FAQ What I wish I knew before I started with the MDR

1. What is the MDR?
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3. Can I use my medical device before having a valid CE mark?
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1. Q&A What is the MDR?

Introduction

The Medical Device Regulation ("MDR") is a EU Regulation that lays down rules concerning the placing on the European Economic Area ("EEA") market, making available on the EEA market or putting into service of medical devices for human use and accessories for such devices in the EU. It also applies to clinical investigations concerning such medical devices and accessories conducted in the EU. A 'medical device' is, in short, any article intended by its (legal) manufacturer to be used, alone or in combination, for a specific medical purpose 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.[1] [refereren naar Q&A What is a medical device]. The MDR can be found on the website of the European Union. Please make sure to select the current consolidated version to get the most recent text.

What roles can be distinguished by the MDR?

The legal obligations that follow from the MDR differ per 'role'. The MDR makes a distinction between, for instance, Manufacturers, Importers, Distributors and Notified Bodies. It is of crucial importance for each economic operator to identify it's role under the MDR as they will be held accountable for fulfilling it properly.

- **Manufacturers:** Manufacturers are natural or legal persons who manufacture or fully refurbish a device or have a device designed, manufactured or fully refurbished, and market that device under their name or trade mark.[2] Article 10 of the MDR establishes the general obligations of manufacturers. Please note that the term 'legal manufacturer' is often used to refer to the defined 'role' in the MDR and should not be mixed up with the factual manufacturer, often being one or more suppliers of components or the whole device to the 'legal manufacturer'. Suppliers do not have an official role defined in the MDR. However, suppliers do play a crucial role in the quality management system;
- **Importers:** Importers are natural or legal persons established within the EU that place a device from a third country on the EEA market.[3] Article 13 of the MDR establishes the general obligations of Importers;
- **Distributors:** Distributors are natural or legal persons in the supply chain, other than the manufacturer or the importer, that make a device available on the EU market, up until the point of putting into service.[4] Article 14 of the MDR establishes the general obligations of Distributors;
- **Notified Bodies:** Notified Bodies are accredited conformity assessment bodies designated in accordance with the MDR. For the conformity assessment procedure of most medical device software, a Notified Body must be involved.

What is the relation to the Regulation on in vitro diagnostic medical devices (IVDR)

The IVDR contains regulations on in vitro diagnostic medical devices. '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:

- Concerning a physiological or pathological process or state;
- Concerning congenital physical or mental impairments;
- Concerning the predisposition to a medical condition or a disease;
- To determine the safety and compatibility with potential recipients;

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[1] Art. 2(1) MDR.
[2] Art. 2(30) MDR.
[3] Art. 2(33) MDR.
[4] Art. 2(34) MDR.

- To predict treatment response or reactions;
- To define or monitoring therapeutic measures[5].

For the purpose of this Q&A, we will not further elaborate on the IVDR. However, do note that software may be regulated as an in vitro diagnostic medical device instead of a 'regular' medical device.

Is there other relevant legislation
Aside from the MDR, other EU and/or national legislation could be relevant to (legal) manufacturers of medical devices. Even though we will not elaborate on these in much detail in this Q&A, please find below a short non-exhaustive list of potential relevant non-MDR topics (other than those that will be touched upon in this Q&A such as advertising and favours):

- Intellectual Property (IP) law concerning software patents and copyrights;
- Privacy legislation (GDPR) relevant to software processing personal data;
- Consumer rights legislation providing information obligations and other requirements when contracting with consumers;
- E-Privacy legislation covering electronic communications such as telemedicine or remote monitoring applications; and
- Upcoming AI legislation about the regulation of the usage of artificial intelligence within the EU.

Are guidance documents and standards important?
Yes, guidance documents and standards should be taken into account when getting into conformity with the MDR. The following applies:

- Guidance documents: Guidance documents regarding the MDR or other relevant legislation can be very helpful in understanding the law. Even though guidance documents are not legally binding themselves, national and EU courts, supervisory authorities and Notified Bodies usually take them into account when performing their duties. It is, however, important to take note of the source of the guidance documents you want to use. Guidance documents published by the European Commission's Medical Device Coordination group ("MDCG") or national competent and supervisory authorities have significant authority. Guidance documents published by your local law firm do usually not.
- ISO-standards: When getting into compliance with EU and Member State legislation, ISO-standards are oftentimes used. ISO standards are a set of internationally recognized (mostly technical) guidelines developed by the International Organization for Standardization (ISO) that ensure products, processes, and services are safe, reliable, of high quality and in compliance with the relevant laws. Devices that are in conformity with ISO standards that are adopted by the European standardisation organisation and published in the Official Journal of the European Union (OJEU) are called 'harmonized standards' and are presumed to be in conformity with the requirements of the MDR covered by those standards or parts thereof. Examples of such standards relevant to medical device software are:
    - EN ISO 13485:2016 on Quality Management Systems;
    - EN ISO 14971:2019 on Application of risk management to medical devices; and
    - IEC 62304:2006 on Software life cycle processes (not harmonized)

[5] Art. 2(2) IVDR.

2. Q&A What is a medical device? (qualification)

Introduction

If you are wondering whether you are dealing with a medical device, you need to refer to the definition in Article 2(1) of the MDR. For various reasons (business case, compliance, planning the product launch), it is important to determine in an early stage of the product development process whether you are working with a medical device. So preferably during the ideation or feasibility phase, and at least at the design and before the development phase. Do not procrastinate on this qualification, even though it is a tricky and sometimes "gray" area in discussions, and bite the bullet.

Who determines whether the device is a "medical device"?

Determining correctly whether a device is a 'medical device' is a manufacturer's own responsibility. You cannot address this question, for example, to a government office or a notified body. You can, of course, seek help [reference to Q&A Where can I find help?].

How does the qualification work?

It is relevant that the qualification process is documented, both the conclusion (medical device/not medical device) and the reasoning towards this conclusion. Documenting ensures that (i) the reasoning becomes logical, (ii) you are better able to discuss efficiently with others involved and (iii) you are able to prove to, for instance, supervisory authorities why you came to certain conclusions.

To do this, work on a report in which you first describe the "intended purpose"[1]. The second part of the report consists of an analysis of whether the described intended use falls within the 'medical device' definition. Specify explicitly which part of the definition matches with the intended use of the device. Involve parties with relevant roles in the qualification process: the determination can best be done by a quality assurance or regulatory assurance staff member. Also try to involve a product specialist, marketing staff member, and possibly a physician as well.

If your device is not a medical device according to the definition in Article 2.1, do another check to be sure it is not still covered by the MDR by looking at Article 2.2 ("accessories to a medical device") and Annex 16 (certain product groups without a medical purpose that are medical devices nonetheless).

Any tips on "the gray area" and qualification of software?

Qualification of software as a medical device can be tricky. There is valuable guidance from the European Commission for a few borderline devices[2]. It may also be useful to seek comparison with devices with a similar purpose already in use in healthcare. Another possibility is to look up devices with a similar intended purpose in the European database for medical devices (EUDAMED). Also getting second opinions can be useful.

Specific guidance is available for software as a medical device[3]. When in doubt, be sure to look at Figure 1 of this guidance.

Can anyone help me qualify?

Asking advise to a lawyer specialized in the MDR can be considered when in doubt. This can also add a more legal reasoning to the qualification. Partners of d-Health can also seek

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[1] Art. 2(12) MDR.
[2] See Manual on Borderline and Classification in the Community Regulatory Framework for Medical Devices (September 2022) (europa.eu)
[3] For more guidance, see MDCG 2019-11: Guidance on Qualification and Classification of Software.

independent advice from employees of the RUG and UMCG with experience in these issues. Please contact d-Health to get this started.

3. Q&A Can I use my medical device before having a valid CE mark?

Introduction

According to the MDR, a medical device may be placed on the market or put into service only if it complies with the MDR.[1] One of the MDR requirements are that a medical device considered to be in conformity with the requirements of the MDR shall bear the CE marking of conformity. The CE mark must be affixed before the medical device is placed on the market.[2]

The EU Member States have laid down rules regarding penalties applicable for acting contrary to the MDR. For instance, under Dutch law, not affixing a CE mark before marketing a device can lead to an administrative fine or an order subject to penalty.[3] Depending on the risk to the health or safety of patients, users or other persons, Member State supervisory authorities have additional means of enforcement following from the MDR, potentially leading up to a product recall and/or sales ban.[4]

However, in some cases, a medical device does not need a CE mark in order to be used legally.

What is an investigational device?

A device that is assessed in a clinical investigation ("Investigational Device") does not need to bear a CE mark.[5] Investigational devices are however subject to the requirements set out in Articles 62 to 80 and 82 of the MDR regulating clinical investigations including general safety and performance requirements regarding aspects of the device that are not covered by the clinical investigation. In principle, investigational devices may only be used by patients participating in a clinical investigation. [reference to Q&A How do I approach clinical evaluation including contact with hospitals?]

What is a custom-made device?

A device specifically made in accordance with a written prescription of any person authorised by national law by virtue of that person's professional qualifications which gives, under that person's responsibility, specific design characteristics, and is intended for the sole use of a particular patient exclusively to meet their individual conditions and needs ("Custom-made device") does not need to bear a CE mark.[6] That being said, manufacturers of custom-made devices do need to comply with the procedure set forth in Annex XIII of the MDR regarding information, documentation, manufacturing and post-market clinical follow-up requirements. Even more rules apply to custom-made implantable devices.[7]

What is in-house development?

Devices, manufactured and used only within health institutions that are not manufactured on an industrial scale, are exempted from the provisions laid down in the MDR (including affixing a CE mark) except for Annex I on general safety and performance requirements if certain conditions are met.[8] One such condition is the restriction to not transfer the device to another

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[1] Art. 5(1) MDR.
[2] Art. 20(1 and 4) MDR.
[3] Art. 12 and 14 Dutch Medical Device Act ("*Wet medische hulpmiddelen*").
[4] See for more information Art. 93-98 MDR.
[5] Art. 20(1) MDR.
[6] Ibid. Please note that mass-produced devices which need to be adapted to meet the specific requirements of any professional user and devices which are mass-produced by means of industrial manufacturing processes in accordance with the written prescriptions of any authorised person are not considered to be custom-made devices. For more guidance, see MDCG 2021-3: Questions and Answers on Custom-Made Device.
[7] Art. 52(8) MDR.
[8] Art. 5(5) MDR.

legal entity. Detailed guidance on these conditions is provided by the Medical Device Coordination Group.[9]

What about compassionate use (article 59 derogation)?
Before placing a device on the market or putting it into service (and legally affixing a CE mark), manufacturers need to undertake a conformity assessment procedure.[10] However, according to Article 59 of the MDR, a competent authority may authorise the placing on the market and putting into service of a specific device for which the conformity assessment procedure has not been carried out, when there is a duly justified request and the use of the device is in the interest of public health or patient safety or health. In the Netherlands, the competent authority is the Healthcare and Youth Inspectorate (IGJ). If the derogation is not limited to a single patient, the Member State authority must inform the Commission and the other Member States.[11] Please note that a derogation based on Article 59 MDR is granted in exceptional cases.

[9] MDCG 2023-1, Guidance on the health institution exemption under Article 5(5) of Regulation (EU) 2017/745 and Regulation (EU) 2017/746.
[10] Art. 52 MDR.
[11] Further information about 'due justification' can be found in the 'Guidelines on the adoption of Union-wide derogations for medical devices in accordance with Article 59 of Regulation (EU) 2017/745 (2020/C171/01)'.

4. Q&A What risk class does my device belong to and what is the consequence?

Introduction
The MDR introduces different risk classes for medical devices, based on the potential risk to the patient and user. The risk classes determine the level of monitoring and assessment manufacturers must undergo to comply with the MDR. This helps ensure patient and user safety.

What are the risk classes?
Below are the different risk classes stated with examples for software as medical device[1].

- Risk Class I: Lowest risk, simple devices such as an app to higher chance on conception by calculating the user's fertility status based on a validated statistical algorithm. Within Class 1, a device may fall into a specific subcategory:
    - Class 1 measurement function: lowest risk devices that serve to measure or detect physiological parameters, such as body temperature, blood pressure. These devices are not invasive in nature and are intended for use outside the body.
    - Class 1 sterile: devices that must be sterile before use, such as sterile dressings, gauze, catheters and hypodermic needles.
- Risk class IIa: Moderate risk, such as a serious game with virtual reality glasses where a specialists determines the necessary cognitive therapy bases on the outcome.
- Risk class IIb: Considerable risk, such as an app that detects abnormalities in an user's heartbeat to inform a physician.
- Risk class III: Highest risk, for example image analysis intended to perform diagnosis for making treatment decisions in patients with acute stroke.

How does the classification go?
To do the classification, follow step-by-step the classification rules in Annex VIII of the MDR. Similar to the qualification process: document the findings. If more than one classification rule applies to your product, go with the highest classification. More information and visual flow charts are in the European Commission guidance[2].

What effect does the height of the class have?
The biggest consequence of the class is the extent of testing by a notified body in conformity assessment procedure (see Annexes IX to XI). The degree of intensity of the notified body's review affects product certification costs and review turnaround times. Check the following reports to get an idea of this:

- Estimation of the costs: MDR Guide.pdf (fme.nl)[3].
- Review-times in 2022: MedTech Europe Survey Report - MedTech Europe.

In addition, the class affects requirements on the manufacturer regarding clinical trials[4], UDI[5] and post-market surveillance[6].

	Class 1	Class 2a	Class 2b	Class 3

[1] For more guidance, see MDCG 2021-24: Guidance on classification of medical devices.
[2] For more guidance, see MDCG 2021-2 Guidance on classification of medical devices and MDCG 2019-11 Guidance on Qualification and Classification of Software.
[3] See an estimation of the costs page 77 'Table 18 Estimation of resource needs', where the first row is the notified body cost ('Out of pocket cost'). Note that this is a general estimate and may vary for your product development.
[4] Art. 61 to 63 and Annex XV MDR.
[5] Art. 27 MDR.
[6] Art. 85 and 86 MDR.

NB conformity assessment	No, the manufacturers notifies the device via EUDAMED or CIBG /Farmatec NOTIS[7]	Yes, conformity assessment by reviewing the technical documentation	Yes, extensive conformity assessment	Ja, thorough conformity assessment including clinical evaluation
NB review times 2022 (see MedTech Europe Survey Report - MedTech Europe)	If applicable, average between 6 and 18 months	On average between 6 and 18 months	On average between 10 and 19 months	On average between 13 and 24 months
Clinical investigation in clinical evaluation	Clinical evaluation plan	Clinical evaluation plan	Clinical evaluation plan (clinical investigation required for implants)	Clinical evaluation plan with additional requirement of clinical investigation
UDI	Transition period after MDR			Mandatory from start MDR
Post market surveillance	Post market surveillance plan	Post market surveillance plan with periodic safety report to NB 1x/2 years	Post market surveillance plan with periodic safety report to NB 1x/2 years	Post market surveillance plan with periodic safety report to NB 1x/year

[7] See for the notification: Medical devices and in vitro diagnostic medical devices | Farmatec). Note, device with measurement function, reusable or sterile needs assessment NB of technical file for these parts.

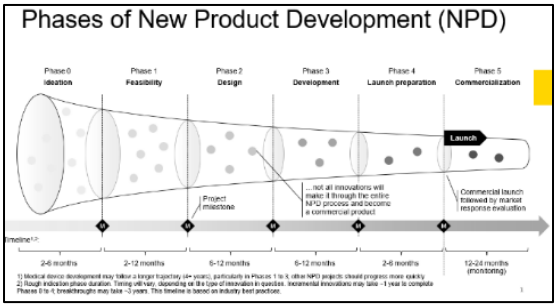
5. Q&A Is there an overview of everything needed?

Introduction

To become or remain competitive, companies must constantly innovate by developing new products. Unfortunately, many development projects fail prematurely, it is important to use a systematic and strategic product development process, to reduce ineffective deployment of resources.

Product development projects have many types of risks. In terms of development time and costs, in terms of technical feasibility, competitive products, obtaining market access (being allowed to place the product on the market), legislations and regulations that the product must comply with and not having the right knowledge and skills in-house.

To limit the risks, it is advisable to phase the development project according to a product development model such as the Phase Gate Process model. Each phase has its own mandatory documents, and each phase has its own go/no go moments.



This Q&A describes high level basic requirements, tips and pitfalls, companies encounter during the development and distribution of a medical device. The operation, advantages, and disadvantages are only explained to a limited extent, including why and how having a strategic development model strengthens the company's quality management system (QMS).

What is needed for the technical documentation?

In accordance with Article 10.4 MDR (EU) 2017-745, the manufacturer of a medical device is obliged to draw up a technical file (TD) and keep it up to date. The content of the TD is described in Annex II and III of the MDR (EU) 2017-745.

Having a fixed format on a network drive, where all the necessary technical documentation can be stored, provides an overview, and helps collect and categorize the information for the Notified Body. Please note that each development phase should have its own folder structure. This ensures that it is easy to find out in which development phase what happened. Note, creating files from scratch, linking requirements and risks, and keeping track of all changes is not an easy task. It is smart to use a 'medical device document management system' to keep track of the required documentation. There are a lot of suppliers that provide this kind of software, you should create a list of requirements/ features that the document management software should offer.

Since the TD and the QMS must be assessed/audited by a Notified Body for most medical device software and it is unlikely that the Notified Body its auditors can speak the Dutch language, you need to draw the required documentation up in the English language.

During an QMS audit, or during product certification, the auditor may require evidence that the development plan has been followed or explain why certain development choices have been made. To prevent documents from being unusable, when they are written in Dutch, it is advisable to draw up all documents, including meeting minutes, in the English language. If

there are operational reasons to have documents available in Dutch, such as assembly instructions, they you can deviate from this rule. However, the test protocols (such as IAT and FAT) will have to be available in English. These are quality records.

What are the design history file and design master records?
In order to get a medical device certified to be placed on the market, the MDR contains documents that the legal manufacturer must provide. To ensure that the TD is complete, and to monitor the progress of writing the TD documents, it is useful to make a checklist of the documents to be delivered, which can then be allocated to a specialist per part. When the checklist is expanded with start and expected end dates, this list can be used as an action list to monitor the progress of documentation.

The TD must be divided into design choices made during the development of prototypes (the design history file) and the technical data of the end product (design master record). Having a Phase Gate Process model makes the control and construction sequence of these files a lot easier. When it has been demonstrated that the product idea is both economically and technically feasible, which has been demonstrated in phases 0 and 1, the development documents that are generated in phases 2 and 3 are the documents that will be placed in the design history file.

At the end of each product development phase, an evaluation should be made about the progress of the project. The findings are described and report, after sharing with the steering committee, is added to the project file. The lessons learned should be addressed in the QMS (as part of continuous improvement).

Checklist deliverables Medical Devices - New Product Development

Note, this checklist describes the documents needed for product market approval and excludes documents and procedures required for the C

Phase	Medical device	A/NA	13485 Norm reference	Statu
Phase 0 Ideation	**Phase 0 one-pagers:**			
	o Concept one-pager (incl. jobs-to-be-done, ideas shortlist)		6.1	
	o Planning one-pager (incl. consequenses for ZiuZ (complexity, resourses, regulatorial, marketability))		6,1	
	o Planning one-pager		6.2	
	Phase 0 project evaluation summary		8.2.5, 8.2.6	
	Key questions defined for Phase 1			
	Stakeholder input:			
	o Customer & user input (User Requirement Specification)		7.2, 7.2.1, 7.2.2, 7.3.3	
	o Maintenance & Support input		7.5.9, 7.5.10, 7.5.11	
	o Shareholder input		7.2.1, 7.3.3	
	Technical feasibility:			
	o Assessment of alternatives (concepts, solutions, technologies)		7.3.5	
	o Proof-of-concept/ demonstrator(s)		7.3.4, 7.3.5, 7.3.6, 7.3.7	
	o Proof-of-concept evaluation report		7.3.7, 7.3.9	
	Business intelligence:			
	o Business case		6.1	
	o Assessment of competitive landscape (incl. substitutes and interesting markets)		7.3	
	o Identify key opinion leaders		7.2.1	
	Quality management:			
	o Quality and Regulatory plan (country/ continent specific)		7.2.1	
	o Requirement Specification		7.2.1	
se 1 bility	o Essential requirement matrix		7.2.1	
	o List of applicable standards		7.2.1	

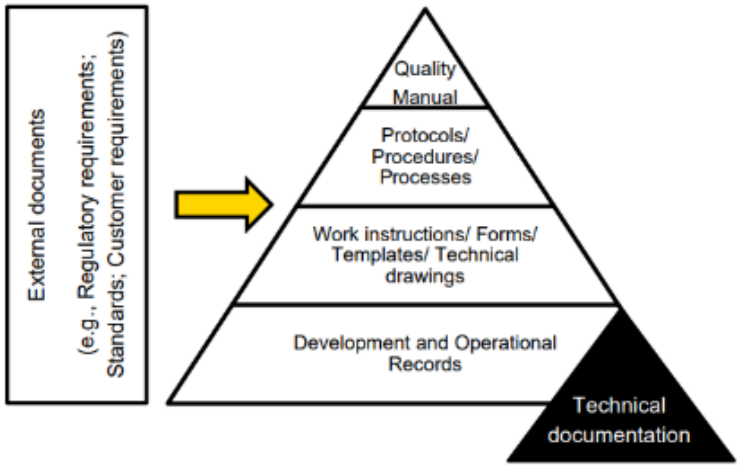
At the end of phase 3 is the 'Design Transfer' takes place[1]. The product is production ready meaning that all technical drawings are available, the bill of materials has been drawn up, the safety critical components have been identified and the device has been verified and validated[2]. The documents required for the production of the first production series are placed in the design master record. Note, all technical documents that are drawn up from this point are placed in the design master record. The contents of the design history file and design master record, which will be described later.

[1] ISO13485:2016 (7.3.8)
[2] ISO13485:2016 (7.3.5, 7.3.6)

Having a phase-out model to stop technical support of the device is an important part of the quality management process, especially since mandatory post-market surveillance can be organized through this model (timelines, frequency, and reporting (periodic safety update reporting (PSUR)).

The safety critical components, as listed in the TD, (provided and approved by the Notified Body), require periodic checks, to determine if the datasheets are still the latest versions, and the approval marks are still valid. Note, it is not allowed to change the safety critical components without the approval of the Notified Body.

What is needed for a quality management system?
The development of a medical device must follow a demonstrably assured process. Having a Quality Management System (QMS) in place is mandatory and is audited by the Notified Body. The legal manufacturer of a medical device draws up, for each product that will be developed and for each market that product will be placed on the market, a quality- and regulatory plan. In this plan the quality management methodology must be described. The choice must be made whether the QMS will be certified according to the international ISO13485:2015 standard, or whether it will be chosen not to have the QMS certified, but to have the Notified Body assess the QMS during the product certification. Do make sure that the QMS has a document-based structure, since you will need to be able to demonstrate the interaction between the processes and on what basis your QMS is founded. Quality records will provide evidence that the quality policy is followed.



Do I need QMS certification?
QMS certification has the advantage that only one audit needs to be carried out for the CE certification of the medical device. If the manufacturer of the medical device wants to bring multiple variants or different products to the market, ISO13485 certification is more (costs) efficient. If the product of a medical device is a one-off activity, the manufacturer can choose to set up the QMS in accordance with the ISO13485 standard, but not to have it certified. During the product certification process, two audits (stages 1 and 2) will be carried out by the Notified Body to assess the QMS. For an ISO13485 certified product, this will be one audit.

The biggest risk of not certifying is the time lost if it turns out that the QMS does not meet the requirements. Implementing an improvement plan (corrective action plan) to ensure a major non-conformity is effective, measurable, and verifiable can take several months. As a result, the marketing plan (phase 4 and 5) cannot be implemented.

6. Q&A Where to start?

Introduction
An important starting point within the development project is the business case. Depending on the business activities, the scope of the quality management system (QMS) is determined (by the Quality Assurance Manager). Both the QMS and product development must have a risk-based control mechanism. With that, work processes for the QMS can be made.

Where to think about for the business case?
What will the (total) product development cost, the product its cost price, when and on which market can and do I want to bring the device? Who are my customers and how much and at what price am I going to sell my product? When the business case is (sufficiently) positive, the product can be further developed. The business case requires to be updated at the end of phase 1, 2 and 3. The main purpose of the business case is to rationalize whether the deployment of resources is justified.

Are there important factors to keep in mind for defining the scope of the QMS?
When the development process is fully outsourced, or when the production of the medical device is outsourced, the QMS does not have to comply with this process-wise and standard elements of, for example, ISO13485:2016 can be declared inapplicable in the quality manual. This makes implementing and maintaining the quality management system more manageable, but an effective supplier management system must be in place (see ISO13485:2016, §7.4). If the activities are eventually brought in-house, the scope of the quality management system can be expanded in consultation with the Notified Body.

Please note, when the business is legally divided into entities, then all subsidiaries must be brought within the scope / use the same QMS. Example the dHealth Holding B.V. has the entities dHealth Medical B.V., dHealth Research B.V.. and dHealh Manufacturing B.V.. In this example, dHealth Medical B.V. is the legal manufacturer of the Medical Device, dHealth Research B.V. is the developer and dHealth Manufacturing B.V. takes care of the production of the Medical Device. This means that dHealth Research and dHealth Manufacturing become suppliers of dHealth Medical. As part of supplier management, dHealth Medical will have to make written agreements and assess/ audit its ‘suppliers' QMS on a regular base (e.g., once a year).

How to start with a risk-based control mechanism?
A distinction can be made between business risks such as the risk of production disruptions and product risks that can affect the patient or user.

To assess product risks, it is advisable to use the methodology as described in ISO14971:2019. Multiply the probability that the hazard will occur by the probability of damage upon occurrence by the damage caused by the hazard upon occurrence, see the tables in the presentation for how this is calculated.

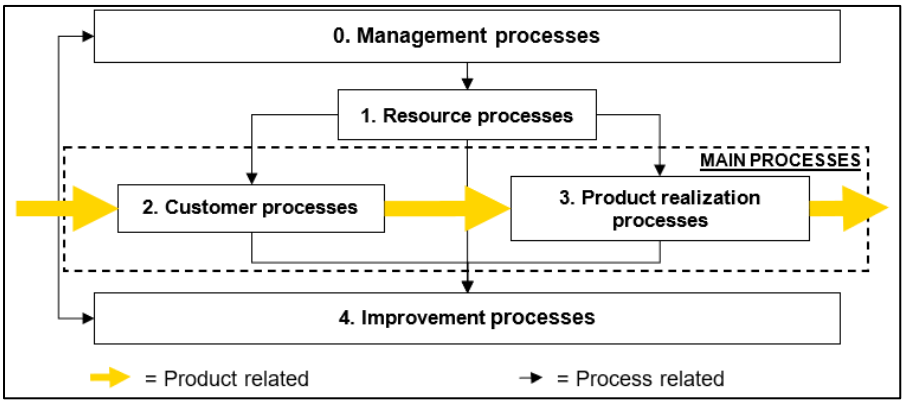
For the business risks, you can make an inventory of the operational risks, and these are easily estimated via probability estimation multiplied by the impact estimation (on a Likert scale). It is advisable to divide business risks into categories. This so that you get an overall picture of the risk areas and get more certainty of completeness. Examples of risk areas are the risk of: Management and reputational damage, financial damage such as: liability, fraud, costs or profit loss, physical damage such as health, safety or productivity and damage caused by non-compliance with laws and regulations. The multiplication shows the risk class. The amount of

risk mitigating measures to be taken depends on the level of risk and the effectiveness of the mitigation.

What is good to keep in mind for the work processes?
A risk based QMS (both product and business risks) has the advantage that not all work processes need to be described in detail, usually a flowchart is sufficient to describe the process. Policy documents or protocols are written out, but no more than necessary in terms of textual description. High risk mitigation usually requires a protocol or procedure that describes the boundaries and actions that need to be taken within the company policy.

When an Enterprise Resource Planning (ERP) system is used that enforces order of action and completeness, it is not necessary to turn all work activities into process flows, for example the creation of a purchase order. Exception applies to processes in which several colleagues / departments are involved, so when a purchase order needs approval or needs to be transferred to another department, it is necessary to describe a process of this.
Internal auditing is also made easier by risk assessment, depending on the risk, processes are audited / revised annually, biennially, triennially, or quadrennially. Only the high-risk processes are reassessed annually.

The work processes should be categorized into management processes, resource processes, customer processes, product realization processes and improvement processes, (chapter 4, 5, 6, 7 and 8 of the ISO13485:2016 standard). This will provide to structure to your QMS. A QMS that complies with the requirements for medical device development and production will include a large amount of work processes. Having a structure provides an overview of the available processes and demonstrates completeness.



For each work process, make a reference to the standard (9001 or 13485). Multiple standard paragraphs can apply to one process flow. Depending on the program used for process management, an analysis can then be made of the set-up business processes and this helps with the external audit, since the auditor of the Notified Body can specifically ask questions about certain standard elements.

If your QMS database allows you to create reports, then adding references to work processes will allow you to create a report that you can use to verify if all the required processes are there and will allow you to easily create an overview that you can use during audits.

7Q&A What happens after starting?

Introduction

Most mandatory documents can only be finalized at the end of the development project. However, it is not wise to draw up all documents at the end of the development project. As a result, not only is a lot of time lost – after all, the product is ready, but cannot yet be sent to the Notified Body for assessment – the development process has also not demonstrably proceeded according to a development plan. Writing a (software) development plan, after the test reports (Validation and Verification) are already available, can cause problems with product certification, especially when dates are overlapping, and signatures are missing. In addition, a lot of ready knowledge is lost when planned and unplanned events are not immediately recorded.

It is wise to start drawing up a technical documentation (TD) from development phase 0, how this is possible and which documents must be drawn up per phase, depends on the product that is being made, but should include the Quality and Regulatory plan (including the regulatory requirements), the soft- and hardware design plan, a general product description and the validation and verification plan. The checklist should include, for each phase, which documents must be present before the decision can be made to proceed to the next phase. These are documents that must all be added to the TD and are of such quality that they can be offered to a Notified Body (so no drafts).

In product development phase 4, the product, including the device master record, will be offered to the Notified Body.

What to expect from maintaining and auditing the QMS?

Maintaining product development and the QMS requires a high time/resource investment. To keep this manageable, it is advisable to carefully check which documents/processes are required and which documents are 'nice to have'. The fact that documents are not necessary does not mean that it has no added value to draw them up. An example of this is the IEC62304:2006 standard. This standard applies to software used in or as a medical device. The standard describes how to classify the software. The software class then determines which documents need to be drawn up. E.g., for software that has been categorized as class A then it is not required to create a document that describes the architectural design. Creating such a document could be beneficial (nice to have) for customers, technical support or to be reused in other products.

Clause	Software documentation	Class A	Class B	Class C
5.1	Software development planning	X	X	X
5.2	Software requirements analysis	X	X	X
5.3	Software architectural design		X	X
5.4	Software detailed design			X
5.5	Software unit implementation	X	X	X
5.5	Software unit verification		X	X
5.6	Software integration and integration testing		X	X
5.7	Software system testing	X	X	X
5.8	Software release	X	X	X

The work processes within the QMS must be audited according to an audit calendar. It is impossible to audit all protocol processes individually. This can also be done with conducting department audits. The department manager is audited on part of the work processes and one audit report is written. The following year you select other work processes for the audit, so all processes are covered, without a department having to do several audits per year.

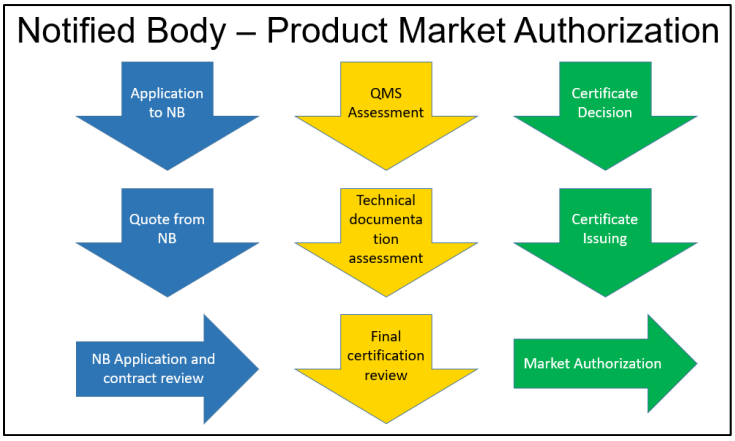
- Management
- Human Resource Management
- Development – Software en hardware
- Supply Chain Management
- Production processes
- Maintenance & Support

The management review can be used to audit the management processes. During the management review, the risk mitigating measures, the status of the QMS and the possibilities for improvement are discussed. Where the members of the management can indicate which processes need to be adjusted. If it turns out that a process is not going correctly, a non-conformity can be created.

In addition to checking whether production documents are created, the workflow processes have been followed, and key performance Indicators are achieved, department audits provide a (reasonably) conclusive picture of the quality and compliance of the work processes and the audits are carried out efficiently and effectively.

8. Q&A How much time and money does this whole story cost?

When the technical documentation (TD) contains all mandatory documents and the QMS meets the requirements, the medical device can be offered for CE certification to the Notified Body.

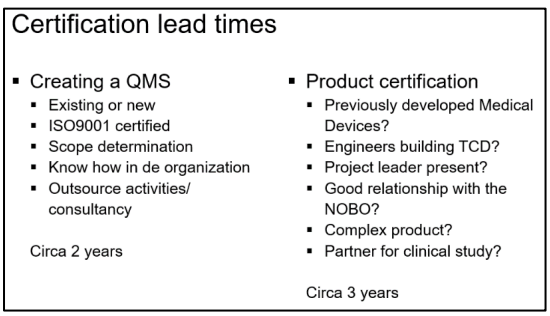


Unfortunately, applying for a CE certification has a very long lead time. It starts with contacting a Notified Body that is allowed to certify the type of medical device and the class. The Notified Body does not have to be located in the Netherlands. In terms of lead time, it may be advisable to check outside the Netherlands whether there is a Notified Body that can indicate in advance what the lead times are.

Please note, a Notified Body must assess product safety and electromagnetic compatibility (EMC). However, this does not have to be the same Notified Body as the CE certification body. Also pay close attention to the marketing communications. It is not allowed to advertise or make claims for products that do not yet have market access. The Notified Body checks this.

Depending on the maturity of the organization and whether an existing QMS can be used, such as an ISO9001:2015 certified QMS which can be supplemented with a QMS suitable for developing a medical device and the availability of a quality department that can set up the necessary work processes, it will take an average organization about two years (1 FTE) to build the necessary QMS.

The speed that determines when a medical device can be brought to market depends on many factors. Overall, this will take three to six years of lead time. This also depends on the product class[1].



[1] For more information, see MedTech Europe Survey Report - MedTech Europe (page 8) and MDR Guide.pdf (fme.nl) (table 18, page 77)

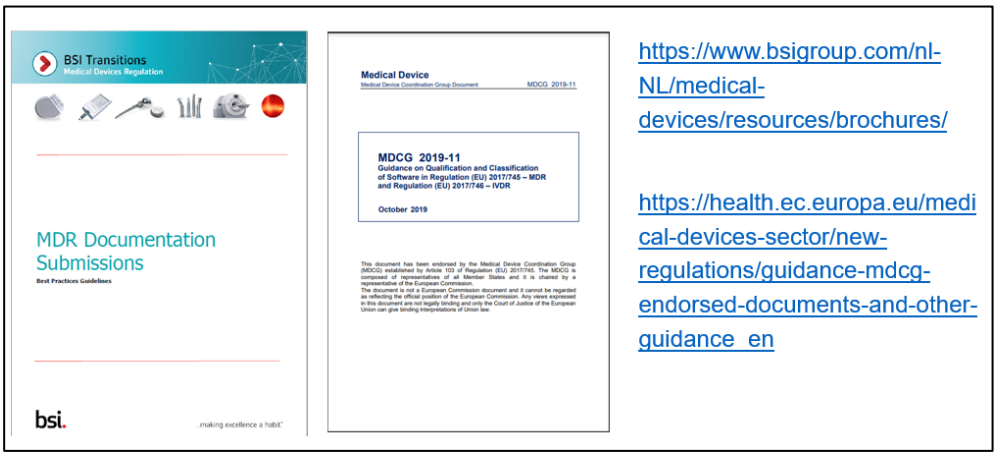
9. Q&A How can I build up knowledge?

Introduction

Like any product placed on the market, medical devices must also comply with laws and regulations. It can be quite difficult to find out exactly which laws and regulations the product must comply with. Unfortunately, the Notified Body is not going to help you with this either. You have to do your own research into the legislation that applies. In this Q&A you can find information about building up knowledge internally. For finding help from external partners see [reference to Q&A Where can I find help?].

Where to find more information?

On the internet there is a lot of information about setting up a quality management system, drawing up the technical documentation or interpreting other legal requirements. There are also templates that can be used to create these documents. In particular, guidance documents provided by Notified Bodies or the European Commission contain useful information to help understand the legislation (Guidance - MDCG endorsed documents and other guidance (europa.eu)). Do note that a lot of information is generalized, since the requirements have been drawn up for a very wide range of Medical Devices. It does give direction to how to comply with the MDR, the QMS or the TCD and how to set this up.



https://www.bsigroup.com/nl-NL/medical-devices/resources/brochures/

https://health.ec.europa.eu/medical-devices-sector/new-regulations/guidance-mdcg-endorsed-documents-and-other-guidance_en

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Where to find education?

Following a training on standards can be a helpful method to get you started on the topic. Think about ISO13485, ISO27001 (for example by the Nederlandse Normalisatie Instituut, NEN), IEC60601 and IEC62304.

Where to find events?

Events organized to inform about the MDR exist at regional (by e.g. d-Health, HTRIC, Life Cooperative), national (for e.g. the NEN, professional groups such as BMTZ) and European level (by e.g. MedTech Europe, RASP). Below are two immediate tips:

- Watch the records of DASH Sparkle Event: Software as a Medical Device - YouTube
- Sign up for the newsletter and events of the official professional group of QA and QA called RAPS (Regulatory Affairs Professionals Society) the Dutch section. You can subscribe via rachapternedvl@gmail.com.

10. Q&A Where can I find help?

Introduction
There are many tasks that must be performed to comply with the MDR before a medical device can be placed on the market or put into service. A non-exhaustive list of these tasks include: starting with qualification and classification, identifying standards and recording evidence, establishing and maintaining contact with the Notified Body (if needed), building and monitoring a quality management system, risk management, clinical evaluation, creating a technical dossier, convincing auditors during audits and setting up and performing post-market surveillance including timely reporting to notified bodies after market authorization. Experience and knowledge is useful for all these tasks. See also [reference to Q&A How can I build up knowledge?].

Should I contact partners?
As a start-up in the medtech sector or when instructing an existing company in the medical industry, it is useful to build a trusted relationship with other companies regarding the MDR so that knowledge and experience can be shared. This is best done with companies in the same phase as you and with companies ahead of you with a product that is similar to your product in terms of risk class and technical area (for example, when developing a wearable, look for a company that is also developing a product with a hardware and software component in the same risk class). In addition, you can be of service to each other by doing test audits for each other.

Where do I find consultant and what do I look for?
Manufacturers who are introducing themselves to the MDR would do themselves a favor having a quality manager internally in the company. The extent of this task, depends on the extent of the requirements the MDR places on the manufacturer in question. Factors that influence this include the level of risk class, complexity of the technique, degree of clinical novelty of the product and the manager's experience. It may well be that the manager will eventually employ a Quality Assurance (QA) & Regulatory Assurance (QA) team.

Internal staff will need to be trained to meet MDR requirements. To relieve the workload, "fly in" missing expertise and/or increase speed to market, help from external consultants can be beneficial. The trick is to ensure a good balance between the knowledge and skills of your own staff and external help. When hiring help externally, think carefully about the scope of the question and which consultant would be able to help out. Our advice is to ask several consultants who fit your needs, rather than trying to find one who (in their own words) specializes in everything. Examples of different types of experts with an indication of which part of MDR compliance they could help with:

- Expert regulatory assurance - Help with qualification, classification and exclusion of ambiguities in the interpretation of MDR requirements or the relationship with other legislation.
- Expert quality assurance - Help with quality management (note: sub-expertise of consultants is likely, such as identifying standards and recording evidence according to Annex I, setting up risk management, creating technical dossier, setting up PMS).
- QMS consultant - Assistance in setting up QMS, such as ISO 13485.
- Clinical evaluator - Assistance in performing clinical evaluation, and guidance at each step of clinical research (note that there are requirements for this person, see MDR Article 61).
- Contract research organization - company that provides support in the form of research services outsourced on a contract basis.

- Full service - Full assistance or even take over manufacturer responsibility (note the dependency that arises).

If the product will also (eventually) be marketed outside the European Economic Area (EU + Norway, Iceland, and Lichtenstein), it is advisable to include the additional legal requirements in the requirements/the quality and regulatory plan.

Finding a good consultant can be tricky: they are scarce, busy, may have vendor lock-in, have varying degrees of experience, high hourly rates and/or may just bring other expertise than you require. Contact dHealth if you'd like to spar about which consultant is right for you; we may be able to suggest a good match.

11. Q&A How do I approach clinical evaluation including contact with hospitals?

Introduction
A clinical evaluation provides clinical evidence that the medical device performs as claimed by the manufacturer and that it is safe to be used in clinical setting. Sometimes, especially when clinical investigation is needed, the clinical evaluation requires collaboration with healthcare institutions.

What does clinical evaluation entail?
What a clinical evaluation entails is recorded in Article 61 of the MDR. Three components are required in the evaluation:

1. assessment of clinical performance and safety of the device using relevant scientific literature;
2. available data from clinical studies already conducted; and
3. available alternative treatment options for the intended purpose.

Clinical investigations are required only for Class IIB and Class III; for the other classes, they are not required by law, if the manufacturer provided sufficient evidence based on other sources. For more novel techniques, however, clinical trials may be necessary because there is less chance of existing clinical trials. For clinical investigations with a medical devices the MDR directly refers to Good Clinical Practice (GCP) according to ISO. So, it is highly recommendable to use this standard to comply with the MDR's requirements for clinical investigations.

Any investigation of a medical device according to an article under the MDR must be authorized by the government (State Members). In the Netherlands, supervision is carried out by the Centrale Commissie Mensgebonden Onderzoek (CCMO) and permission must be obtained from medical ethics review committees (METc's). What the requirements are for submission to a METc (standard research file) depends on the MDR article that's applicable[1].

Note that hospitals may have their own requirements for the trial separate from the METc. With in-house development, this approval is usually obtained before the METc review; with an external manufacturer for clinical trials, it is the other way around.

Good to realize is that an investigation with a medical device can have two different goals: to be part of a Clinical Evaluation Plan (CEP) according to the MDR or to add scientific value by publishing in journals. A study can have both goals, but it does not have to. To gather evidence under the MDR, you don't necessarily have to publish, but you do have to comply with the MDR.

How do I contact a healthcare institution?
Even if a new medical device is fantastic, this does not mean that all hospitals will want to collaborate with the manufacturer immediately. More is needed for a good collaboration, such as: the research must fit within the hospital's vision and mission, future plans and availability of a relevant research group.

Through a central coordinating point within healthcare institutions, manufacturers have the greatest chance of finding a collaboration that bears fruit. Conferences offer opportunities to engage directly with healthcare organizations. If you already have a contact lead, it is still recommended to contact a central point for efficient affiliation with the organization. UMCs (and possibly top clinical hospitals) may additionally be able to help with drafting research contracts,

[1] For information Standard research file medical devices | Investigators | The Central Committee on Research Involving Human Subjects (ccmo.nl)

referral to technical entry approvals and other internal approvals, joint finding of grants and other resources needed to realize development/innovation.
Here are some hints stated for central coordinating points for innovation within hospitals:

- UMC Groningen: Innovation Center (umcgresearch.org).
- Martiniziekenhuis Groningen: MartiniLab (martiniziekenhuis.nl)
- ISALA Zwolle: ISALA Innovatieloket
- Medisch Centrum Leeuwarden: MCL Academie
- Other UMCs and (top clinical) healthcare institutions can usually also be contacted at a central point: search the internet for “the name of the healthcare institution” and "innovation”.

12. Q&A What does contact with a Notified Body look like?

Introduction
Before a manufacturer can place a medical device on the European Economic Area ("EEA") market or put the medical device into service, a conformity assessment must be performed with a positive result. Depending on the applicable conformity assessment procedure, a designated Notified Body must be involved in this procedure. Please note that putting medical devices on markets outside the EEA requires compliance with local medical device laws which are not subject to this Q&A.

List of Notified Bodies
In the Nando database of Notified Bodies on the website of the European Commission, one can find a list of certified Notified Bodies in the EU. In the Netherlands there are three Notified Bodies: DEKRA Certification, Kiwa Dare and BSI Group The Netherlands. However, please note that, even if you are located in the Netherlands, you can contact a Notified Body in another Member State without this having effect on the validity or scope of the declaration of conformity you hope to receive. That being said, not all Notified Bodies are accredited for all types of medical devices.

When to contact a Notified Body?
It is advisable not to wait too long before contacting a Notified Body. The waiting times for Notified Body services is, since the introduction of the MDR, notoriously long, partially because Notified Bodies themselves had to recertify under the MDR. Even though a Notified Body is not allowed to provide you with advise on your conformity assessment, it is very helpful to discuss your planning with them as soon as possible so you can make sure the Notified Body has sufficient recourses at the time you need their services.

How to contact a Notified Body?
A Notified Body can usually be contacted as you would contact any service provider, though their website, by e-mail or by phone. If you have hired a consultant to help you with the conformity assessment procedure, they may have contacts within a Notified Body already. However, please note that having contacts within a Notified Body does not mean you will be helped earlier. In addition, even though your consultant could have established contacts within a Notified Body already, another Notified Body might be a better fit for your company.

What does the process with a Notified Body typically look like?
Generally, the process looks as follows:

1. Getting a spot on the Notified Body's waiting list.
2. Formal application to Notified Body: Submitting your product certification requirements and a part of your technical file.
3. Receive Notified Body's proposal: This proposal will form the basis of the contractual agreement with the Notified Body.
4. Get a team and timeslot assigned after acceptance of the proposal.
5. Assessment of technical documentation and QMS: During the review, the Notified Body will inspect the manufacturing site and audit the Quality Management System.
6. Certification decision: Once the review of the technical documentation has been completed, all questions raised by the Notified Body reviewers have been answered, the factory inspection has been completed and the Quality Management System has been reviewed, the Notified body will, if positive, issue a certificate of conformity.

For the exact conformity process, you can ask for information to the Notified Body in question.

13 Q&A. What do I have to think about after the device hits the market?

Introduction
Congratulations, you are marketing your device! You have successfully followed the MDR conformity assessment procedure, affixed the CE mark and are now in compliance with the MDR. There are, however, a lot of things to keep in mind when marketing a product. Some following from the MDR, others from other legislation. Do keep in mind that most rules also apply/are relevant in the pre-marketing phase.

What are the requirements of post-market surveillance according to the MDR?
According to the MDR, manufacturers are required to maintain a comprehensive post-market surveillance system, collecting and analysing data on the quality, performance, and safety of the device.[1] This involves activities such as vigilance reporting, i.e., reporting serious incidents and field safety corrective actions, periodic safety update reports, and post-market clinical follow-ups.[2] The MDR also emphasizes the importance of taking corrective actions if necessary, to protect the health and safety of patients and users. This may include device modifications, recalls, or even withdrawals from the market.

Is advertising for a medical device permitted?
Advertising can be a crucial aspect of getting the device to the relevant user. Advertising is, however, regulated. In the European Union the MDR provides rules on certain device-related claims.[3] For instance with regard to misleading information, the omission of certain risk-related information and the suggestion of uses other than those stated to form part of the intended purpose for which the conformity assessment was carried out. Advertising is further regulated on Member State level. This means that advertising in, for example, Germany could be regulated differently than in the Netherlands. In the Netherlands, medical device advertisement is regulated partially in statutory laws on general advertisement and partially in codes of conduct with regard to general and medical device specific advertisement.

Am I allowed to provide favors to healthcare professionals?
How success rate of any product generally depends on whether its potential users are inclined to use it. This can be achieved by pricing and advertising but also by offering money, services or goods for the purpose of promoting the sale of a medical device to healthcare professionals ("Favors"). Favors can range from paying for services, participation fees for a conference, sponsoring a project, giving a product discount to a birthday present. On EU level, there is no binding regulation on favors. That being said, member of certain associations could bind themselves to codes of conduct such as the Medtech Europe Code of Ethical Business Practice. Favors are, like advertising, regulated on a Member State level. In the Netherlands, for example, favors are strictly regulated in the Dutch Medical Device Act.[4] In addition, the Netherlands knows the 'Code of Conduct for Medical Devices'. The rules on favors in this code are comparable to the rules on favors in the Dutch Medical Devices Act, but are a bit more extensive.

What steps do I need to consider for the pricing and reimbursement of the device?
Healthcare systems and reimbursement processes can vary significantly between EU Member States. Before a medical device can be sold in a particular Member State, it not only needs to comply with the MDR, but it also often needs to go through a separate process to be eligible for reimbursement under that Member State's healthcare system. This typically involves demonstrating the device's cost-effectiveness and clinical benefits. The criteria for

[1] Art. 83(2) MDR.
[2] Art. 83 to 90 MDR.
[3] Art. 7 MDR.
[4] Art. 6 Dutch Medical Device Act.

reimbursement can be highly variable and may depend on factors such as the type of device, the intended patient population, and the specifics of the national healthcare system. In some EU Member States, the price of a medical device may be negotiated as part of the reimbursement process. This can depend on factors such as the perceived value of the device and the prices of comparable products on the market.

In the Netherlands, for example, with regard to reimbursement for the use of medical devices in hospital settings, the following steps must be taken for a medical device manufacturer seeking reimbursement for its device in the Netherlands:

- In-hospital use:
    - Determine if the device falls within an existing Diagnosis Treatment Combination ("DBC") code. A DBC is an instrument in the Netherlands used to calculate and bill for the cost of hospital care. It includes all activities from diagnosis to treatment for a particular condition. If a medical device is part of a procedure that is covered under a DBC, the product can be covered and manufacturer should engage with healthcare providers to promote the adoption of their device and with insurers to negotiate prices.
    - If a device isn't covered under a DBC, the manufacturer may need to submit an application for reimbursement to the Healthcare Institute Netherlands. This body assesses whether a particular treatment (not a single medical device) should be included in the basic health insurance package based on need for treatment, effectiveness of the treatment, cost-effectiveness and feasibility. After the assessment, a new DBC can be created. Hospitals and insurers negotiate prices for DBCs. These prices aren't fixed and can vary between hospitals and insurers.
- For devices for other uses than in-hospital use, for instance those being reimbursed based on the Dutch Health Insurance Order (in Dutch: "*Regeling Zorgverzekeringswet*"), negotiations should be started with health insurers. It is primarily up to the health insurance company to assess whether a (new) medical device qualifies for reimbursement from the basic health insurance package.

How to deal with making changes to the device?

Making changes to the device's function, intended use, essential design and manufacturing characteristics may have serious consequences from a regulatory perspective. A change to or the addition of functionality may lead to the device to be qualified as a medical device (if it was not already) or a revision of the classification of the medical device.

Even minor changes should be documented, including the reason for the change, an assessment of the impact of the change and an outline for a plan for implementation. Major changes can lead to the obligation to perform a new conformity assessment procedure, including having a Notified Body assessing the device and manufacturer again.