

Guideline

Digital Health Regulatory Navigator (EU)

Scope

This guideline is designed to assist in using the **Digital Health Regulatory Navigator (EU)**. It is targeted at **early-stage digital health startups** that are developing **(standalone) software solutions**, offering general guidance on creating a regulatory strategy by navigating through the high-level requirements of **European Union medical device regulations for software**.

This guideline provides general advice for completing each of the nine navigator sections. An **example illustrating how to fill out the navigator** is included in the **appendix**. The navigator is intended for iterative use.

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0. Scope

This navigator is targeted at early-stage digital health startups that are developing (standalone) software solutions, offering guidance on creating a regulatory strategy by navigating through the high-level requirements of European Union medical device regulations for software. The navigator is primarily focused on standalone software (running on general-purpose devices or hardware medical devices that do not need the standalone software to achieve its intended purpose). Complex systems that combine hardware and embedded software are subject to additional and distinct regulatory requirements for medical devices, which are beyond the navigator's scope. Attention: The EU medical device regulations introduce the term Medical Device Software (MDSW), which includes two types of solutions: 1) software with at least one medical purpose that is standalone and 2) software that is intended to drive or influence the use of a hardware medical device while also having at least one own medical purpose (see section 2 for a definition of a medical purpose). As mentioned before, this navigator focuses only on standalone software and helps understand the EU medical device regulatory requirements for what is known as Software as a Medical Device (SaMD). The following gives an overview of key questions that you will answer through the nine steps of the navigator.

1. Intended Purpose <i>For what purpose is your software intended?</i>	2. Medical Device Regulations Qualification <i>Is your software a medical device?</i>	3. Type of Medical Device Regulation <i>Which EU medical device regulation applies?</i>
4. Risk Classification <i>What risk class applies to your software?</i>	5. Evaluation <i>Will you need a premarket clinical study?</i>	6. Regulatory Roadmap <i>What are the next steps to become a medical device?</i>
7. Stakeholders and Costs <i>Which regulatory stakeholders and costs will be involved?</i>	8. Synthesis <i>What are your key learnings from the previous steps?</i>	9. Pivoting <i>Do you plan to adjust your strategy based on previous findings?</i>

1. Intended Purpose

The **intended purpose** is a text written by the digital health startup and states for which usage its solution is intended. The **intended purpose**, as described in the instructions for use or marketing material, determines whether the product falls under **medical device regulations**. This also includes public information and company marketing material, which should be in line with the **intended purpose**. It is best to describe the **intended purpose** in a technical way. For example, it is better to write that the device performs a specific therapy instead of stating that the device cures the patient. All fields of the **intended purpose** section make up the **intended purpose**. Keep the intended purpose concise, ensuring it is neither too broad nor too specific so it remains relevant even if the device changes. Adjusting the intended purpose after market launch can be expensive, but it may occasionally be a strategic decision.

Start by filling out each step of the section and finally create a summary of an **intended purpose** in no more than three sentences.

1.1 Main Purpose and Claims

Describe the main purpose of your solutions and consider whether it serves a **medical purpose** (providing information, alone or in combination, to: treat, diagnose, predict, prevent, monitor, or alleviate a disease, injury, or disability; investigate an anatomy, a physiological or pathological process or state; or providing information by means of in vitro examination). Medical device regulations must be considered if the device serves a medical purpose (see Section 2 Medical Device Regulations Qualification).

Furthermore, include statements about **claims** (e.g., the device reduces symptoms as a clinical benefit claim) and disclaimers (e.g., the device does not replace medical treatment) concerning the performance of the software device, the clinical benefits, and the non-clinical benefits. These claims can later be used to market the product. Attention: You must provide evidence for the clinical benefits you claim. Please refer to section 5. Evaluation for details.

1.2 Intended Medical Indication

Describe the condition(s) and/or disease(s) addressed by your software. These might be based on ICD codes (International Classification of Diseases codes). These codes refer to a comprehensive list of medical classifications established by the World Health Organization (WHO). These codes are regularly updated through revisions, so it is crucial to refer to the latest version.

1.3 Contraindications

List which conditions prevent safe and efficient use. Which borderline cases exist for which the product should not be used? Under which other circumstances should it not be used?

1.4 Patient Population

Please outline the patient population for whom your software is intended. This group may or may not intersect with the user profile in section 1.5. The patient population primarily encompasses demographic information, while the user profile refers to the skills required for operating the software. If the software is exclusively used by patients, the patient population and the user profile will be similar. If the software is used by physicians or nurses, they should be mentioned under the user profile. Patients indirectly impacted by the software should then be described as the patient population. Typical characteristics that might be mentioned here are age group, gender, health conditions, weight, diseases, ethnic differences, and physical limitations.

1.5 User Profiles and Qualification

Describe the typical user of the software. Users might be patients, doctors, or nurses. If your product has multiple users, list all of them here. The user profile refers to the skills needed to use the software. Some ideas could be: Qualifications, prior training (for your software), technical proficiency, time spent using the software, education, language, language complexity, special relevant skills, and typical tasks. Additionally, the targeted country might be relevant.

1.6 Part of Body

How does the solution come in contact with the patient? This also mainly applies to hardware. Interfaces can be physical (energy, material) or immaterial (signals, information). Describe the body parts the device has contact with or at least the ones it has an impact on.

1.7 Context of Use and Environment

Outline the usual context and environment in which the software is utilized. Specify the types of devices on which the software operates and the number of these devices. Additionally, mention any other software or hardware necessary for your device to function. Typically, applications require users to possess a device with a compatible operating system. Furthermore, you might describe the frequency of use, workload, results to be achieved, place of use, environmental conditions, or visibility. It might be relevant to distinguish mobile or stationary use and the clinical environment (protective gear and sterility).

1.8 Connected Devices and Accessories

If applicable, describe connected devices or accessories that are used together with the device. Some examples of accessories include wearables like smartwatches, other sensors, and tools for installing, calibrating, and maintaining medical devices.

1.9 Operating Principle

Describe the operating principle on a high level. For software, you might state the inputs and outputs. An example could be the processing of images and outputting a diagnosis. Additionally, you could describe typical workflows for using your software.

1.10 Intended Purpose Summary

Provide a summary of the previous fields in no more than three sentences, including the medical purpose, claims, patient population, user profiles, context and environment of use, and the operating principle

2. Medical Device Regulations Qualification

Section 2 is a decision tree based on an official guidance document, MDCG 2019-11, by the Medical Device Coordination Group (MDCG). This expert committee supports the European Commission and Member States in the uniform implementation of medical device regulations. The tree helps to decide whether the software is subject to medical device regulations based on the **intended purpose**. The element of the **intended purpose** that determines whether the software qualifies as a medical device is its medical purpose (see section 1.1). Accordingly, the definition of a medical device (see question 2.5) includes several specific medical purposes. The important question to ask yourself is: Does my software serve one of the medical purposes that are mentioned in the definition of a medical device of the European Union (see question 2.5 definition)? Additionally, the decision tree highlights important questions that are not immediately evident from the medical device definition alone but

are crucial to consider for the software, such as the requirement that individual patients must benefit (see question 2.4).

Software is often paired with sensors from general-purpose consumer electronics or wearable digital products. For more information on the regulatory requirements for software and sensor combinations, refer to MDCG 2023-4. This consideration is important for answering question 3 of the decision tree.

The following points give an overview of what it means to fall under medical device regulations:

- Medical device regulations ensure EU market functionality and set high quality and safety standards
- Falling under these regulations increases time and costs (CE marking for high-risk devices together with a notified body alone costs approx. €30 000 to €100 000)
- Developing medical devices demands a unique business model approach
- Regulated products access the market after proving performance and safety, which can be a competitive advantage and unique selling proposition and often is a prerequisite for reimbursement
- Borderline cases may adjust their strategy (and with that, the **intended purpose**) to avoid or fit within regulations based on their business case, target customers, resources, and market considerations (especially patient apps fall under these borderline cases)
- Unregulated market access is quicker and cheaper
- Medical devices can have modules, with some subject to regulations and others not

In the following, important definitions and examples are given to help answer the questions shown in the decision tree of the navigator.

Question 2.1 Definitions

Input data

Any data provided to software in order to obtain output data after computation of this data can be considered as input data. Input data examples (non-exhaustive):

- Data given through the use of a human data-input device such as a keyboard, mouse, stylus, or touch screen;
- Data given through speech recognition;
- Digital document: formatted for general purpose such as Word file or pdf file or jpeg image, formatted for medical purpose such as DICOM file or ECG records or Electronic Health Record, unformatted document. Note that digital documents have to be differentiated from software able to read such documents;
- Data received from/transmitted by devices.

[MDCG 2019-11]

Output Data

Any data produced by a software can be considered as an output data. Output data examples (nonexhaustive):

- Screen display data (such as layout with number, characters, picture, graphics, etc.);
- Print data (such as layout with number, characters, picture, graphics, etc.);
- Audio data;
- Digital document (formatted for a general purpose such as Word file or pdf file or jpeg image, or formatted for medical purpose such as DICOM file or ECG records or Electronic Health Record, unformatted document).
- Haptic buzzing as an alternative to audio sound

[MDCG 2019-11]

Question 2.2 Definition**Accessory for a medical device**

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).

[Regulation (EU) 2017/745 on medical devices (MDR) Article 2(2)]

Software driving or influencing the use of a (hardware) medical device

Software which is intended to drive or influence the use of a (hardware) medical device.

Additionally, this type of software can, but must not, have or perform a medical purpose on its own or create information on its own for one or more of the medical purposes described in the definition of a medical device or an in vitro diagnostic medical device. This software can, but is not limited to: (a) operate, modify the state of, or control the device either through an interface (e.g., software, hardware) or via the operator of this device (b) or supply output-related to the (hardware) functioning of that device.

[adapted for this navigator from MDCG 2019-11]

Question 2.3 Example

Example: Software which alters the representation of data for a medical purpose would qualify as a medical device software (e.g. "searching image for findings that support a clinical hypothesis as to the diagnosis or evolution of therapy" or "software which locally amplifies the contrast of the finding on an image display so that it serves as a decision support or suggests an action to be taken by the user"). However, altering the representation of data for embellishment/cosmetic or compatibility purposes does not readily qualify the software as medical device software.

[MDCG 2019-11]

Question 2.4 Example

Software examples not considered as being for the benefit of individual patients: Those which are intended only to aggregate population data, provide generic diagnostic or treatment pathways (not directed to individual patients), scientific literature, medical atlases, models and templates as well as software intended only for epidemiological studies or registers.

[MDCG 2019-11]

Question 2.5 Definition**Medical Device**

'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) and of those referred to in the first paragraph of this point.

[MDCG 2019-11]

3. Type of Medical Device Regulations

Section 3 is a similar decision tree to the previous section and is also based on MDCG 2019-11. There are two types of medical device regulations in the European Union: The **Regulation (EU) 2017/745 on medical devices (MDR)** and the **Regulation (EU) 2017/746 on in vitro diagnostic medical devices (IVDR)**. While they share some similarities, they are also different in some aspects. The key differences are:

- The MDR applies to all medical devices for human use, except for medical devices that use biological samples from the human body or information from these samples (like DNA data or microscopic cell images), which are covered by the IVDR
- While both regulations share similarities in their structure, they also exhibit notable differences
- MDR software examples: Software supporting diagnosis through medical images, diagnostic software for scoring depression based inputted mood data, cognitive therapy software that treats depression, software that monitors heart rate and blood pressure
- IVDR software examples: Software to support diagnosis based on genetic data, software providing information on the statistical predisposition for Down syndrome based on various in vitro diagnostic medical device assays

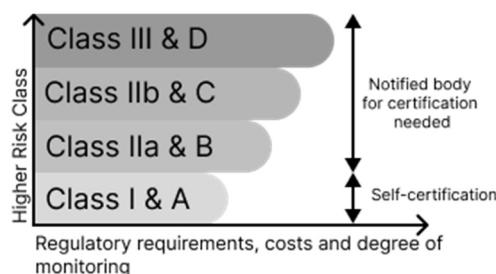
In the following, important definitions and examples are given to help answer the questions shown in the decision tree. The tree helps to decide the applicable type of medical device regulations.

Question 3.1 Definitions
<p>In Vitro Diagnostic (IVD) Medical Device</p> <p>'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:</p> <ul style="list-style-type: none"> - 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; - to predict treatment response or reactions; - to define or monitoring therapeutic measures. <p>Specimen receptacles shall also be deemed to be in vitro diagnostic medical devices. [Regulation (EU) 2017/746 on in vitro diagnostic medical devices (IVDR) Article 2(2)]</p>
<p>In vitro diagnostic (IVD)</p> <p>Experiments or processes conducted outside a living organism using biological materials from the human body, such as cells, tissues, or organs in an artificial environment (test tubes, Petri dishes, and other artificial containers)</p>
<p>Physiological processes and states</p> <p>Bodily and biological functions within an organism's body (e.g., body temperature, heart rate, blood pressure, respiration, senses or reflexes)</p>
<p>Pathological processes and states</p> <p>Abnormal anatomical or physiological conditions such as inflammation, infection, tumors, or neurological disorders (e.g., Alzheimer's disease)</p>

4. Risk Classification

There are different risk classes in the medical device regulations. For the MDR, the risk classes are I, IIa, IIb, and III, and for the IVDR, they are A, B, C, and D. The most important differences between these risk classes are:

- Higher risk class means more requirements according to the regulations
- **All risk classes except Class I and A:** A notified body, which is a private company designated by an EU member state to assess the conformity of medical devices, must be involved in the CE marking (Exception: Subclasses Is, Im, Ir and As also need to involve a notified body)
- Class I and A manufacturers sign their **own** MDR conformity; a state authority only checks the **intended purpose** and risk class without looking into the entire documentation. This means lower costs and faster market entry. Still, the requirements are high for Class I & A



To determine the risk class, 22 MDR and 7 IVDR rules exist, which you find in the appendix of this document or the annexes of the respective regulations. **All rules** must be considered based on the **intended purpose**, and the **highest risk class based on all rules is the final risk class of the product**.

4.1 Medical Device Regulation (MDR) Software Risk Class

For software, MDR Rule 11 often applies, but all other MDR rules should be considered based on the **intended purpose** (all rules see Appendix 2). Rule 11 is depicted in the following because of its importance for standalone software. For further information, see MDCG 2019-11 and MDCG 2021-24.

MDR Rule 11

- a)** Software intended to provide information which is used to take **decisions with diagnosis or therapeutic purposes** is classified as class IIa, except if such decisions have an impact that may cause:
death or an irreversible deterioration of a person's state of health, in which case it is in class III; or a **serious deterioration of a person's state of health** or a surgical intervention, in which case it is classified as class IIb.
- b)** Software intended to monitor physiological processes is classified as class IIa, except if it is intended for monitoring of **vital physiological parameters**, where the nature of variations of those parameters is such that it could result in immediate danger to the patient, in which case it is classified as class IIb.
- c)** All other software is classified as class I.

[Regulation (EU) 2017/745 on medical devices (MDR) Annex VIII Article 6(3)]

Rule 11 Supporting Definition Serious Deterioration in Health

Serious deterioration in the health of the subject, that resulted in any of the following:

- (i) life-threatening illness or injury,
- (ii) permanent impairment of a body structure or a body function,
- (iii) hospitalisation or prolongation of patient hospitalisation,
- (iv) medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function,
- (v) chronic disease

[Regulation (EU) 2017/745 on medical devices (MDR) Article 2(58)]

Rule 11 Supporting Definition Vital Physiological Process

Vital physiological process means a process that is necessary to sustain life, the indicators of which may include any one or more of the following: respiration, heart rate, cerebral function, blood gases, blood pressure, body temperature.

[Global Harmonization Task Force GHTF/SG1/N77:2012]

ONLY if Rule 11 a) applies (**the software is intended to provide information that is used to make decisions with diagnostic or decisions with therapeutic purposes**) then the following table taken from MDCG 2019-11 can be used to classify the product.

Rule 11 a) Decision Table	Significance of information provided		
	High Treat or diagnose	Medium Drives clinical management	Low Informs clinical management
Critical situation or patient condition	Class III	Class IIb	Class IIa
Serious situation or patient	Class IIb	Class IIa	Class IIa
Non-serious situation or patient condition	Class IIa	Class IIa	Class IIa

The following list gives guidance on the most relevant software classification rules and states some examples of MDR software with their respective risk class:

- Rule 11 is most relevant for software, but in some cases, Rule 10 for active medical devices or Rule 22 might apply (see MDCG 2021-24 p. 22/25)
- Software used for contraception or the prevention of the transmission of sexually transmitted diseases is classified as class IIb (Rule 15)
- Software used to control the hardware of a medical device has the same risk class as the medical device
- Little software is Class I: An example of Class I software is aimed at conception. Software with a focus on primary prevention (preventing disease onset) or treating conditions without providing information for therapeutic decisions or diagnosis decisions (for example, because a diagnosis or type of treatment decision has already been made by a healthcare professional) is still at risk of being classified as Class IIa or higher
- Example Class IIa: Software that treats depression through cognitive therapy and a specialist determines the necessary therapy based on the software's output (Rule 11a)
- Example Class IIb: Software intended to analyze a user's heartbeat, detect abnormalities, and guide the physician in the diagnosis (Rule 11a)

- Example Class III: Software intended for the diagnosis of acute stroke through image analysis (Rule 11a)

4.2 In Vitro Diagnostic Medical Device Regulation (IVDR) Software Risk Class

Seven rules must be considered based on the **intended purpose** of in vitro diagnostic software (all rules see Appendix 3). For further information, see MDCG 2020-16.

The following list gives examples of IVDR devices based on their risk class.

- Class A: Includes specimen receptacles and laboratory equipment.
- Class B: Covers IVDs intended for self-testing that pose a lower risk to patients compared to Class C, such as pregnancy test kits, fertility testing instruments, and cholesterol test kits. This class also includes IVDs not governed by other rules.
- Class C: Encompasses devices used to detect infectious agents that do not spread rapidly, as well as those that identify highly dangerous pathogens capable of causing permanent disability if results are inaccurate.
- Class D: Comprises devices specifically designed to identify life-threatening or highly contagious infectious agents that spread easily

5. Evaluation

Execution of **Clinical Evaluations** under MDR and **Performance Evaluations** under IVDR is a mandatory activity to demonstrate the **safety** and **performance** of software by generating sufficient **clinical evidence**. The **clinical evidence** should be sufficient and appropriate in view of the characteristics of the device, clinical risks, and its **intended purpose**. This evaluation is a continuous process conducted throughout the lifecycle of the software. This section is based on MDCG 2020-1.

Clinical Evidence

Clinical data and CLINICAL EVALUATION (MDR) / PERFORMANCE EVALUATION (IVDR) 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.

[MDCG 2020-1]

For software that is considered a medical device (= own medical purpose), the evaluation is performed on three components:

Data on **(1) Valid Clinical Association/Scientific Validity** (Is there a well-founded association between the software's output and the targeted clinical condition? Do you have scientific data for acceptance of the underlying principle of the algorithm?) demonstrates that the software's use is based on sound scientific principles. Evidence can possibly be gathered through a literature search on scientific databases, professional guidelines, state-of-the-art, and proof-of-concept studies. If insufficient evidence is available, data can be collected through a **clinical investigation** under MDR or a **performance study** under IVDR (this can then be combined with evidence collection in **(3) Clinical Performance**).

Evidence on **(2) Technical/Analytical Performance** (Can the software accurately, reliably, and precisely generate the intended output from the input data? Does the software reliably, accurately, and

consistently meet the intended purpose in real-world usage?) is generated through verification and validation as part of software development. Typically, this involves activities like verification and validation tests (unit tests, system tests). The **Technical/Analytical Performance** must be demonstrated through parameters such as accuracy, analytical specificity, measuring interval (range), generalisability, availability, reliability, absence of cybersecurity, human factors engineering and others (see MDCG 2020-1).

Data on **(3) Clinical Performance** (Does the software achieve its intended purpose in the target population and lead to a clinical benefit?) aims to show that clinically relevant outputs, such as **clinical benefits**, can be achieved in line with the **intended purpose**. Clinical data is needed to back up **clinical benefit** claims (see table below for the definition of a clinical benefit), which are specified by a **measurable, patient-specific clinical outcome for an individual**. This data can possibly be found in the scientific literature (this typically applies to less innovative devices) or other sources and must come from equivalent devices (criteria for equivalent devices are strict, and medical device regulations definition for equivalence must be followed; see MDCG 2020-5). Data is not always available for more innovative devices. In these cases, data can be collected through a **clinical investigation** under the MDR or a **performance study** under the IVDR before entering the market (in the navigator, referred to as "premarket clinical study"). Such studies often involve potential users and may take the form of a **cohort study** or, if more extensive clinical evidence is needed, a **randomized controlled trial (RCT)**. It is important to note that these studies can require the approval of local authorities and ethics committees before being executed. In addition, a study execution partner such as a university hospital can be necessary. Attention: Class III devices almost always require a clinical investigation.

If **clinical benefits** are claimed that are **related to patient management or public health** or if the **clinical benefits** are related to a positive impact related to the function (screening, monitoring, diagnosis, or aid to the diagnosis of patients), clinically relevant outputs are achieved through demonstrated **predictable and reliable use and usability**.

The **Clinical Performance** must be demonstrated through parameters such as clinical/diagnostic sensitivity, usability, positive predictive value, confidence intervals, number needed to treat, and others (see MDCG 2020-1).

Clinical Benefit

Article 2 (53) MDR defines CLINICAL BENEFIT as the positive impact of a device on the health of an individual, expressed in the 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; whereas Article 2 (37) IVDR defines CLINICAL BENEFIT as 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.

[MDCG 2020-1]

Examples of measurable, patient-relevant clinical benefit claims

- The symptoms of the disease are reduced
- The wound heals 50% faster
- Reduces pain
- Detects more cancer than without

Examples of clinical benefit claims related to patient management or public health

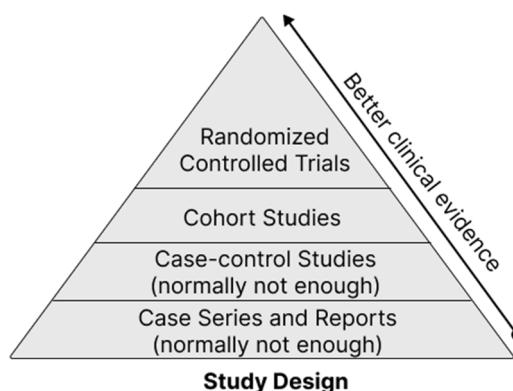
- Support management of diabetes
- Helps to identify patients who benefit from further diagnostic procedures
- Informs physicians on treatment options based on patient data
- It is used for pain and cramps

Examples of non-clinical benefit claims

- Journal function to track changes
- Screening in the hospital is twice as fast

Attention: Some reimbursement pathways, where health insurers cover the costs of digital health solutions, require high-quality evidence for a product to be eligible for reimbursement, or at least it is advantageous to present such evidence to generate trust. As a result, even if medical device regulations don't always mandate extensive evidence, generating it before or after market entry can be beneficial when financial resources permit. However, caution is advised, as Randomized Controlled Trials (RCTs) are often very costly, potentially running into several hundred thousand euros or more. Ultimately, the decision should be guided by country-specific requirements and the intended revenue model.

Collected evidence for the safety and performance of the device needs to be evaluated, a benefit-risk analysis must be conducted, and all results must be documented in a report, which is a mandatory part of the device's technical documentation.



6. Regulatory Roadmap

The regulatory roadmap should include the most important milestones and their estimated dates. Activities like software development and risk management are continuous and should **extend beyond market access** (see Appendix 1 for an example of how to fill out the roadmap). The following points try to give an overview of the most important aspects.

- Medical device regulations require compliance with general safety and performance requirements (GSPR) and recommend following EU-harmonized industry standards (ISO and IEC) and common specifications
- They require the establishment of a Quality Management System (QMS), often based on EN ISO 13485, early on to ensure all necessary activities related to the GSPR are completed
- State-of-the-art practices must be followed: Activities for software development (EN IEC 62304, optionally and additionally IEC 82304), risk management (EN ISO 14971), usability evaluation (EN IEC 62366-1), clinical/performance evaluation, cybersecurity management (IEC 81001-1-5 including related technical reports, e.g., penetration testing) and other essential activities must be documented in the QMS and a technical documentation
- Additional standards are applicable for non-standalone software. This results in a significant amount of additional work

- A user manual for the software must be created
- Product-related activities must be documented in technical documentation. After completion, CE marking through a notified body is required, leading to a market access certificate, which is typically granted months later. Class I and Class A manufacturers self-certify, requiring only high-level state authority involvement, which is much faster and less costly
- Together with the CE marking, the software must be registered in EUDAMED, which is a central database of medical products
- Establishing a QMS and completing documentation can take 2 to 12 months or longer, depending on the manufacturer's efficiency. Audits by notified bodies may add another 3 to 10 months
- Post-market activities are required after market access as per medical device regulations, such as post-market surveillance and incident reporting

Besides the MDR and IVDR, other regulations, such as the General Data Protection Regulation (GDPR) and the Artificial Intelligence Act (AI Act), might apply to your software. Optionally, identify these regulations and include them in your regulatory roadmap. Also, further standards and requirements might be relevant, for example, regarding organizational information security (ISO 27001) for manufacturers aiming to become a digital health application (DiGA) in Germany. These depend on the country-specific regulatory environment. Optionally, identify these additional country-specific requirements and add them to your regulatory roadmap.

7. Stakeholders and Costs

This section includes a **stakeholder map** for compliance with medical device regulations. It is separated into startup internal stakeholders and stakeholders external to the startup. Include key regulatory stakeholders like notified bodies, state authorities, research institutions, regulatory consultants (external), and internal team members like quality managers, risk managers, and the Person Responsible for Regulatory Compliance (PRRC), which is a startup internal person required by the regulations. Also, **regulatory cost** factors should be identified, such as costs for CE-marking with notified bodies (30 000€ to 100 000€, except for Class I and A, which do not require a notified body), regulatory and medical personnel, standards, consulting (up to 50 000€ depending on the intensity), clinical investigations/performance studies, and post-market activities. List these factors in the table with their frequency (one-time, ongoing, as needed) and relative cost magnitude (high, medium, low).

8. Synthesis

The synthesis section aims to help summarize the key insights from previous sections into one concise statement. Therefore, it might be necessary to revisit previous sections.

Afterward, identify the key challenges related to your regulatory and the broader business strategy that you will be facing based on your current findings. These could be specific challenges that you discovered while filling out previous sections or more general ones, such as uncertainty about risk classification, cost of compliance, costs of involving notified bodies, time constraints, or missing expert knowledge.

9. Pivoting

The last section should help you reflect on whether a change to the **intended purpose** and the regulatory strategy might be beneficial. Several types of changes and reasons are listed to support the decision. Besides changing the **intended purpose** or specific strategy elements, it can also be considered to primarily enter a non-European market like North America, where distinct regulations apply. Based on all the information available to you, identify the next steps regarding the **intended purpose**, your regulatory strategy, and the related challenges.

Advantages of falling under medical device regulations	Disadvantages of falling under medical device regulations
<ul style="list-style-type: none"> • CE marking can be a competitive advantage (proves quality and benefits) • CE marking opens revenue streams through reimbursement with health insurers (reimbursement is country-specific) • Clinical benefit claims can be used in marketing and public information 	<ul style="list-style-type: none"> • CE marking is time-consuming, resource-intensive, and expensive • Possibly expensive studies with real users required

Guideline Disclaimer

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The information and interpretations presented in this guide are based on the current understanding of the MDR, IVDR, and MDCG guidance documents. The navigator and this guide are intended for informational purposes only and do not constitute advice. Before using the information, please verify it against official publications. Likewise, interpretations should be confirmed with the relevant authorities before application. The author accepts no liability for any losses, actions, expenses, damages, or other liabilities arising directly or indirectly from using this guide. The content reflects the author's personal views and experiences that were discussed with experts and was created independently. It should not be relied upon as a basis for drawing conclusions.

Appendix 1:

Example

Digital Health

Regulatory

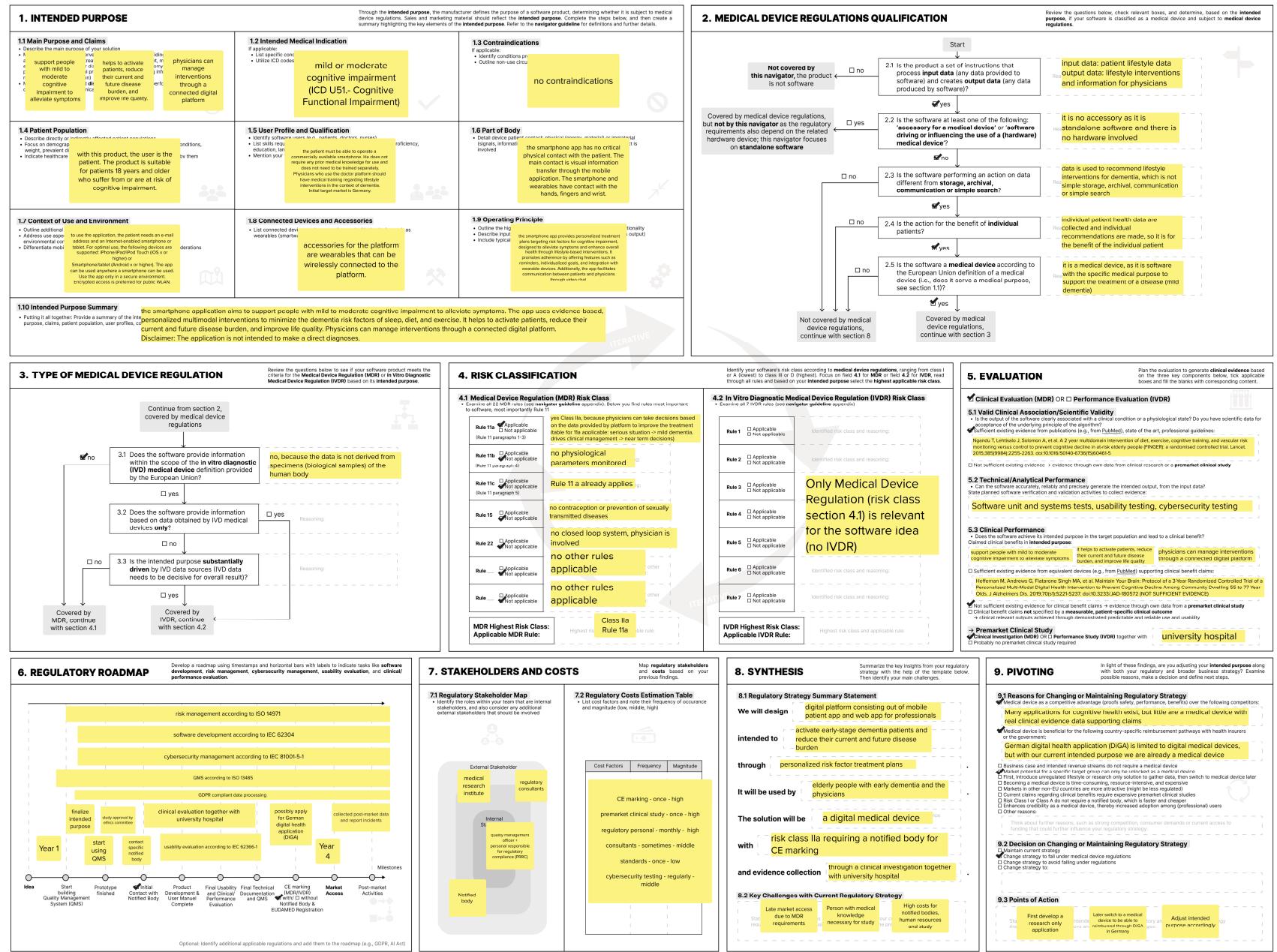
Navigator

(EU)

Digital Health Regulatory Navigator (EU)

Nine steps to assess if your standalone software is subject to medical device regulations of the European Union and to develop a regulatory strategy.

Idea Name	Dementia platform	Date	23/01/2024	Iteration	2
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Appendix 2: Medical Device Regulation Risk Class Rules

CLASSIFICATION RULES (MDR, Annex VIII)

4. NON-INVASIVE DEVICES

4.1. Rule 1

All non-invasive devices are classified as class I, unless one of the rules set out hereinafter applies.

4.2. Rule 2

All non-invasive devices intended for channelling or storing blood, body liquids, cells or tissues, liquids or gases for the purpose of eventual infusion, administration or introduction into the body are classified as class IIa:

- if they may be connected to a class IIa, class IIb or class III active device; or
- if they are intended for use for channelling or storing blood or other body liquids or for storing organs, parts of organs or body cells and tissues, except for blood bags; blood bags are classified as class IIb.

In all other cases, such devices are classified as class I.

4.3. Rule 3

All non-invasive devices intended for modifying the biological or chemical composition of human tissues or cells, blood, other body liquids or other liquids intended for implantation or administration into the body are classified as class IIb, unless the treatment for which the device is used consists of filtration, centrifugation or exchanges of gas, heat, in which case they are classified as class IIa.

All non-invasive devices consisting of a substance or a mixture of substances intended to be used in vitro in direct contact with human cells, tissues or organs taken from the human body or used in vitro with human embryos before their implantation or administration into the body are classified as class III.

4.4. Rule 4

All non-invasive devices which come into contact with injured skin or mucous membrane are classified as:

- class I if they are intended to be used as a mechanical barrier, for compression or for absorption of exudates;
- class IIb if they are intended to be used principally for injuries to skin which have breached the dermis or mucous membrane and can only heal by secondary intent;
- class IIa if they are principally intended to manage the micro-environment of injured skin or mucous membrane; and
- class IIa in all other cases.

This rule applies also to the invasive devices that come into contact with injured mucous membrane.

5. INVASIVE DEVICES

5.1. Rule 5

All invasive devices with respect to body orifices, other than surgically invasive devices, which are not intended for connection to an active device or which are intended for connection to a class I active device are classified as:

- class I if they are intended for transient use;
- class IIa if they are intended for short-term use, except if they are used in the oral cavity as far as the pharynx, in an ear canal up to the ear drum or in the nasal cavity, in which case they are classified as class I; and
- class IIb if they are intended for long-term use, except if they are used in the oral cavity as far as the pharynx, in an ear canal up to the ear drum or in the nasal cavity and are not liable to be absorbed by the mucous membrane, in which case they are classified as class IIa.

All invasive devices with respect to body orifices, other than surgically invasive devices, intended for connection to a class IIa, class IIb or class III active device, are classified as class IIa.

5.2. Rule 6

All surgically invasive devices intended for transient use are classified as class IIa unless they:

- are intended specifically to control, diagnose, monitor or correct a defect of the heart or of the central circulatory system through direct contact with those parts of the body, in which case they are classified as class III;
- are reusable surgical instruments, in which case they are classified as class I;
- are intended specifically for use in direct contact with the heart or central circulatory system or the central nervous system, in which case they are classified as class III;
- are intended to supply energy in the form of ionising radiation in which case they are classified as class IIb;
- have a biological effect or are wholly or mainly absorbed in which case they are classified as class IIb; or
- are intended to administer medicinal products by means of a delivery system, if such administration of a medicinal product is done in a manner that is potentially hazardous taking account of the mode of application, in which case they are classified as class IIb.

5.3. Rule 7

All surgically invasive devices intended for short-term use are classified as class IIa unless they:

- are intended specifically to control, diagnose, monitor or correct a defect of the heart or of the central circulatory system through direct contact with those parts of the body, in which case they are classified as class III;
- are intended specifically for use in direct contact with the heart or central circulatory system or the central nervous system, in which case they are classified as class III;
- are intended to supply energy in the form of ionizing radiation in which case they are classified as class IIb;

- have a biological effect or are wholly or mainly absorbed in which case they are classified as class III;
- are intended to undergo chemical change in the body in which case they are classified as class IIb, except if the devices are placed in the teeth; or
- are intended to administer medicines, in which case they are classified as class IIb.

5.4. Rule 8

All implantable devices and long-term surgically invasive devices are classified as class IIb unless they:

- are intended to be placed in the teeth, in which case they are classified as class IIa;
- are intended to be used in direct contact with the heart, the central circulatory system or the central nervous system, in which case they are classified as class III;
- have a biological effect or are wholly or mainly absorbed, in which case they are classified as class III;
- are intended to undergo chemical change in the body in which case they are classified as class III, except if the devices are placed in the teeth;
- are intended to administer medicinal products, in which case they are classified as class III;
- are active implantable devices or their accessories, in which cases they are classified as class III;
- are breast implants or surgical meshes, in which cases they are classified as class III;
- are total or partial joint replacements, in which case they are classified as class III, with the exception of ancillary components such as screws, wedges, plates and instruments; or
- are spinal disc replacement implants or are implantable devices that come into contact with the spinal column, in which case they are classified as class III with the exception of components such as screws, wedges, plates and instruments.

6. ACTIVE DEVICES

6.1. Rule 9

All active therapeutic devices intended to administer or exchange energy are classified as class IIa unless their characteristics are such that they may administer energy to or exchange energy with the human body in a potentially hazardous way, taking account of the nature, the density and site of application of the energy, in which case they are classified as class IIb.

All active devices intended to control or monitor the performance of active therapeutic class IIb devices, or intended directly to influence the performance of such devices are classified as class IIb.

All active devices intended to emit ionizing radiation for therapeutic purposes, including devices which control or monitor such devices, or which directly influence their performance, are classified as class IIb.

All active devices that are intended for controlling, monitoring or directly influencing the performance of active implantable devices are classified as class III.

6.2. Rule 10

Active devices intended for diagnosis and monitoring are classified as class IIa:

- if they are intended to supply energy which will be absorbed by the human body, except for devices intended to illuminate the patient's body, in the visible spectrum, in which case they are classified as class I;
- if they are intended to image in vivo distribution of radiopharmaceuticals; or
- if they are intended to allow direct diagnosis or monitoring of vital physiological processes, unless they are specifically intended for monitoring of vital physiological parameters and the nature of variations of those parameters is such that it could result in immediate danger to the patient, for instance variations in cardiac performance, respiration, activity of the central nervous system, or they are intended for diagnosis in clinical situations where the patient is in immediate danger, in which cases they are classified as class IIb.

Active devices intended to emit ionizing radiation and intended for diagnostic or therapeutic radiology, including interventional radiology devices and devices which control or monitor such devices, or which directly influence their performance, are classified as class IIb.

6.3. Rule 11

Software intended to provide information which is used to take decisions with diagnosis or therapeutic purposes is classified as class IIa, except if such decisions have an impact that may cause:

- death or an irreversible deterioration of a person's state of health, in which case it is in class III; or
- a serious deterioration of a person's state of health or a surgical intervention, in which case it is classified as class IIb.

Software intended to monitor physiological processes is classified as class IIa, except if it is intended for monitoring of vital physiological parameters, where the nature of variations of those parameters is such that it could result in immediate danger to the patient, in which case it is classified as class IIb.

All other software is classified as class I.

6.4. Rule 12

All active devices intended to administer and/or remove medicinal products, body liquids or other substances to or from the body are classified as class IIa, unless this is done in a manner that is potentially hazardous, taking account of the nature of the substances involved, of the part of the body concerned and of the mode of application in which case they are classified as class IIb.

6.5. Rule 13

All other active devices are classified as class I.

7. SPECIAL RULES

7.1. Rule 14

All devices incorporating, as an integral part, a substance which, if used separately, can be considered to be a medicinal product, as defined in point 2 of Article 1 of Directive 2001/83/EC, including a medicinal product derived from human blood or human plasma, as defined in point 10 of Article 1 of that Directive, and that has an action ancillary to that of the devices, are classified as class III.

7.2. Rule 15

All devices used for contraception or prevention of the transmission of sexually transmitted diseases are classified as class IIb, unless they are implantable or long term invasive devices, in which case they are classified as class III.

7.3. Rule 16

All devices intended specifically to be used for disinfecting, cleaning, rinsing or, where appropriate, hydrating contact lenses are classified as class IIb.

All devices intended specifically to be used for disinfecting or sterilising medical devices are classified as class IIa, unless they are disinfecting solutions or washer-disinfectors intended specifically to be used for disinfecting invasive devices, as the end point of processing, in which case they are classified as class IIb.

This rule does not apply to devices that are intended to clean devices other than contact lenses by means of physical action only.

7.4. Rule 17

Devices specifically intended for recording of diagnostic images generated by X-ray radiation are classified as class IIa.

7.5. Rule 18

All devices manufactured utilising tissues or cells of human or animal origin, or their derivatives, which are non-viable or rendered non-viable, are classified as class III, unless such devices are manufactured utilising tissues or cells of animal origin, or their derivatives, which are non-viable or rendered non-viable and are devices intended to come into contact with intact skin only.

7.6. Rule 19

All devices incorporating or consisting of nanomaterial are classified as:

- class III if they present a high or medium potential for internal exposure;
- class IIb if they present a low potential for internal exposure; and
- class IIa if they present a negligible potential for internal exposure.

7.7. Rule 20

All invasive devices with respect to body orifices, other than surgically invasive devices, which are intended to administer medicinal products by inhalation are classified as class IIa, unless their mode of action has an essential impact on the efficacy and safety of the administered medicinal product or they are intended to treat life-threatening conditions, in which case they are classified as class IIb.

7.8. Rule 21

Devices that are composed of substances or of combinations of substances that are intended to be introduced into the human body via a body orifice or applied to the skin and that are absorbed by or locally dispersed in the human body are classified as:

- class III if they, or their products of metabolism, are systemically absorbed by the human body in order to achieve the intended purpose;

- class III if they achieve their intended purpose in the stomach or lower gastrointestinal tract and they, or their products of metabolism, are systemically absorbed by the human body;
- class IIa if they are applied to the skin or if they are applied in the nasal or oral cavity as far as the pharynx, and achieve their intended purpose on those cavities; and
- class IIb in all other cases.

7.9. Rule 22

Active therapeutic devices with an integrated or incorporated diagnostic function which significantly determines the patient management by the device, such as closed loop systems or automated external defibrillators, are classified as class III.

Appendix 3: In Vitro Diagnostic Medical Device Regulation Risk Class Rules

CLASSIFICATION RULES (IVDR, Annex VIII)

2.1. Rule 1

Devices intended to be used for the following purposes are classified as class D:

- detection of the presence of, or exposure to, a transmissible agent in blood, blood components, cells, tissues or organs, or in any of their derivatives, in order to assess their suitability for transfusion, transplantation or cell administration;
- detection of the presence of, or exposure to, a transmissible agent that causes a life-threatening disease with a high or suspected high risk of propagation;
- determining the infectious load of a life-threatening disease where monitoring is critical in the process of patient management.

2.2. Rule 2

Devices intended to be used for blood grouping, or tissue typing to ensure the immunological compatibility of blood, blood components, cells, tissue or organs that are intended for transfusion or transplantation or cell administration, are classified as class C, except when intended to determine any of the following markers:

- ABO system [A (ABO1), B (ABO2), AB (ABO3)];
- Rhesus system [RH1 (D), RHW1, RH2 (C), RH3 (E), RH4 (c), RH5 (e)];
- Kell system [Kel1 (K)];
- Kidd system [JK1 (Jka), JK2 (Jkb)];
- Duffy system [FY1 (Fya), FY2 (Fyb)];

in which case they are classified as class D.

2.3. Rule 3

Devices are classified as class C if they are intended:

- (a) for detecting the presence of, or exposure to, a sexually transmitted agent;
- (b) for detecting the presence in cerebrospinal fluid or blood of an infectious agent without a high or suspected high risk of propagation;
- (c) for detecting the presence of an infectious agent, if there is a significant risk that an erroneous result would cause death or severe disability to the individual, foetus or embryo being tested, or to the individual's offspring;
- (d) for pre-natal screening of women in order to determine their immune status towards transmissible agents;

- (e) for determining infective disease status or immune status, where there is a risk that an erroneous result would lead to a patient management decision resulting in a life-threatening situation for the patient or for the patient's offspring;
- (f) to be used as companion diagnostics;
- (g) to be used for disease staging, where there is a risk that an erroneous result would lead to a patient management decision resulting in a life-threatening situation for the patient or for the patient's offspring;
- (h) to be used in screening, diagnosis, or staging of cancer;
- (i) for human genetic testing;
- (j) for monitoring of levels of medicinal products, substances or biological components, when there is a risk that an erroneous result will lead to a patient management decision resulting in a life-threatening situation for the patient or for the patient's offspring;
- (k) for management of patients suffering from a life-threatening disease or condition;
- (l) for screening for congenital disorders in the embryo or foetus;
- (m) for screening for congenital disorders in new-born babies where failure to detect and treat such disorders could lead to life-threatening situations or severe disabilities.

2.4. Rule 4

(a) Devices intended for self-testing are classified as class C, except for devices for the detection of pregnancy, for fertility testing and for determining cholesterol level, and devices for the detection of glucose, erythrocytes, leucocytes and bacteria in urine, which are classified as class B.

(b) Devices intended for near-patient testing are classified in their own right.

2.5. Rule 5

The following devices are classified as class A:

- (a) products for general laboratory use, accessories which possess no critical characteristics, buffer solutions, washing solutions, and general culture media and histological stains, intended by the manufacturer to make them suitable for in vitro diagnostic procedures relating to a specific examination;
- (b) instruments intended by the manufacturer specifically to be used for in vitro diagnostic procedures;
- (c) specimen receptacles.

2.6. Rule 6

Devices not covered by the above-mentioned classification rules are classified as class B.

2.7. Rule 7

Devices which are controls without a quantitative or qualitative assigned value are classified as class B.