Regarding Northern Ireland, please see the MHRA guidance.

Regarding more detailed instructions on transitioning certification from UK Notified Bodies to EU-recognised Notified Bodies, please see the MHRA guidance.

## 2.3. THE EFFECT OF EU LEGISLATION OUTSIDE THE EEA

Many countries outside Europe allow the marketing of medical devices within their area if those devices are lawfully CE marked. The manufacturer, however, must be able to prove the lawfulness of their CE marking to the local authority. For that purpose, the manufacturer may place a request to their EU Member State competent authority (Fimea in Finland) for a Certificate of Free Sales (or Free Sales Certificate, Free Trade Certificate, Export Certificate, depending on the country and authority). The Certificate of Free Sales will carry the unique number of the EU certificate provided by the Notified Body as well as the Basic UDI-DI of the medical device (see Chapter 6.2.10 for the unique device identifier).

Through this practice, the meaning and strength of the CE mark is emphasized outside the European economic area. Nevertheless, an increasing number of countries globally hold requirements for device registration and approval, but it makes a positive difference if the device is CE marked.

It is not possible to extrapolate from the EU and assume that other countries have the same kind of medical device regulations. Despite the ongoing global harmonization efforts there may be very significant differences. Not even the definition of a medical device is necessarily the same outside the EU and, as an example, the classification may differ between countries. In such cases, it would be advisable to turn to regulatory experts with knowledge of that specific market area.

## 2.4. COMPETENT AUTHORITIES AND OTHER STAKEHOLDERS IN FINLAND AND THE EU

### 2.4.1. Finland as an EU Member State

As a part of the Finnish Government, the Ministry of Social Affairs and Health manages the preparation and implementation of Finland's social welfare and health care policy, gender equality policy, and occupational safety and health policy. The Ministry of Social Affairs and Health is in charge of its sectoral matters in the EU in terms of preparation, follow-up, defining Finland's standpoint, drafting EU legislation, and implementing EU legislation in Finland.

Each EU Member State has its own competent authority whose mission is to monitor the compliance of medical devices on the market. The competent authority in Finland is [Fimea](#). Fimea is a central administrative agency operating under the Finnish Ministry of Social Affairs and Health regulating medicinal products, medical devices, blood and tissue products and biobanks. Fimea's position as an authority is defined in Finnish law.


Finnish law and Fimea's role are further discussed in Chapter 2.5.3.

### 2.4.2. EU Institutions

EU institutions play a variety of roles regarding the MDR and the IVDR, and for that reason it is good to understand the structure of the European Union. The most important institutions related to medical devices are found on the EU website:

- [EU institutions and bodies in brief](#)
- [European Parliament](#)
- [Council of the European Union](#)
- [European Commission \(EC\)](#)
- [Court of Justice of the European Union \(CJEU\)](#)

The Council of the European Commission together with the European Parliament is the main decision-making body of the EU.



The European Commission is the EU's politically independent executive arm. It alone is responsible for drawing up proposals for new European legislation, such as those for medical devices, and it implements the decisions of the European Parliament and the Council of the EU. The Council represents the EU Member States, the Parliament represents the people, and the Commission represents the EU.

The Court of Justice of the European Union (CJEU) interprets EU law to ensure that it is applied in the same way in all EU countries. It settles legal disputes between national governments and EU institutions. This includes any disputes related to the interpretation and implementation of the MDR and the IVDR.

### 2.4.3. European Commission and Directorates-General (DG)

The European Commission (EC) proposes new laws, such as the MDR and the IVDR, for adoption by the Parliament and the Council. Then, together with the Court of Justice of the EU, the EC ensures that the law is properly applied throughout the EU Member States. The EC holds a key role in interpreting and guiding the MDR and the IVDR.

The EC is organised into several departments known as Directorates-General (DG). DG SANTE is responsible for EU policy on food safety and health and for monitoring the implementation of the related laws. Medical devices belong to their area of responsibility.

The Medical Device Coordination Group (MDCG) and its tasks are defined in the MDR and the IVDR. The MDCG deals with key issues of the medical devices sector, including Notified Body oversight, standardisation, borderline and classification, new technologies, clinical investigation and market surveillance. There are 13 working groups within the MDCG providing advice and guidance in their field of expertise. The members of the working groups are appointed by the EU Member States. Other stakeholders, such as the major European industry associations, participate as observers and are appointed following a call for applications. All members of the MDCG are appointed for the duration of three years. They meet regularly with the European Commission as the Chair.

Furthermore, the MDR and the IVDR require that the EC creates expert panels to advise and support the scientific assessment in the field of medical devices and IVD devices. Expert panels are designated by means of the [Commission Implementing Decision \(EU\) 2019/1396](#) for the relevant medical fields (e.g., for orthopaedics, neurology, ophthalmology). One expert panel is a 'screening panel' that determines whether there is a need for a scientific opinion by one of the panels.

The expert panels hold the following responsibilities, depending on the need:

- Providing opinions on the Notified Bodies' assessments of clinical evaluation of certain high-risk medical devices, and the performance evaluation of certain IVD devices
- Providing advice to the Medical Device Coordination Group (MDCG) and the European Commission concerning safety and performance of medical devices and IVD devices
- Providing advice to manufacturers on their clinical development strategy and proposals for clinical investigations
- Providing advice to EU countries, manufacturers and Notified Bodies on various scientific and technical matters
- Contributing to the development and maintenance of relevant guidance documents, common specifications (CS) and international standards
- Providing opinions in response to consultations from manufacturers, EU countries and Notified Bodies

Expert panel members are senior experts in their own field, appointed by the European Commission on the basis of their scientific, clinical and technical expertise, following a call for expression of interests.

A medical device manufacturer should acknowledge, at least, the following DGs, the Medical Device Coordination Group (MDCG) and its working groups, as well as the expert panels and their tasks.

- [Health and Food Safety \(DG SANTE\)](#)
  - [Public health](#)
    - [Medical Devices - Sector](#)
    - [Medical Devices – New regulations](#)
      - [Guidance – MDCG endorsed documents](#)
    - [Medical Devices – Dialogue between interested parties](#)
      - [MDCG Working Groups](#)
      - [International Cooperation](#)
    - [Medical Devices – Expert Panels](#)
- [Internal Market, Industry, Entrepreneurship and SMEs \(DG GROW\)](#)
- [Research and Innovation \(DG RTD\)](#)
- [Research Executive Agency \(DG REA\)](#)
- [Trade \(DG TRADE\)](#)

#### 2.4.4. Notified Bodies

Placing a medical device or an in vitro diagnostic (IVD) device on the European Union market may require a conformity assessment performed by a third party, a Notified Body (NB). Notified Bodies are conformity assessment bodies (CAB) officially designated by the national authority of an EU Member State to carry out conformity assessments within applicable European Union legislation, such as the medical device regulations (MDR and IVDR). These CABs are often private businesses performing calibration, testing, auditing, inspection and/or certification, and they may provide several other such services than conformity assessment according to one or more EU legislations.

Notification is an act whereby an EU Member State informs the European Commission and other EU Member States, that a body, which fulfils the relevant requirements, has been designated to carry out conformity assessments according to a specific European Union legislation (Hence the name *Notified Body*). Some countries outside the EU can also designate Notified Bodies through arrangements described on the NANDO website (For Brexit and UK Notified Bodies, please see Chapter 2.2.3). The medical device manufacturers can use any Notified Body for their conformity assessment, regardless of the home country of the manufacturer or the Notified Body. Many of these also hold staff to provide services internationally.

Other considerations for choosing a Notified Body may be their queues and speed of services, as well as the manufacturer's lingual and cultural preferences. Two Notified Bodies are designated for their task by Fimea as the Finnish designating authority:

- [Eurofins Expert Services Oy](#) (NB number 0537)
- [SGS Fimko Oy](#) (NB number 0598)

At the time of publishing this book, they are not yet designated for the MDR or the IVDR. It is also worth noting that Eurofins is currently designated to the IVDD and has applied for designation to the IVDR, whereas SGS Fimko does not provide IVD certification services. Neither of them holds a scope of competence to assess class III medical devices or active implantable medical devices. Read more on Notified Body scopes of competence below.

At the time of publishing this book, there are 18 Notified Bodies nominated for their tasks according to the MDR and five for the IVDR (For Brexit and UK Notified Bodies, please see Chapter 2.2.3). In comparison, the same numbers currently are 54 for the MDD, 12 for the AIMDD and 21 for the IVDD. All in all, given the timelines for the MDR and the IVDR, the number of Notified Bodies is alarmingly low and the speed of their designation in the joint effort of the EU Members States and the European Commission is lagging behind. In particular, those manufacturers who do not yet hold a relationship with a Notified Body designated for the MDR or the IVDR, and who cannot take advantage of the transition times provided for devices with CE marking according to the former directives, should take this into account in their CE marking schedules.

## Notified Body Scope of Competence and the NB Scope Expression Codes

The [NANDO \(New Approach Notified and Designated Organisations\) Information System website](#) holds the lists of Notified Bodies by country, legislation, and body. In the medical device sector, the Notified Bodies carry a scope of competence that is expressed by 'NB scope expression codes'. To make searches in NANDO, the manufacturer must know the 'NB scope expression codes' that match with their medical device to know which Notified Bodies can assess them. In addition to the 'NB scope expression codes', NANDO also reveals the conformity assessment options (indicated as annexes of the specific medical device legislation) and any limitations a Notified Body may have in their scope regarding a specific code (such as limiting the scope to devices up to class IIb only or ruling out certain technologies from the scope).

The 'NB scope expression codes' are defined in Regulation (EU) 2017/2185, and the codes (e.g., 'MDA 0307 Active non-implantable respiratory devices') are grouped in the following categories:

- MDA - Active medical devices
- MDN - Non-active medical devices
- MDS - Medical devices with specific characteristics
- MDT - Medical devices for which specific technologies or processes are used
- IVR - In vitro diagnostic devices
- IVS - In vitro diagnostic devices with specific characteristics
- IVT - In vitro diagnostic devices for which specific technologies are used
- IVP - In vitro diagnostic devices which require specific knowledge in examination procedures
- IVD - In vitro diagnostic devices which require specific knowledge in laboratory and clinical disciplines for the purpose of product verification

When a medical device manufacturer lodges an application for certification with a Notified Body, the device types and technologies are to be indicated. Usually, at the application review stage (as defined in section 4.3 of Annex VII of the MDR) the Notified Body will verify the codes provided by the manufacturer, or will assign the codes to the devices themselves. This verification is carried out by the Notified Body in order to ensure that it holds the scope of competence to assess the manufacturer's application, and that it holds the qualified assessors and specialists to carry out the relevant conformity assessment activities.

The *MDCG 2019-14 Explanatory note on MDR codes* provides instructions on the use of the 'NB scope expression codes' in relation to the MDR. At the time of publishing this book, a similar guidance document is being prepared by the European Commission for the IVDR. It is advisable for the manufacturer of medical devices to know in advance which codes match their device and how to check the scope of competence of Notified Bodies. This will save time when applying for a conformity assessment as the manufacturer then knows to contact Notified Bodies with a matching scope of competence.

Information regarding Notified Bodies, their contact information, scopes of competence and the NB scope expression codes can be found in the following sources (Please note that the last three sources may be affected by Brexit on 31 Dec 2020, since the Notified Body Operations Group (NBOG) server locates in the United Kingdom):

- [NANDO \(New Approach Notified and Designated Organisations\) Information System website](#)
- [Regulation 2017/2185 on Notified Body scope expression codes](#)
- MDCG 2019-14 (Dec 2019) – Explanatory note on MDR codes
- NBOG F 2017-3 – Applied-for scope of designation and notification of a conformity assessment body – MDR
- NBOG F 2017-4 – Applied-for scope of designation and notification of a conformity assessment body – IVDR
- [NBOG \(Notified Body Operations Group\) Documents website](#)

## Notified Body Sampling of Technical Documentations

Sampling of MDR Class IIa medical devices and IVDR Class B IVD devices for the assessment of the Technical Documentation by the Notified Body is based on the 'category of devices' which is defined by the above MDA, MDN or IVR codes. Sampling of MDR Class IIb medical devices and IVDR Class C IVD devices is based on the 'generic device group' which is defined by the European Nomenclature on Medical Devices (EMDN) codes. Please see the MDCG 2019-13 guidance document for further information regarding the 'categories of devices' and 'generic device groups' and how they affect the conformity assessment by Notified Bodies. In addition, please note at the time of publishing this book, the device registration module of EUDAMED is not yet in use, and the EMDN codes are not yet made available by the European Commission. The codes are expected to be published at the launch of the EUDAMED device registration module.

## 2.5. INFORMATION ON EU LEGISLATION

### 2.5.1. Create a Knowledge Bank into Your QMS

The international Quality Management System (QMS) standard ISO 13485 for the medical device sector, intended for regulatory purposes, requires that a manufacturer defines the regulatory requirements related to its devices and activities. In practice, the manufacturer must be aware of the applicable legislation and of any forthcoming changes to be able to define the inputs for the device design and the relevant processes. In addition, the manufacturer would need to acknowledge and study the applicable state of the art standards (harmonised or not, see Chapter 3.6) that concern their device.

The ISO 13485 further defines that a manufacturer must create a documented system to collect and manage the regulatory requirements that apply to its medical devices and processes. In practice, this means to manage the current requirements as well as to follow-up and prepare for any changing legislation and standards regarding the market areas where they do business.

The Person Responsible for Regulatory Compliance (PRRC, see Chapter 4.6), whether a person or a team, holds the responsibility on the collection and management of the requirements. The system should be efficient to support the commercial activities of the manufacturer. The company's employees would need to trust that the QMS provides them with up-to-date and accurate information on regulatory and other requirements.

### 2.5.2. EUR-Lex Database

The primary source of EU legislation is the [EUR-Lex database](#), the home for EU regulations, directives, other legal acts, EU case law, and other public documents. The Person Responsible for Regulatory Compliance (PRRC) or the regulatory team of the manufacturer must learn to search the database and interpret the relevant information regarding, for example, a specific regulation. Consolidated texts of the regulations are useful and different language versions are found in html and pdf format. The EUR-Lex also provides useful electronic tables of contents for legislation, such as the MDR and the IVDR. It is worth creating an EUR-Lex account and utilise the 'Save', 'Follow' (RSS feed), and other functionalities to remain up to date and organised with the relevant EU legislation.

[The Publications Office of the EU](#) sets another database worth searching for legislation and other information regarding the market.

See also the websites of the Directorates General (DG) in Chapter 2.4.3.



### 2.5.3. Finnish Law and Fimea

A Finnish manufacturer should still study the [Finnish legislation on medical devices at the FINLEX web service](#). This national legislation leans on the former medical device directives (MDD, AIMDD, IVDD) that currently apply until full application of the MDR and the IVDR. However, while manufacturers have begun to follow the medical device regulations (MDR and IVDR), the need to study the national legislation has become less relevant. However, the MDR and the IVDR give some leeway to national law, which the manufacturer or the hospitals and clinics may need to remain aware of.

[Fimea](#) is the Finnish competent authority for medical devices. Its website provides valuable information and links for the Finnish medical device manufacturers and for the industry in general (for example, regarding exports, legislation, placing on the market, clinical investigations, registration of devices, incident reporting, language requirements, and market surveillance programs). Some of the information on the site that is in Finnish may not, however, be available in English. While the former medical device directives are still applied, the Finnish law and the ordinances ('määräys' in Finnish) published by Fimea remain important for the manufacturers.

Fimea's role is not only to maintain but also to improve the health of the Finnish population. Therefore, it is in Fimea's interest and duty to develop the medical device sector. The Fimea personnel is easy to contact and the guidance they provide as an authority is highly valuable. A general advice for a manufacturer, when contacting any authorities, is to prepare well and form an educated interpretation on the requirements at hand.

### 2.5.4. How to Stay Up-to-Date?

Following up on all applicable and changing EU and international legislation, standards and guidance documents may be nearly an impossible task, especially for small manufacturers. Therefore, it is recommended to become involved with industry associations and their regulatory working groups. Some of the most important associations from the perspective of a Finnish medical device manufacturer are:

- [Healthtech Finland](#)
- [Sailab - MedTech Finland](#)
- [MedTech Europe](#)
- [COCIR](#)



**3. LEGISLATION, GUIDANCE AND  
STANDARDS FOR MEDICAL  
DEVICES**

## 3.1. MDR AND IVDR

MDR and IVDR are regulations, which means that they are binding legislative acts which must be applied in their entirety as such across the EU. This is a major change compared to the MDD, IVDD, and AIMDD, which are directives and have been transposed to national legislation in the all EU Member States.

**MDR** – Regulation (EU) 2017/745 on medical devices – [Consolidated version of the MDR](#)

**IVDR** – Regulation (EU) 2017/746 on in vitro diagnostic medical devices – [Consolidated version of the IVDR](#)

At the time of writing this book, both MDR and IVDR have been updated twice by two corrigenda. The most notable change so far has been the one-year extension for the applicability of the MDD, delaying the MDR date of application from 26 May 2020 to 26 May 2021.

After the MDR and IVDR become applicable, the MDD, IVDD, and AIMDD are repealed. Any certificates issued by Notified Bodies in accordance with the MDD, IVDD and AIMDD remain valid until the end of the period indicated on the certificate, but new certificates can no longer be issued under those directives.

Devices which are class I according to the MDD and which move to a higher risk class under the MDR, hence requiring a conformity assessment by a Notified Body, may be placed on the market or put into service until 26 May 2024, assuming their Declaration of Conformity (DoC) was drawn up before 26 May 2020. However, if during this time period the manufacturer makes 'significant changes' in the device design, its intended purpose, or related processes, compliance and certification according to the MDR is required. See the MDCG 2020-3 for guidance regarding 'significant change'

Devices which are class I devices under the MDR, and will not require Notified Body assessment, need to comply to the MDR from the date of application 26 May 2021.

It should be noted that the requirements in the MDR and IVDR related to post-market surveillance, market surveillance, vigilance, and registration of economic operators and devices begin to apply for all medical devices on the date of application of the MDR or the IVDR, or as specified in the regulations. This applies also to devices that are on the market according to the MDD, AIMDD, or IVDD.

## 3.2. OTHER CE MARKING LEGISLATION

It is very important to understand that medical devices may be subject to several other directives and/or regulations that must be complied with. One product may have features that are controlled by multiple different pieces of legislation.

CE marking is not reserved for medical devices alone – devices of multiple other product categories need to be CE marked. If a product is covered by the scope of one or more of the European Union harmonisation acts providing for CE marking (also known as 'CE marking legislation'), it must be CE marked in order to be placed on the EU market. Products that are not covered by CE marking legislation cannot be affixed with the CE marking.

CE marking legislation covers a wide range of legal acts which overlap and complement each other. Because of this, several pieces of legislation may have to be taken into consideration for one product. A product can be made available or put into service only when the product complies with all applicable provisions, and when the conformity assessment has been carried out in accordance with all applicable CE marking legislation. The manufacturer's Declaration of Conformity must also state that the requirements of all applicable CE marking regulations and directives have been fulfilled in relation to the device in question, listing the aforementioned regulations and directives.

To avoid application of duplicate requirements, certain pieces of CE marking legislation exclude products covered by other acts from their scope. For example, medical devices are excluded from the scope of the Low Voltage Directive (2014/35/EU) since the necessary requirements are already covered by the MDR and the IVDR.

Some common pieces of CE marking legislation that might apply to medical devices are presented in this chapter.

### Radio Equipment Directive (RED)

If the medical device is considered a radio equipment, it must also comply with the Radio Equipment Directive (RED) 2014/53/EU.

*'Radio equipment' means an electrical or electronic product, which intentionally emits and/or receives radio waves for the purpose of radio communication and/or radiodetermination, or an electrical or electronic product which must be completed with an accessory, such as antenna, so as to intentionally emit and/or receive radio waves for the purpose of radio communication and/or radiodetermination.*

More information can be found at the following sources:

- [EU website for Radio Equipment Directive \(RED\)](#)
- [Consolidated version of Radio Equipment Directive 2014/53/EU](#)
- [List of harmonised standards under RED](#)

### Machinery Directive

If the medical device contains parts which fit the scope and definitions of the Machinery Directive 2006/42/EC, this directive must be followed. This applies to machinery, interchangeable equipment, safety components, lifting accessories, chains robes and webbing (for lifting purposes), removable mechanical transmission devices, and partly completed machinery. More detailed scope and definitions are found in Articles 1 and 2 of that directive.

More information can be found at the following sources:

- [EU website for Machinery](#)
- [Consolidated version of Machinery Directive 2006/42/EC](#)
- [List of harmonised standards under Machinery Directive](#)

### RoHS Directive

If the medical device is an electrical or electronic piece of equipment, it must also comply with the RoHS Directive 2011/65/EU. The restriction of the use of lead, mercury, cadmium, hexavalent chromium, polybrominated biphenyls (PBB), and polybrominated diphenyl ethers (PBDE) apply to all electronic devices, including medical devices with certain exemptions. The restriction of the use of four phthalates (DEHP, BBP, DBP and DIBP), which already applies to other electrical devices, will apply to medical devices from 22 July 2021 onwards.

*'Electrical and electronic equipment' or 'EEE' means equipment which is dependent on electric currents or electromagnetic fields in order to work properly and equipment for the generation, transfer and measurement of such currents and fields and designed for use with a voltage rating not exceeding 1 000 volts for alternating current and 1 500 volts for direct current.*

*EN IEC 63000:2018 Technical documentation for the assessment of electrical and electronic products with respect to the restriction of hazardous substances* specifies the technical documentation that the manufacturer needs to compile in order to declare compliance with the applicable substance restrictions.

More information can be found at the following sources:

- [EU website for RoHS Directive](#)
- [Consolidated version of RoHS Directive 2011/65/EU](#)

### Personal Protective Equipment (PPE) Regulation

Some devices may be intended to be used both as a personal protective equipment (PPE) and as a medical device for preventing disease. In this case, they need to comply with the PPE Regulation in addition to the Medical Device Regulation (MDR). Examples of such devices are gloves and masks used by surgeons during an operation, or an epidemic or pandemic, intended to protect both the patient (making them a medical device) as well as the user (making them a PPE). Sunglasses or other protective glasses with vision correction are another good example of devices which fit into the scope of both regulations.

*'Personal protective equipment' (PPE) means:*

- a) equipment designed and manufactured to be worn or held by a person for protection against one or more risks to that person's health or safety;*
- b) interchangeable components for equipment referred to in point (a) which are essential for its protective function;*
- c) connexion systems for equipment referred to in point (a) that are not held or worn by a person, which are designed to connect that equipment to an external device or to a reliable anchorage point, which are not designed to be permanently fixed, and which do not require fastening works before use.*

More information can be found at the following sources:

- [EU website for Personal protective equipment \(PPE\)](#)
- [Personal Protective Equipment Regulation \(EU\) 2016/425](#)

## 3.3. OTHER EU LEGISLATION

In addition to CE marking legislation, a medical device may also be subject to a number of other directives and regulations. This list is non-exhaustive, only some of the most relevant ones are listed in this chapter. It is important for the manufacturer to study and identify all pieces of legislation that may affect their products, as well as the related guidance documents and standards. In addition, legislation not related to products themselves should be considered and studied. These are related to topics such as product liability, public procurement, patent law, and taxation.

### Medicinal Products Legislation

As a general rule, the MDR does not apply to medicinal products as they are governed by the Medicinal Products Directive 2001/83/EC. However, combination products have become more and more common. In borderline cases, the principal mode of action of the product is key in deciding which legislation to apply. Furthermore, if the device consists of or incorporates 'advanced therapy medicinal products', it falls under the respective Regulation (EC) No 1394/2007.

*'Medicinal product':*

- a) Any substance or combination of substances presented as having properties for treating or preventing disease in human beings; or*
- b) Any substance or combination of substances which may be used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis.*

Devices which are intended to administer a medicinal product are governed by the MDR. However, there are two exceptions:

- If the device intended to administer a medicinal product and the medicinal product are placed on the market in such a way that they form a single integral product which is intended exclusively for use in the given combination and which is not reusable, that single integral product shall be governed by the Medicinal Products Directive 2001/83/EC or Regulation (EC) No 726/2004, as applicable.
- If the action of that substance is principal and not ancillary to that of the device, the integral product shall be governed by the Medicinal Products Directive 2001/83/EC or Regulation (EC) No 726/2004, as applicable.

In both cases, the relevant general safety and performance requirements set out in Annex I of the MDR shall apply as far as the safety and performance of the device part are concerned.

See the following related legislation:

- Directive 2001/83/EC relating to **medicinal products for human use** – [Consolidated version of Directive 2001/83/EC](#)
- Regulation (EC) No 726/2004 laying down Community procedures for the **authorisation and supervision of medicinal products** for human and veterinary use and establishing a European Medicines Agency – [Consolidated version of Regulation \(EC\) No 726/2004](#)
- Regulation (EC) No 1394/2007 on **advanced therapy medicinal products** – [Consolidated version of Regulation \(EC\) No 1394/2007](#)

## Human Blood and Plasma Legislation

MDR does not apply to human blood, blood products, plasma or blood cells of human origin. Nor does it apply to devices that incorporate such items when placed on the market or put into service. The only exceptions are devices that incorporate as an integral part a substance which, if used separately, would be considered a 'medicinal product derived from human blood or human plasma' that has an action ancillary to that of the device. Such devices are governed by the MDR.

*'Medicinal products derived from human blood or human plasma': Medicinal products based on blood constituents which are prepared industrially by public or private establishments, such medicinal products including, in particular, albumin, coagulating factors and immunoglobulins of human origin.*

However, if the action of that substance is principal and not ancillary to that of the device, the integral product shall be governed by the Medicinal Products Directive 2001/83/EC or Regulation (EC) No 726/2004, as applicable. In that case, the relevant general safety and performance requirements set out in Annex I to the MDR shall apply as far as the safety and performance of the device part are concerned.

See the following related legislation:

- Directive 2000/70/EC amending Directive 93/42/EEC as regards **medical devices incorporating stable derivatives of human blood or human plasma** – [Directive 2000/70/EC](#)
- Directive 2002/98/EC setting standards of quality and safety for the **collection, testing, processing, storage and distribution of human blood and blood components** and amending Directive 2001/83/EC – [Consolidated version of Directive 2002/98/EC](#)
- Commission Directive 2004/33/EC implementing Directive 2002/98/EC as regards certain **technical requirements for blood and blood components** – [Consolidated version of Directive 2004/33/EC](#)
- Commission Directive 2005/62/EC implementing Directive 2002/98/EC as regards Community standards and specifications relating to a **quality system for blood establishments** – [Consolidated version of Directive 2005/62/EC](#)

## Human Tissue and Cells Legislation

MDR does not apply to transplants, tissues or cells of human origin, or their derivatives. However, MDR does apply to devices manufactured utilising derivatives of tissues or cells of human origin which are non-viable or are rendered non-viable.

Any device which, when placed on the market or put into service, incorporates as an integral part non-viable tissues or cells of human origin or their derivatives that have an action ancillary to that of the device shall be assessed and authorised in accordance with the MDR. In that case, the provisions for donation, procurement and testing laid down in Directive 2004/23/EC shall apply in addition to the MDR.

However, if the action of those tissues or cells or their derivatives is principal and not ancillary to that of the device and the product is not governed by Regulation (EC) No 1394/2007 (on advanced therapy medicinal products), the product shall be governed by Directive 2004/23/EC. In that case, the relevant general safety and performance requirements set out in Annex I to the MDR shall apply as far as the safety and performance of the device part are concerned.

See the following related legislation:

- Directive 2004/23/EC on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells – [Consolidated version of Directive 2004/23/EC](#)

## Legislation Related to Animal Tissues and Animal By-products

Transplants, tissues or cells of animal origin, or their derivatives, or products containing or consisting of such are not in the scope of the MDR or IVDR. However, medical devices manufactured utilising tissues or cells of animal origin, or their derivatives, which are non-viable or are rendered non-viable are in the scope of the MDR or IVDR. The General Safety and Performance Requirements in Annex I of the MDR and IVDR contain specific requirements for these types of devices.

See the following related legislation:

- Commission Regulation (EU) No 722/2012 concerning particular requirements as regards the requirements laid down in Council Directives 90/385/EEC and 93/42/EEC with respect to **active implantable medical devices and medical devices manufactured utilising tissues of animal origin** – [Regulation \(EU\) No 722/2012](#)
- Regulation (EC) No 1069/2009 laying down health rules as regards **animal by-products and derived products** not intended for human consumption (Animal by-products Regulation) – [Consolidated version of Regulation \(EC\) No 1069/2009](#)
- Commission Regulation (EU) No 142/2011 implementing Regulation (EC) No 1069/2009 laying down **health rules as regards animal by-products and derived products** not intended for human consumption and implementing Directive 97/78/EC as regards certain samples and items exempt from veterinary checks at the border under that Directive – [Consolidated version of Regulation \(EU\) No 142/2011](#)
- Regulation (EC) No 999/2001 laying down rules for the prevention, control and eradication of certain **transmissible spongiform encephalopathies** – [Consolidated version of Regulation \(EC\) No 999/2001](#)
- Directive 2010/63/EU on the **protection of animals used for scientific purposes** – [Consolidated version of Directive 2010/63/EU](#)

## REACH Regulation

Regulation (EC) No 1907/2006 concerning the **Registration, Evaluation, Authorisation and Restriction of Chemicals** (REACH) – [Consolidated version of REACH Regulation \(EC\) No 1907/2006](#)

## Directives Related to Waste and End of Life

Directive 2008/98/EC on **waste** (Waste Framework Directive) – [Consolidated version of Waste Framework Directive 2008/98/EC](#)

Directive 2012/19/EU on **waste electrical and electronic equipment (WEEE)** – [Consolidated version of WEEE Directive 2012/19/EU](#)

Directive 94/62/EC on **packaging and packaging waste** – [Consolidated version of Packaging Directive 94/62/EC](#)

## Regulation on Biocidal Products

Regulation (EU) No 528/2012 concerning the making available on the market and use of **biocidal products** – [Consolidated version of Regulation \(EU\) No 528/2012](#)

## Legislation Concerning Personal Data

General Data Protection Regulation (GDPR) (EU) 2016/679 on the protection of natural persons with regard to the **processing of personal data and on the free movement of such data** – [Consolidated version of GDPR \(EU\) 2016/679](#)

Directive 2002/58/EC concerning the **processing of personal data and the protection of privacy in the electronic communications sector** (Directive on privacy and electronic communications) – [Consolidated version of Directive 2002/58/EC](#)

## Directives Concerning Radiation

Council Directive 2013/59/Euratom laying down basic safety standards for protection against the dangers arising from **exposure to ionising radiation** – [Consolidated version of Euratom Directive 2013/59/Euratom](#)

Directive 2006/25/EC on the minimum health and safety requirements regarding the **exposure of workers to risks arising from physical agents (artificial optical radiation)** – [Consolidated version of Directive 2006/25/EC](#)

## 3.4. MDCG (MEDICAL DEVICE COORDINATION GROUP) GUIDANCE DOCUMENTS

The European Commission provides a range of guidance documents to assist in the implementation of the medical device regulations. One of the tasks appointed to the Medical Device Coordination Group (MDCG) is to contribute to the development of guidance aimed at ensuring effective and harmonised implementation of the MDR and the IVDR. The regulations further state that guidance should, in particular, contain information regarding:

- the designation and monitoring of Notified Bodies,
- application of the General Safety and Performance Requirements (Annex I of the MDR and IVDR),
- conduct of clinical evaluations and investigations by manufacturers,
- assessment by Notified Bodies, and
- vigilance activities.



Guidance documents endorsed by the MDCG can be found on the [Guidance page](#) of the Medical Devices Sector websites. New guidance documents are being constantly created and old ones updated, so one should be aware of the emerging guidance and updates.

Former medical device directive guidance documents were called MEDDEV guidance documents. At the time of writing this book, some of these are still widely used because the updated MDCG guidance documents do not yet exist for certain topics. However, when using MEDDEV guidance documents, care must be exercised to stay compliant with the current regulations.

It should be considered that regulations always come before guidance documents. Guidance documents are legally non-binding and one could deviate from them as long as the regulation was followed. However, in practice, the Notified Bodies and competent authorities expect the manufacturers to comply with these guidance documents. In addition, it is recommended to utilise the MDCG guidance documents rather than to reinvent the wheel. The documents have been written in cooperation with the European Commission, Notified Bodies, representatives of the industry, and other relevant experts. Following the MDCG guidance documents should make your journey to regulatory compliance and CE marking more fluent.

### 3.5. COMMON SPECIFICATIONS

The MDR and IVDR define 'common specifications' (CS) as a set of technical and/or clinical requirements, other than a standard, that provides a means of complying with the legal obligations applicable to a device, process, or system. If (harmonised) standards do not exist, or are not considered sufficient, or there is a need to address public health concerns, the European Commission may adopt common specifications. They are adopted by means of 'implementing acts'.

Common specifications may apply to the following:

- General Safety and Performance Requirements
- Technical documentation
- Clinical evaluation, clinical investigation, or post-market clinical follow-up (MDR)
- Performance evaluation, performance studies, or post-market performance follow-up (IVDR)

Similar to harmonised standards, the devices that are in conformity with the common specifications are presumed to be in conformity with the requirements they cover. Manufacturers are expected to comply with the common specifications unless they can duly justify that they have adopted solutions that ensure a level of safety and performance that is at least equivalent thereto.

At the time of writing of this book, the first and the only adopted CS is for reprocessing of single-use medical devices: [\(EU\) 2020/1207 common specifications for the reprocessing of single-use devices](#).

### 3.6. THE USE OF HARMONIZED EN AND OTHER STANDARDS

To address the General Safety and Performance Requirements (Annex I of MDR or IVDR) and many other requirements in the MDR and the IVDR, internationally recognised standards may be considered state of the art. The majority of these standards are results of multinational working groups of the International Organisation for Standardization (ISO) and the International Electrotechnical Commission (IEC). Where such an international standard exists, it is good business practice to exploit this instead of reinventing the means to comply with regulations. Stakeholders in the medical device industry, from authorities to hospitals, mainly expect compliance with international standards and evidence thereof.

To comply with European Union legislation, it would be advisable to utilize the harmonised EN version of the standard that applies to your device. 'EN' stands for 'European Standard', which are standards ratified by one of the three European

Standardization Organisations (ESOs): [CEN](#), [CENELEC](#) or [ETSI](#). EN standards, when published in the [Official Journal \(OJ\) of the European Union](#), provide 'presumption of conformity' to European Union legislation (i.e., are harmonised to the legislation, Article 8.1 of the MDR and the IVDR). However, the contents of the EN standard are rarely altered from the original, making the EN version easy to utilise for your global compliance purposes. When harmonised, the presumption of conformity is expressed in Annex Z (or ZA, ZB, ZZ, etc.) of the EN standard, stating to which requirements, under which conditions, and to what extent presumption of conformity to specific EU legislation can be claimed. For more details, study the Official Journal or the [Blue Guide on the implementation of EU products rules](#).

On a global level, harmonization of standards in the EU can be compared to the concept of 'recognized standards', for example, in the USA and Canada. These standards are to a large extent the same international standards.

The lists of standards harmonized to the former medical device directives and published in the Official Journal can be accessed from here:

- [Harmonised Standards to the MDD](#)
- [Harmonised Standards to the AIMDD](#)
- [Harmonised Standards to the IVDD](#)

However, note that the harmonization of standards against the current medical device directives has been dramatically delayed in the EU during the past few years, and none which have been harmonised against the MDR or the IVDR to date. The European Commission and CEN-CENELEC, who together hold the responsibility over the harmonisation process, have entered a long debate on the contents and legality of Annexes Z. This has, in effect, eroded one of the foundations of EU product legislation, even for years to come, in regard to the medical device industry. This casts doubt on the uniform interpretation of standards across Europe, causing uncertainty in medical device development, hospital procurement and, eventually, patient safety. While the concept of 'presumption of conformity' is malfunctioning – though the European regulations refer to it as one of the foundations to ensure the safety of its citizens – the stakeholders, including Notified Bodies and EU Member State authorities, are forced to make their own interpretations on what are considered state of the art standards in safety.

In the absence of harmonized standards to the MDR and the IVDR, it is advisable to explore the lists of harmonized standards to the MDD, AIMDD, or the IVDD. One must remember that there may be more recent versions of those standards published, for instance, by the ISO or the IEC. The more recent versions may be regarded state of the art in safety and may be justified to be utilized instead of any previous version. In fact, the Notified Bodies may expect the manufacturer to follow the more recent version due to the "state of the art in safety" requirement defined by Annex I of the MDR and IVDR. This requirement is generally considered to "overrule" the reference for the use of harmonized standards in Article 8 of the MDR and the IVDR. However, it is recommended to provide a detailed justification to the Notified Body why a specific version of the standard can be used to assume compliance to the regulatory requirements when it differs from the version that is not currently harmonised to the MDD, AIMDD, or the IVDD.

When purchasing a standard, pay attention to which publication of the standard would best function as a tool for your compliance purposes:

- Where corrigenda or amendments to the original standard have been published, consider purchasing the 'consolidated' version of the standard, if available. This provides a single uniform version of the text and is, therefore, by far the easiest to read. If a consolidated version of the EN standard is not available, it may be wiser to purchase both, the consolidated original, e.g., from the ISO, and the harmonized EN version for the sake of Annex Z.
- The year of publication of the EN version of the standard, its corrigenda and amendments, may be different from that of the original. Be sure to purchase the most recent version. If the EN version is not yet available or harmonised (which can take a substantial amount of time), but your product development continues, we encourage you to purchase the recent 'original' to study it and make the gap-analysis between the recent and earlier version.

- Standards may be published and sold in your native language by one of the national standardization bodies of CEN-CENELEC. All standards may not be translated to your national language. But even if you use translations to interpret the requirements, consider utilising English as your default language for all documentation. Your entry to the global market will become easier.

Standards may come heavy with information. It is advisable to begin reading a standard from its figures and annexes, as they provide the clearest description on the purpose, the contents, and the application of the standard. They mainly describe principles rather than accurate requirements, and it remains the responsibility of the manufacturers to translate those principles into practice, taking into account the specific nature of their devices and organisation.

A harmonized EN standard can be distinguished from its international version by the so-called Annex Z. Annex Z explains the relationship of the standard to an Annex or other requirements of the directive or regulation. See Figure 1 for an example.

Figure 1 Caption from Annex ZB of the EN ISO 13485:2016, explaining the presumption of conformity of the standard with Annex II ('Full quality assurance system') of the MDD (93/42/EEC)

**ZB.1 Relationship with Annex II of Directive 93/42/EEC (as amended)**

Compliance with this European Standard does not provide a presumption of conformity with all the aspects of Annex II, as outlined in Table ZB.1. Therefore, a manufacturer or a Notified Body has to take additional provisions to ensure conformity, and claim or certify conformance, with Annex II of this Directive. The legal requirements must be examined, applied and verified one by one and the solutions adopted must become part of the quality system in the meaning of the Directive.

**Table ZB.1 — Correspondence between this European Standard and Annex II of Directive 93/42/EEC (as amended)**

Paragraph of Directive 93/42/EEC, Annex II	Clause(s) of this European Standard	Comments/Qualifying remarks
3.1, 1st sentence		Not covered.
3.1, 2nd sentence, 1st indent		Not covered.
3.1, 2nd sentence, 2nd indent		Not covered.
3.1, 2nd sentence, 3rd indent		Not covered.
3.1, 2nd sentence, 4th indent	4.1.1, 4.1.2, 4.1.3, 4.1.4, 4.1.6, 4.2.1, 4.2.2, 4.2.3, 4.2.4, 4.2.5	Covered. The documentation required in this European Standard covers the quality system documentation meant in 3.2 of Annex II when the explicit legal requirements are incorporated into the quality system documentation. See also coverage of 3.2 below.
3.1, 2nd sentence, 5th indent	4.1, 5.1, 5.4, 5.5, 5.6	Covered.
3.1, 2nd sentence, 6th indent	4.1, 5.1, 5.4, 5.5, 5.6	Covered.
3.1, 2nd sentence, 7th indent 3.1, 7th indent (i)		Not covered. This European Standard includes requirements on post market surveillance, and reporting adverse events and field safety corrective actions to authorities but does not cover all the details required by

### 3.7. EUROPEAN MEDICAL DEVICE DATABASE, EUDAMED

Transparency is a key objective of the new medical device regulations aiming to provide a large access to relevant information for the public, and strengthening the confidence of the public and patients in the safety of medical devices placed on the EU market. [EUDAMED is the European Medical Device Database, developed by the European Commission \(EC\)](#). It has been set up to provide public information on the following:

- Devices placed on the market, certificates issued by Notified Bodies and the relevant economic operators (manufacturer, importer and, where relevant, authorised representative)

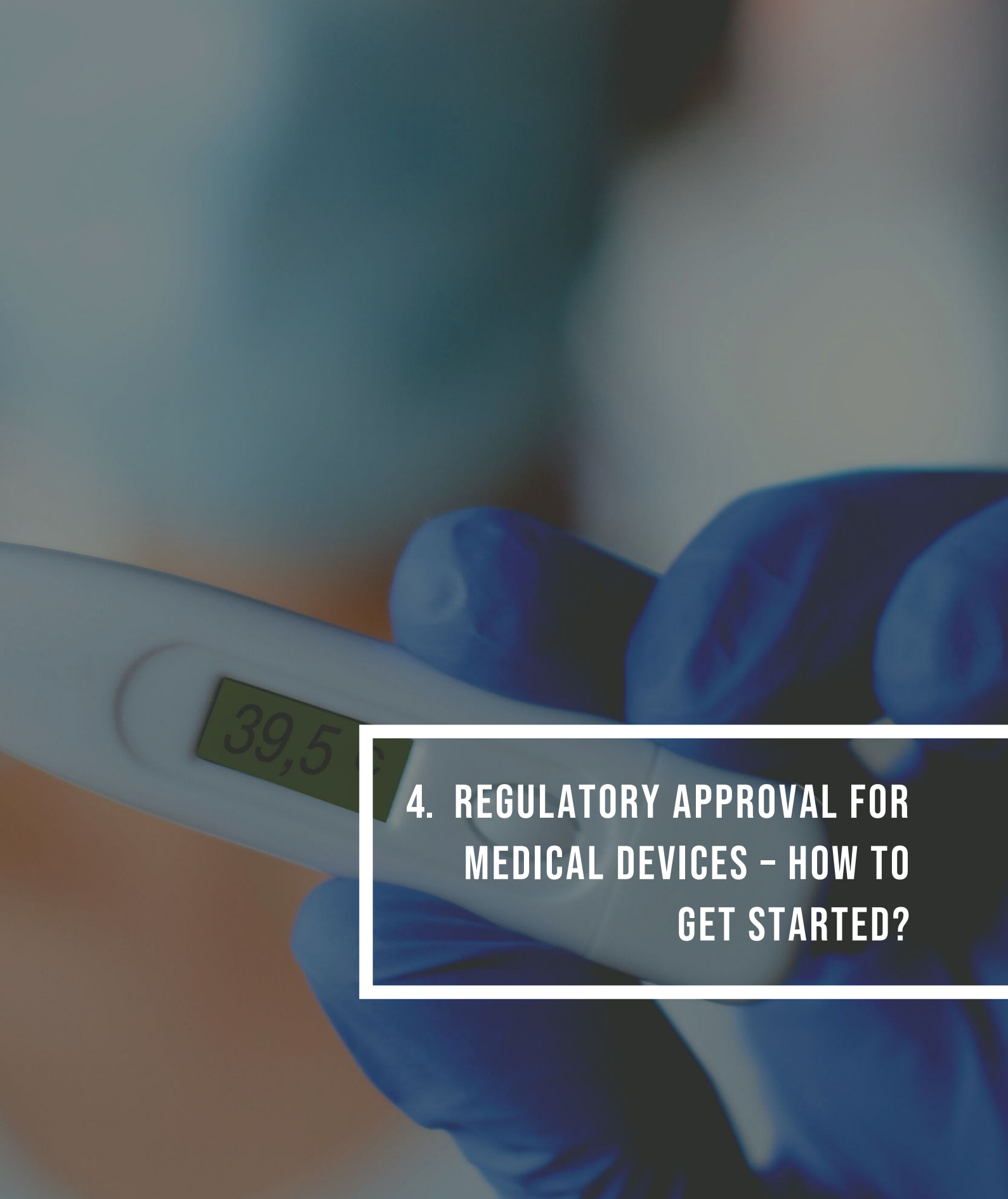
- Unique identification of devices to facilitate their traceability
- Clinical investigations on medical devices in the EU
- Incident reports (partial access) and the field safety notices for vigilance activities by manufacturers

In addition, EUDAMED is established to enable the EU Member State competent authorities and the European Commission to carry out their tasks on a well-informed basis and to enhance their cooperation.

EUDAMED consists of the following six electronic interconnected modules:

- Registration of economic operators (“Actors registration”)
- UDI and devices registration
- Notified Bodies and the EU certificates they have granted to manufacturers
- Clinical investigations and performance studies
- Vigilance and post-market surveillance
- Market surveillance

The work for the development and implementation of EUDAMED is still ongoing. At the time of writing this book, only the ‘Actors registration’ module is in use. Please note that until EUDAMED is fully functional, the corresponding provisions of the former MDD, AIMDD, and IVDD continue to apply for (in particular) information regarding vigilance reporting, clinical investigations (medical devices), performance studies (IVDs), registration of devices and economic operators, and certificate notifications.



**4. REGULATORY APPROVAL FOR  
MEDICAL DEVICES – HOW TO  
GET STARTED?**

## 4.1. MARKETING AND REGULATORY STRATEGIES

A medical device manufacturer ought to create its regulatory strategy early on and cover its entire device portfolio in the strategy. With the manufacturer's marketing strategy the regulatory strategy forms the preconditions for its product development process. An innovation without the marketing and regulatory strategies leads to a proof-of-concept at best, with few chances to reach the market. There is a long path from research and concepts to professional product development that transforms the user needs and every regulatory requirement into a successfully marketed medical device.

In this book, we do not go into details of creating a marketing strategy, but it must be clear that the chosen customer or patient segment and the envisioned international markets lay the foundation for the regulatory strategy. And vice versa, the regulatory strategy will likely reveal opportunities and threats that adjust the marketing strategy. But the transition from an innovative product idea into a business concept and a marketing strategy must come first. What is the added value offered to the end user and who is the client? Remember that a medical device is comparable to any product and its commercial success follows the same economic principles. However, the intended purpose of the device, its medical benefits and potential risks in the healthcare setting create distinct marketing challenges.

The regulatory requirements and the healthcare market have their differences from country to country. To prepare well, it would be necessary to know, which countries and markets the device is targeted to in the short and long time frame. By narrowing down the targeted markets, there is a better chance to bring the product faster to the market, but this decision should leave enough room for opportunities to expand. CE marking is a rational target for a Finnish medical device manufacturer, as it also supports market access in countries outside the European Union (see Chapter 2.3 for the Certificate of Free Sales). Europe itself contains many different healthcare market mechanics and requires thorough investigation on the most potential entries. Outside Europe, the manufacturer should use care in defining the other targeted markets. Where the US market used to be by far the largest, other global markets have grown substantially to make the US less dominant. In addition, the mechanics of market entry to the USA are often strict and not always that straight forward. Then again, with the more stringent requirements brought by the MDR and IVDR for medical device software in the EU, especially for machine learning (ML) and artificial intelligence (AI), the US market may provide a better option for the first market entry. Whatever the case, by investing a little more on top of the MDR or IVDR requirements at the early product development stages, the doors to approach several other markets remain open. By filling those gaps later, the manufacturer may come to pay a multiple price, as they may need to take the device back to the drawing board.

The decision on whether or not to create a regulatory strategy is now easier than ever. Article 10 and Annex IX of the MDR and the IVDR define that a medical device manufacturer must hold a strategy for regulatory compliance. This regulatory strategy shall contain at least the following aspects:

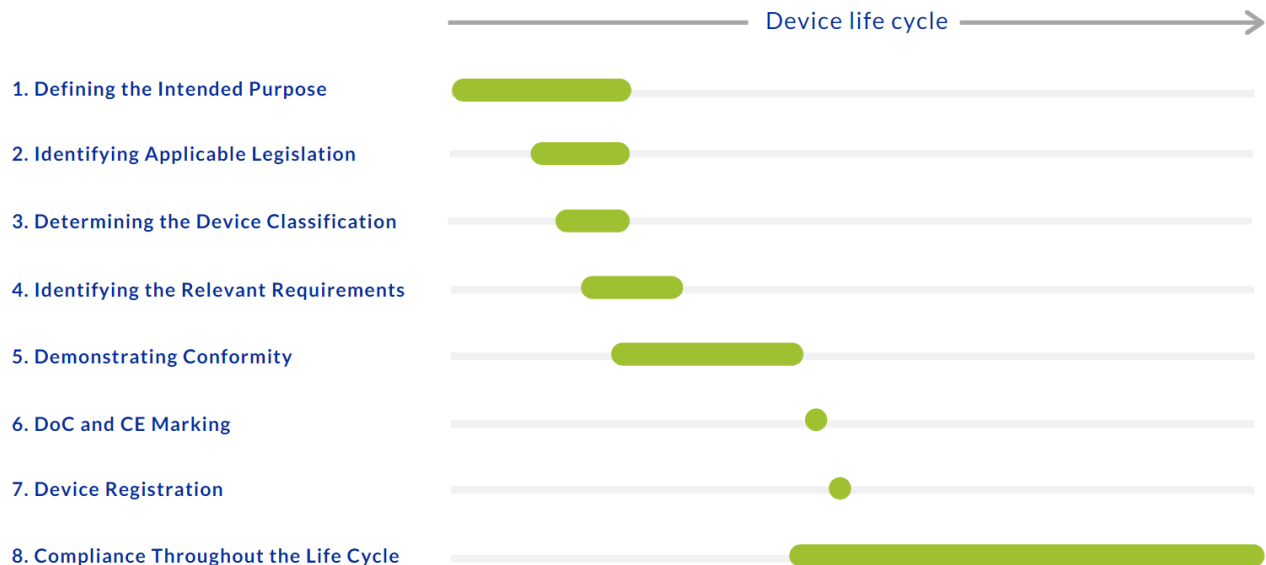
- Processes for the identification of relevant legal requirements
- Processes for the qualification of devices
- Processes for the classification of devices
- Processes for the handling of equivalence (See Chapter 6.2.5 for a description of challenges related to equivalence)
- The manufacturer's choice of and compliance with the conformity assessment procedure (It is advisable to consider Annex IX as the default conformity assessment option)
- Procedures for the management of device modifications

To set up the first draft of the regulatory strategy, the manufacturer must consider the following path described in the next chapter into CE marking and the basic steps it contains.

## 4.2. THE REGULATORY PATH TO CE MARKING

The regulatory path to CE Marking can be roughly described using eight steps. These steps, including their timing in the device life cycle, are depicted in Figure 2 and are described in more detail in this chapter.

Figure 2 Eight steps to CE marking



### Step 1: Defining the Intended Purpose

The intended purpose of the medical device is the single most important item the manufacturer must pay attention to. The intended purpose determines whether the product qualifies as a medical device or not. It is the responsibility of the manufacturer to define the intended purpose of the device. However, the intended purpose should describe the actual use of the device as accurately as possible. It is hard to argue that the intended purpose of a device is not medical if all the features of the device indicate the opposite, and vice versa. In some cases, the difference between a medical device and a general wellness product might be dependent on the intended purpose alone.

The intended purpose also determines the risk class of the medical device, which correlates with the extent of work required to demonstrate that the device is safe and effective for its intended purpose. The intended purpose also indicates the clinical benefit that must outweigh the risks associated with the device. Intended purpose is discussed in more detail in Chapter 5.1.

### Step 2: Identifying Applicable Legislation

The intended purpose also indicates whether the product falls into the scope of the MDR or the IVDR (discussed in more detail in Chapter 3.1).

Medical devices may be subject to several other directives and regulations that must be complied with. One product may have features and properties that are controlled by multiple different pieces of legislation. It is important to recognize all applicable legislation. EU legislation in general is discussed in Chapter 2. Other relevant directives and regulations are discussed in Chapters and 3.2 and 3.3.



### Step 3: Determining the Device Classification

Devices are classified according to their associated risks. The level of requirements as well as the extent of Notified Body involvement in assessing the conformity of the device and the manufacturer's Quality Management System (QMS) is dependent on the device class.

According to the MDR, devices are divided into the following four classes, from lowest risk to highest: Class I, Class IIa, Class IIb, and Class III. The IVDR also presents four classes for in vitro diagnostic (IVD) devices, from lowest risk to highest: Class A, Class B, Class C, and Class D.

Medical device software classification is an art in itself explained further in Chapter 5.4. It is important to correctly identify the product class as early as possible in product development. Device classification is discussed in more detail in Chapter 5.3.

### Step 4: Identifying the Relevant Requirements

The relevant requirements of the MDR and the IVDR are dictated by the intended purpose and the classification of the device. Requirements are partly related to the product (General Safety and Performance Requirements, Annex 1 of the MDR and IVDR) and partly related to the Quality Management System (QMS). All relevant requirements must be identified, and justification given if the manufacturer deems any General Safety and Performance Requirements non applicable.

### Step 5: Demonstrating Conformity

According to Annex I of the MDR and IVDR, the device must meet the General Safety and Performance Requirements (GSPR) which apply to it, considering its intended purpose. The manufacturer must prepare the Technical Documentation for the device to demonstrate how these requirements have been fulfilled. Some of the most notable processes related to device conformity are risk management, usability engineering, clinical evaluation (for medical devices), and performance evaluation (for IVDs). It is not enough to consider the requirements for the product or software. In addition, purchasing, production, quality assurance, transport, storage, installation, and maintenance activities must be considered to ensure that the device continues to achieve its intended performance and remains safe for patients and users.

The most convenient way to demonstrate conformity is achieved by applying state of the art standards (Chapter 3.6) and guidelines (Chapter 3.4). For the Quality Management System (QMS), the most sensible option is to create a QMS on the basis of the ISO 13485 QMS standard, which is designed specifically for medical devices.

For class I devices, the manufacturer alone makes the decision on the adequate demonstration of conformity. For the higher risk class devices (classes Is, Ir, Im, IIa, IIb and III), a Notified Body assessment is always required before moving on to the next step and CE marking the device.

More information on how to demonstrate conformity can be found in Chapter 6.

### Step 6: Declaration of Conformity and CE Marking

After the manufacturer has ensured that all requirements have been fulfilled and documented accordingly, it is time to draw up the EU Declaration of Conformity (DoC). By drawing up the EU DoC, the manufacturer assumes exclusive responsibility for the compliance of the device. Declaration of Conformity is discussed in Chapter 6.4.

Before placing the medical device on the market, it must be affixed with the CE marking. Exceptions to this rule are custom-made devices and devices manufactured by health institutions for their own use which are not CE marked (see Chapter 4.3). Medical devices that do not carry the CE mark may be used only in clinical investigations or performance evaluations (in case of IVDs). CE marking is discussed in more detail in Chapter 6.5.

## Step 7: Device Registration

Registration is the last step before the device can be placed on the market. Registration is performed through EUDAMED (the European Medical Device Database). More information on registration is found in Chapter 6.6.

Note that until EUDAMED is fully functional, the corresponding provisions of the former MDD, AIMDD, and IVDD continue to apply for device registration. According to these directives, devices are registered to the competent authority of the EU Member State in which the manufacturer has its registered place of business (for example, Fimea in Finland).

## Step 8: Compliance throughout the Life Cycle

The manufacturer's work on compliance does not end when the device is placed on the market. On the contrary, the life cycle of the device has merely started.

It must be ensured that the device is delivered with adequate instructions for installing and putting into service. If users are to be trained prior to using the device, the manufacturer must plan for it in advance. The manufacturer must also take maintenance into account, both routine periodic maintenance and maintenance in the case of device faults.

Processes for post-market surveillance and complaint handling need to be in place and linked to the corrective and preventive actions (CAPA) process, risk management and vigilance reporting. Post-market surveillance and vigilance are discussed in more detail in Chapter 7.

Since compliance needs to be achieved throughout the device life cycle, post-market surveillance must be conducted proactively. The manufacturer's responsibility only ends once the product has been taken out of use and disposed of, or entirely removed from the market.

## 4.3. WHO IS THE MANUFACTURER?

From the regulatory perspective, the manufacturer is ultimately always responsible for their own products. For this reason, it is important to define the 'manufacturer' from the responsibility perspective. A 'manufacturer' is the natural or legal person who markets a device under their name or trade mark and carries the responsibility for the device, regardless of whether they design and manufacture or fully refurbish the medical device or have outsourced any or all of these activities to external parties. This means that a subcontractor can even design or manufacture the device and perform other activities on behalf of the manufacturer, but the responsibility remains with the legal entity who prints their name or trade mark on the device.

The 'manufacturer' is always responsible for the design, manufacture, packaging, and labelling of the medical device when they place the device on the market under their own name, and this responsibility cannot be transferred from the manufacturer to any outsourced providers. The manufacturer is ultimately responsible also for the activities performed on their behalf, by the supplier or subcontractor, regarding the specific medical device. It does not make a difference if the only activity a company does is to place their trade mark on a device that is fully designed and manufactured by others. Even in such case, the 'manufacturer' must be in full control of the device and, for example, hold all Technical Documentation related to the device.

Additionally, in cases where the manufacturer fully refurbishes a device and markets the device under their label, the refurbisher is considered the 'manufacturer'. 'Fully refurbishing' means the complete rebuilding of a device that has already been placed on the market, or the making of a new medical device from used medical devices or other products. Please note that a distributor who significantly modifies a device or a health institution who distributes their devices to other entities are considered to fulfil the criteria of a 'manufacturer'.

A device is considered to be placed on the market regardless of whether it is provided in return for payment or free of charge. However, a medical device is not considered to be placed on the market if it is being assessed in a clinical investigation, or, in the case of in vitro diagnostic (IVD) devices, in a performance study. Nonetheless, the manufacturer carries the responsibility over such investigational devices, as the purpose of the investigations is to make the device available on the EU market. Prior to CE marking a device, taking into account appropriate legal requirements, such investigations are the only means to having the device used according to its intended purpose. The device can be presented for targeted users prior to CE marking, for example, at trade fairs, but it needs to bear a clear indication that it is not yet CE marked and that the device cannot therefore be used even for experimental purposes.

If the manufacturer is not established in the European Union, they cannot operate alone in the EU market. In these cases, the manufacturer needs to designate an 'authorised representative' to act on the manufacturer's behalf in relation to specified tasks with regard to the manufacturer's obligations under the medical device regulations. The authorised representative is any natural or legal person established within the EU who has received and accepted a written mandate from the manufacturer that locates outside the EU to perform this task. Authorised representatives are typically importers or distributors, or consulting firms that provide other regulatory services aside the authorised representative services. The authorised representative acts as the manufacturer's representative towards the European authorities and holds much responsibility under the regulations. Therefore, the agreement between the manufacturer and the authorised representative should be precise and clear. One manufacturer may hold agreements with several authorised representatives, but one device or generic device group may only have one authorised representative.

A health institution, meaning hospitals and other organisations, the primary purpose of which is the care or treatment of patients or the promotion of public health, may manufacture and use medical devices within their institution. Such devices are considered to having been 'put into service' and therefore are required to comply with the medical device regulations and to develop an appropriate Quality Management System (QMS). However, such devices are not to be CE marked and not all requirements of the MDR or IVDR apply. Article 5 of the MDR or IVDR, concerning the responsibilities of the health institution, should be studied in detail. It must be considered that instantly on providing the device for use outside their health institution, the institution would need to CE mark the device and bear the responsibilities of a 'manufacturer'.

Additionally, if the device is custom-made, it shall not bear the CE mark. A 'custom-made device' means any device specifically made in accordance with a written prescription by a person authorised to give such a prescription (e.g., a clinician). This person would claim responsibility on the safety and performance of the device. The device would bear specific design characteristics as it would be intended for the exclusive use of a particular patient. Please note that any mass-produced devices which need to be adapted to meet the specific requirements of a professional user shall not be considered to be 'custom-made devices'. In comparison to CE marked devices, the requirements for custom-made devices are limited.

Please note that in many cases the manufacturer also takes the role as an 'importer' or 'distributor', for example, when the device is a system comprised of CE marked and non-CE marked components.

## 4.4. RESPONSIBILITIES OF AUTHORISED REPRESENTATIVES, IMPORTERS AND DISTRIBUTORS

### 4.4.1. Authorised representative

A manufacturer that is located outside the EU must appoint an authorised representative to be able to place devices on the market in the EU. An authorised representative means any natural or legal person established within the EU, mandated by a manufacturer to act on its behalf in relation to specified tasks defined in the MDR and IVDR. A different authorised

representative may represent different medical devices from one manufacture, but devices belonging to the same generic device group should have the same authorised representative.

At a minimum, authorised representatives' obligations include verifying that for the medical device the

- the EU Declaration of Conformity (DoC) is drawn up,
- the Technical Documentation is drawn up, and
- where applicable, an appropriate conformity assessment procedure has been carried out for the manufacturer by a Notified Body.

Similar to manufacturers, an authorised representative should have permanent and continuous access to a Person Responsible for Regulatory Compliance (PRRC). An authorised representative must also keep copies of the Technical Documentation, Declarations of Conformity, and EU certificates from Notified Bodies and make them accessible to authorities on request. In addition, authorised representatives will have to register themselves to EUDAMED as an economic operator and verify that the manufacturer has registered the requested information on the company and the devices to EUDAMED.

An authorised representative must cooperate with authorities on corrective and preventive actions (CAPA) and inform the manufacturer immediately about complaints. The authorised representative will be liable for defective devices together with the manufacturer if the manufacturer has not complied with the regulations. An authorised representative should terminate the mandate if the manufacturer acts contrary to its obligations, and inform competent authorities and the Notified Body of the termination and the reasons behind it.

It should be noted that elements that are the exclusive responsibility of the manufacturer cannot be delegated to the authorised representative.

#### 4.4.2. Importer

An importer is defined as any natural or legal person established in the EU that places a device from a third country on the EU market.

The importer is responsible for making sure that the devices they place on the market

- bear the CE marking,
- are accompanied by the required information and labelled in accordance with the MDR or the IVDR, taking into account appropriate language requirements, and
- have been assigned a UDI where applicable.

Importers shall indicate on the device or its packaging, or in a document accompanying the device, their name, registered trade name or registered trademark, their registered place of business, and the address at which they can be contacted. In addition, importers should register themselves to EUDAMED as an economic operator and verify that the imported devices are registered.

Importers should make sure that storage and transport conditions, when under their responsibility, do not jeopardise compliance. Importers also have the responsibility to inform manufacturers and their authorised representatives in the event of complaints. They should also keep a register of complaints, non-conforming devices, recalls and withdrawals, and escalate non-compliance with authorities if they suspect that a device has been falsified or that there is a serious risk to health. Importers are also required to cooperate with authorities and provide samples or grant access to the devices. If an importer considers that a device is not compliant with the MDR or the IVDR, the device shall not be placed on the market and the importer shall inform the manufacturer and the authorised representative. The importer should also inform the authorities if they suspect that a device has been falsified or that there is a serious risk to health.

While these are the requirements for an importer, they also lay the foundation for the manufacturer on their oversight towards the importers. It would be good business practice to choose an importer that is able to comply with the requirements of the MDR or the IVDR.

### 4.4.3. Distributor

A distributor is defined as any natural or legal person in the supply chain, other than the manufacturer or the importer that makes a device available on the market, up until the point of putting it into service.

Distributors should verify that

- the devices have been CE marked,
- an EU Declaration of Conformity has been drawn up,
- labels and instructions for use are provided in the official languages or other languages accepted by the EU country, and
- the importer's name, where applicable, is indicated on each device or in the accompanying documentation, and that the device bears a UDI.

Distributors shall ensure that storage and transport conditions, when under their responsibility, are appropriate and in line with the recommendations of the manufacturer.

If a distributor considers a device to be non-compliant with the MDR or the IVDR, the device shall not be made available on the market. In this case, the distributor should inform the other economic operators. Distributors should inform the authorities if they suspect that a device has been falsified or that there is a serious risk to health. They should also keep a register of complaints, non-conforming devices, recalls and withdrawals. Distributors shall cooperate with authorities and make available all the documentation and information they have at their disposal.

While these are the requirements for a distributor, they also lay the foundation for the manufacturer on their oversight towards the distributors. It would be good business practice to choose distributors that are able to comply with the requirements of the MDR or the IVDR.

## 4.5. PLACING ON THE MARKET

The medical device regulations specify 'making available on the market', 'placing on the market', and 'putting into service' of medical devices. Each of these definitions bare a distinctive meaning and purpose under the regulations and are important for the manufacturer to understand. Investigational devices aside, the definitions read as follows:

- 'Making available on the market' means any supply of a device for distribution, consumption, or use on the EU market in the course of a commercial activity, whether in return for payment or free of charge.
- 'Placing on the market' means the first time a device is made available on the EU market.
- 'Putting into service' means the stage at which a device has been made available to the final user as being ready for use on the EU market for the first time for its intended purpose.

The distinction between 'placing on the market' and 'putting into service' is important as, according to the MDR or IVDR, they bear different consequences.

Prior to placing a device on the market, the manufacturer (and where applicable, the authorised representative) must ensure that:

- The product is intended to be used for a purpose that fulfils the definition of a medical device as it is laid out in the regulations. Only then can the product qualify as a medical device and become regulated by either the MDR or the IVDR.
- All regulations that apply for the device are identified, also including others than the MDR or the IVDR.
- The device is correctly classified according to the classification rules of the MDR or the IVDR.
- The General Safety and Performance Requirements (Annex I of the MDR or the IVDR) and other requirements applicable to the device have been identified, taking into account the intended purpose and technology of the device.
- All of these requirements have been fulfilled.
- The necessary documents exist to prove the compliance of the device to those requirements.
- A proper Quality Management System (QMS) has been put in place, also for the lowest risk class devices (which is a new requirement in the MDR and the IVDR compared to the former medical device directives).
- EU certification is granted by a Notified Body (if the device class requires a Notified Body's involvement in assessing the conformity of the device).
- The manufacturer's Declaration of Conformity (DoC) is in place and bears the required contents.
- The device bears the CE mark.
- The device bears a Unique Device Identifier (UDI).
- The applicable registrations are made into the EUDAMED database (which is not yet available and therefore interim guidelines exist to fulfil the registration requirements). This requirement is gradually enforced during the coming years, starting from the highest risk class devices.

A medical device must therefore fulfil the requirements of CE marking and the CE marking must be done prior to placing the device on the market. Furthermore, 'putting the device into service' requires that the device is supplied, installed, and maintained as defined by the manufacturer, making it ready for use by the end user according to the intended purpose of the device.

Special attention must be paid to the marketing claims and marketing activities for the medical device. The labelling, instructions for use and advertising must stick to the intended purpose of the device, as it is specifically forbidden by the medical device regulations (MDR and IVDR) to mislead the user or the patient and to suggest other uses for the device. The manufacturer cannot ascribe functions and properties which the device does not have, nor create false impressions regarding treatment or diagnosis. The manufacturer must furthermore inform the user or the patient on likely risks associated with the use of the device.

## 4.6. PERSON RESPONSIBLE FOR REGULATORY COMPLIANCE (PRRC)

Manufacturers are required to appoint a Person Responsible for Regulatory Compliance. At least one such person must be available within the organisation. If several persons are jointly responsible for regulatory compliance, their respective areas of responsibility shall be defined. PRRC has the responsibility to ensure that the manufacturer fulfils its obligations over:

- Conformity of the devices under the QMS
- Technical Documentation and the EU
- Declaration of Conformity (DoC)
- Post-Market Surveillance
- Reporting to authorities and customers (e.g., in vigilance cases)
- PRRC shall suffer no disadvantage within the manufacturer's organisation in relation to the proper fulfilment of their duties.
- PRRC must have necessary expertise in the field of medical devices. Qualification requirements for PRRC are:

- Relevant (university) degree together with 1-year experience in a regulatory or quality position related to medical devices, or
- 4 years of experience in a regulatory or quality position related to medical devices

The addition of such a requirement into the MDR and the IVDR highlights the need for the top management of the manufacturer to deepen their knowledge on regulatory compliance. To be able to make decisions, where the PRRC carries such responsibility, the top management and the PRRC have to agree on compliance principles on a more practical level. The PRRC, or one member of the PRRC team, is likely the same person as the Management Representative discussed in Chapter 8.

Micro and small enterprises (SME) are not required to have the PRRC within their organization but must have such person permanently and continuously at their disposal. If a manufacturer decides to subcontract the responsibilities of a PRRC to a third party, they still need to be able to demonstrate that they can meet their legal obligations. This is achieved through a contract defining the responsibilities and ensuring the relevant qualification and permanent and continuous availability of the PRRC.

Also authorised representatives are required to have a PRRC at their disposal. The PRRC of an authorised representative should be responsible for ensuring that the tasks of an authorised representative as specified in the given mandate are fulfilled. The responsibilities of an authorised representative include supervision and control for placing the device on market and conducting the relevant post-market surveillance and vigilance activities. This adds an additional level of scrutiny and therefore the PRRC for an authorised representative and for a manufacturer located outside EU cannot be the same person.

The *MDCG 2019-7 Guidance on Article 15 of the Medical Device Regulation (MDR) and in vitro Diagnostic Device Regulation (IVDR) regarding a 'person responsible for regulatory compliance' (PRRC)* further clarifies the responsibilities and qualification of a PRRC.

# Health monitor

Doctor



Ok, let's get started.  
How can I help you today?

I have a sore throat

Do you have any other symptoms?

Diet

PROGRESS

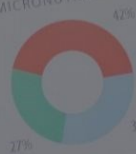
412 REMAINING OF 1200

812 Consumed   -220 Burned   592 Net

▶ FOOD DIARY

▶ TRAINING SCHEDULE

MICRONUTRIENTS CHART



Protein: 53.97  
Carbs: 32.18  
Fats: 95.34

heart beats: 72   blood pressure: 120/80   temperature: 36.9

Exercises

STEPS

282 steps

WALKING DISTANCE

0.54 km

CLIMBED

3 floors

5. INTENDED PURPOSE,  
QUALIFICATION AND  
CLASSIFICATION





## 5.1. INTENDED PURPOSE

The intended purpose of the medical device is the single most important item the manufacturer must pay attention to. It is the responsibility of the manufacturer to define the intended purpose of the device. The intended purpose identifies in detail which purposes the device may be used for and for which it may not. If the device is used for other purposes than those intended by the manufacturer, the responsibility on such misuse or off-label use falls at least partly on the user.

The intended purpose dictates, for example:

- Whether or not the product qualifies as a medical device (see Chapter 5.2).
- Under which regulation the device falls, the MDR or the IVDR.
- To which risk class the device belongs.
- For which medical purposes the device can be used.
- To which patient groups the device can be used.

It is worth noting that a product which is not intended to be used as a medical device may not be used for such purposes. On the other hand, if a product qualifies as a medical device, even though this is not the intention of the manufacturer, it cannot avoid the requirements of the MDR or IVDR. In borderline cases, the distinction may be very hard to make (see Chapter 5.2.3).

Furthermore, the intended purpose comes to define, for example:

- The scope of evidence to prove compliance
  - The broader the intended purpose (e.g., targeting both adults and children), the greater the burden to show that all areas within the intended purpose are covered.
- The depth of evidence to prove compliance which depends on the risk class and type of the device (e.g., implant)
  - The higher the risk class, the more stringent the General Safety and Performance Requirements (Annex I of the MDR and IVDR) for the device.
  - Particularly regarding risk management and clinical evaluation, the level of evidence and requirements increase according to the risk class and device type.
  - Respectively, the level of Notified Body involvement required for CE marking increases, even triggering the need for the Notified Body to consult a specific expert panel named by the European Commission for certain types of devices bearing high risk class.
- Whether the device can be used by laymen or if the use is restricted to professional users only.
- To which purposes and to which target groups the device may be advertised and marketed.
- Whether the device can be used at home or in clinical environments.
- What is the intended use environment regarding cybersecurity, connections to hospital networks, wireless transmission of data, and privacy.

The amount of work in product development may be reduced by narrowing down the intended purpose, or vice versa. This correlates directly with the resources and time required in development. On the other hand, by expanding the intended purpose, the targeted market may be greater. The manufacturer should therefore make the decisions on the intended purpose with caution and take into account consequences during the entire life cycle of the device. One may also plan ahead to extend the intended purpose of the device along the life cycle to distribute resources on a longer time frame.

## 5.2. THE DEFINITION AND QUALIFICATION OF A MEDICAL DEVICE AND IVD DEVICE

### 5.2.1. The Definition and Qualification of a Medical Device in the MDR

To qualify as a medical device, and hence to be regulated by the MDR, the product must fulfil the definition of a medical device as it stands in the MDR:

*“Medical device’ means any instrument, apparatus, appliance, software, implant, reagent, material or other article intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the following specific medical purposes:*

- *diagnosis, prevention, monitoring, prediction, prognosis, treatment or alleviation of disease,*
- *diagnosis, monitoring, treatment, alleviation of, or compensation for, an injury or disability,*
- *investigation, replacement or modification of the anatomy or of a physiological or pathological process or state,*
- *providing information by means of in vitro examination of specimens derived from the human body, including organ, blood and tissue donations,*

*and which does not achieve its principal intended action by pharmacological, immunological or metabolic means, in or on the human body, but which may be assisted in its function by such means.*

*The following products shall also be deemed to be medical devices:*

- *devices for the control or support of conception;*
- *products specifically intended for the cleaning, disinfection or sterilisation of devices as referred to in Article 1(4) (i.e. medical devices, accessories for medical devices and products listed in Annex XVI of the MDR) and of those referred to in the first paragraph of this point (i.e. devices for the control or support of conception).”*

The last bullet point refers to medical devices and their ‘accessories’ as well as to products listed in Annex XVI of the MDR which hold the risk profile of a medical device but do not bear an intended medical purpose (e.g., an implant with a purely cosmetic purpose), and are therefore brought under the MDR.

In addition, please note that the medical device definition holds a description of in vitro diagnostic (IVD) medical devices. By definition IVD devices are medical devices, but they apply the IVDR instead of the MDR.

It is also imperative to understand the concept of an ‘accessory’ since accessories are required to comply with the MDR all the same. The MDR refers to both medical devices and accessories as ‘devices’, making no distinction in the requirements they need to comply with:

*“Accessory for a medical device’ means an article which, whilst not being itself a medical device, is intended by its manufacturer to be used together with one or several particular medical device(s) to specifically enable the medical device(s) to be used in accordance with its/their intended purpose(s) or to specifically and directly assist the medical functionality of the medical device(s) in terms of its/their intended purpose(s).”*

Despite the challenges related to the qualification of many types of products as medical devices, the new medical device regulations (MDR and IVDR) provide a more harmonised basis for interpreting these definitions. In the past, the mix of EU Member State legislation, EU directives, and European Commission (EC) guidelines created a myriad of information to follow. However, not all guidance documents related to the qualification of medical devices according to the regulations are published by the EC at the time this book was published.

For the qualification of medical device software, please see Chapter [5.4.1](#).

## 5.2.2. The Definition and Qualification of an IVD Device in the IVDR

If a medical device falls under the definition of an IVD device, it is the IVDR and not the MDR the manufacturer needs to apply. To qualify as an in vitro diagnostic (IVD) medical device, and, hence, to be regulated by the IVDR, the product must fulfil the definition of an IVD device as it stands in the IVDR:

*“In vitro diagnostic medical device’ means any medical device which is a reagent, reagent product, calibrator, control material, kit, instrument, apparatus, piece of equipment, software or system, whether used alone or in combination, intended by the manufacturer to be used in vitro for the examination of specimens, including blood and tissue donations, derived from the human body, solely or principally for the purpose of providing information on one or more of the following:*

- a) *concerning a physiological or pathological process or state;*
- b) *concerning congenital physical or mental impairments;*
- c) *concerning the predisposition to a medical condition or a disease;*
- d) *to determine the safety and compatibility with potential recipients;*
- e) *to predict treatment response or reactions;*
- f) *to define or monitoring therapeutic measures.*

*Specimen receptacles shall also be deemed to be in vitro diagnostic medical devices.”*

To simplify this definition, in vitro diagnostics (IVD) means the laboratory testing that is performed on a clinical specimen that is taken from a patient or a healthy individual. It is important to note that invasive sampling products, or products which are directly applied to the human body for the purpose of obtaining a specimen, do not fall under the IVDR but under the MDR (e.g., syringes with needles for blood specimen collection).

Specimen receptacles are IVD devices specifically intended for the primary containment and preservation of specimens derived from the human body for the purpose of IVD examination.

Products for general laboratory use or products intended to research-use only are not considered IVD devices, unless such products, in view of their characteristics, are specifically intended by their manufacturer to be used for in vitro diagnostic examination.

It is also imperative to understand the concept of an ‘accessory’ since they need to comply with the IVDR all the same. The IVDR refers to both IVD devices and accessories as ‘devices’, making no distinction in the requirements they need to comply with:

*“Accessory for an in vitro diagnostic medical device’ means an article which, whilst not being itself an in vitro diagnostic medical device, is intended by its manufacturer to be used together with one or several particular in vitro diagnostic medical device(s) to specifically enable the in vitro diagnostic medical device(s) to be used in accordance with its/their intended purpose(s) or to specifically and directly assist the medical functionality of the in vitro diagnostic medical device(s) in terms of its/their intended purpose(s).”*

For the qualification of IVD software, please see Chapter [5.4.1](#).

## 5.2.3. Borderline Cases

The qualification of products as medical devices often becomes challenging. There may be borderline cases in relation to, for example:

- non-regulated products (e.g., products intended for wellness purposes)
- medicinal products
- cosmetic products

- products containing human or animal cells or tissue or their derivatives
- advanced therapeutics or biologics (e.g., gene therapy medicinal products)
- personal protective equipment (PPE)
- biocidal products
- in vitro diagnostic (IVD) devices versus other medical devices

Some devices may contain, as an integral part, substances which, if used separately, would be considered medicinal products. But when the intended action of the drug is only ancillary to that of the principal intended purpose of the medical device, the combination is considered to fall under the MDR (e.g., soft tissue fillers incorporating local anaesthetics). However, in such cases, there are requirements regarding the ancillary drug that a manufacturer and its Notified Body need to take into account prior to CE marking.

Guidance on borderline cases may be found in the [European Commission's MDCG guidance documents](#) published by the commission's medical device coordination group (MDCG).

The [Manual on Borderline and Classification in the Community Regulatory Framework for Medical Devices](#) may come handy in borderline cases, but it is very important to acknowledge that, at the time of publishing this book, the manual is not yet updated to align with the MDR and the IVDR. An updated version of the Manual on Borderline by the European Commission is in the making by the European Commission.

In case of uncertainty on whether or not the product falls under the medical device regulations, a manufacturer can first approach their own Notified Body and thereafter, in case of unresolved qualification or disagreement, the competent authority of their home EU Member State (which is Fimea in Finland). If the manufacturer does not yet hold an agreement with a Notified Body, they may still be reached to give their opinion on the qualification (and classification) of the device. Even though the application process for Notified Body assessment is stringent, they are given the flexibility to address qualification and classification requests beforehand. For choosing the right Notified Body to reach, one should study their scopes of competence (see Chapter 2.4.4). Later, the application for conformity assessment can be sent to only one Notified Body at a time.

If the request was addressed to the competent authority, they have the option to further approach the European Commission, which will consult its medical device working group on Borderline and Classification, or, where relevant, European authorities such as the European Medicines Agency (EMA). Ultimately, it is the European Court of Justice that may be approached to resolve disputes over borderline cases. Therefore, in addition, it may be relevant to study earlier cases, even though they likely relate to the former medical device directives.

## 5.3. CLASSIFICATION OF MEDICAL DEVICES AND IVD DEVICES

### 5.3.1. The Implications of Device Classes

The classification of medical devices is highly important, because the level of requirements as well as the extent of Notified Body involvement in assessing the conformity of the device and the manufacturer's Quality Management System (QMS) is dependent on the device class. Device classification defines the procedures the manufacturer must follow to be able to place the device on the market.

Prior to classification, the manufacturer should focus on the qualification of the product as a medical device (see previous chapters). This should be done as early as possible before investing a lot into product development. Immediately thereafter, it is just as important to know the device class to be able to plan ahead in product development with a correct understanding of the level of requirements applicable to the device. For devices in class III (MDR) or class D (IVDR), there is a multitude of requirements compared to class I or class A and, therefore, the classification should be done correctly at the start. As an

example, when the risk class is revealed to be higher than that initially chosen, the design inputs originally collected may not match the requirements, causing a major re-design of the device and the QMS at worst.

The MDR and the IVDR also require the manufacturer to contain a rationale on the qualification and classification of the device within its Technical Documentation.

Please see Chapter 6.3.3 for more details on conformity assessment routes to market.

### 5.3.2. Medical Device Classification in MDR

In the MDR, devices are divided into the following four classes, from lowest risk to highest:

- Class I (see more guidance regarding class I further below)
- Class IIa
- Class IIb
- Class III

Medical device classification is defined in Annex VIII of the MDR. Annex VIII begins from the definitions and implementing rules, followed by classification rules from 1 to 22. The classification rules are based on the vulnerability of the human body, taking into account the potential risks associated with the technical design and manufacture of the devices. This allows a set of criteria, such as the duration of contact, degree of invasiveness, and the part of the body affected (e.g., local vs. systemic effect) in various combinations as a basis for classification. It is also worth noting that active implantable medical devices, which are now drawn under the MDR (from the former directive 80/385/EEC specific for active implants), are placed in class III. Overall, the classification in the EU is well in line with medical device classifications internationally. Notable differences apply to the classification of software as a medical device according to the Rule 11 of the MDR, where the EU recognises practically no software falling below class IIa. The *MDCG 2019-11 Guidance on Qualification and Classification of Software in MDR and IVDR* document further clarifies this and other important interpretations regarding software (providing also one example of a class I medical device software). See Chapter 5.4.3 for more information on the classification of medical device software.

The conformity assessment procedure for class I devices is carried out, as a general rule, under the sole responsibility of the manufacturer in view of the low level of risk associated with such devices. A Notified Body is therefore not involved in the assessment. However, additional requirements apply to class I devices that are placed on the market in a sterile condition that contain a measuring function, or that are reusable surgical instruments. In such cases, a Notified Body is required to carry out conformity assessment regarding these aspects, including an audit on the Quality Management System (QMS) through all applicable chapters of the ISO 13485 QMS standard.

These subcategories of class I devices are generally referred to as:

- Class I (s) for devices that are placed on the market in (s)terile condition
- Class I (m) for devices with a (m)easuring function
- Class I (r) for (r)eusable surgical instruments

The classification rules are grouped in Chapter III of Annex VIII of the MDR as follows:

- Rules 1 to 4: Non-invasive devices
- Rules 5 to 8: Invasive devices
- Rules 9 to 13: Active devices (including software)
- Rules 14 to 22: Special rules

However, to begin classification, the following definitions presented in Chapter I of Annex VIII are relevant:

- Duration of continuous use of the device, where attention should be paid to the definition (see implementation rule 3.6) and examples of ‘continuous use’ (see implementation rule 3.6) if this plays a meaningful part for classification of the device.
- Invasiveness of the device, whether surgically or through a body orifice (which also includes the external surface of the eyeball, or any permanent artificial opening, such as a stoma).
- Whether or not the device is considered active (mainly electromedicals and software, but also devices dependent on any other sources of energy than that directly generated by human body or gravity, such as thermal, chemical or radioactive sources).
- On which parts of the human body the device comes into contact, where, for instance, contact with the central nervous systems or the central circulatory system causes a higher risk.

Please note that the interpretation of these definitions can be quite complex, and therefore all guidance documents defined in Chapter 5.5 would need to be studied in detail, in case of any uncertainty of the application of the definitions.

Furthermore, the implementing rules in Chapter II of Annex VIII are essential in classifying any medical device, in particular for taking into account the (most critical) intended purpose of the device and cases where several classification rules may apply to one device:

- *“3.1. Application of the classification rules shall be governed by the intended purpose of the devices.*
- *3.2. If the device in question is intended to be used in combination with another device, the classification rules shall apply separately to each of the devices. Accessories for a medical device shall be classified in their own right separately from the device with which they are used.*
- *3.3. Software, which drives a device or influences the use of a device, shall fall within the same class as the device. If the software is independent of any other device, it shall be classified in its own right.*
- *3.4. If the device is not intended to be used solely or principally in a specific part of the body, it shall be considered and classified on the basis of the most critical specified use.*
- *3.5. If several rules, or if, within the same rule, several sub-rules, apply to the same device based on the device's intended purpose, the strictest rule and sub-rule resulting in the higher classification shall apply.*
- *3.6. In calculating the duration referred to in Section 1, continuous use shall mean:*
  - (a) the entire duration of use of the same device without regard to temporary interruption of use during a procedure or temporary removal for purposes such as cleaning or disinfection of the device. Whether the interruption of use or the removal is temporary shall be established in relation to the duration of the use prior to and after the period when the use is interrupted or the device removed; and*
  - (b) the accumulated use of a device that is intended by the manufacturer to be replaced immediately with another of the same type.*
- *3.7. A device is considered to allow direct diagnosis when it provides the diagnosis of the disease or condition in question by itself or when it provides decisive information for the diagnosis.”*

### 5.3.3. IVD Device Classification in IVDR

In the IVDR, devices are divided into the following four classes, from low to high:

- Class A (see more guidance regarding class A further below)
- Class B
- Class C
- Class D

The classification of in vitro diagnostic (IVD) medical devices is defined in Annex VIII of the IVDR, where it begins from the definitions and implementing rules, followed by classification rules from 1 to 7. The classification system takes into account the intended purpose of the devices and their inherent risks.

The classification system for IVD devices has been fundamentally changed in the IVDR compared to the former IVD medical device directive (IVDD). This has been done to enhance patient safety and to take account of technological progress, but also to put the system in line with international practice, where, in particular, the guidance developed by the Global Harmonization Task Force (GHTF) and its follow-up initiative, the [International Medical Devices Regulators Forum \(IMDRF\)](#), has been taken into account. As a consequence of the new IVD classification in the EU, a Notified Body is required for most IVD devices, whereas previously a Notified Body was required for the minority of IVDs.

Guidance on the classification rules for IVD devices under the IVDR is provided in the MDCG 2020-16 guidance document.

The conformity assessment procedure for class A devices is carried out, as a general rule, under the sole responsibility of the manufacturer, since such devices pose a low risk to patients. A Notified Body is therefore not involved in the assessment. However, additional requirements apply to class A devices that are placed on the market in a sterile condition. In such cases, a Notified Body is required to carry out conformity assessment regarding these aspects, including an audit on the Quality Management System (QMS) through all applicable chapters of the ISO 13485 QMS standard. This subcategory is generally referred to as Class A (s) or Class A sterile.

The classification rules in Chapter 2 of Annex VIII of the IVDR run from rule 1 to 7.

The implementing rules in Chapter 1 of Annex VIII are essential in classifying any IVDs, in particular for taking into account the intended purpose(s) of the device and cases where several classification rules may apply to one device:

- *“1.1. Application of the classification rules shall be governed by the intended purpose of the devices.*
- *1.2. If the device in question is intended to be used in combination with another device, the classification rules shall apply separately to each of the devices.*
- *1.3. Accessories for an in vitro diagnostic medical device shall be classified in their own right separately from the device with which they are used.*
- *1.4. Software, which drives a device or influences the use of a device, shall fall within the same class as the device. If the software is independent of any other device, it shall be classified in its own right.*
- *1.5. Calibrators intended to be used with a device shall be classified in the same class as the device.*
- *1.6. Control materials with quantitative or qualitative assigned values intended for one specific analyte or multiple analytes shall be classified in the same class as the device.*
- *1.7. The manufacturer shall take into consideration all classification and implementation rules in order to establish the proper classification for the device.*
- *1.8. Where a manufacturer states multiple intended purposes for a device, and as a result the device falls into more than one class, it shall be classified in the higher class.*
- *1.9. If several classification rules apply to the same device, the rule resulting in the higher classification shall apply.*
- *1.10. Each of the classification rules shall apply to first line assays, confirmatory assays and supplemental assays.”*

Please note that the interpretation of the classification rules together with the implementing rules can be complex, and therefore the guidance documents defined in Chapter 2.14.2 that relate to IVDs would need to be studied in detail in case of any uncertainty of the application of the rules.

## 5.4. QUALIFICATION AND CLASSIFICATION OF MEDICAL DEVICE SOFTWARE (MDSW)

The health tech sector sees a vastly increasing number of innovations related to software, both stand-alone and embedded. Many of these innovations are considered medical devices and are therefore regulated under either the MDR or the IVDR. To many of the entrants, who may be start-ups, clinics, health service providers, IT service providers, or pharma manufacturers, the medical device regulations pose new and notable challenges. By introducing a specific classification rule (rule 11 of the MDR) for software and publishing the *MDCG 2019-11 Guidance on Qualification and Classification of Software in MDR and IVDR*, the European Commission has made it clear that the EU directives on medical devices were not up to date regarding software, and that there are concerns related to the use of software that is intended for therapeutic and diagnostic purposes. In effect, a medical device software (MDSW) manufacturer regulated by the MDR must now assume their software falls in class IIa at a minimum, and is therefore required to be assessed by a Notified Body. Software regulated by the IVDR do not face this rule, but are most likely classified in class B at a minimum, also requiring a Notified Body assessment.

Therefore, it has become highly important for the entire healthcare sector to understand that the MDR and the IVDR with their novel classification affecting software also affects the many hospitals and clinics throughout Europe who are the buyers of that software. Still, today some hospitals require CE marking for a broad range of software which might not, in effect, all qualify as medical devices. Under the MDD, class I has been the prominent software class and neither a QMS nor a Notified Body has been required for class I devices. As a consequence, a market has been formed where the CE mark is applied even to software that could not qualify as a medical device. Now that the MDR is applied and class IIa is the minimum device class, Notified Bodies step in to assess basically all medical device software, though they may not agree with the manufacturers' claims that certain software can be CE marked.

It is the MDCG 2019-11 guidance document the entire health tech industry should follow, including the buyers, to be able to maintain the flow of both regulated and non-regulated software goods on the market. Due to the intervention by Notified Bodies, all parties are eventually forced to follow the same guidelines, but it would be for the benefit of the healthcare sector that this would happen sooner. However, even if the software that is sold to a hospital did not qualify as a medical device, it would be advisable to utilise the same or similar methods and standards to develop and maintain the software. This is to maximise the safety and performance of the software and to reduce risks for the hospital, the patients, the healthcare professionals and the business.

### 5.4.1. Qualification of Medical Device Software


Medical device software (MDSW) is *“software that is intended to be used, alone or in combination, for a purpose as specified in the definition of a ‘medical device’ in the MDR or an ‘in vitro diagnostic (IVD) medical device’ in the IVDR”*.

A software may be qualified as a MDSW regardless of its location (e.g., operating in the cloud, on a computer, on a mobile phone, or as an additional functionality on a hardware medical device). Please note that MDSW should be classified in the same way, regardless of the software's location and the type of interconnection between the software and a (hardware) device. This means, for instance, that embedded software should be taken into account in classification and this may affect the device class.

Furthermore, MDSW that is intended specifically to replace a part or component of a device and that significantly changes the performance or safety characteristics or the intended purpose of the device shall be considered to be a medical device.

To qualify a software as a medical device, one should follow the MDCG 2019-11 guidance document and the decision diagrams it provides, starting from Figure 3 below. Interpretation of each of the steps can sometimes be very challenging, and experience in qualification of software will come handy. One particularly important point of view in the MDCG 2019-11 guidance document is that not all software used within healthcare is qualified as a medical device. It is highlighted that the risk of harm



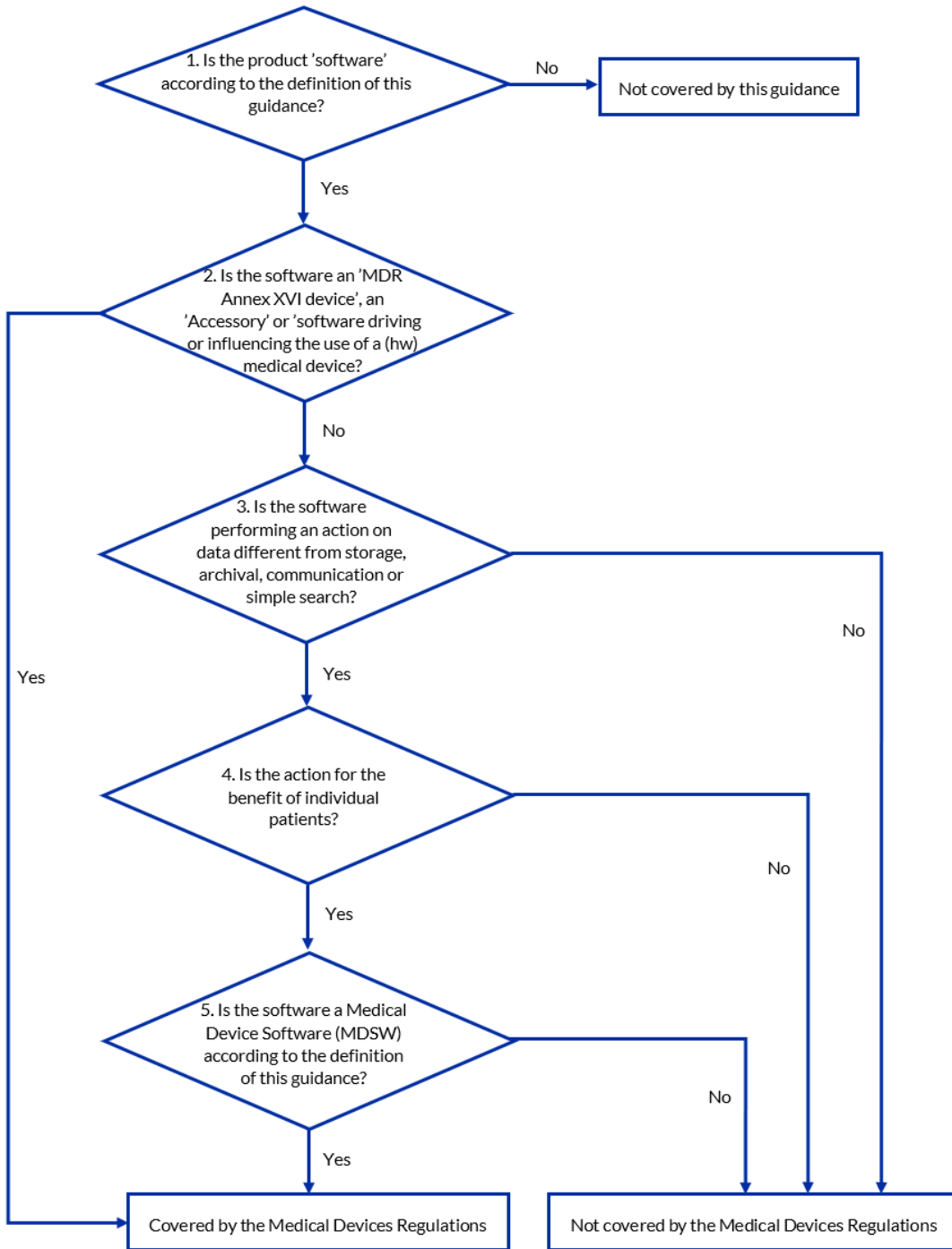


to patients, users of the software, or any other person related to the use of the software within healthcare (including a possible malfunction) is not a criterion on whether the software qualifies as a medical device.

If the software is intended to drive or influence the use of another medical device, but it also carries a medical intended purpose, the software may qualify as a medical device software (MDSW). This would need to be taken into account at Step 2 of Figure 3.

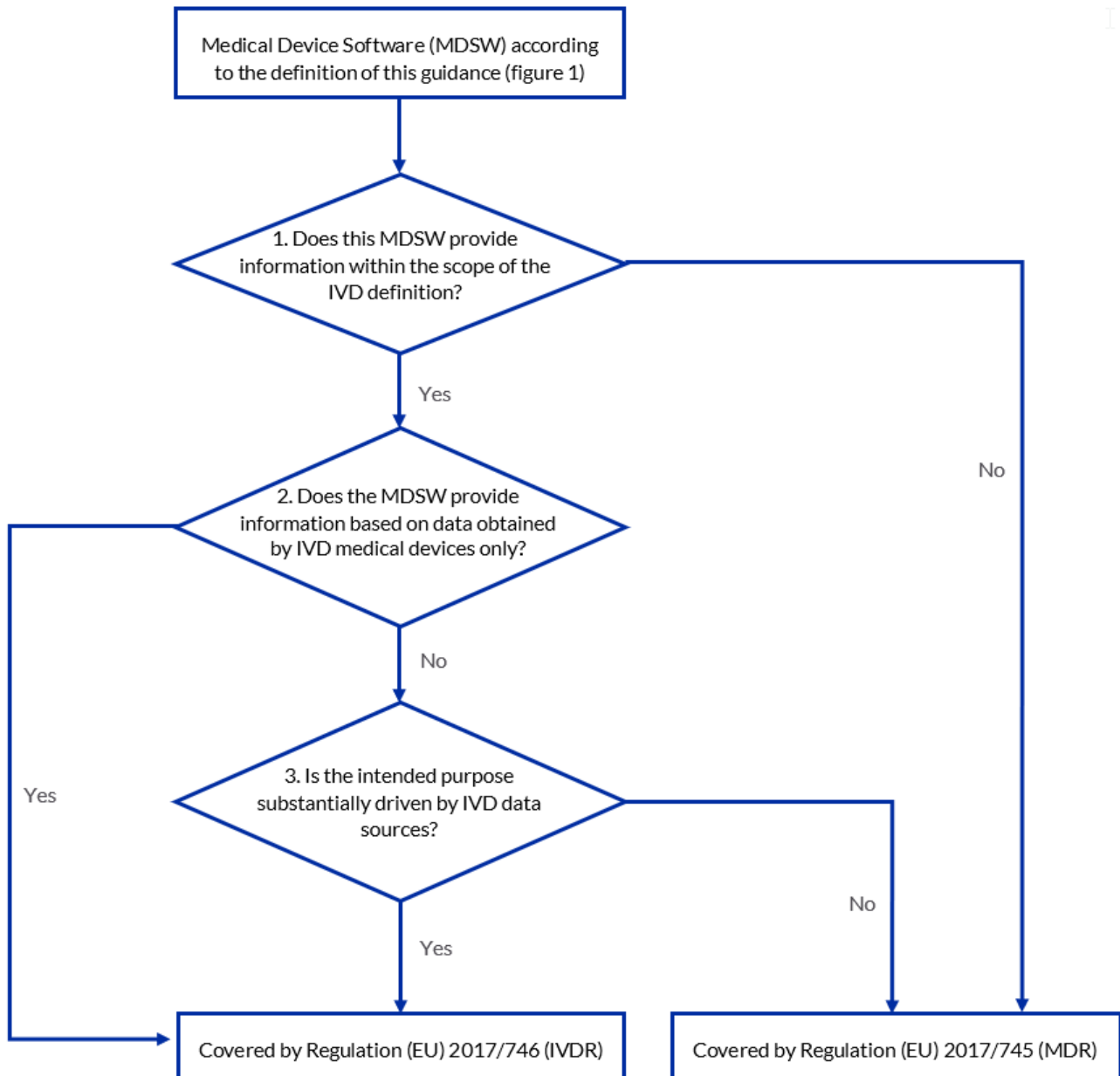
Regarding steps 3 (action on data), 4 (for the benefit of individual patients), and 5 (medical purpose), these must all apply for the software to be considered medical device software (MDSW), and all steps may be very difficult to interpret, depending on the software and its intended purpose.

Figure 3 Decision steps to assist the qualification of MDSW as either an IVD device, regulated by the IVDR, or other medical device, regulated by the MDR (MDCG 2019-11)



After defining if the software is covered by the medical device regulations (MDR or IVDR), the next step is to define which one of these regulations should be applied. In case the software provides information based on in vitro diagnostic (IVD) data, this may fall under the IVDR. Room is left for consideration on which source of data is dominant if some of the clinically relevant data is drawn from sources other than IVD sources. One should follow the MDCG 2019-11 guidance document and the decision diagram it provides below in Figure 4.

Figure 4 Decision steps to assist the qualification of MDSW (MDCG 2019-11)



In addition, bear in mind that manufacturers must evaluate the potential impact of any future changes to the function, intended purpose, and essential design and manufacturing characteristics on its qualification and classification, and not forget combinations of the MDSW with other medical devices or products.

### 5.4.2. Modularity of Software

Some medical device software may be segregated into a number of modules. Some of these modules may have a medical purpose, some not. This raises the issue as to whether the whole product can be CE marked when not all the applications have a medical purpose.

The medical device modules must comply with the MDR or the IVDR and carry the CE marking. The non-medical device modules are not subject to the requirements for medical devices. The boundaries of the modules which are subject to the medical device regulations should be clearly identified by the manufacturer based on their intended purpose.

However, if the medical device modules are intended for use in combination with other modules within a software structure, other devices or equipment, the entire combination including the connection system must be safe and must not impair the specified performances of the medical device modules.

For the above reasons, the MDCG 2019-11 guidance document suggests using a modular approach for software development when operating in the health tech sector.

### 5.4.3. Classification of Medical Device Software

The classification of medical devices regulated under the MDR are most notably affected by the new software classification rule 11. The MDCG 2019-11 guidance document explains that the rule 11a wording “intended to provide information which is used to take decisions with diagnosis or therapeutic purposes” describes, in very general terms, the “mode of action” which is characteristic of basically all medical device software (MDSW). Therefore, this subrule 11a is generally applicable to all MDSW, making them class IIa at a minimum. The one exception falling in class I is MDSW that is intended to ‘support conception’, which the guidance document does not regard a ‘medical purpose’, but which falls under the definition of a ‘medical device’. In addition, please note that software that is an ‘accessory’ to a hardware medical device may fall in class I.

The subrule 11a, in particular, describes and categorises (1) the significance of the information provided by the device to the healthcare decision making (patient management) in combination with (2) the healthcare situation (patient condition). See Table 1 below, which is provided in the MDCG 2019-11 for guidance on applying the subrule 11a. The origins of this table and the applicable categories are in the [IMDRF Software as a Medical Device](#) guidance document. Class I does not appear in the table simply because the subrule 11a does not recognise it as an option.

Table 3 Classification guidance on subrule 11a (MDCG 2019-11) \*) Please note that the numbering of the IMDRF categories in the original table in the MDCG 2019-11 document contains errors which have been corrected in this table and indicated with asterisk.

		Significance of information provided by the MDSW to a healthcare situation related to diagnosis/therapy		
		High Treat or Diagnose ~IMDRF 5.1.1	Medium Drives clinical management ~IMDRF 5.1.2	Low Informs clinical management (everything else)
State of Healthcare situation or patient condition	Critical situation or patient condition ~IMDRF 5.2.1	Class III Category IV.i	Class IIb Category III.ii *	Class IIa Category II.iii *
	Serious situation or patient condition ~IMDRF 5.2.2	Class IIb Category III.i *	Class IIa Category II.ii	Class IIa Category I.ii
	Non-serious situation or patient condition (everything else)	Class IIa Category II.i *	Class IIa Category I.i *	Class IIa Category I.iii *


A clear example of a class III medical device software according to subrule 11a is an automated closed loop medication software for patients in critical condition, where the software determines the amount of medicine (treatment) based on the diagnosis made by the same or another device or software, whereby the significance of this information is high (Such an example is not provided in the MDCG 2019-11 guidance document, but the classification rule 22 for closed loop systems, which also applies to such software, confirms the interpretation.). An example of a class IIa software provided in the MDCG 2019-11 guidance document is a cognitive therapy MDSW that includes a diagnostic function, but a specialist determines the necessary cognitive therapy based on the outcome provided by the MDSW. In this example, reference is given to Table 3 and IMDRF Risk Category II.ii, since the healthcare situation is considered 'serious' and the significance of the information to 'drive clinical management'.

While many manufacturers must now focus on rule 11 of the MDR, it has to be remembered that software is also defined as an 'active device'. Therefore, all classification rules for active devices (rules 9, 10, 11, 12, 13, 15 and 22) and their subrules should be considered. In line with implementation rule 3.5, the strictest applicable rule or subrule shall then apply.

In the case of IVD medical device software, unless classified to a higher class than class B by any of the specific rules, rule 6 of the IVDR is the fallback rule making the device at a minimum a class B device. This is unless the software is an 'accessory' to another IVD device and may therefore be classified as class A IVD device.

## 5.5. WHERE TO GET HELP FOR CLASSIFICATION?

The classification of a medical device or an IVD device may be very simple, when the classification rule casts no doubt (e.g., joint replacements specified in rule 8 of the MDR are clearly class III devices) or the European Commission guidance documents provides a clear classification example. However, medical devices come in hundreds of thousands of different types and in many, if not most, of the cases, classification of devices is challenging and requires experience.



As we have learnt earlier, the manufacturer should work to get the classification right the first time. When in doubt, it is imperative to approach their Notified Body and thereafter, in the case of unresolved classification or disagreement, the competent authority of their home EU Member State (which is Fimea in Finland). If the manufacturer does not yet hold a contract with a Notified Body, they may still be reached to give their opinion on the classification (and qualification) of the device. Even though the application process for Notified Body assessment is stringent, they are given the flexibility to address qualification and classification requests beforehand. For choosing the right Notified Body to reach, one should study their scopes of competence (see Chapter 2.4.4). Later, the application for conformity assessment can be sent to only one Notified Body at a time. If the request was addressed to the competent authority, they have the option to further approach the European Commission which will consult its medical device working group on Borderline and Classification. Ultimately, it is the European Court of Justice that may be approached to resolve disputes over classification. Therefore, it may also be relevant to study earlier cases even though they likely relate to the former medical device directives.

Classification is defined in Annex VIII of the MDR and the IVDR. It is worth studying Annex VIII and utilising the following central guidance documents to find advice. However, notice that in the list below, MEDDEV 2.4/1 and the Manual on Borderline refer to the former directives and not the MDR or the IVDR. At the time of publishing this book, the new versions of these guidance documents are being processed by the European Commission working groups. One must, therefore, use extreme caution not to draw false conclusions from the previous guidelines, as some of these principles have changed dramatically and the numbering of the classification rules may have altered.

- MEDDEV 2.4/1 Rev. 9 Classification of medical devices (June 2010) (Please use caution, as this document refers to the former medical device directives.)
- MDCG 2020-16 Guidance on Classification Rules for In Vitro Diagnostic Medical Devices under IVDR
- MDCG 2019-11 Guidance on Qualification and Classification of Software in MDR and IVDR
- Manual on Borderline and Classification in the Community Regulatory Framework for Medical Devices (Please use caution, as this document refers to the former medical device directives.)



**6. MEDICAL DEVICE CONFORMITY  
AND CE MARKING**

## 6.1. DEMONSTRATING CONFORMITY

A medical device must be designed, manufactured, packaged, and labelled in such way that it is suitable for its intended purpose. The device must remain suitable for its intended use for its entire life cycle. The manufacturer's work does not end when the device has been placed on the market. On the contrary the life cycle of the device has just started.

In practice, these requirements highlight that the manufacturer is responsible for the device

- is suitable for its intended purpose under normal conditions of use
- is effective, i.e., achieves the performance intended by the manufacturer, and
- is safe, i.e., does not compromise the clinical condition or the safety of patients, users or other persons

This means that

- the product must meet the applicable requirements of the MDR or the IVDR, and
- the manufacturer must have an efficient Quality Management System (QMS).

Hence, compliance must be demonstrated from the product's perspective (Chapter 6.2) as well as from the QMS perspective (Chapter 6.3).

The manufacturer must draw up the Technical Documentation to demonstrate the product's compliance. This is usually achieved by applying state of the art standards (Chapter 3.6) and guidelines (Chapter 3.4).

## 6.2. DEMONSTRATING CONFORMITY OF THE PRODUCT

This chapter focuses on the product requirements for demonstrating conformity to the MDR and IVDR. The requirements are discussed on a generic level, highlighting some of the most important areas. The General Safety and Performance Requirements (Chapter 6.2.1) set the basis for all device specific requirements. Risk management (Chapter 6.2.2) and usability engineering (Chapter 6.2.3) are especially important activities in identifying and controlling the risks that your device or its use might cause. There are very specific requirements and standards for the development and maintenance of medical device software (Chapter 6.2.4), which help ensure that MDSW is safe and effective to use. Clinical evaluation (for MDs) and performance evaluation (for IVDs) is essential in demonstrating the clinical benefits of the device and validating its suitability for its intended purpose.

### 6.2.1. General Safety and Performance Requirements

According to Annex I of the MDR and IVDR, the device must meet the General Safety and Performance Requirements (GSPR) which apply to it, considering its intended purpose. These were called Essential Requirements in the MDD and IVDD. The manufacturer of the medical device must prepare technical documentation for the product to demonstrate how these requirements have been fulfilled. It is considered good practice to use a checklist prepared for this purpose for assessing applicable requirements for your product and demonstrating that the requirements have been fulfilled. Note that the requirements are generic principles and that need to be translated into specific requirements for your particular product, leaning on possible more specific requirements defined in applicable standards. You must also be aware of the state of art of similar products on the market and, when applicable, alternative solutions in also other kinds of products. The ultimate goal is to demonstrate that your product is fit for its intended purpose, that the medical benefits outweigh the risks and that the device is in line with the state of art.



The checklist can be used to demonstrate:

- That all General Safety and Performance Requirements have been considered and a rationale is provided where the requirements are not applicable
- Which method (e.g., verification, validation or clinical evaluation) has been used to demonstrate conformity to each applicable requirement
- Which standards or other solutions have been applied to demonstrate conformity, and
- Which document (e.g., test report) within the Technical Documentation supports the conclusion of conformity to each applicable requirement.

You can download and use, for example, the [Lean Entries GSPR Checklist](#) for this purpose.

If your medical device is also in the scope of another CE marking legislation, a similar kind of checklist approach can be utilised to demonstrate compliance to the Essential Requirements of that legislation. See Chapter 3.2 for more information about other directives and regulations.

## 6.2.2. Risk Management

Risk management activities are mentioned in multiple different paragraphs of the General Safety and Performance Requirements and several other Articles in the MDR and IVDR. Risk management can be considered as one of the core activities of medical device development and for ensuring its continuous safety and performance once the device has been placed on the market. Furthermore, it is an essential cornerstone of a well-functioning QMS, bridging pre- and post-market activities together. It needs to be an essential driver throughout the product life cycle and a natural part of a company's culture and decision-making.

It is crucial that medical devices do not compromise the clinical condition or the safety of patients, or the safety and health of users or other persons. All risks associated with their use must be carefully considered by the manufacturer and weighed against the benefits to the patient. According to the medical device regulations, risks need to be reduced as far as possible without adversely affecting the benefit-risk ratio of the device.

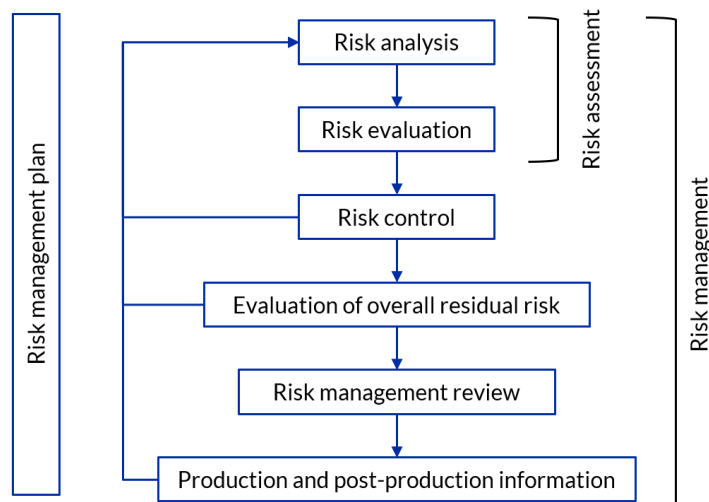
To achieve this goal, manufacturers must establish, implement, document, and maintain a risk management system. According to MDR, risk management shall be understood as a continuous iterative process throughout the entire life cycle of a device, requiring regular systematic updating. MDR defines that in carrying out risk management, manufacturers shall:

- Establish and document a **risk management plan** for each device.
- **Identify and analyse** the known and foreseeable hazards associated with each device.
- **Estimate and evaluate the risks** associated with, and occurring during, the intended use and during reasonably foreseeable misuse.
- Eliminate or control the risks.
- **Evaluate the impact of information** on hazards and their frequency from the production phase and the **post-market surveillance system** through estimates on their associated risks, the overall risk, benefit-risk ratio and risk acceptability, and amend control measures based on these findings if necessary.

The international state of the art standard for risk management is the *ISO 14971:2019 - Medical devices - Application of risk management to medical devices*. It contains information on the general requirements for a risk management system and processes, covering the entire life cycle of the device, from writing up the risk management plan to post-production activities regarding a device.

The technical report *ISO/TR 24971:2020 Medical devices – Guidance on the application of ISO 14971* provides practical guidance on the development, implementation and maintenance of a risk management system for medical devices according to the ISO 14971 standard. Much of its contents were included in the annexes of the previous version of the ISO 14971 standard.

Figure 5 Stages of risk management (originally from the ISO 14971:2019)



When selecting the most appropriate risk control solutions, the following order or priority of measures shall be followed:

1. Eliminating or reducing risks as far as possible through the safe design and manufacture of the device.
2. Taking adequate protection measures, including alarms if necessary, in relation to risks that cannot be eliminated.
3. Providing information for safety (warnings/precautions/contra-indications) and/or training to users.

Since these are the risk control categories that are presented in both Annex I of the MDR and the IVDR and the ISO 14971 standard, it is good practice by the manufacturer to document the risk controls in matching categories.

According to the MDR and IVDR, all known and foreseeable risks, and any undesirable side-effects, shall be minimised. They must be acceptable when weighed against the evaluated benefits to the patient and/or user arising from the achieved performance of the device during normal conditions of use. This is documented in the form of a benefit-risk analysis. This analysis and its conclusions are also part of the Technical Documentation for the device.

It is critical to understand that risk management is an iterative process starting within product development and continuing throughout the entire product life cycle. During the product development, the first initial risk management work gives important input to the user requirements and consecutive product specifications. It also guides to the right level of various efforts in the field of verification, validation as well as the best touch to clinical evaluation. During the post-market phase it is of special importance when analysing the impact of changes to the device, in non-conformance situations as well as e.g. when evaluating the need for revalidation of various manufacturing processes. It is the glue keeping everything under proper control.

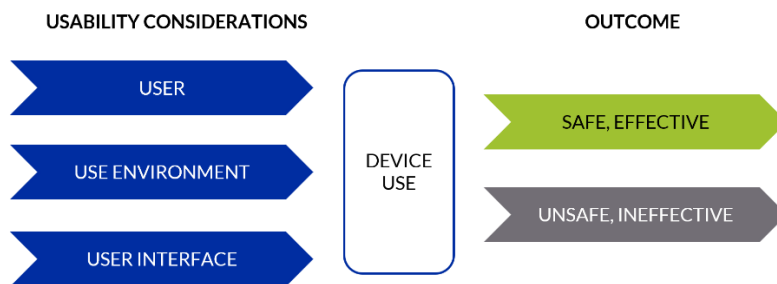
It is of uttermost importance that the original risk management file is actively used during the post-market stage, e.g. in complaint handling and when considering possible vigilance actions. It must be kept updated, i.e. if new hazards are recognized or if the risk level is changed due to a recognized change in the occurrence or severity. Risk management, technical documentation and post-market surveillance need to be an integrated entity, also linked as an input to new product development and clinical evaluation and post-market clinical follow-up.

### 6.2.3. Usability Engineering

Usability engineering is an important part of the product development for any medical device. Although the requirement to conduct usability engineering activities has not been explicitly stated in the MDR, it is still required. This is implied in General Safety and Performance Requirements which states that the manufacturer must, in their effort to eliminate or reduce risks related to use error:

- reduce as far as possible risks related to the ergonomic features of the device and the environment in which the device is intended to be used, and
- consider the use environment and the technical knowledge, experience, education, training, and the medical and physical conditions of the intended users.

Figure 6 Usability engineering (figure originally from FDA guidance for human factors engineering)



The standard *IEC 62366-1 - Medical devices – Part 1: Application of usability engineering to medical devices* is considered state of the art for planning usability engineering activities for a medical device.

The level of effort within usability engineering should be proportionate to the characteristics of the device, complexity of the user specification, and the severity of the harm associated with the use of the device. It is important that usability is considered for all steps of the product life cycle, including transport, storage, installation, operation, maintenance and disposal. In addition, it is good to keep in mind that all user interfaces of the device should be considered, not just the graphical user interface.

Usability engineering is very closely linked to risk management, presented in Chapter 6.2.2. Usability engineering activities consider and mitigate risks caused by problems in user interaction associated with normal use. Risk management also considers abnormal use as part of reasonably foreseeable misuse.

### 6.2.4. Medical Device Software

Software applications have become increasingly popular in the health tech sector during recent years. It is crucial to identify early in development if the software qualifies as a medical device. More information about the qualification and classification of medical device software (MDSW) can be found in Chapter 5.4.

If the software qualifies as a medical device, is part of a medical device (embedded software), or is an accessory to a medical device, it must meet the requirements set in MDR or IVDR. All requirements set in Annex I need to be assessed for applicability. Risk management and usability engineering, already covered in previous chapters, are essential for software medical devices, as well as clinical evaluation, covered in the next chapter.

The state of the art standard for developing and maintaining medical device software is *IEC 62304 Medical device software – Software life cycle processes*. The IEC 62304 contains requirements on how to conduct specific phases of software development and maintenance, including level of required documentation and verification. It describes the following:

- **Software development process:** including development planning, requirements analysis, architectural design, detailed design, unit implementation, integration and integration testing, software system testing and software release.
- **Software maintenance process:** including maintenance planning and how to analyse and implement modifications.
- **Software risk management:** including a link to the ISO 14971 risk management standard and risk management activities related to software specifically.
- **Software configuration management:** including control of configuration items and their version and documenting software of unknown provenance (SOUP).
- **Software problem resolution:** including how to document problem reports, investigate problems, and take appropriate actions.

It should be noted that this standard does not cover validation and final release of the medical device, which are nevertheless required by the ISO 13485 and MDR/IVDR.

The IEC 62304 divides software into safety classes A, B, and C (from lowest risk to highest). These are unique to the standard, and not to be confused with medical device classes, although some similarities behind the logic of these two exist. The safety class of a software is determined based on results of the risk analysis and its worst-case scenarios:

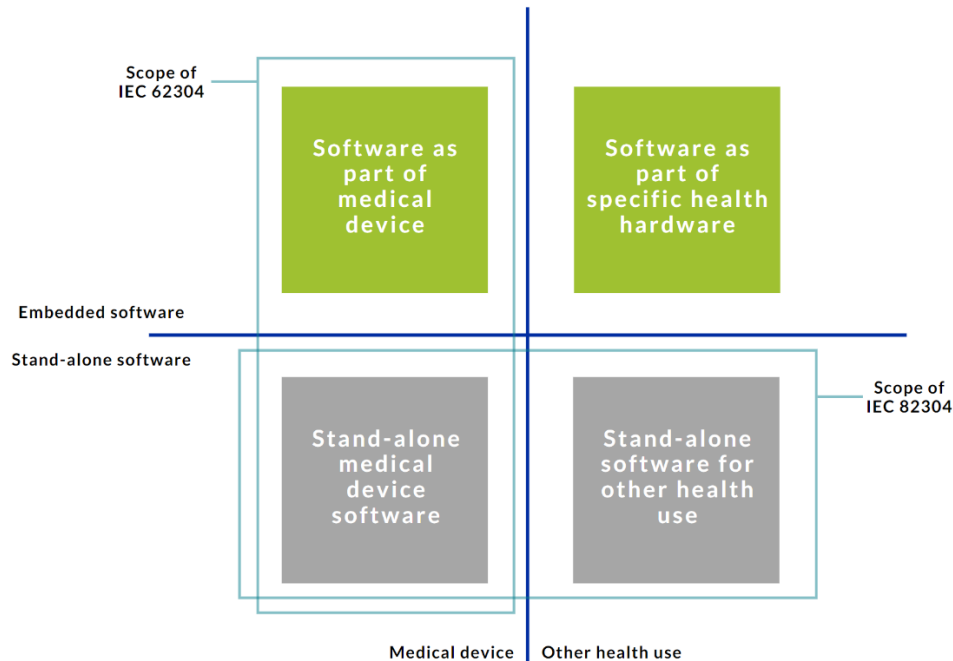
- If the failure of the software cannot result in unacceptable risk after evaluating the effectiveness of risk control measures external to the software, the software belongs in safety class A.
- If failure of the software can result in unacceptable risk after considering risk controls external to the software system, the software belongs in safety class B if these cases can only result in non-serious injury, and in safety class C if these cases can result in serious injury or death.

Those external risk control measures mentioned can be, for example, hardware, independent software or health care procedures. During software architecture design, complex software can be partitioned into modules which may have different software classifications if segregation is possible.

Software safety class determines which requirements of the IEC 62304 are applicable. All requirements set in the standard apply for class C software. Class B software is exempted from some of the requirements, such as developing detailed design for interfaces. Class A software on the other hand is exempted from multiple requirements, including all requirements related to architectural design.

Another standard worth mentioning is the *IEC 82304-1 Health Software – Part 1: General requirements for products safety*. This has been written for stand-alone health software to provide requirements to ensure their safety and security. For software life cycle processes, the IEC 82304-1 refers directly to IEC 62304. The standard encourages manufacturers to develop devices for health use with the same controlled methods and to utilize risk management activities to minimize risks to patients and users. The scope of the IEC 62304 and the IEC 82304 is depicted in Figure 7.

Figure 7 Scope of the IEC 62304 and the IEC 82304



### 6.2.5. Clinical Evaluation (MDR)

The MDR requires that the demonstration of conformity with the General Safety and Performance Requirements (Annex I of the MDR) must also include a clinical evaluation. Clinical evaluation is performed to ensure both the safety and performance of the medical device. It is an ongoing process that continues throughout the life cycle of the device. The clinical evaluation plan and the resulting clinical evaluation report form a crucial part of the Technical Documentation of a medical device.

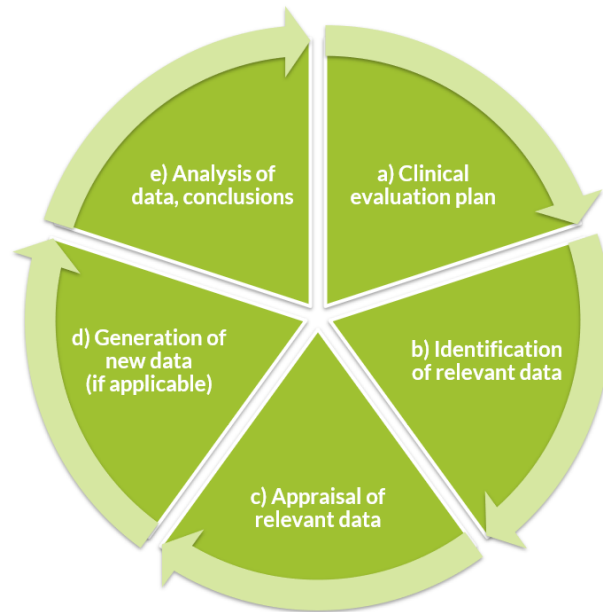
It is important to note that clinical evaluation is mandatory for all devices, regardless of their risk class. The level of clinical evidence that is necessary and the depth of the clinical evaluation shall be proportionate to the risk class of the device, as well as its characteristics and intended purpose. It might be necessary to perform a clinical investigation as part of the clinical evaluation if gaps are identified in the gathered and analysed data or if more clinical data is needed. However, clinical investigation is only one source of clinical data and one part of clinical evaluation. The evaluation itself is key in demonstrating conformity and determining the benefit risk ratio.

The steps for conducting and documenting clinical evaluation are defined in the MDR as follows:

- a) Establish and update a clinical evaluation plan.
- b) Identify available clinical data relevant to the device and its intended purpose, and any gaps in clinical evidence through a systematic scientific literature review.
- c) Appraise all relevant clinical data by evaluating their suitability for establishing the safety and performance of the device.
- d) Generate, through properly designed clinical investigations in accordance with the clinical development plan, any new or additional clinical data necessary to address outstanding issues (if applicable).

- e) Analyse all relevant clinical data in order to reach conclusions about the safety and clinical performance of the device, including its clinical benefits.

Figure 8 Steps for conducting and documenting clinical evaluation according to MDR



Clinical evaluation must follow a defined and methodologically sound procedure. The clinical evaluation shall be thorough and objective and take into account both favourable and unfavourable data. It is based on the following:

- A critical evaluation of the relevant scientific literature currently available, relating to the safety, performance, design characteristics, and intended purpose of the device (on the device itself or, in rare cases, an equivalent device).
- A critical evaluation of the results of all available clinical investigations.
- A consideration of currently available alternative treatment options for that purpose (the clinical state of the art practice).
- Historical data related to the device or similar devices (e.g. post-market surveillance data and data found in adverse event databases).

In some cases, clinical data used in the clinical evaluation may be the data of an equivalent device. In such a case, equivalence must be clearly demonstrated, and the technical, biological and clinical characteristics of the two devices shall be similar to the extent that there would be no clinically significant difference in the safety and clinical performance of the device. However, the MDR takes a far stricter approach on equivalence than the former MDD and requires manufacturers to demonstrate that they have sufficient levels of access to that data relating to devices with which they are claiming equivalence to. This, in most cases, makes equivalency an impossible method to support the clinical claims, unless both devices are placed on the market by the same manufacturer. However, information on equivalent or similar devices remains a relevant source of information in the clinical evaluation process, not to mention the importance of competitor screening for business purposes.

There is also a notable difference in the level of requirements for clinical evaluation between the MDD and the MDR. However, guidance document MEDDEV 2.7/1 revision 4 that was released concerning clinical evaluations under the MDD and AIMDD in 2016 has significantly bridged this difference. Practically all Notified Bodies require clinical evaluations to be conducted according to the level of requirements presented in MEDDEV 2.7/1 rev 4 and it remains the state of the art guidance document

for clinical evaluation until a new guidance document is published by the MDCG. The requirements in the MDR for clinical evaluation need to be studied carefully to consider all relevant requirements related to clinical evaluation.

Important definitions from MDR regarding clinical evaluation:

- *'Clinical evaluation' means a systematic and planned process to continuously generate, collect, analyse and assess the clinical data pertaining to a device in order to verify the safety and performance, including clinical benefits, of the device when used as intended by the manufacturer*
- *'Clinical evidence' means clinical data and clinical evaluation results pertaining to a device of a sufficient amount and quality to allow a qualified assessment of whether the device is safe and achieves the intended clinical benefit(s), when used as intended by the manufacturer*
- *'Clinical performance' means the ability of a device, resulting from any direct or indirect medical effects which stem from its technical or functional characteristics, including diagnostic characteristics, to achieve its intended purpose as claimed by the manufacturer, thereby leading to a clinical benefit for patients, when used as intended by the manufacturer*
- *'Clinical benefit' means the positive impact of a device on the health of an individual, expressed in terms of a meaningful, measurable, patient-relevant clinical outcome(s), including outcome(s) related to diagnosis, or a positive impact on patient management or public health;*

The [MDCG guidance documents](#) that are published, prior to this book being published, concerning clinical evaluation include:

- *MDCG 2020-13 Clinical evaluation assessment report template* – While this template has been created for Notified Bodies to document conclusions of their assessment of the clinical evidence and clinical evaluation report presented by the manufacturer, it may prove useful also for manufacturers when utilised as a checklist for the clinical evaluation report.
- *MDCG 2020-6 Guidance on sufficient clinical evidence for legacy devices* – The purpose of this document is to help manufacturers of medical devices previously CE marked under the medical device directives to determine the level of clinical evidence required under the MDR or IVDR. Appendix III of this guidance document contains a suggested hierarchy of clinical evidence for conformation of conformity with relevant General Safety and Performance Requirements (GSPR, Annex I of the MDR). This may prove useful when considering the sufficient level of clinical evidence for any device, also those other than legacy devices.
- *MDCG 2020-5 Guidance on clinical evaluation – Equivalence* – This guidance covers the demonstration of equivalence for the purposes of using the clinical data of a device that is already placed on the market to CE marking.
- *MDCG 2020-1 Guidance on Clinical Evaluation (MDR) / Performance evaluation (IVDR) of medical device software* – This guidance provides the framework for conducting clinical evaluation and determining the appropriate level of clinical evidence required for medical device software (MDSW).

As a reminder, a general MDCG guidance document for conducting a clinical evaluation and preparing a clinical evaluation report has not yet been released by the MDCG. Therefore, *MEDDEV 2.7/1 revision 4 - Clinical evaluation: A Guide for Manufacturers and Notified Bodies under Directives 93/42/EEC (MDD) and 90/385/EEC (AIMDD)* remains the state of the art guidance document for this purpose.

## 6.2.6. Clinical Investigation (MDR)

If the data gathered during the clinical evaluation of a device suggests that more clinical data is needed, it might be necessary to perform a clinical investigation. The conduct of clinical investigations has been regulated in great detail, as they involve human subjects. The decision of whether to conduct a clinical investigation must not be taken lightly and must be based on a clear need for additional clinical data identified during clinical evaluation. Unnecessary clinical investigations should be avoided for obvious ethical reasons.

The general requirements for clinical investigations have not been changed greatly from the former MDD and AIMDD to the new MDR. Clinical investigations might need to be conducted somewhat more often because of the changes to requirements concerning clinical evaluation. Additionally, the application and reporting processes will change with the implementation of EUDAMED.

Clinical investigations might be carried out for one or more of the following purposes:

- To establish and verify that, under normal conditions of use, a device is designed, manufactured and packaged in such a way that it is suitable for one or more of the specific purposes listed in the medical device definition, and achieves the performance intended as specified by its manufacturer.
- To establish and verify the clinical benefits of a device as specified by its manufacturer.
- To establish and verify the clinical safety of the device and to determine any undesirable side-effects under normal conditions of use of the device, and assess whether they constitute acceptable risks when weighed against the benefits to be achieved by the device.

If the device in question is a new implantable device or class III device, a clinical investigation must generally always be performed. An exception to the rule might be the very specific case where the device is a modification of a device already marketed by the same manufacturer. Even then the manufacturer must demonstrate the modified device to be equivalent to the marketed device, and that its original clinical evaluation is sufficient.

A clinical investigation must always be designed, authorised, conducted, recorded, and reported in accordance with the MDR. Clinical investigations shall be designed and conducted in such a way that the rights, safety, dignity, and well-being of the subjects participating in a clinical investigation are protected and prevail over all other interests, and the clinical data generated are scientifically valid, reliable, and robust. The informed consent of the subjects (or their legally designated representative) must always be obtained and recorded in order to proceed with the investigation.

Clinical investigations are subject to a scientific and ethical review. The ethical review shall be performed by an ethics committee in accordance with national law.

If a clinical investigation is conducted regarding an already CE marked device, the exact requirements for the investigation depends on whether the assessment is done:

- a) within the scope of its intended purpose ('PMCF investigation') or
- b) outside the scope of its intended purpose.

*Article 74 Clinical investigations regarding devices bearing the CE marking* defines the requirements for both these cases.

## **Application for Clinical Investigations**

An application must be submitted to the EU member state or states in which the clinical investigation is planned to be conducted. The documentation for the application has been described in detail in MDR Annex XV Chapter II. The application includes the following items:

- Application form
- Investigator's Brochure (IB)
- Clinical Investigation Plan (CIP), including its annexes
- Patient information sheet, documents for obtaining informed consent and description of arrangements to comply with applicable rules on the protection and confidentiality of personal data
- A signed statement that the investigational device conforms to the General Safety and Performance Requirements (GSPR, Annex I of the MDR), apart from those aspects covered by the clinical investigation and full details of available Technical Documentation for the device



- Statement from the ethics committee or committees concerned
- Proof of insurance coverage

The application shall be submitted via EUDAMED (which at the time of publishing this book is in the making by the EC). The authorities of the EU Member State concerned notifies the applicant within 10 days of them receiving the application, whether the clinical investigation falls within the scope of MDR, and whether the application is complete in accordance with the content requirements. The date of receiving an affirmative answer is referred to as the 'validation date'. If no answer is received, validation date can be considered to be the 10<sup>th</sup> day after sending the application. Unless otherwise specified in national law, the clinical investigation of class I and non-invasive class IIa and IIb devices may be started immediately after the validation date, assuming that no negative opinions have been issued by an ethics committee. In case of all other devices, the applicant must wait for a separate authorisation, which should be granted within 45 days of the validation date (or 65 days in specific cases where additional experts need to be consulted).

If further information is required to complete the application, these timelines change. Further information can be found in MDR *Article 70 Application for clinical investigation*.

## Conduct of a Clinical Investigation

The state of the art standard for designing, conducting, recording, and reporting clinical investigations of medical devices is the *ISO 14155:2020 - Clinical investigation of medical devices for human subjects – Good clinical practice*. The standard specifies general requirements intended to

- Protect the rights, safety, and well-being of human subjects
- Ensure the scientific conduct of the clinical investigation and the credibility of the clinical investigation results
- Define the responsibilities of the sponsor and principal investigator
- Assist sponsors, investigators, ethics committees, regulatory authorities, and other bodies involved in the conformity assessment of medical devices

The standard also contains templates for documents such as clinical investigation plan (CIP), investigator's brochure (IB) and clinical investigation report.

A clinical investigation must always be conducted in accordance with the approved clinical investigation plan. The conduct of a clinical investigation must be adequately monitored to ensure that the rights, safety, and well-being of subjects is protected, that the reported data is reliable and robust, and that the conduct of the clinical investigation is in compliance with MDR. The extent and nature of the monitoring is considered case by case, taking into consideration all characteristics of the clinical investigation, including the objective and methodology of the clinical investigation and the degree of deviation of the intervention from normal clinical practice.

Care must be taken in recording, processing, handling, and storing the clinical investigation information. It must be done in a manner that the information can be accurately reported, interpreted, and verified. At the same time, the confidentiality of records and the personal data of the subjects must remain protected in accordance with the applicable law on personal data protection.

## Incidents during Clinical Investigations

Incidents that have taken place during a clinical investigation must be analysed and reported. The report shall be submitted to all EU countries in which the clinical investigation is being conducted and contain the following:

- Any serious adverse event that has a causal relationship with the investigational device, the comparator device or the investigation procedure, or where such causal relationship is reasonably possible.

- Any device deficiency that might have led to a serious adverse event if appropriate action had not been taken, intervention had not occurred, or circumstances had been less fortunate.
- Any new findings in relation to the events listed above.

This information shall be submitted via EUDAMED (once it becomes available). The deadline for reporting depends on the severity of the event. Further information and guidance can be found in *MDCG 2020-10/1 Safety reporting in clinical investigations of medical devices under the Regulation (EU) 2017/745*.

All serious adverse events and device deficiencies must be assessed to determine whether to modify, suspend or terminate the clinical investigation. The EU Member States concerned assess any serious adverse events based on the received reports and decide on needed actions, including whether to revoke the authorisation for that clinical investigation completely.

### Procedures for the End of the Clinical Investigation

A notification must be made to the EU country concerned when ending the clinical investigation. That notification shall be made within 15 days of the end of the clinical investigation (usually calculated from the last visit of the last subject). The clinical investigation report and a summary of the clinical investigation shall be submitted to the EU country concerned within one year of the end of the clinical investigation.

If the clinical investigation is halted or terminated early, a notification must be submitted as well. Timelines for this notification vary depending on the reason for the early termination. More information can be found in the *MDR Article 77 Information from the sponsor at the end of a clinical investigation or in the event of a temporary halt or early termination*.

### 6.2.7. Performance Evaluation (IVDR)

The IVDR requires that the demonstration of conformity with the General Safety and Performance Requirements must also include a performance evaluation. It is conducted to ensure that the intended clinical benefits will be achieved, and that the device is safe to use. Performance evaluation of a device is a continuous process by which data are assessed and analysed to demonstrate the scientific validity, analytical performance and clinical performance of an IVD device for its intended purpose. Its conduct is documented in the form of a performance evaluation plan, and its results in the form of a performance evaluation report. Both of these become a part of the technical documentation.

The performance evaluation shall be thorough and objective, considering both favourable and unfavourable data. Its depth and extent shall be proportionate and appropriate to the characteristics of the device including the risks, risk class, performance and its intended purpose. All relevant data needs to be identified through a systematic scientific literature review, and needs to be appraised for suitability to the device in question. Gaps in the data need to be identified, and new data generated if necessary to address these gaps.

The three main areas of a performance evaluation are:

#### 1. Scientific validity

Scientific validity means the association of an analyte or marker with a clinical condition or a physiological state. This can be demonstrated through a literature search if enough information with adequate quality can be found to establish the validity. Additionally, consensus expert opinions, results from proof of concept, and clinical performance studies may be utilized as sources of data.

The scientific validity of the analyte or marker is documented in the scientific validity report.

#### 2. Analytical performance

Analytical performance means the ability of a device to correctly detect or measure a particular analyte. The analytical performance of the device shall be demonstrated in relation to the following parameters (unless any of them can be justified as not applicable): analytical sensitivity, analytical specificity, trueness (bias), precision (repeatability and reproducibility), accuracy (resulting from trueness and precision), limits of detection and quantitation, measuring range, linearity, cut-off (including determination of appropriate criteria for specimen collection, and handling and control of known relevant endogenous and exogenous interference), and cross-reactions.

Generally, the analytical performance is always demonstrated on the basis of analytical performance studies. Analytical performance shall be demonstrated and documented in the analytical performance report.

### 3. Clinical performance

Clinical performance means the ability of a device to yield results that are correlated with a particular clinical condition or a physiological or pathological process or state in accordance with the target population and intended user. The clinical performance of the device shall be demonstrated in relation to the following parameters (unless any of them can be justified as not applicable): diagnostic sensitivity, diagnostic specificity, positive predictive value, negative predictive value, likelihood ratio, expected values in normal and affected populations.

Demonstration of clinical performance must be based on clinical performance studies, scientific peer-reviewed literature and/or published experience gained by routine diagnostic testing. Clinical performance studies shall always be performed unless it is justified why a demonstration based on other sources of clinical data is sufficient. The clinical performance shall be demonstrated and documented in the clinical performance report.

The performance evaluation report shall be updated throughout the life cycle of the device, whenever necessary. The performance evaluation report for class C and D devices needs to be updated at least annually.

Important definitions from IVDR regarding performance evaluation:

- *'performance evaluation'* means an assessment and analysis of data to establish or verify the scientific validity, the analytical and, where applicable, the clinical performance of a device
- *'clinical evidence'* means clinical data and performance evaluation results, pertaining to a device of a sufficient amount and quality to allow a qualified assessment of whether the device is safe and achieves the intended clinical benefit(s), when used as intended by the manufacturer
- *'clinical benefit'* means the positive impact of a device related to its function, such as that of screening, monitoring, diagnosis or aid to diagnosis of patients, or a positive impact on patient management or public health
- *'scientific validity of an analyte'* means the association of an analyte with a clinical condition or a physiological state
- *'performance of a device'* means the ability of a device to achieve its intended purpose as claimed by the manufacturer. It consists of the analytical and, where applicable, the clinical performance supporting that intended purpose
- *'analytical performance'* means the ability of a device to correctly detect or measure a particular analyte
- *'clinical performance'* means the ability of a device to yield results that are correlated with a particular clinical condition or a physiological or pathological process or state in accordance with the target population and intended user
- *'performance study'* means a study undertaken to establish or confirm the analytical or clinical performance of a device

The currently published [MDCG guidance documents](#) related to performance evaluation include:

- *MDCG 2020-6 Guidance on sufficient clinical evidence for legacy devices* – The purpose of this document is to help manufacturers of medical devices previously CE marked under MDD or IVD to determine the level of clinical evidence needed under MDR or IVDR.
- *MDCG 2020-1 Guidance on Clinical Evaluation (MDR) / Performance evaluation (IVDR) of medical device software* – This guidance provides framework for conducting clinical evaluation and determining the appropriate level of clinical evidence required for medical device software (MDSW).

Standard EN 13612:2002 *Performance evaluation of in vitro diagnostic medical devices* defines performance evaluation requirements on high level and more specific requirements for performance studies. However, it should be kept in mind that this standard has not been updated recently and might not be completely in line with IVDR requirements.

### 6.2.8. Performance Study (IVDR)

The purpose of clinical performance studies is to establish or confirm aspects of device performance which cannot be determined by analytical performance studies, literature and/or previous experience gained by routine diagnostic testing. This information is used to demonstrate compliance with the relevant general safety and performance requirements with respect to clinical performance. When clinical performance studies are conducted, the data obtained shall be used in the performance evaluation process and be part of the clinical evidence for the device.

Performance studies must be conducted only using devices that comply with the General Safety and Performance requirements set out in Annex I of IVDR, apart from the aspects that the performance study is attempting to cover. In case of devices which are not yet CE market, the label of the device must contain a clear indication that the device is 'device for performance study'.

Performance studies shall be designed and conducted in such a way that the rights, safety, dignity and well-being of the subjects participating in such performance studies are protected and prevail over all other interests and the data generated are scientifically valid, reliable and robust. Clinical performance studies shall also be designed in such a way as to maximize the relevance of the data while minimising potential bias.

Performance studies are subject to scientific and ethical review. The ethical review shall be performed by an ethics committee in accordance with national law. It is also worth noting that applicable laws on data protection must be applied when conducting performance studies, including performance studies that use left-over samples.

The depth of requirements for a performance study depend on its level of impact to its subjects. All performance studies must be designed, conducted and recorded according to general requirements set out in Article 57 and Annex XIII of IVDR. However, there are stricter requirements for performance studies:

- a) where surgically invasive samples are taken only for the purpose of the performance study
- b) that are interventional clinical performance studies (where the test results may influence patient management decisions and/or may be used to guide treatment) or
- c) where the conduct of the study involves additional invasive procedures or other risks for the subjects of the studies

These stricter requirements are presented in Articles 59 to 77 and Annex XIV of IVDR. Performances studies involving companion diagnostics are subject to the same stricter requirements as well (unless they are using left-over samples only).

*'companion diagnostic' means a device which is essential for the safe and effective use of a corresponding medicinal product to:*

- a) *identify, before and/or during treatment, patients who are most likely to benefit from the corresponding medicinal product or*
- b) *identify, before and/or during treatment, patients likely to be at increased risk of serious adverse reactions as a result of treatment with the corresponding medicinal product*

### Application for Performances Studies

An application must be submitted to the EU Member State(s) in which the performance study is going to be conducted. The documentation for the application has been described in detail in IVDR Annex XIII (Sections 2 and 3) and Annex XIV. The application includes the following item:

- Application form
- Investigator's Brochure (IB)
- Performance Study Plan (CPSP) including its annexes
- Patient information sheet, documents for obtaining informed consent and description of arrangements to comply with applicable rules on the protection and confidentiality of personal data
- A signed statement that the investigational device conforms to the General Safety and Performance Requirements (GSPR, Annex I of the IVDR) apart from the aspects covered by the performance study and full details of available Technical Documentation for the device
- Statement from the ethics committee or committees concerned
- Proof of insurance coverage

The application shall be submitted via EUDAMED (which at the time of publishing this book is in the making by the EC). The authorities of the EU Member State concerned notifies the applicant within 10 days of it receiving the application, whether the performance study falls within the scope of IVDR and whether the application is complete in accordance with the content requirements.

Unless otherwise specified in the national law:

- the performance study where surgically invasive samples are taken only for the purpose of the performance study (point a of performance studies falling under stricter requirements) may be started immediately after the validation day, assuming that no negative opinions have been issued by an ethics committee and assuming that the specimen collection does not represent a major clinical risk to the subject of the study
- all other performance studies (falling under stricter requirements) may be started only when the applicant has received a separate authorisation, which should be granted within 45 days of the validation date (or 65 days in specific cases where additional experts need to be consulted).

If further information is needed to complete the application, these timelines change. Further information can be found from IVDR Article 66 - *Application for performance studies*.

### Conduct of a Performance Study

ISO 20916:2019 In vitro diagnostic medical devices – Clinical performance studies using specimens from human subjects – Good study practice is a new standard that defines good study practice for the planning, design, conduct, recording and reporting of clinical performance studies carried out to assess the clinical performance and safety of in vitro diagnostic (IVD) medical devices for regulatory purposes.

Also standard *EN 13612:2002 Performance evaluation of in vitro diagnostic medical devices* should be taken into account for performance studies, as it describes how the manufacturer can fulfil his obligation to conduct a scientifically sound performance study, if a performance study is necessary and appropriate to support performance claims of the IVD device. However, it should be kept in mind that this standard has not been updated recently and might not be completely in line with the IVDR requirements.

The performance study must always be conducted in accordance with the approved performance study plan. The conduct of a performance study must be adequately monitored to ensure that the rights, safety and well-being of subjects is protected, that the reported data is reliable and robust, and that the conduct of the performance study is in compliance with IVDR. The extent and nature of the monitoring is considered case by case taking into consideration all characteristics of the study, including the objective and methodology of the performance study and the degree of deviation of the intervention from normal clinical practice.

Care must be taken in recording, processing, handling and storing the performance study information. It must be done in a manner that the information can be accurately reported, interpreted, and verified. At the same time, the confidentiality of records and the personal data of the subjects must remain protected in accordance with the applicable law on personal data protection.

### Adverse Events During Performance Studies

Incidents that have taken place during a performance study must be reported. The report shall be submitted to all EU countries in which the performance study is being conducted and contain the following:

- Any serious adverse event that has a causal relationship with the device, the comparator or the study procedure or where such causal relationship is reasonably possible
- Any device deficiency that might have led to a serious adverse event if appropriate action had not been taken, intervention had not occurred, or circumstances had been less fortunate
- Any new findings in relation to the events listed above

This information shall be submitted via EUDAMED (once it becomes available). The deadline for reporting depends on the severity of the event.

All serious adverse events and device deficiencies must be assessed to determine whether to modify, suspend or terminate the performance study. EU Member States concerned assess any serious adverse events based on the received reports and decide on needed actions, including whether to revoke the authorisation for that performance study completely.

### Procedures for the End of the Performance Study

A notification must be made to the EU Member States concerned about ending the performance study. That notification shall be made within 15 days of the end of the performance study (usually calculated from the last visit of the last subject). The performance study report and a summary of the performance study shall be submitted to the EU country concerned within one year of the end of the performance study.

If the performance study is halted or terminated early, a notification must be submitted as well. Timelines for this notification vary depending on the reason of the early termination. More information can be found from the *IVDR Article 73 Information from the sponsor at the end of a performance study or in the event of a temporary halt or early termination*.

### 6.2.9. Labelling and Instructions for Use (IFU)

The MDR and IVDR require that each device shall be accompanied by the information needed to identify the device and its manufacturer, and by any safety and performance information relevant to the user. Such information may appear on the device itself, on the device labels or packaging or in the instructions for use (IFU). The General Safety and Performance Requirements (GSPR, Annex I of the MDR and IVDR) contains a list of information to be included both in the IFU and labels.

Instructions for use (or 'user manual') means the information provided to the user on the intended purpose of the device, target groups and intended users, proper use, expected performance and of any precautions to be taken. Residual risks based on the risk analysis, that are required to be communicated to user, must be included in IFU or labels as limitations, contraindications, precautions or warnings.

The IFU should be provided with each device. Exceptions are the IVD devices and Class I and IIa medical devices that can be justified to be used safely and as intended by the manufacturer without instructions. When the device is intended for professional use only, the IFU may be provided to the user in non-paper format (e.g., electronic), except when the use of

electronic IFU reduces the level of safety when compared to a paper IFU or the device is intended for near-patient testing (IVD). For medical devices, the aspects related to the use of electronic IFU are defined in [Regulation \(EU\) No 207/2012](#).

Label means the printed or graphic information on the device or packaging containing the name or trade name of the device, details to identify the device and contents of packaging, name and address of the manufacturer and where applicable other special information related to the device. The label must also include a Unique Device Identifier (UDI). UDI is a series of numeric or alphanumeric characters that is created through internationally accepted device identification and coding standards and that allows unambiguous identification of specific devices on the market. Contents of the UDI are described later in [Chapter 6.2.10](#).

The IFU and the labels must be provided in official national languages of those EU member states where the device is envisaged to be sold. Within their national legislation, the EU Member States may define a list of alternative languages that are also accepted. However, information on safe use of the device (e.g. precautions, warnings) must always appear in national languages.

The labelling and the IFU are part of the medical device. Their applicability needs to be validated as part of the usability evaluation.

## Implant Card

The manufacturer of an implantable device (other than sutures, staples, dental fillings, dental braces, tooth crowns, screws, wedges, plates, wires, pins, clips and connectors) must provide an implant card together with the device. Implant card has the size of a credit card or an ID card and contains information of the patient's identity and the implanted device. The implant card is provided for following purposes:

1. Enabling the patient to identify the implanted devices and to get access to other information related to the implanted device (e.g. via EUDAMED, and other websites).
2. Enabling patients to identify themselves as persons, who require special attention or care in relevant situations e.g. in airport security checks.
3. Enabling e.g. the emergency clinical staff or first responder to be informed about the special care or needs for the patient in case of emergency situations.

The following information is provided on the implant card (preferably on the card itself or, alternatively, as stickers to be placed by the clinician):

- Device name
- Serial number, lot number
- Unique device identification (UDI)
- Name, address and the website of the manufacturer
- Device type

The implant card should also include the identity of the patient and therefore it should include blank fields which are then filled out by the healthcare professional. The healthcare institution should fill out the following information:

- Name of the patient or patient ID
- Name and address of the health institution or healthcare provider who performed the implantation
- Date of implantation.

It is the responsibility of the health institutions to fill the patient information and implantation details to the implant card and provide it to the patient.

The following information must be provided with the device and maintained in the webpages mentioned in the implant card:

- Information allowing the identification of the device
- Warnings, precautions or measures to be taken by the patient or a healthcare professional with regard to reciprocal interference with reasonably foreseeable external influences, medical examinations or environmental conditions
- Any information about the expected lifetime of the device and any necessary follow-up
- Any other information to ensure safe use of the device by the patient

The information must be described in a way that is readily understood by a lay person and is updated when appropriate. The patient or other interested parties can access this information via the webpages provided in the implant card.

## 6.2.10. Unique Device Identifier (UDI)

The purpose of the Unique Device Identifier (UDI) is to allow unambiguous identification of a device. The UDI system facilitates easier traceability of medical devices, significantly enhances the effectiveness of the post-market safety-related activities for devices and allows for better monitoring by competent authorities. It will also help to reduce medical errors and to fight against falsified devices. The use of the UDI system finally should also improve purchasing and waste disposal policies and stock-management by health institutions and other economic operators. The UDI will be applied to all medical devices except custom-made and investigational devices.

Elements of the UDI system are:

- Basic UDI-DI
- UDI-DI - Device Identifier
- UDI-PI - Production Identifier
- UDI carrier

Each of these elements are described in more detail below.

### Basic UDI-DI

The basic UDI-DI is an identifier that identifies a device group with same intended purpose, risk class, essential design and manufacturing characteristics. The basic UDI-DI is the main access key for all device info in the European Database on Medical Devices (EUDAMED). However, it is separate from device packaging and labelling and it does not appear on the device itself.

The Basic UDI-DI is referenced in relevant documentation by the manufacturer, e.g. the Declaration of Conformity (DoC), certificates and Technical Documentation.

Basic UDI-DI is applied for from one of the following designated entities:

- GS1
- HIBCC (Health Industry Business Communications Council)
- ICCBBA
- IFA GmbH (Informationsstelle für Arzneispezialitäten)

### UDI-DI Device Identifier and UDI-PI Production Identifier

UDI-DI (Device Identifier) and UDI-PI (Production Identifier) are visible on the device or its package. UDI-DI is the static part of the UDI. It is applied for from one of the designated entities together with the Basic UDI-DI. Each component that is



considered to be a device and is commercially available on its own shall be assigned a separate UDI unless the components are part of a configurable device that is marked with its own UDI.

A new UDI-DI is required whenever there is a change in the device that could lead to misidentification of the device and/or ambiguity in its traceability. Those are, for example, changes in the following:

- Name or trade name of the device
- Device version or model
- Labelled as single-use
- Packaged sterile
- Need for sterilisation before use
- Quantity in a package
- Critical warnings or contra-indications
- Carcinogenic, mutagenic, reprotoxic (CMR) / Endocrine disruptors

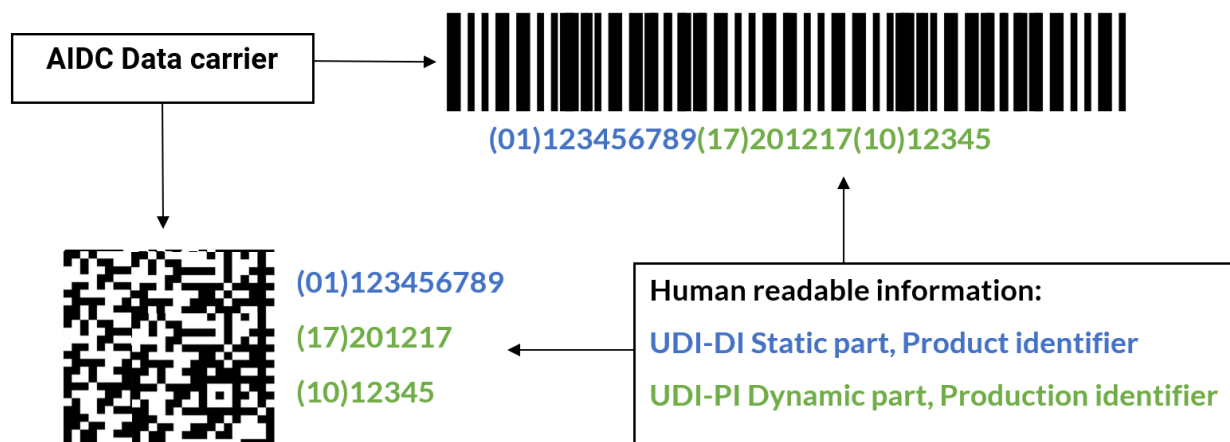
UDI-PI is the dynamic part of the UDI and identifies the manufactured device unit. UDI-PI is defined by the manufacturer. If a lot number, serial number, software identification or expiry date appears on the label, it must be part of the UDI-PI. Similarly, if there is only a manufacturing date on the label, this shall be used as the UDI-PI.

### UDI carrier

UDI carrier means representation of the UDI that appears in a plain-text version/human readable information (HRI) and in a format that uses AIDC technology (Automated Identification for Data Capture). AIDC means any technology that conveys the unique device identifier or the device identifier of a device in a format that can be entered into an electronic patient record or another computer system via an automated process. The HRI consists of legible characters that can easily be read by people.

The UDI carrier is placed on the label or on the device itself and on all higher levels of device packaging. Higher levels do not include shipping containers.

Figure 9 Examples of UDI carriers



The Figure 9 presents examples of UDI carriers using the system of GS1, one of the designated issuing entities. In their system, the numbers in the parentheses indicate the different parts of the UDI:

- (01) Device identifier, UDI-DI
- (17) Expiration date
- (10) Lot number

### UDI in software

The previously presented Basic UDI-DI, UDI-DI and UDI-PI requirements apply also for software which constitutes a medical device in itself. If the software is delivered on a physical medium, for example via a CD or DVD, each packaging level shall bear the human readable and AIDC representation of the complete UDI. On display, only Human Readable Interpretation (HRI) is required.

The UDI is provided on a readily accessible screen for the user in an easily-readable plain-text format such as an 'about' file, or is included on the start-up screen. Software lacking a user interface such as middleware for image conversion, shall be capable of transmitting the UDI through an application programming interface (API).

A new UDI-DI is required for a software whenever there is a modification that changes:

- The original performance
- The safety or the intended purpose of the software
- Interpretation of data

Minor software revisions are generally associated with bug fixes, usability enhancements that are not for safety purposes, security patches or operating efficiency. Minor revisions require a new UDI-PI and not a new UDI-DI.

### International approach to UDI

A UDI system is planned or already implemented in the USA and other countries internationally. The different UDI systems usually have a similar approach and are based on the same issuing entities. Still, it is important to remember that each market area has their own regulation on the use of the UDI. UDI systems from other market areas are not automatically applicable to another area. Information from UDI system in the USA can be found in the [US FDA Global Unique Device Identification Database \(GUDID\)](#).

## 6.3. DEMONSTRATING CONFORMITY OF THE QUALITY MANAGEMENT SYSTEM

### 6.3.1. Quality Management System Provides the Foundation for Your Business

According to the MDR and IVDR, a Quality Management System (QMS, described in more detail in Chapter 8) is mandatory for all manufacturers of medical devices, regardless of product classification. Setting up a QMS is a new requirement for Class I devices (that are not one of the specific types of Class I devices defined in Chapter 2.14), but an old one for all the rest. Fortunately, there is also a very valid reason to voluntarily develop an appropriate QMS from a business points of view: The success of a company depends, to a large extent, on the efficient and professional management of the company. A modern QMS provides an effective means to managing the business and creates a framework for the company's efficient and, thus, commercially successful operations. Only a well-run company creates growth.

A QMS, as required by the MDR and IVDR, should cover all parts and elements of a manufacturer's organisation dealing with the quality of processes, procedures, and end products, the medical devices. It shall govern the management, structure,

responsibilities, procedures, processes, and resources required to implement the principles and actions necessary to achieve compliance with the regulation.

The QMS shall address at least the following aspects:

- A strategy for regulatory compliance
- Identification of applicable General Safety and Performance Requirements (GSPR, Annex I of the MDR and IVDR) and exploration of options to address those requirements
- Responsibility of the management
- Resource management, including selection and control of suppliers and sub-contractors
- Risk management as set out in Section 3 of Annex I of the MDR and IVDR
- Clinical Evaluation (according to the MDR) including Post-Market Clinical Follow-up (PMCF), or Performance Evaluation (according to IVDR) including Post-Market Performance Follow-up (PMPF)
- Product realisation, including planning, design, development, production, and service provision
- Unique Device Identification (UDI) system
- Setting-up, implementation, and maintenance of a Post-Market Surveillance system
- Handling communication with Competent Authorities, Notified Bodies, economic operators (importers, distributors, Authorised Representatives), customers, and/or other stakeholders
- Processes for reporting of serious incidents and field safety corrective actions in the context of vigilance
- Management of Corrective and Preventive Actions (CAPA) and verification of their effectiveness
- Processes for monitoring and measurement of output, data analysis and product improvement.

Even though most of these elements are also present in the *ISO 13485 Quality Management System standard for medical devices*, the standard is not mandatory to be implemented. However, the most sensible thing is to create a QMS specifically on the basis of this well-established standard and not to reinvent the wheel (as is the case with most standards). Notified Bodies and other interested parties will immediately identify a valid QMS if it meets the requirements of the standard – otherwise it can be overwhelmingly difficult to prove that all regulatory requirements regarding a QMS have been met. However, it must be kept in mind that not all the quality management system requirements of the MDR and the IVDR are met by following the ISO 13485 standard alone.

### 6.3.2. Quality Management System is Mandatory

A Quality Management System (QMS) is mandatory for all product categories (article 10 of the MDR and the IVDR) but certification of the QMS is always not mandatory. For MDR Class I and IVDR Class A devices, an assessment of the QMS by a Notified Body is not required. However, if those devices are

- placed on the market in sterile condition (Class I (s))
- have a measuring function (Class I (m)), or
- are reusable surgical instruments (Class I (r)),

an assessment by a Notified Body is required. In these cases, the involvement of the Notified Body is limited to the following aspects:

- In the case of devices placed on the market in sterile condition, to those aspects relating to establishing, securing, and maintaining sterile conditions.
- In the case of devices with a measuring function, to those aspects relating to the conformity of the devices with the metrological requirements.
- In the case of reusable surgical instruments, to those aspects relating to the reuse of the device, in particular cleaning, disinfection, sterilisation, maintenance, and functional testing, and the related instructions for use.

Even though an assessment of the QMS by a Notified Body is not required, it might still make sense to receive an objective assessment from a third party. For such a purpose, an ISO 13485 audit by an accredited conformity assessment body (which may be the same organisation as your Notified Body) is the most typical choice, as the subsequent ISO 13485 certification also holds value in the eyes of your clients and other stakeholders. To an extent, non-conformities from your assessment bodies should not be regarded as negative either – they should be considered as opportunities for improvement to develop the compliance and efficacy of your QMS.

For all other product classes, the Notified Body audit is part of the conformity assessment procedure. Following an approved audit, the Notified Body issues an EU quality management certificate for the QMS. The certificate is valid for a specified period, provided that annual surveillance audits have been carried out. The EU certificate is manufacturer-specific and includes the identification of the devices or groups of devices that are subject to the same processes.

### 6.3.3. Involvement of a Notified Body Depends on the Device Classification

#### a. MDR Class I and IVDR Class A

The manufacturer must develop a Quality Management System (QMS) in alignment with article 10, meet all the General Safety and Performance Requirements (Annex I of the MDR and IVDR) relating to the product, draw up the relevant Technical Documentation for the device, and issue a Declaration of Conformity (DoC). It should also be borne in mind that if the product belongs to category MDR I (s) (sterile), I (m) (measuring function), I (r) (reusable surgical instrument) or IVDR A (s) (sterile) these properties require an assessment by a Notified Body.

Further guidance on class I devices is provided in the *MDCG 2019-15 Guidance Notes for Manufacturers of Class I Medical Devices* guidance document.

#### b. MDR, Class IIa

The manufacturer must build a Quality Management System (QMS) in alignment with article 10, meet all the General Safety and Performance Requirements (Annex I of the MDR and IVDR) relating to the product, draw up the relevant Technical Documentation for the device and issue a Declaration of Conformity (DoC). In addition, the assessment by a Notified Body is mandatory. The manufacturer has three different alternative approaches to the assessment of a Notified Body:

1. Full QMS audit as described in MDR Annex IX and according to requirements in the ISO 13485. This, in practice, would be the first line of choice for any medical device manufacturer.
2. Partial audit of the QMS, which applies to the production quality assurance, in accordance with MDR Annex XI Part A. Simplified, the audit can be considered to cover the ISO 13485 standard with the exception of product development (However, it is worth reading the details in Annex XI of the MDR!).
3. Partial audit of the QMS for product verification in accordance with Annex XI of the MDR Part B. Simplified, the audit can be considered to cover the ISO 13485, with the exception of product development and production (However, it is worth reading the details in Annex XI of the MDR!).

Full QMS in alignment with the ISO 13485 is the most widely used and recommended option. Partial implementation is applicable in exceptional cases where for example the manufacturing is fully outsourced.

#### c. MDR, Class IIb and III

The manufacturer must build a Quality Management System (QMS) in alignment with article 10, meet all the General Safety and Performance Requirements (Annex I of the MDR and IVDR) relating to the product, draw up the relevant Technical Documentation for the device, and issue a Declaration of Conformity (DoC). In addition, the assessment by a Notified Body is

mandatory. The manufacturer has two different alternative approaches to the assessment of a Notified Body, one of which has two alternative options:

1. Full QMS audit as described in MDR Annex IX and according to requirements in the ISO 13485. This, in practice, would be the first line of choice for any medical device manufacturer.
2. EU type examination in alignment with MDR Annex X. Inspection by examination and testing of every product or statistical inspection (requires the manufacturer to supply the manufactured products in homogeneous lots). The Notified Body examines or tests the device and examine the related documentation supplied by the manufacturer, and issue an EU type-examination certificate. The certificate is valid for five years and then requires a new assessment. The EU type examination is coupled with:
  - a) Partial audit of the QMS, which applies to the production quality assurance, in accordance with MDR Annex XI Part A. Simplified, the audit can be considered to cover the ISO 13485 standard with the exception of product development (However, it is worth reading the details in Annex XI of the MDR!). Manufacturer describes a QMS that is applied throughout the whole manufacturing process. With these processes, the manufactured products comply with the type described in the EU type-examination certificate.
  - b) Partial audit of the QMS for product verification in accordance with Annex XI of the MDR Part B. Simplified, the audit can be considered to cover the ISO 13485, with the exception of product development and production (However, it is worth reading the details in Annex XI of the MDR!). The Notified Body reviews all manufactured products or their manufacturing and testing documentation to evaluate if the device conforms to the type described in the EU type-examination certificate.

Again, the full QMS is the most recommended option. EU type examination may be applicable for example, for devices that are manufactured rarely and in low quantities, such as large MRI equipment.

#### d. IVD Class B, C and D

The manufacturer must build a Quality Management System (QMS) in alignment with article 10, meet all the General Safety and Performance Requirements (Annex I of the MDR and IVDR) relating to the product, draw up the relevant Technical Documentation for the device, and issue a Declaration of Conformity (DoC). The Notified Body involved consists of the assessment of Technical Documentation for device category, generic device group, or every device and full QMS audit as described in MDR Annex IX and according to requirements in the ISO 13485.

For class D devices, the conformity assessment includes also a verification by an EU reference laboratory (Annex IX, section 4.9).

## 6.4. DECLARATION OF CONFORMITY

A precondition for CE marking is that the manufacturer draws up an EU declaration of conformity (DoC). In this declaration, the manufacturer must state that the requirements of all applicable CE marking regulations and/or directives have been fulfilled in relation to the device in question. By drawing up the EU DoC, the manufacturer assumes exclusive responsibility for the compliance of the device.

Annex IV of the MDR and IVDR outlines the minimum contents of the EU DoC. These are:

- The name, registered trade name or registered trademark and, if already issued, single registration number (SRN) of the manufacturer and, if the manufacturer is located outside the European Economic Area, the name and address of the European authorised representative
- A statement that the EU declaration of conformity is issued under the sole responsibility of the manufacturer

- The Basic UDI-DI (See Chapter 6.2.10 for unique device identification)
- The product and trade name, product code, catalogue number or other unambiguous reference of the device covered by the EU DoC, such as a photograph (where appropriate) as well as the intended purpose of the device. Except for the product or trade name, the other information may be provided by the Basic UDI-DI.
- The risk class of the device
- A statement that the device that is covered by the present DoC is in conformity with the MDR and, if applicable, with any other relevant Union CE marking legislation
- References to any common specifications (CS) used and in relation to which conformity is declared (See Chapter 3.5 for more information on CS)
- If applicable, the name and identification number of the Notified Body (NB), a description of the conformity assessment procedure performed (Annex IX, X or XI of the MDR or IVDR), and identification of the EU certificate or certificates issued by the NB
- If applicable, additional information
- The place and date of issue of the DoC, name and function of the person who signed it, as well as an indication for the signature and on behalf of whom that person signed.

The original signed EU DoC must be kept for at least 10 years from the date the last device was placed on the market. In the case of implantable devices, the DoC must be kept for at least 15 years from the date the last device was placed on the market. A copy of the DoC must be made available to the competent authority upon request.

## 6.5. CE MARKING TO INDICATE COMPLIANCE

### 6.5.1. CE marking and Its Meaning

'CE' comes from the French words 'Conformité Européenne' and is used as a declaration to demonstrate compliance. General principles of the CE marking have been established in Article 30 of *Regulation (EC) No 765/2008*, setting out the requirements for accreditation and market surveillance relating to the marketing of products.

The CE mark shall be affixed before the medical device is placed on the market. By affixing the CE mark, the manufacturer indicates that the healthcare device satisfies the requirements relating to it from the MDR, the IVDR, and/or any other EU directives and legislation relevant to the device in question. It should be borne in mind that the medical device may also be subject to requirements from other legislation than to the MDR or IVDR. It is good to remember that in cases where the involvement of a Notified Body is not required, the company alone determines that the requirements of the CE marking have been met.

If the CE marking has been made incorrectly or if it is missing, the competent authority may prohibit the manufacture, sale, export, or other distribution of the device.

The CE marking means that the device is ready to be placed on the market. The manufacturer must ensure that the meaning of the CE marking is respected in all situations.

Situations where a product shall **not** be CE marked:

- A custom-made device (since such a device is made for a named individual patient and not for the general public, and is therefore not placed on the market).
- A device intended for clinical investigation or performance evaluation. The product is not yet ready to be placed on the market at this stage but is used for the sole purpose of validating its intended use and characteristics for CE marking.

- The device can be presented to customers before it meets all the MDR or IVDR requirements, e.g., at exhibitions. Such a device cannot be CE marked, but instead it must be clearly identified that it cannot be placed on the market or put into service until all the MDR requirements have been met.
- Devices manufactured by health institutions for their own use.

## 6.5.2. Rules for the Use and Visual Representation of the CE Mark

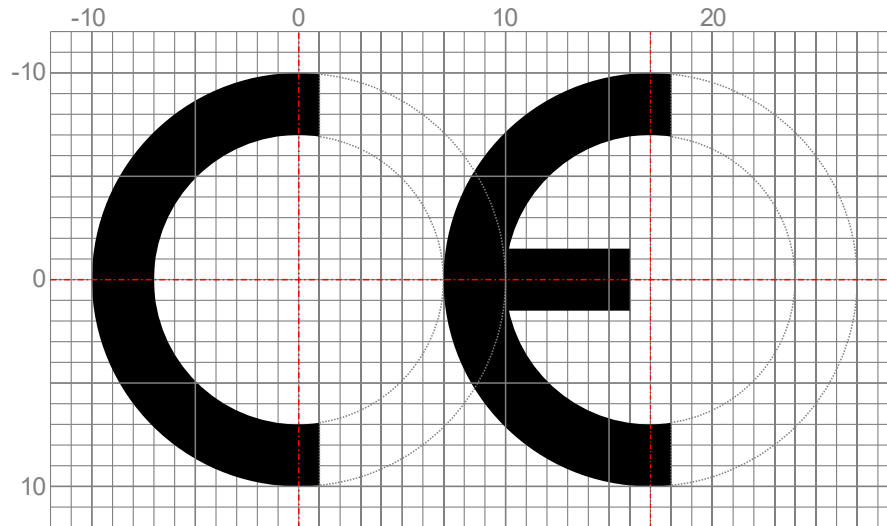
Rules regarding the use and affixing of the CE mark are defined as follows:

- The CE marking shall be affixed visibly, legibly, and indelibly to the device or its sterile packaging.
- If such affixing is not possible or not warranted on account of the nature of the device (e.g., very small device, implantable device or other properties), the CE mark shall be affixed to the packaging.
- The CE mark shall also appear in any instructions for use and on any sales packaging.
- The CE mark must also appear in medical device software (MDSW).
- It is prohibited to affix to a product a marking which is similar to the CE marking and which are therefore likely to be misleading. One must also be careful when affixing other markings or logos to the product. They are allowed, and in some cases required, but they must not impede the visibility and legibility of the CE mark in any way.

Rules regarding the visual representation of the CE mark:

- The CE mark shall consist of the initials 'CE', taking the form presented in Figure 10.
- If the size of the CE mark is reduced or enlarged, the proportions shall be respected.
- The components of the CE mark shall have the same vertical dimension, which may not be less than 5 mm. The minimum dimension may be waived for small-scale devices.
- The CE mark can take different forms (e.g., in terms of colour, solid/hollow) as long as it remains visible, legible, and respects the given proportions.
- If a Notified Body (NB) has been involved in the conformity assessment, the CE mark shall be followed by the four-digit identification number of the NB responsible for the conformity assessment.
- If a Notified Body has not been involved in the conformity assessment, only the CE mark is affixed

Figure 10 CE Marking



### 6.5.3. Presenting the Device to Public Before CE Marking

A medical device can be used without CE marking in clinical investigations, or in the case of IVD device, in performance evaluations. Because the investigation or evaluation is done specifically to demonstrate the conformity of the device for CE marking, the device cannot be CE marked yet at this stage. Please note that these investigations and evaluations are controlled by precise rules, which are presented in Chapters 6.2.6 and 6.2.7.

The device may also be presented at trade fairs, exhibitions and demonstrations, as well as at scientific or technical seminars. In this case, a clear indication must be displayed clearly indicating that the device cannot be placed on the market or put into service until it has been brought into conformity. However, such a device must not be used for its intended purpose. For example, an IVD device cannot be used at the trade fair to examine samples received from participants.

## 6.6. REGISTRATION OF OPERATORS AND DEVICES


Registration is the final step before a device can be placed on the market. The registration is performed through EUDAMED (the European Medical Device Database) and it consists of these two elements:

- Registration of the economic operators (manufacturer, importers and, where relevant, authorised representative).
- Registration of devices into the UDI/Device database using the Basic UDI-DI of the device (See Chapter x for UDI).

The manufacturers, authorised representatives, and importers shall register themselves to EUDAMED. Based on the registration, the competent authority issues a single registration number (SRN) to the registrant. Manufacturers use the SRN when applying to a Notified Body for conformity assessment or for accessing EUDAMED in order to fulfil its obligations.

The manufacturers must issue a Basic UDI-DI to all devices (other than custom made and investigational devices), as well as to systems and procedure packs, where applicable. Basic UDI-DI is the primary identifier of the device model. It is the main key





for records in the UDI database and is referenced in relevant certificates by the Notified Body and the EU Declaration of Conformity by the manufacturer. The device is first registered into the UDI database with the Basic UDI-DI together with other required data elements.

If the device requires a conformity assessment by a Notified Body before it can be placed on the market, the economic operator registration and the UDI database registration must be done before the manufacturer applies to a Notified Body for the assessment. The Notified Body shall include a reference to the Basic UDI-DI on the certificate issued.

Finally, before the device can be placed on the market, the manufacturer needs to enter, or if already provided, verify the information on the device in EUDAMED. If the manufacturer is located outside the EU, the authorised representative and the importer are responsible for ensuring that the registration has been performed properly.

The data entered in EUDAMED needs to be reviewed periodically and kept up to date. Device registration is not applied to custom made or investigational devices.



**7. POST-MARKET SURVEILLANCE  
AND VIGILANCE**

Post-market surveillance (PMS) is a broad concept and includes many different concepts to ensure patient safety after a medical device has been placed on the market. It includes vigilance activities, feedback handling, post-market clinical follow-up (PMCF) for medical devices, and post-market performance follow-up (PMPF) for IVDs. It also takes the form of various different types of reports.

## 7.1. POST-MARKET SURVEILLANCE

Post-market surveillance is a systematic procedure within the QMS to proactively collect and analyse data on the quality, performance and safety of devices throughout their life cycle to take necessary actions. It also ensures that the residual risks remain acceptable. It is carried out by manufacturers in cooperation with other 'economic operators' (importers, distributors, authorised representatives). The post-market surveillance activities must be proportionate to the risk class and appropriate for the type of device.

Data gathered by the manufacturer's post-market surveillance system shall in particular be used

- to update the benefit-risk determination and to improve the risk management,
- to update the design and manufacturing information, the instructions for use and the labelling,
- to update the clinical evaluation (MDR) / performance evaluation (IVDR),
- to update the summary of safety and clinical performance (presented in Chapter 7.2),
- to identify needs for corrective and preventive action (CAPA) or field safety corrective action,
- to identify options to improve the usability, performance, and safety of the device,
- when relevant, to contribute to the post-market surveillance of other devices, and
- to detect and report trends.

The ISO/TR 20416:2020 Medical devices – Post-market surveillance for manufacturers is a technical report (not a standard) that provides guidance on the post-market surveillance process and its implementation. This guidance document was published in July 2020 and provides a highly useful systematic view on post-market surveillance in practice as well as a collection of information on setting up the relevant processes. Again, it must be highlighted, how valuable it can be for a medical device manufacturer to study the experiences poured into a standard or a guidance document. Particularly on topics, such as post-market surveillance, it has been challenging for manufacturers to come up with efficient means to make the best of it. The systematic views presented in the ISO/TR 20416 can be of high value for both the safety and efficacy aspects of a device and the business considerations through the follow-up of market success.

### 7.1.1. Post-Market Surveillance Plan

Post-market surveillance for a specific device shall be based on a post-market surveillance plan. The first version of the plan is to be written already during the product development phase. The plan shall address the collection and utilisation of available information, in particular:

- Information concerning serious incidents, including information from periodic safety update reports (PSURs), and field safety corrective actions.
- Records referring to non-serious incidents and data on any undesirable side-effects.
- Information from trend reporting.
- Relevant specialist or technical literature, databases and/or registers.
- Information, including feedbacks and complaints, provided by users, distributors and importers.
- Publicly available information about similar medical devices.

The post-market surveillance plan shall cover:

- A proactive and systematic process to collect this information.
- Effective and appropriate methods and processes to assess the collected data.
- Suitable indicators and threshold values for continuous reassessment of the benefit-risk analysis and of the risk management.
- Effective and appropriate methods and tools to investigate complaints and analyse market-related experience collected in the field.
- Methods and protocols to manage the incidents subject to the trend report, including the methods and protocols to be used to establish any statistically significant increase in the frequency or severity of incidents as well as the observation period.
- Methods and protocols to communicate effectively with competent authorities, Notified Bodies, economic operators and users.
- Reference to procedures to fulfil the manufacturers obligations according to the MDR.
- Systematic procedures to identify and initiate appropriate measures including corrective actions.
- Effective tools to trace and identify devices for which corrective actions might be necessary.
- A post-market clinical follow-up (PMCF) plan or a justification as to why a PMCF is not applicable (PMCF will be discussed more closely in Chapter 7.3).

### 7.1.2. Post-Market Surveillance Report – Class I / Class A, B

Manufacturers of class I medical devices class A and B in vitro diagnostic devices shall document the results and conclusion done based on the post-market surveillance data in a post-market surveillance report. This should also contain a rationale and description of any corrective and preventive actions (CAPA) taken based on the results. The report shall be updated when necessary and made available to the EU Member State competent authority upon request.

### 7.1.3. Periodic Safety Update Report (PSUR) – Class IIa, IIb, III / Class C, D

Manufacturers of class IIa, class IIb, and class III medical devices and class C and D in vitro diagnostic devices shall prepare a periodic safety update report (PSUR) for each device and, if applicable, for each category or group of devices. The purpose of a PSUR is to summarise the results and conclusions done based on the post-market surveillance data, as well as to provide a rationale and description of any corrective and preventive actions (CAPA) taken. This purpose is identical to the purpose of the post-market surveillance report.

In addition to this, the PSUR shall also contain:

- The conclusions of the benefit-risk determination
- The main findings of the PMCF (MDR) / PMPF (IVDR)
- The volume of sales of the device and an estimate evaluation of the size and other characteristics of the population using the device and, where practicable, the usage frequency of the device

The PSUR shall be updated at least annually for class IIb and class III medical devices and class C and D IVDs, and at least biannually for class IIa devices. Manufacturers of class III and implantable medical devices and class D IVDs shall submit the PSUR to their Notified Body via EUDAMED (which is not yet set up at the publication of this book), where the Notified Body shall add its evaluation with details of any action taken. Such PSURs and evaluations shall be made available to EU Member State competent authorities through EUDAMED. For other devices than class III and implantable medical devices and class D IVDs, the manufacturers shall make PSURs available to their Notified Body, and upon request, to the competent authority.

## 7.1.4. Trend Reporting

Following possible trends is an important and required part of post-market surveillance. This must also be addressed in the post-market surveillance plan.

Even small incidents can have a large impact if they occur frequently, or they can be a sign of a latent bigger issue. Therefore, trend reporting should focus on these incidents and not on serious reportable incidents or expected undesirable side-effects. The purpose of trend reporting is to catch statistically significant increase in the frequency or severity of incidents that could have a significant impact on the benefit-risk analysis and which have led or may lead to unacceptable risks when weighed against the intended benefits. The significant increase shall be compared to the foreseeable frequency or severity of incidents for the type of device in question (or category or group of devices). Any significant increase is reported to EUDAMED (not yet available at the time of publishing this book). The *ISO/TR 20416:2020 Medical devices – Post-market surveillance for manufacturers* provides practical examples of methods that can be utilised for trend reporting.

## 7.2. SUMMARY OF SAFETY AND (CLINICAL) PERFORMANCE – CLASS III AND IMPLANTS / CLASS C

A summary of safety and clinical performance (SSCP) must be prepared for implantable devices and for class III devices (excluding custom-made or investigational devices). For IVDs, a summary of safety and performance (SSP) must be prepared for class C and D devices (excluding devices for performance studies). The SSCP/SSP is intended to provide public access to an updated summary of clinical data and other information about the safety and clinical performance of the medical device. The SSCP/SSP will be an important source of information for intended users – both healthcare professionals and, if relevant, for patients. It is one of the several means intended to fulfil the objectives of the MDR and IVDR to enhance transparency and provide adequate access to information. The draft of the SSCP/SSP shall be submitted to the Notified Body to be validated by them. After validation, the Notified Body shall upload the summary to EUDAMED. The manufacturer shall mention on the label or instructions for use where the summary is available. It is important to note that it should be written in such language that it is clear to the intended users.

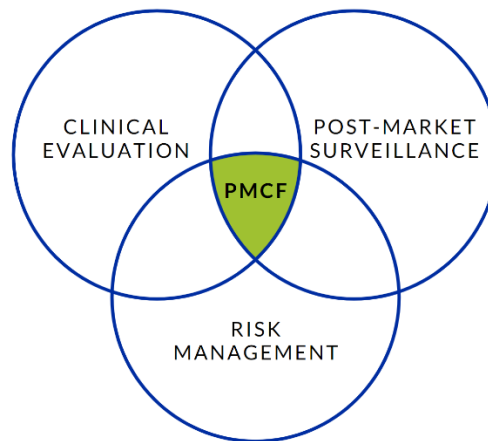
The following guidance documents have been published concerning this summary and they provide guidance on the presentation, content, and validation of the SSCP: *MDCG 2019-9 Summary of safety and clinical performance A guide for manufacturers and notified bodies*.

- The SSCP and SSP have similar content. They shall include:
- Identification of the device and manufacturer, including Basic UDI-DI and SRN (if already issued) (See Chapter 6.2.10 for UDI).
- Intended purpose of the device, including indications, contraindications and target populations.
- Description of the device, including reference of previous generations or variants and their differences, accessories and devices intended to be used in combination with the device.
- Possible diagnostic or therapeutic alternatives (SSCP for medical devices only).
- Reference to any harmonised standards or common specifications (CS) applied (See Chapter 3.5 for CS and Chapter 3.6 for harmonised standards).
- Summary of clinical evaluation (MDR) or performance evaluation (IVDR) and relevant information on the PMCF or the PMPF, respectively.
- The metrological traceability of assigned values (SSP for IVDs only).
- Suggested profile and training for users.
- Information on residual risks and undesirable effects, warnings, and precautions.

### 7.3. POST-MARKET CLINICAL FOLLOW-UP (MDR)

Post-market clinical follow-up (PMCF) is a continuous process that updates the clinical evaluation for medical devices. The PMCF shall be included in the post-market surveillance plan. The purpose of the PMCF is for the manufacturer to proactively collect and evaluate clinical data from the use in or on humans of a device which bears the CE marking and that has been placed on the market or put into service according to its intended purpose. The PMCF is performed to confirm the safety and performance throughout the expected life cycle of the device, to ensure the continued acceptability of identified risks, and to detect emerging risks on the basis of factual evidence.

Figure 11 Role of PMCF in relation to clinical evaluation, post-market surveillance and risk management activities



Two guidance documents have been published by the Commission related to the PMCF which provide the suggested template for both the plan and the report:

- *MDCG 2020-7 Post-market clinical follow-up (PMCF) Plan Template*
- *MDCG 2020-8 Post-market clinical follow-up (PMCF) Evaluation Report Template*

The PMCF plan shall specify the methods and procedures for proactively collecting and evaluating clinical data with the aim of:

- Confirming the safety and performance of the device throughout its expected life cycle
- Identifying previously unknown side-effects and monitoring the identified side-effects and contraindications
- Identifying and analysing emergent risks on the basis of factual evidence
- Ensuring the continued acceptability of the benefit-risk ratio
- Identifying possible systematic misuse or off-label use of the device with a view to verifying that the intended purpose is correct

The PMCF plan shall include at least:

- The general methods and procedures of the PMCF to be applied (such as the gathering of clinical experience gained, feedback from users, screening of scientific literature and of other sources of clinical data).
- The specific methods and procedures of the PMCF to be applied (such as the evaluation of suitable registers or PMCF studies).
- A rationale for the appropriateness of the selected methods and procedures.
- A reference to the relevant parts of the clinical evaluation report and to the risk management.

- The specific objectives to be addressed by the PMCF.
- An evaluation of the clinical data relating to equivalent or similar devices.
- Reference to any relevant common specifications (CS, see Chapter 3.5), harmonised standards when used by the manufacturer (see Chapter 3.6), and relevant guidance on the PMCF.
- A detailed and adequately justified schedule for PMCF activities (e.g., analysis of PMCF data and reporting) to be undertaken by the manufacturer.

These findings shall be analysed and documented in the form of a PMCF evaluation report, which is a part of the clinical evaluation report and all Technical Documentation. The conclusions of the PMCF evaluation report shall be taken into account in the clinical evaluation and risk management activities. The PMCF may also raise the need for corrective and/or preventive action (CAPA).

Sometimes there is a need to conduct a specific clinical study as part of the PMCF activities. These are discussed in more detail in the guidance document *MEDDEV 2.12/2 rev. 2 Post Market Clinical Follow-up Studies*. It should be noted that this document has been written in alignment with the former MDD and not the new MDR. An updated version for the MDR has not yet been published.

According to the MEDDEV 2.12/2, the decision to conduct PMCF studies must always be based on the identification of possible residual risks and/or unclarity on long term clinical performance that may impact the benefit-risk ratio. Therefore, there must be a specific question that the study is aiming to answer. According to the same guidance, circumstances that may require PMCF studies include, for example:

- Innovation (novel materials, technology, medical indications, etc.)
- Significant changes to the product
- High risk anatomical locations or target populations
- Unanswered questions of long-term safety and performance
- Emergence of new information on safety or performance
- If the CE marking was based on equivalence (especially when transitioning from the MDD to the MDR)

## 7.4. POST-MARKET PERFORMANCE FOLLOW-UP (IVDR)

Post-market performance follow-up (PMPF) is very similar to post-market clinical follow-up (PMCF) as a concept but has been presented in a separate chapter because there are differences in the details.

The PMPF is a continuous process that updates the performance evaluation for IVDs. The PMCF shall be included in the post-market surveillance plan. The purpose of the PMPF is for the manufacturer to proactively collect and evaluate performance and scientific data from the use of a device which bears the CE marking and that has been placed on the market or put into service according to its intended purpose. The PMCF is performed to confirm the safety, performance and scientific validity throughout the expected lifetime of the device, to ensure the continued acceptability of the benefit-risk ratio and to detect emerging risks on the basis of factual evidence.

The PMCF plan shall specify the methods and procedures for proactively collecting and evaluating safety, performance and scientific data with the aim of:

- Confirming the safety and performance of the device throughout its expected life cycle.
- Identifying previously unknown risks or limits to performance and contraindications.
- Identifying and analysing emergent risks on the basis of factual evidence.
- Ensuring the continued acceptability of the benefit-risk ratio.
- Identifying possible systematic misuse.

The PMCF plan shall include at least:

- The general methods and procedures of the PMCF to be applied (such as the gathering of clinical experience gained, feedback from users, screening of scientific literature and of other sources of scientific data).
- The specific methods and procedures of the PMCF to be applied (such as ring trials and other quality assurance activities, epidemiological studies, evaluation of suitable patient or disease registers, genetic databanks or PMPF studies).
- A rationale for the appropriateness of the selected methods and procedures.
- A reference to the relevant parts of the performance evaluation report and to the risk management.
- The specific objectives to be addressed by the PMPF.
- An evaluation of the performance data relating to equivalent or similar devices and the current state of the art.
- Reference to any relevant common specifications (CS, see Chapter 3.5), harmonised standards used by the manufacturer (see Chapter 3.6), and relevant guidance on the PMPF.
- A detailed and adequately justified schedule for PMPF activities (e.g., analysis of PMPF data and reporting) to be undertaken by the manufacturer.

These findings shall be analysed and documented in the form of a PMPF evaluation report, which is a part of the performance evaluation report and all Technical Documentation. The conclusions of the PMPF evaluation report shall be taken into account in the performance evaluation and risk management activities. The PMPF may also raise the need for corrective and/or preventive action (CAPA).

Sometimes there is a need to conduct a PMPF study as part of the PMPF activities. PMPF study is a performance study to further assess, within the scope of its intended purpose, a device which already bears the CE marking. If the PMPF study involves submitting subjects to procedures additional to those performed under the normal conditions of use of the device and those additional procedures are invasive or burdensome, requirements about documentation and notification laid down in the *Article 70 Performance studies regarding devices bearing the CE marking* must be observed.

## 7.5. VIGILANCE: REPORTING OF SERIOUS INCIDENTS AND FIELD SAFETY CORRECTIVE ACTIONS

Vigilance is extremely important to maintain product safety in problematic situations. The procedure can prevent the occurrence of injuries and other adverse effects on patients and end users in general. After the product has been placed on the market, the manufacturer's most important responsibility is considered to be the ability to perform vigilance: To take appropriate measures and submit timely incident reports when necessary. The manufacturer and, if applicable, their authorised representative must take actions effectively and in a timely manner within a strict framework. A good rule of thumb is to make one too many incident reports than one too few. Patient safety must not be compromised!

### When to Report and How?

Manufacturers of devices that are made available on the EU market (other than investigational devices) shall report to the relevant EU Member State competent authorities:

- Any serious incident involving devices, except expected side-effects which are clearly documented in the product information and quantified in the technical documentation and are subject to trend reporting.
- Any field safety corrective action (including also field safety corrective action taken outside of EU market area, if the reason for the field safety corrective action is not limited to the device made available in that area).



These reports shall be submitted to the competent authority of the country where the incident has occurred. They shall be submitted through EUDAMED, once this becomes available. These reports will also be automatically transmitted through EUDAMED to the notified body that issued the certificate for the device in question (if any). The Manufacturer shall co-operate with the competent authority and, if applicable, the notified body concerned during the investigation of a serious incident. It is important to note that until the EUDAMED is fully functional, the corresponding provisions of the former MDD, AIMDD and IVDD continue to apply for vigilance and incident reporting.

Professional users (clinicians, nurses, etc., hospitals and other places of care in general) of medical devices are also obliged to report incidents to their country's competent authority. They must also notify the manufacturer or their authorised representative of the incident, as the manufacturer bears the responsibility for the conformity of the device.

### Timelines for Reporting

The clock starts ticking immediately after the manufacturer has received information about the incident. It is often necessary to decide whether to report or not report before a thorough investigation of the event has been carried out. Where necessary to ensure timely reporting, the manufacturer may submit an initial report that may be incomplete, followed up by a complete report.

In the EU, there are three different timelines for reporting, depending on the severity of the serious incident. The strictest applicable timeline shall apply:

- **Any serious incidents** shall be reported immediately after a causal relationship (or a reasonably possible causal relationship) between the incident and the device has been established, no later than **15 days** after becoming aware of the incident.
- In the event of **death or an unanticipated serious deterioration** in a person's state of health, the report shall be provided immediately after the manufacturer has established (or as soon as it suspects) a causal relationship between the device and the serious incident, no later than **10 days** after becoming aware of the incident.
- In the event of a **serious public health threat** the report shall be provided immediately, no later than **2 days** after the manufacturer becomes aware of that threat.

It is worth noting, that the timelines for reporting have changed from the former MDD, AIMDD, and IVDD. The 15-day timeline for reporting any serious incidents has replaced the previous 30-day timeline. All other timelines have remained the same. The timelines for MDD/IVDD were not stated in the directives themselves, but instead introduced by *MEDDEV 2.12-1 rev 8 Guidelines on a medical devices vigilance system*.

It is important that manufacturers are prepared for incident reporting in advance. In practice this means having a procedure in place within their Quality Management System (QMS) with clear responsibilities and having employees appropriately familiar with the process. It is also important to ensure that the procedure of collecting information from users and distributors of the medical device is effective in order to receive timely incident reports. Investigation of incidents must be given the highest priority.

### Guidance on Reporting Serious Incidents

Further details on the reporting of serious incidents and field safety corrective actions can be found in MDR Article 87. MDCG guidance concerning vigilance has not been published, but the old guidance document *MEDDEV 2.12-1 rev 8 Guidelines on a Medical Devices Vigilance System* does contain good practical information. However, this guidance does not fully apply as it has been written to align with the former MDD, AIMDD and IVDD. It contains a list of details that must be included in the report, as well as a template for reporting.

## Incidents During Clinical Investigations

Incidents that have happened during a clinical investigation must be reported as well. The report shall be submitted to all EU countries in which the clinical investigation is being conducted. The following must be reported:

- Any serious adverse event that has a causal relationship with the investigational device, the comparator device or the investigation procedure, or where such causal relationship is reasonably possible.
- Any device deficiency that might have led to a serious adverse event if appropriate action had not been taken, intervention had not occurred, or circumstances had been less fortunate.
- Any new findings in relation to the events listed above.

These shall be submitted via EUDAMED once it becomes available. The period for reporting shall take account of the severity of the event. Further information and guidance can be found in *MDCG 2020-10/1 Safety reporting in clinical investigations of medical devices under the Regulation (EU) 2017/745*. The guidance also contains an appendix: *MDCG 2020-10/2 Clinical Investigation Summary Safety Report Form v1.0*.



## 8. QUALITY MANAGEMENT SYSTEM (QMS)

## 8.1. DEVICE SAFETY AND PERFORMANCE ENABLED BY AN EFFICIENT QMS

Medical device manufacturers should bear in mind the main points required by the authorities:

- Medical devices must be safe.
- Medical devices must have adequate performance as intended by the manufacturer.

These two points play an essential role in practically all international regulations – the devices must be “safe” and “effective”. When is a product safe and compliant in performance? Approaches to meet the safety and performance requirements are complementary:

- On the one hand, the product requirements are in place for the product itself to be safe and perform in accordance with its intended purpose.
- On the other hand, a Quality Management System (QMS) is in place to ensure that the ability of the manufacturer to meet the product requirements throughout its entire life cycle is maintained, even when facing challenges.

A Quality Management System (QMS), or ‘quality system’, provides the manufacturer with a tool to establish a framework for its operations and to ensure that all regulatory requirements are met. At its best, the ‘quality system’ also serves as an effective ‘management system’ which makes it possible for the company to operate more successfully in business. Throughout the decades, the focus in conformity assessment has shifted from the control of individual medical devices to the assessment and approval of the manufacturer’s QMS, i.e., their capability to continuously produce devices of high-quality. As an example, type testing of medical devices has reduced in many countries and has been replaced by the assessment of the QMS.

The Article 10 of the MDR and IVDR presents ‘General obligations of manufacturers’. Among those obligations, a QMS has become mandatory to all medical device manufacturers independent of the product class. Article 10 lists the minimum elements a QMS needs to address:

- Strategy for regulatory compliance
- Management responsibility
- Resource management
- Risk management
- Clinical evaluation
- Product design, development, and realization and change control
- Post-market surveillance
- Communications with competent authorities and Notified Bodies
- Vigilance reporting
- Corrective and preventive actions
- Measuring and acting upon data relating to product performance and the need for product improvement

The article further defines, that the QMS needs to be kept up to date and continually improved, which aligns with the requirements of the ISO 13485 standard. A manufacturer should pay attention to this list of minimum requirements and other relevant QMS requirements within the regulations, because they are dominant to any requirements in a standard. Notice also that this list overlaps with many of the requirements in the ISO 13485.

## 8.2. QMS STANDARDS

The ISO 9001 Quality Management System standard is widely used in other industries but it is not sufficient for medical device manufacturers. Medical devices have their own QMS standard, the *ISO 13485:2016 - Medical devices - Quality management systems - Requirements for regulatory purposes*. The ISO 13485 was originally based on the ISO 9001 standard but holds a higher level and more detailed requirements. This ensures that the specific requirements to medical devices are taken into account in the development and maintenance of the QMS. On the other hand, the ISO 9001 standard holds features that have been dropped from the ISO 13485 standard. In addition, in public procurement tenders, the ISO 9001 certification may appear as a mandatory requirement, but due to the differences in standard requirements, a manufacturer that meets the ISO 13485 may not meet the ISO 9001 standard. Where relevant for business, these differences are to be taken into account. Other examples of QMS standards that may be relevant to your business are the ISO 14001 for environmental management, the ISO/IEC 27001 for information security management, and the ISO 45001 for occupational health and safety. It is worth comparing standards and ensuring you use the concepts and content of the correct standards.

The ISO 13485 standard is internationally the state of the art QMS standard in the field of medical devices. It is a harmonised standard in the EU (although not yet for the MDR and IVDR due to delays in harmonisation, see Chapter 3.6), a recognised standard in the USA and Canada (CSA ISO 13485), and is to be applied in most countries that have specific regulations on medical devices. Successful product development, production and compliance at all stages of the device life cycle call for a QMS based on this standard. The ISO 13485 standard requires that the safety and performance requirements, as well as clinical performance and risk management through the entire product life cycle, are fully taken into account.

Note that compliance to legislation and regulation is mandatory, complying to a standard is not. However, standards often represent the state-of-the art implementation of specific part of a regulation. The title of ISO 13485 standard includes the expression “for regulatory purposes”. This means that the requirements applied throughout the QMS must take into account all applicable regulations. This naturally includes the requirements of Article 10 and other parts of the MDR and IVDR, but also requirements from other applicable regulations, such as the GDPR, the national legislation of a specific EU country or the US FDA requirements, if the manufacturer claims to place devices on the US market. The ISO 13485 also provides a tool for the Notified Bodies to implement QMS assessment taking into account the applicable regulations.

In the past, compliance with Good Manufacturing Practice (GMP), originally the American and British GMP regulations, was also required for medical devices. Although the GMP code is still very strong in the pharmaceutical industry, its importance for medical devices today is marginal. In the U.S. a medical device manufacturer must comply with the Quality System Regulation (QSR) legislation, Act 21 CFR Part 820 (Code of Federal Regulations Title 21) to which the ISO 13485 aligns with in most parts.

The currently valid versions of the standard are the ISO 13485:2016 internationally and the EN ISO 13485:2016 in the EU. The difference between the international and EU versions is that the latter includes the so-called Annex Z, which describes the extent to which the standard covers the requirements of the European medical device directives (and soon hopefully the new medical device regulations). See example of an Annex Z of the EN ISO 13485:2016 standard in Figure 1 of Chapter 3.6. The ISO 210 Committee, which is responsible for the ISO 13485 standard, has also prepared a Practical Guide (*ISO 13485:2016 - Medical Devices - A Practical Guide*), which provides information to facilitate the implementation of the standard. It is highly recommended to study this guidance document (and Technical Reports (TRs) where they have been published alongside a standard), as it holds more practical information on establishing an actual QMS than the standard itself. For the same reason, it is good practice to pay early attention to the figures and annexes of a standard, as they may hold the most visual and practical information on compliance.

## 8.3. ISO 13485 AND CONFORMITY ASSESSMENT OPTIONS

The ISO 13485 standard can be applied in full or with certain exclusions, depending on the device class and type and the conformity assessment option chosen by the manufacturer, as the options are laid out in the MDR and IVDR. However, it cannot be emphasised enough how an efficient QMS, covering all activities affecting the safety and performance of the device, provides the foundation for business in the medical device sector. Furthermore, in different market areas, such as the USA or Canada, the requirements for the completeness of a QMS may differ from those in the EU. A full QMS according to the ISO 13485 can be viewed as good business strategy and a means to controlling many business-related risks.

The mandatory nature of a QMS and its dependence on device classification is discussed in more detail in Chapter 6.3.2. Conformity assessments, which include the QMS approach, are discussed in more detail in Chapter 6.3.3.

## 8.4. HOW TO DEVELOP AN EFFECTIVE QMS?

A QMS may have a significant effect on methods of working throughout the organisation. Implementing a QMS often requires a change in the organisation culture, and it might take time for employees to adapt to the new way of working. To ease the path, it is useful to begin by documenting the current way of working and to add elements required by the regulations or standards on top. This progress into the regulated world is then achieved through incremental steps instead of one giant leap. It also facilitates the acceptance of new procedures if the teams can contribute to the development of the QMS and participate in finding the solutions from the perspective of current practices.

It is essential that the QMS reflects the organisation, its culture and operations, yet meets the applicable regulatory requirements. Ready-made QMS templates are available for purchase online. This might sound like an easy solution to QMS implementation, but for effective implementation and maintenance, a QMS should be customised for the particular organisation. If the QMS is only applied to the surface of the daily operations, this results in an extra burden and it might be difficult to maintain effectively. A well implemented QMS is nothing separate from the daily operations and management and adds value to the organisation through producing safe and effective products. Hiring an experienced medical device consultant supporting the team in the QMS ramp-up is often the most efficient way for a successful QMS project. It is also worth noting that developing a QMS should not be seen as a one-time effort but rather as a continuous project. The applicability of the QMS is periodically evaluated and the QMS should evolve with the organisation.

## 8.5. ISO 13485 – GENERAL FEATURES

The ISO 13485 standard is written for the needs of the medical device industry. It can be used in the design and development of medical devices and related services, in production, installation, and in the post-market phase. It can also be used by subcontractors where applicable. It is of great benefit to the manufacturer that its subcontractors hold a QMS based on the ISO 13485 standard, but it is nevertheless worth ensuring that the most essential requirements are taken into account in a contract between the parties. If a subcontractor is able to show evidence on compliance according to the ISO 13485 standard and other medical device standards, for instance, by certification from an accredited conformity assessment body (CAB), the less need there is for the manufacturer to perform compliance audits on the supplier, and the better the opportunity there is to rely mostly on the contract. The more critical the role the supplied activity plays for the device safety and performance, the more relevant this notion becomes.

Naturally, the standard, along with the MDR or IVDR, also provides the basis for Notified Bodies to conduct conformity assessment audits.

The ISO 13485 is based on a process approach to quality management and is primarily intended to be used to comply with regulatory requirements for medical devices. The goal of the standard is to ensure compliance. The size or type of the manufacturer does not affect the requirements – even a small company faces the same requirements as a large one. The manufacturer must also cover the outsourced functions, i.e., the responsibility of the outsourced party has to be reflected in the QMS. However, it is possible for all companies to exclude some standard requirements if they are not applicable, but the justification must be documented. Where in the standard a requirement applies “if necessary” or “where appropriate”, the requirements should be considered mandatory unless the manufacturer can document otherwise.

Other relevant topics should also be considered within the QMS, as the ISO 13485 does not cover, e.g.

- environmental management,
- information security,
- occupational health and safety, or
- financial management.

The Practical Guide (*ISO 13485:2016 – Medical Devices – A Practical Guide*) provides guidance on the application of the ISO 13485 standard.

Some essentials regarding an ISO 13485 compliant QMS:

- The necessary regulatory requirements must be known and, if necessary, taken into account in the QMS. By following the QMS, the organisation must be able to trust that all regulatory requirements will be taken into account.
- All necessary processes must be identified and the relationships between them defined (using flowcharts for clarity). It is also worth noting that the interfaces between processes are often problematic and defining those interfaces well will enhance the efficiency of the QMS.
- The most important processes would be management, product development, production, material management (including the purchasing process), document control, corrective and preventive actions (CAPA), and infrastructure, naturally depending on the company's operations.
- The manufacturer must ensure the control of outsourced processes if the processes affect the conformity of the product.
- Procedures must be documented and comprehensible from top to bottom (e.g., the flow through quality policy & objectives - quality manual - upper to lower level procedural instructions - work instructions - measurement - analysis of data - management review).
- All documentation (not only operating procedures) including records must be properly controlled.
- The role of management and leadership and related issues are key to ensuring the functioning of the QMS (management commitment, customer focus, quality policy & objectives, QMS design and effectiveness, resource management, responsibilities and authority, management representative, communication, management review)
- Risk management throughout the device life cycle is another key issue, and risk management must be strongly involved in all activities. Reliance on the ISO 14971:2020 risk management standard and ISO/TR 24971:2020 guidance document is best practice.
- Ability to manage corrective and preventive actions (CAPA) procedures and incident reporting must be effective.
- A QMS is recommended to be initiated in the operations of a company from day one, for applicable parts, starting at the beginning of product development.
- It is essential for the company to understand the meaning and value of the QMS, the means for its effective use and control and the need for its continuous maintenance at all levels of the organisation.
- Functionality of the QMS is monitored through management reviews, internal audits, product reviews and process validations.

## 8.6. MANAGEMENT

At its best, a Quality Management System (QMS) provides tools for the overall management of the company. Management responsibility plays a key role in the ISO 13485 standard, which is something even a start-up company should prepare for from day one - A poorly managed company will not produce devices that comply with regulatory requirements which can be commercially destructive. These are some of the most important management-related requirements in the ISO 13485 and medical device regulations:

- The management must be committed to developing, implementing, and maintaining an effective QMS.
- Commitment is shown by efficiently setting up the quality policy and quality objectives, holding the management reviews according to plan, enabling the necessary resources, and identifying and communicating operational requirements.
- Customer (patient or end user) requirements are defined and met.
- The quality policy may be concise, but it must emphasise compliance with regulatory requirements (safety and efficacy of devices) and the effectiveness of the QMS, and be appropriate to the manufacturer's business.
- Quality objectives must be in line with the quality policy, they must be measurable and defined for all levels of the organisation.
- The organisation's responsibilities and authorities shall be defined and documented and shall be communicated within the organisation.
- The management shall appoint at least one Person Responsible for Regulatory Compliance (PRRC) in their organisation, which is a requirement in article 15 of the MDR and IVDR. The regulations set requirements for qualification and expertise of the PRRC. In case of micro and small enterprises, PRRC can also be an outsourced person permanently and continuously at their disposal. The ISO 13485 also requires the management to appoint a Management Representative who is responsible for the implementation and maintenance of the QMS, reporting to management, and ensuring that the organisation complies with regulatory and customer (patient or end user) requirements. The management representative shares mainly the same responsibilities as the PRRC and is in many cases the same person.
- The management is responsible for proper communication related to the QMS.
- A post-market surveillance system is implemented for actively and systematically gathering and analysing relevant data on the quality, performance and safety of a device throughout its entire lifetime. The post-market data is analysed periodically for drawing the necessary conclusions and for determining the need for any preventive, corrective or other actions.
- Management reviews must be held at pre-planned intervals to ensure that the QMS is fully functional. The input for the review relates to the current operations through audit results, customer feedback, process performance, product compliance, corrective and preventive actions (CAPA), follow-up actions, changes, and recommendations for improvement, but also includes information on new or amended statutory requirements.

## 8.7. DOCUMENTATION

A medical device manufacturer should follow the basic principle on documentation that “everything must be documented and what is not documented does not exist”. The scope of documentation can still vary between companies, taking into account the size of the company, the way it operates, and the complexity of the processes, for example. Yet, the QMS documentation must cover all functions in the company. The quality manual and the quality policy set the basis, with operating procedures derived from the policy, and the related work instructions. In addition, the documentation covers all documents and records related to processes and products.

Important requirements in the ISO 13485 regarding documentation:



- The quality manual defines the scope of the QMS and justifies the non-applications and exclusions, provides the high level description of the standard operating procedures (SOPs, as they are typically named) and their interrelations, and the structure of the documentation (i.e., the QMS in a nutshell).
- The manufacturer must hold a procedure for managing internal and external documents to ensure their adequacy, review and approval prior to publication, change control, accessibility, readability, and identification – and also for preventing the inadvertent use of obsolete documents and to keep these for a specified retention period.
- The manufacturer must hold a procedure for managing records for demonstrating the compliance and performance of the devices and the QMS, as well as the readability and identification, availability, retention period, and disposal of the records

It is highly recommended to take these requirements into account from day one, as otherwise the results of product development and other activities may not be usable or applicable in later phases.

## 8.8. RESOURCE MANAGEMENT

Adequate resources must be defined and allocated for implementing and maintaining the effectiveness of the QMS, as well as for meeting the regulatory and customer (patient or end user) requirements. Resources include human resources, infrastructure, and the work environment. The ISO 13485 standard considers human resources only to ensure that the personnel performing work affecting product quality are competent. Because all employees can indirectly influence the product quality, it may sometimes be difficult to draw those boundaries. Therefore, from the management perspective, it makes sense to apply the requirements of the standard beyond what is mandatory. In general, all personnel should have adequate qualifications based on appropriate education, training, and experience.

Competences must be documented. An organisation chart and job descriptions with required competences are created for all employees or positions. Employees must also be aware of the importance and significance of their work tasks and how they contribute to achieving the quality objectives. Sometimes it can be difficult to scale the number of personnel adequately. However, the authorities may pay attention to the lack of resources if, for example, planned schedules for critical tasks are continuously failing.

Buildings, workspaces, equipment, and supporting services are part of the infrastructure that must be organised to achieve product compliance. This also includes maintenance functions if they (or the lack of these) can affect the quality of the product. Particular attention should be paid to sufficient competence by the maintenance functions, as these tasks are often outsourced to parties who do not themselves have experience in medical device requirements.

The working environment must be appropriate to achieve product conformity. For example, adequate requirements should be defined for the clothing of personnel and the working environment. This could mean, i.e., clean room conditions for implantable device or information security requirements for a software device. Some legislations, such as the US FDA QSR and Brazilian requirements are very detailed in this regard. In particular, it should be noted that all temporary personnel also receive appropriate training for their work or work under the supervision of a trained person.

For a start-up company, resource management is also important, but it can be challenging to establish the necessary competences with a limited number of employees present, especially where the regulatory and quality-related work require a certain amount of impartiality from other functions, not to forget the regulatory experience that may be crucial for the company's success, outsourcing, or sharing resources with other companies may be the solution. On the other hand, it can be hard to define the responsibilities and authorities for an outsourced or shared expert. These challenges apply to other roles as well and requires good planning from a medical device start-up.

## 8.9. PRODUCT DEVELOPMENT

### 8.9.1. General Requirements

In the ISO 13485 standard, the term used for product development is “design and development”, and in the US FDA Quality System Regulation (QSR) the term is “design control”. Often, companies focus most of their Quality Management System (QMS) work on this part. However, it is worth remembering that product development cannot take place without proper management, resource management, validated equipment and methods, and documentation. In other words, even the youngest company should invest in building an entire QMS instead of taking the narrow product development perspective. The goal of product development is not only to create a specific medical device, but to produce all the information required for purchasing, production, quality assurance, packing and shipping, warehousing, transportation, sales and marketing, maintenance, installation, etc., to take over the product. On one hand, a holistic approach covering the entire product life cycle is needed sooner than many companies acknowledge, and on the other hand, there is an immediate need for a clear picture of the market and the customers in order to acquire the correct basis for the product development project.

The ISO 13485 describes the product development process in principle, while the US QSR contains much more detailed requirements for product development. It is also worth remembering that in addition to these requirements for product development, there are more QMS-related requirements, for instance, in the ISO 14971 risk management standard, the IEC 62366 for usability engineering, or the IEC 62304 standard for software life cycle, as well as an entire library of technical standards that should be taken into account early on in developing specific types of medical devices.

It is, therefore, necessary to study all applicable regulations and standards at an early phase to create the appropriate processes necessary for successful product development. Attention must be paid to the product-related quality objectives and requirements for safety and performance, processes, resources, and required documentation and records. Of particular importance are product specific verification, validation, monitoring, inspection and testing activities, as well as the product acceptance criteria. Clinical evaluation is an essential concept in this regard and has already been discussed in detail in Chapter 6.2.5 and Performance Evaluation for IVD devices in Chapter 6.2.7. The aim of the product development processes is also to produce the “cook books” for other parts of the organisation to follow, so that, for example, production can produce devices that meet the set requirements, and purchasing holds standardised procedures to order critical components from suppliers. In the US QSR, such cook books are called Device Master Records (DMR).

### 8.9.2. Design Inputs

The golden rule in the US QSR is that “design output must meet the design input”. This means that the final product must meet the inputs that are specified on an engineering level of detail during the development project. The fastest and economically the most efficient result is achieved when the customer and statutory requirements that make the design inputs are well defined already in the beginning of product development. Every change to the design inputs later on means the development project is potentially delayed or even returned to the starting point. A thoughtful regulatory strategy that is aligned with a solid market strategy provides the basis for the originally innovative idea to be developed into a medical device. In the background, this requires substantial studying of the relevant regulations, the General Safety and Performance Requirements (GSPR) of the MDR or IVDR, and applicable standards early on to make educated choices for the design inputs.

The ISO 13485 requires that the customer-related processes specify inputs defined by the customer, including terms of delivery and post-delivery measures. The targeted markets and customer segments should be well defined in the marketing strategy, as any changes in later phases bear the risk of delaying the project significantly. For medical devices, the customer requirements must be extended to the patient and the medical need - only then can the intended purpose and specifications of the device be determined. This also creates the need to identify requirements that the patient or end user was not able to express, but which are essential for the safe and efficient functioning of the device in the medical context. When defining

customer requirements, it is advisable to obtain documented information from many well-selected customers (taking into account the patient, different users, and different customers) as well as medical literature, competitors, considerations from the early risk assessment, etc. User specifications must include precise information on customer requirements.

It is suggested to perform first rounds of risk analysis and usability engineering at early phases of the product development to achieve further understanding of the product and related requirements. Both risk management and the usability engineering process act as essential sources for design inputs.

The ISO 13485 standard defines at least the following design input data:

- Functional, performance, usability, and safety requirements based on the intended purpose of the device
- Applicable regulatory and statutory requirements
- Information gathered from similar devices
- Other requirements relevant to design and development
- Results of risk management

User specifications are first documented to ensure that user requirements are fully taken into account. The user specifications are then transferred to more technical product specifications, which also take into account technical implementation aspects. It is essential that product requirements are defined and documented. The requirements must be complete, unambiguous, and must not conflict with each other. If the product requirements are changed, the documentation will be updated accordingly. The justification for the change must be properly documented and all concerned parties informed. Frequent changes in design inputs may also appear alarming for the Notified Body or, e.g., the US FDA, so one should invest enough in making the right choices for design inputs. Problems can be avoided, for example, by organising user and product specifications into categories by priority: The highest category is considered mandatory, and if this cannot be reached, the product is not feasible to be developed. However, in such cases, the manufacturer should investigate if a change in the intended purpose of the device would make the needed difference (e.g., excluding children from the targeted end users). The lowest category holds design inputs that can be safely omitted if, for example, there are no resources to implement this.

The design inputs must be reviewed and approved.

### 8.9.3. Product Development Plan and Design Reviews

The ISO 13485 standard requires that an operating procedure is defined within the QMS for product development and that the product is then developed according to this procedure. The stages of product development need to be defined in the product development plan. Each stage includes a design review and the review protocol needs to be defined in the operating procedures for product development. Depending on the nature of the product and the project, several design reviews may be organised. These are examples of design reviews, named according to the topics on their agenda:

- Design input review (which is always mandatory)
- Design verification review
- Design validation review (including the review of clinical evaluation, unless reviewed separately)
- Design transfer review (verification that the outputs of the product development are suitable for production)
- A final review covering the entire product development (held before placing the product on market, always mandatory)
- A possible review after the product has been on the market for a defined time

In the design reviews, it is assessed if the product development outputs meet the inputs. Additionally, the reviews identify potential problems and suggest necessary actions.

The product development plan must also include definition of activities related to verification, validation, transfer to production, product development responsibilities and authorities, cooperation between different parts of the organisation and documentation.

#### 8.9.4. Design Verification and Validation

The goal of design verification is to verify that the design output meets the requirements of the input data. The process includes a verification plan, including acceptance criteria, then implementation in alignment with the plan, then report on the results against the acceptance criteria.

Design validation is performed to ensure that the medical device is suitable for its intended purpose. Validation activities include usability studies and clinical evaluation (medical devices) or performance evaluation (IVDs).

#### 8.9.5. Design Output

The outputs of product development must be presented in a way that that enables their comparison against the design inputs. Design outputs must:

- Meet the input requirements
- Provide appropriate information for purchasing, production and service provision
- Include product acceptance criteria or references to them
- Define the properties that are essential for the safe and proper use of the product

#### 8.9.6. Design Change and Change Control

Design changes can hardly be avoided during product development, but efficient preparations and a systematic approach to product development and to compliance overall can significantly reduce the amount of changes and rework needed due to new or revised design inputs. The more design changes during a project, the clearer the warning signals on poor design and poor product development process. Design changes must always be controlled and documented well. The reason for the change shall be justified, its effects on risk management assessed, and, where appropriate, verified and validated, followed by a review and approval of the change.

If the device is already placed on the market or put into service, the potential impact of the change to such devices must be assessed.

### 8.10. PURCHASING

Purchasing requirements are defined during product development when the technical specifications are determined for the medical device, its components, raw materials, etc. Only when pre-defined and approved, do the purchase requirements form the criteria towards suppliers for the purchased products or services. The extent of control applied to the supplier and to any purchased products is determined by their impact on the quality of the final medical device. Suppliers are categorised on the basis of the criticality of the purchased product or service, and the criteria for selecting, evaluating, and re-evaluating a supplier must be determined. Supplier evaluation often consists of an assessment of product samples and an evaluation of the ability of the supplier in meeting requirements for the purchased product. The evaluation can be a very simple qualification or a comprehensive supplier audit. For critical products or processes, it is important to ensure their availability in all conditions. This could be achieved through reserve stock or by establishing relations to several alternative suppliers.

Especially when the purchased product or service (e.g., sterilisation) is critical, an agreement should be put in place by the parties to confirm all purchasing related information. The purchasing information ensures that the purchased product is suitable for the final medical device or its production. Therefore, it is highly important to generate all purchasing requirements, including the acceptance criteria, and to verify their adequacy before communicating them to the supplier.

Incoming inspection or other activities are performed by the manufacturer to verify that the purchased product meets specified requirements. The purchased products must be kept separate from products that are already approved until it is verified that they meet the applied requirements.

## 8.11. PRODUCTION

All elements of production of a medical device need to be controlled. Processes and their critical control points must be identified and documented. Production procedures, equipment, test methods and other related matters must be properly identified, listed, calibrated, validated, etc. The ISO 13485 standard refers to the availability of appropriate documented procedures, requirements, work instructions, reference materials, and reference measurement procedures. Reference is made to the use of appropriate instruments, the availability and use of monitoring and measuring equipment, and the implementation of monitoring and measurement activities. The standard also requires that delivery, post-delivery, installation, and servicing activities be carried out in a controlled manner.

## 8.12. MEASUREMENT, ANALYSIS AND IMPROVEMENT

The manufacturer must have processes in place for monitoring, measurement, analysis, and improvement. These are required to demonstrate the conformity of the product and to ensure and maintain the conformity and effectiveness of the QMS.

The ISO 13485 standard requires that there is a process in place to monitor customer feedback to be able to determine if customer's requirements are continuously met. Furthermore, the ISO 13485 and the international medical device regulations quite understandably emphasise the handling of complaints. A complaint handling procedure must be in place and adequately resourced by the manufacturer. The procedure must be detailed enough to ensure that any identified incidents or non-conformities related to the device are handled effectively and in a timely manner. Serious incidents meeting the reporting criteria and any field safety corrective actions are reported to the relevant competent authorities. The QMS must include procedures for communicating with competent authorities and Notified Bodies. Complaints should be linked to both the corrective and preventive action (CAPA) process and the incident management process.

Internal audits shall be performed by the manufacturer at scheduled intervals, and by qualified and independent auditors to ensure that

- the QMS meets the criteria of the ISO 13485 standard, the applicable statutory requirements (e.g., the MDR or IVDR) and the manufacturer's own requirements, and
- the QMS is effectively implemented and maintained.

Internal audits are planned by the manufacturer based on the status and importance of its processes and the results of previous audits. Audit criteria, scope, frequency and procedures must be pre-defined. An audit consists of planning, execution, reporting, and applying the possible corrective and preventive actions. The company management is responsible for ensuring that corrective and preventive actions are implemented and that the causes of non-conformities are resolved without undue delay.

## 8.13. CORRECTIVE AND PREVENTIVE ACTIONS (CAPA)

In a well performing company, the emphasis may be on preventive actions. However, most often the chain of events leading to action by the manufacturer starts with a customer complaint, a non-conforming product, or an internal or external audit finding, and then corrective action ensues. Both, corrective and preventive actions are intended to prevent future incidents. Corrective actions prevent the recurrence and preventive action prevent the occurrence of incidents.

The corrective action comprises of:

- A review and investigation of the causes of the non-conformity and, if necessary, immediate correction (such as recalling a product from the market) to prevent further or additional damage.
- Identifying and implementing the necessary corrective actions to prevent the recurrence of the non-conformity by addressing the causes of the non-conformity.
- Records of the results of investigations and actions taken, and reviewing their effectiveness.

The preventive action comprises of:

- Determining potential nonconformities and their causes.
- Assessing, determining, and implementing the need for a preventive action to prevent the occurrence of non-conformities by addressing the cause of the potential non-conformity.
- Recording the results of the investigation and actions taken, and reviewing their effectiveness.

If the corrective or preventive action is related to devices that are already distributed, the need for vigilance activities must also be evaluated.