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Guidance for EU MDR - Software as a Medical Device (SaMD)

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1.0 Introduction

Software has developed considerably since the Council Directive 93/42/EEC (EU MDD) which was released in 1993. Manufacturers of such digital health technologies, medical applications and wearable body sensors as examples, must carefully consider the new rules and regulatory requirements set forth within the EU Medical Devices Regulation 2017/745 (EU MDR), adopted by the European Parliament and Council in May 2017. The new EU MDR, with a mandatory compliance date of 26 May 2020, replaces the former MDD, and introduces new concepts, definitions, classification rules and procedural requirements for medical device software – and particularly for software products regulated as Class I medical devices in Europe. Many digital health technologies will now fall into the scope of the new EU MDR.

2.0 Scope and Objective

The aim of this document is to provide guidance regarding classification and regulatory compliance of software intended to be used as a medical device in accordance with directives and regulations in the medical device regulation 2017/745 (EU MDR). Under the MDD previously there were 18 rules for active devices and now under the EU MDR there are 22 rules. The scope of this document is to help those needing to classify their device under one of the rules of the EU MDR quite clearly with less need for ambiguity.

3.0 What is Software under the MDD?

Under the MDD there were 18 rules in total and the software section was not clearly identified. The rules for software were mainly under the active devices section (as per Med Dev 2.4.1 Rev 9 Classification of Medical Devices), Rule 9 – Rule 12, and Rule 16 under Special rules. However, under section 3.1.4 of Med dev 2.4.1 rev 9 we see –

3.1.4. Active medical devices

Any medical device operation of which depends on a source of electrical energy or any source of power other than that directly generated by the human body or gravity and which acts by converting this energy. Medical devices intended to transmit energy, substances or other elements between an active medical device and the patient, without any significant change, are not considered to be active medical devices. Stand alone software is considered to be an active medical device.

The concept "act by converting energy" includes conversion of energy in the device and/or conversion at the interface between the device and the tissues or in the tissues.

And also under "*Application of the classification of rules":*

"Due to its complexity, classification of standalone software will be covered in a specific guidance document".

It is also worth defining here what an accessory is:
'accessory' means an article which whilst not being a device is intended specifically by its manufacturer to be used together with a device to enable it to be used in accordance with the use of the device intended by the manufacturer of the device;

The specific guidance document is Med Dev 2.1.6 "Guidelines on the qualification and classification of standalone software used in healthcare within the regulatory framework of Medical Devices", however this is not reflective of the EU MDR 2017/745 and the IMDRF guidance documents.

It is worth also looking at the definitions of a medical device in relation to software as per the MDD:

Article 1 (Definitions and Scope) – MDD 93/42 EC

2. (a)*'medical device' means any instrument, apparatus, appliance, software, material or other article, whether used alone or in combination, including the software intended by its manufacturer to be used specifically for diagnostic and/or therapeutic purposes and necessary for its proper application, intended by the manufacturer to be used for human beings for the purpose of:*

— diagnosis, prevention, monitoring, treatment or alleviation of disease,

— diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap,

— investigation, replacement or modification of the anatomy or of a physiological process,

— control of conception, and which does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means;

4.0 What is Software under the EU MDR?

In this section we will begin to look at what the EU MDR 2017/745 describes regarding software. The definitions section is clearly different from the MDD so this shall be described and also compared in Appendix A in tabulated format which shows the MDD reference and the MDR reference and the difference between the two section by section. Using the following flowchart in fig 1.0 we decide whether our product is covered as a Medical Device under the EU MDR 2017/745, using the regulation itself and the definitions in the next few pages.

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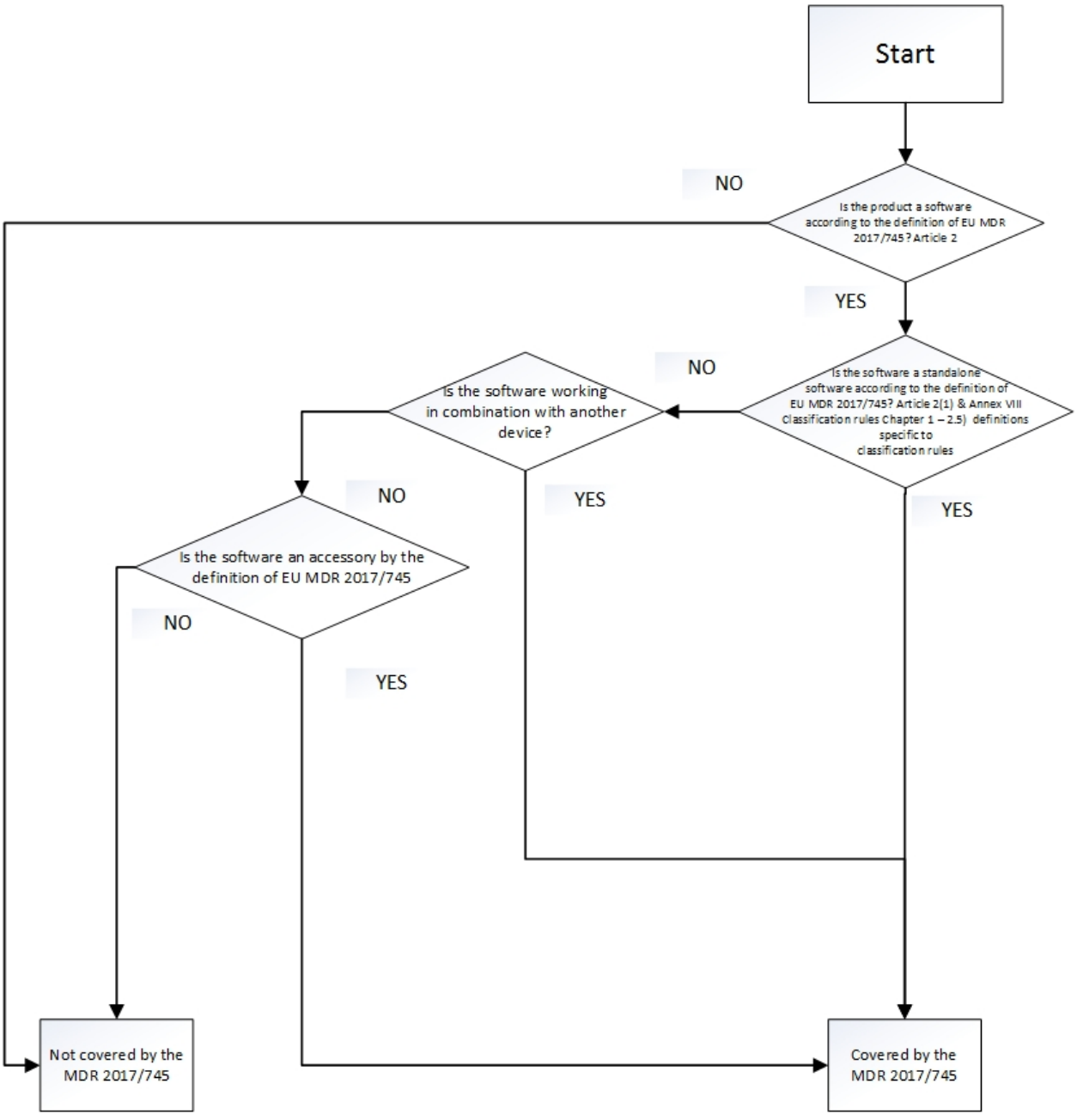

Figure 1.0 Decision flowchart

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Article 2: Definitions (abbreviated) – EU MDR 2017/745

Underlined below is new text

(1) '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 EU MDR adds– Prediction and Prognosis of Disease. These new definitions extend the already established concept of physiological data monitoring, and processing of physiology data, with advanced digital health care technologies capable of potentially predicting or providing a prognosis of potential future states of disease identification, an advanced concept of diagnostics.

Article 2 (4) 'active device' means any device, the operation of which depends on a source of energy other than that generated by the human body for that purpose, or by gravity, and which acts by changing the density of or converting that energy. Devices intended to transmit energy, substances or other elements between an active device and the patient, without any significant change, shall not be deemed to be active devices. *Software shall also be deemed to be an active device*;

Annex VIII Chapter 1, 2.5. 'Active device intended for diagnosis and monitoring' means any active device used, whether alone or in combination with other devices, to supply information for detecting, diagnosing, monitoring or treating physiological conditions, states of health, illnesses or congenital deformities.

This definition in Article 2(4), suggests that the medical device software is connected with dependent hardware including interfaces which provide information. The EU MDR 2017/745 describes the classification of rules related to Active Devices from Rule 9 to Rule 13 with Rule 11 being an additional rule. Using the flowchart in fig 1.0, if the product is an app for wellbeing or lifestyle this will be clarified

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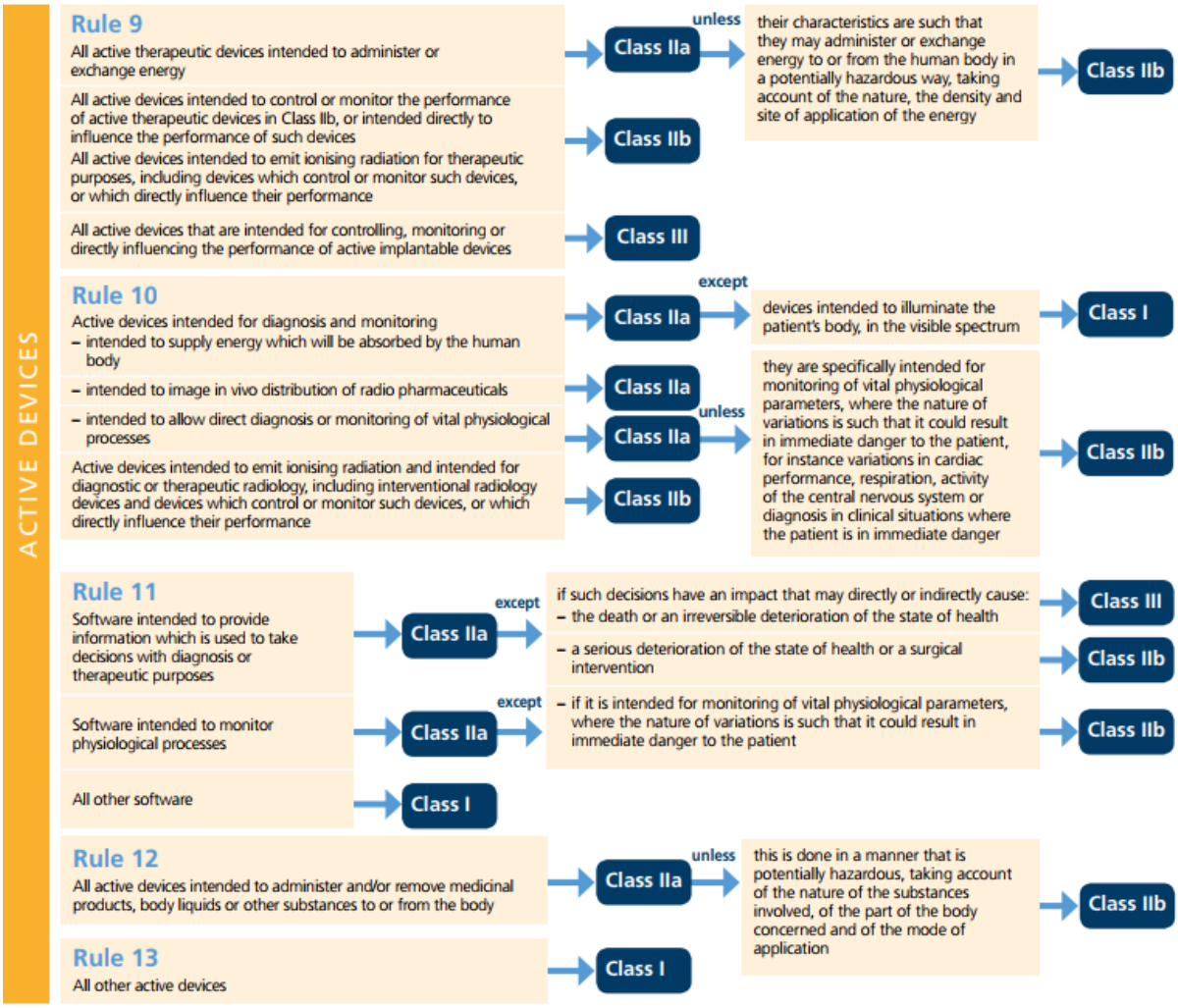
under the definitions and the outcome will be that it is not considered a Medical Device so is outside of the scope of this document.

Definition of accessory under the EU MDR

(2) '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);



Source - LRQA

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Figure 2.0 Active Devices Rules Classifications EU MDR 2017/745

Definitions in MDD 93/42 EC - Annex IX (classification criteria)

The following shows the definition under the MDD:

1. Definitions for the classification rules

1.4. Active medical device

Any medical device operation of which depends on a source of electrical energy or any source of power other than that directly generated by the human body or gravity and which acts by converting this energy. Medical devices intended to transmit energy, substances or other elements between an active medical device and the patient, without any significant change, are not considered to be active medical devices. Stand-alone software is considered to be an active medical device.

II. Implementing rules

2.3. *Software, which drives a device or influences the use of a device, falls automatically in the same class.*

Comparison MDD Vs EU MDR (Active Devices)

Appendix A is a comprehensive section by section comparison of the MDD to the EU MDR in relation to software.

The terminology used in the active devices section of the EU MDR has been expanded to include terms such as (in rule 9) - *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.*

As well as;

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

There are some other additional terms

In the MDD this was only under Rule 10 but now is included in rule 9 as well as Rule 10 as follows with the underlined differences–

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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.

Rule 10 also then expands with the following differences (with examples)–

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.

Rule 11 – This is a new rule and expanded on in Section 5.0 below

Rules 12 and 13 are not much different from the old Rules 11 and 12, with underlined differences.

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.

Special Rules

The old rule 16 is aligned in terminology with the new rule 17 of the EU MDR 2017/745 but with better clarity –

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

5.0 A deeper look at Rules 11, 17 and 22

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Rule 11

Rule 11 is a new rule specifically for standalone software, while the term "standalone" doesn't appear in the text of the regulation; the word alone only appears 3 times in the regulation in the context of active or software applications. This rule sits under the active devices section but is clearly for standalone software which unlike the MDD clearly states "stand-alone software is considered to be an active medical device".

Annex VIII of the EU MDR: Section 6.3. Rule 11

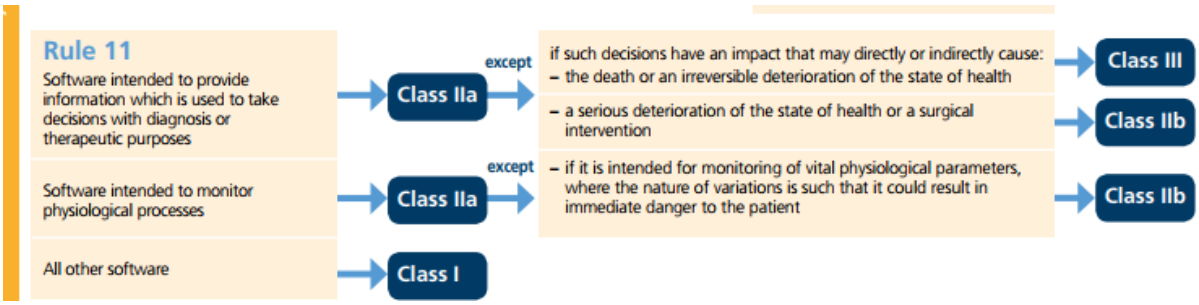

Figure 3.0 Graphical presentation of Rule 11 – Active Devices *Source - LRQA*

As per the above figure, ***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.

The new Rule 11 does not mention or refer to the new terminology '**prognosis and prediction**.' It is assumed the concept of prevention and prognosis for a future disease state are to be included into the

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following definition: "*Software to provide information … used to take decisions with diagnostic or therapeutic purposes.*"

The definitions and classification rules will not allow many standalone software to be classified as class I.

Almost any software used for the purpose of diagnosis, monitoring, prediction, prognosis or treatment also provides information which is used to take decisions with diagnosis or therapeutic purposes will be classified as class IIa or higher under rule 11.

Software that may remain in class I

Some examples of software that may remain in Class 1 are:

- Monitoring, if not used for diagnosis or if there is no vital threat. E.g. if a software monitors a physiological parameter based on which no diagnosis is proposed and which only indicates non-therapeutic actions. An example would be software monitoring the fluid balance and reminding to consume fluids.
- Prognosis not intended for decision making.
- Alleviation, e.g. biofeedback systems not considered as therapy since they "solely" easy symptoms

The EU MDR provides a clear definition in Section 1: Legislative acts (regulations):

(19) It is necessary to clarify that software in its own right, when specifically intended by the manufacturer to be used for one or more of the medical purposes set out in the definition of a medical device, qualifies as a medical device, while software for general purposes, even when used in a healthcare setting, or software intended for life-style and well-being purposes is not. The qualification of software, either as a device or an accessory, is independent of the software's location or the type of interconnection between the software and a device.

Above Paragraph (19) clearly exempts general-purpose software without a medical purpose as defined in Section 1, as well as fitness and wellness apps, from being regulated as medical devices.

Therefore the following table can summarise where software is NOT considered a medical device as opposed to when it is.

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Software considered a Medical Device	Software not considered a Medical Device
Intended Purpose for diagnostic purposes	Intended for Documentation Purposes Only
Intended Purpose for therapeutic purposes	Intended For Research and Education
Monitoring of physiological processes	Not specifically intended for a medical purpose

Software that will be classified higher from the MDD to the EU MDR

In general, software will be classified in higher classes. Here are some examples:

Product	Class according to MDD	Class according to EU MDR
App supporting the selection and dose calculation of cytostatic drugs	I	III
Software suggesting diagnoses based on test results	I	IIb or higher (up to III)
App to diagnose sleep apnoea	I	IIa (or higher)
Therapy or radiation planning software	IIb	IIb or III, depending on the argumentation

<u>Rules 17 and 22</u>

Annex VIII of the EU MDR: Section 7.4 Rule 17 and Section 7.9 Rule 22

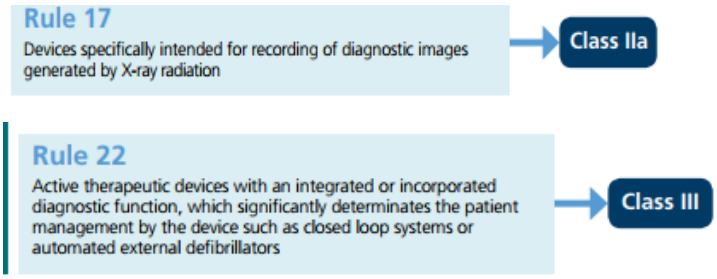

Figure 4.0 Graphical presentation of Special Rules 17, 22 *Source - LRQA*

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Rule 17

As diagnostic images refer to an output which involves complex algorithms this involves software but is specific to X Ray radiation

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

Rule 22

Since rule 22 explicitly describes “integrated or incorporated diagnostic function”, this often refers to some software combined with active devices..

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.

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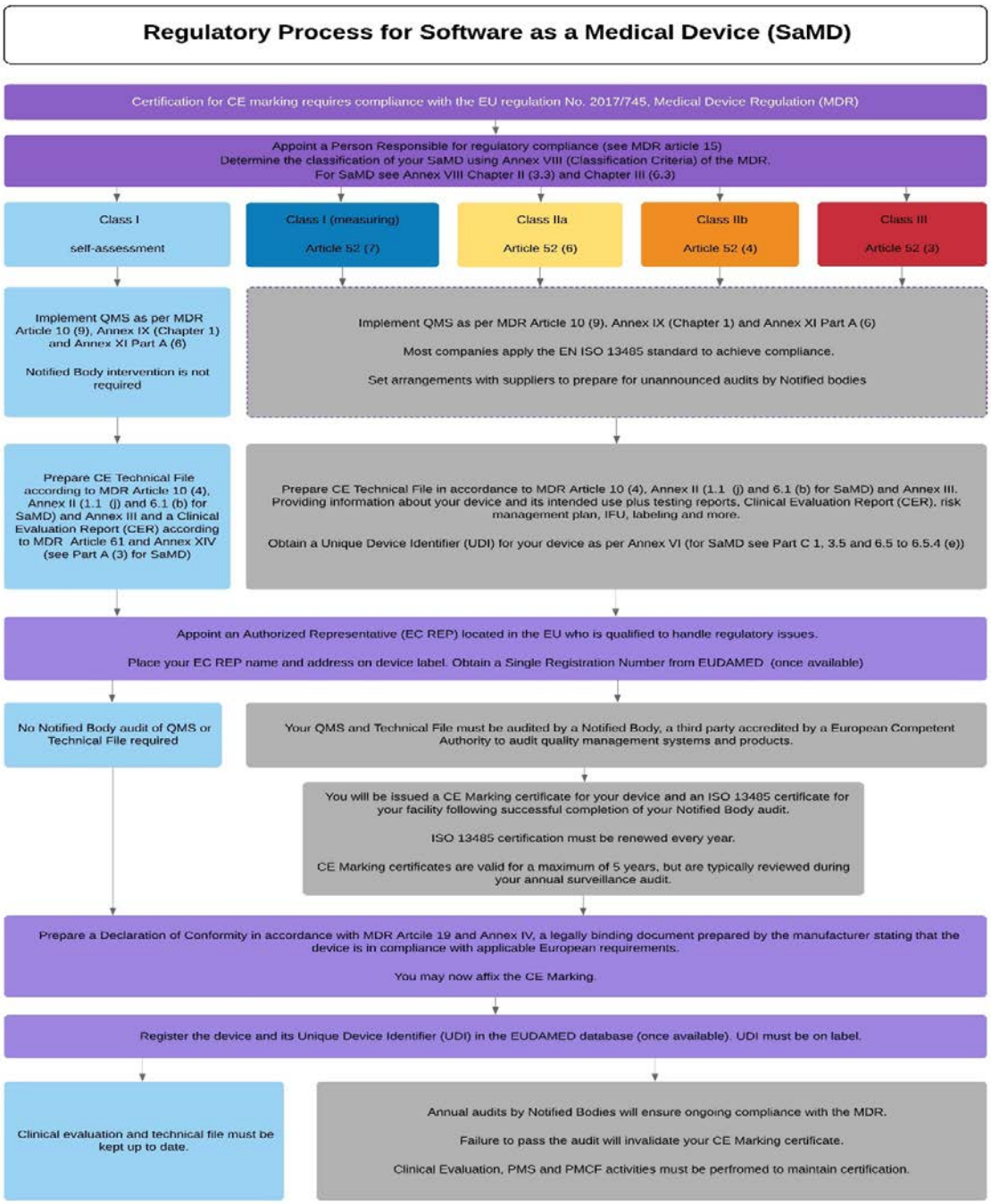
6.0 Regulatory pathway for SaMD



7.0 Examples of Software under the EU MDR

Rule 11 Examples:

1. *As per the above figure,* ***Software intended to provide information*** *which is used to take decisions with diagnosis is classified as class IIa –*

   Name: *Hearing Health Screening Software*

   Class: *IIa*

   Producer: *Ultimate Kiosks*

   Intended use: *Provides hearing tests that classifies results into normal, conductive or sensorineural. The software then provides recommendations for effective follow-up actions*

   Argument: *This software falls into class IIa as it will provide information (recommendations) on the appropriate follow up actions regarding diagnosing and treating any hearing defects but does not impact patients in a way to cause death, irreversible/serious deterioration of health or surgical intervention*

   Link: *http://www.ultimatekiosk.com/site/hearinghealthscreeningsoftwarepage*

2. ***Software intended to provide information*** *which is used to take decisions with diagnosis or therapeutic purposes where 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;*

   Name: *RAPID ™*

   Class: *III*

   Producer: *iSchemaView, Inc.*

   Intended use: *"The RAPID neuroimaging platform creates high-quality images from non-contrast CT, CT angiography, CT perfusion, and MRI diffusion and perfusion studies. The software provides an intuitive and easily interpretable real-time view of brain perfusion, allowing physicians to determine lesion volumes for a wide variety of different thresholds. CT angiography images indicate differences in vessel density between hemispheres and an automated ASPECT score is generated from non-contrast CT.*

   To enhance clinical workflow, the RAPID system allows user-defined settings to generate the initial image maps. Custom installation ensures that the system is properly configured to match your individual CT or MRI systems. RAPID provides efficient processing and easy to interpret output screens.

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Clinical Applications

RAPID provides both viewing and analysis capabilities for functional and dynamic imaging datasets acquired with non-contrast CT, CT Perfusion, CT angiography, and MRI including a Diffusion Weighted MRI (DWI) Module and a Dynamic Analysis Module.

The DWI module is used to visualize local water diffusion properties from the analysis of diffusion-weighted MRI data. The dynamic analysis module is used for visualization and analysis of dynamic imaging data, showing properties of changes in contrast over time. This functionality includes calculation of parameters related to tissue flow and blood volume. "

Argument: *This product can and has been used to allow clinicians to make important decisions regarding diagnosis/treatment of a stroke in patients. See: https://www.ahn.org/innovation/stroke-survivor-credits-life-changing-rapid-software . Decisions based on results from this software can potentially fall into the category of impact that causes "death or an irreversible deterioration of a person's state of health" and thus must be classed as a class III medical device*

Link: *http://www.i-rapid.com/products-rapid-overview*

3. ***Software intended to provide information*** *which is used to take decisions with diagnosis or therapeutic purposes where such decisions have an impact that may cause: a serious deterioration of a person's state of health or a surgical intervention, in which case it is classified as class IIb.*

Name: *PredictBGL Insulin Dose Calculator*

Class: *IIb*

Producer: *ManageBGL Diabetes*

Intended use: "*PredictBGL is a bolus calculator intended to help people with diabetes calculate doses, track patterns, detect trends, reduce the incidence of hypoglycaemia, and help improve doses. The system is intended for use in individual patients, with Type 1 diabetes, or those who use insulin as part of a diabetes regimen such as Type 2 diabetes, LADA/Type 1.5 and gestational diabetes. During use, PredictBGL is customized to one patient's dose regime. It should never be used to calculate doses for another patient. PredictBGL should be used to log blood sugars, carbohydrates and insulin 3 or more times per day."*

Argument: *This software falls into class IIb because it provides information regarding decisions for insulin dosage for patients with diabetes. Miscalculation of such a dose could result in hyperglycaemia or hypoglycaemia which can be regarded as a serious deterioration of a person's state of health.*

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Link: *https://www.managebgl.com/*

4. ***Software intended to monitor physiological processes*** *is classified as class IIa,*

   Name: *VitaDock+*

   Class: *IIa*

   Producer: *Medisana*

   Intended use: "*With the VitaDock+ App, all health and vital data can be monitored at anytime and anywhere. As a user you can supplement each value with comments and display additional graphs and evaluations. This will make health management even more customized.*

   Argument: *This medical device software falls into class IIa as it is used to monitor physiological processes that do not result in immediate danger to the patient*

   Link: *https://www.medisana.com/VitaDock-App-2-0.html*

5. ***Software intended to monitor physiological processes*** *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.*

   Name: *RespiraSense Software Application*

   Class: *IIb*

   Producer: *PMD solutions*

   Intended use: *"Medical professionals can set alert thresholds, interface with RespiraSense and retrieve vital information using the Respirasense software on a tablet. To ensure while using wireless technology that the chain of custody between the patient's information and their medical chart is secure, PMD has created a scan to connect feature. Scan to connect allows medical professionals to rename a lobe from a complex ID to the patient's own medical record number. This enables quick and efficient retrieval of a single patient's vital information with the confidence of knowing it's the right information from the right patient.*

   Using the RespiraSense software to scan the QR code on the back of the Lobe and then scanning the medical record number of the patient achieves this. To retrieve that patient's vital information at any time thereafter simply scan the patient medical record number. Due to PMD's novel signal processing

capabilities, RespiraSense can confidently be used on a variety of body profiles, gender and ages, to truly offer a new industry standard in acute and continuous respiratory rate monitoring."

Argument: *the RespiraSense software application is a class IIb medical device because it monitors a physiological process (respiration) which is vital and where the nature of variations of those parameters is such that it could result in immediate danger to the patient. This is because "Relative changes in respiratory rate are the most sensitive and specific prediction of deterioration in patients" and "Continuous respiratory rate monitoring gives an advanced warning to medical staff at the very earliest stages of patient deterioration."*

Link: *http://www.pmd-solutions.com/respiratory-rate-monitoring/*

6. ***All other software is classified as class I.***

Name: *Migraine Buddy*

Class: *I*

Producer: *Healint*

Intended use: *"Migraine Buddy is an advanced migraine headache diary and tracking app designed with neurologists and data scientists." "Track your migraine, understand your triggers, and share your migraine history with your doctor to get the best possible treatment"*

Argument: *Migraine Buddy is a class I medical device because it simply records and merges data relating to migraines without seeking to diagnose or make decisions for patients, nor does it monitor any vital or naturally occurring physiological process. It was designed to gather many different types of data related to migraines, so patients can consult their doctors by sharing their recorded migraine history.*

Link: *https://healint.com/*

Rule 17 example

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

Name : *Ziehm Solo FD*

Class: IIa

Producer - X OGraph

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Intended Use: *Ziehm Imaging started the paradigm shift of innovative detector technologies for mobile X-ray imaging from image intensifiers (I.I.) to flat-panel detectors. Other C-arm competitors followed and reconfirmed the trend of implementing amorphous silicon (aSi) flat-panel detectors to their mobile systems. Since then, Ziehm Imaging continuously reaffirms this step in further driving innovations for mobile X-ray imaging systems with the latest flat-detector technology*

The Ziehm Solo FD is a great all-rounder for general purpose fluoroscopy. It would be ideal for, but not limited to, the following applications:
· General Orthopaedics
· Urology
· Pain Management
· Pacing Wire Insertion
· Speech & Language (SALT)
· Paediatrics
Cine record and replay ('loop') and a vascular software package with DSA, Maximum Opacification and Roadmap can also be specified

Argument: *The Ziehm Solo FD uses X Ray radiation at low dose but is clearly recording images for diagnosis for multiple areas as described in the intended use*

Link : https://xograph.com/ziehm-solo-fd

Rule 22 example

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.

Name : Zoll R series Defibrillator

Class: III

Producer - Zoll

Intended Use: *Defibrillator Function The R Series system is indicated for defibrillation on victims of cardiac arrest where there is apparent lack of circulation as indicated by: • Unconsciousness. • Absence of breathing. • Absence of pulse. The R Series system in the Manual mode is indicated for synchronized cardioversion of certain atrial or ventricular arrhythmias. A qualified physician must decide when synchronized cardioversion is appropriate. The R Series system Semiautomatic and Manual mode is indicated for use in early defibrillation programs where the delivery of a defibrillator shock during*

resuscitation involving CPR, transportation, and definitive care are incorporated into a medically-approved patient care protocol. The R Series system Semiautomatic and Manual mode is indicated for adult and pediatric patients.

The CPR dashboard is an incorporated diagnostic.

Argument: *Rule 22 itself provides this as an example since it has a diagnostic function*

Link : https://www.zoll.com/medical-products/defibrillators/r-series/

Appendices:

Appendix A : EU MDR vs MDD Comparison Table

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Appendix A: EU MDR vs MDD Comparison Table

MDD	EU MDR	Differences between EU MDR and MDD
	Introductory statements (19) *It is necessary to clarify that software in its own right, when specifically intended by the manufacturer to be used for one or more of the medical purposes set out in the definition of a medical device, qualifies as a medical device, while software for general purposes, even when used in a healthcare setting, or software intended for life-style and well-being purposes is not a medical device. The qualification of software, either as a device or an accessory, is independent of the software's location or the type of interconnection between the software and a device.*	Extra information in the EU MDR on what qualifies a piece of software to be defined as a medical device (SaMD) 1. Software that is used for one or more medical purposes (defined in article 2 (1)) is a medical device 2. While software for general purposes, even when used in a healthcare setting, or software intended for life-style and well-being purposes is not a medical device.

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Article 1 (Definitions and Scope)	**Article 2 (Definitions)**	
2. (a)	(1)	Here the definition of a medical device is similar to that in the MDD but expanded to include *implants* and *reagents.*
'medical device' means any instrument, apparatus, appliance, software, material or other article, whether used alone or in combination, including the software intended by its manufacturer to be used specifically for diagnostic and/or therapeutic purposes and necessary for its proper application, intended by the manufacturer to be used for human beings for the purpose of:	*'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:*	The new definition also includes *prediction* and *prognosis* of disease as a function of the medical device
— diagnosis, prevention, monitoring, treatment or alleviation of disease,	*— diagnosis, prevention, monitoring, prediction, prognosis, treatment or alleviation of disease,*	*Handicap* has been replaced by *disability* [(1)]
— diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap,	*— diagnosis, monitoring, treatment, alleviation of, or compensation for, an injury or disability,*	Investigation, replacement or modification of *physiological state* and *pathological process* or *state* have been added to the EU MDR.
— investigation, replacement or modification of the anatomy or of a physiological process,	*— investigation, replacement or modification of the anatomy or of a physiological or pathological process or state,*	Support of conception has been added to EU MDR [(2)]
	— providing information by means of in vitro examination of specimens derived from the human body, including organ, blood and tissue donations,	Software is considered an 'active device' the definition of which is covered in Annex IX, I (1.4) in the MDD but has been placed under article 2 (4) of the EU MDR. One small difference is that the EU MDR includes devices that

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— control of conception, *and which does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means;*	*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.* (4) *'active device' means any device, the operation of which depends on a source of energy other than that generated by the human body for that purpose, or by gravity, and which acts by changing the density of or converting that energy. Devices intended to transmit energy, substances or other elements between an active device and the patient, without any significant change, shall not be deemed to be active devices. Software shall also be deemed to be an active device;* (25)	change the 'density of the energy' received from the source within the definition of active medical device. The Definition of 'compatibility' of a medical device has been added to the EU MDR under Article 2 (25) and includes software within this definition. The Definition of 'interoperability' of a medical device has been added to the EU MDR under Article 2 (26) and includes software within this definition.

	'compatibility' is the ability of a device, including software, when used together with one or more other devices in accordance with its intended purpose, to: *(a) perform without losing or compromising the ability to perform as intended, and/or* *(b) Integrate and/or operate without the need for modification or adaption of any part of the combined devices, and/or* *(c) Be used together without conflict/interference or adverse reaction.* (26) *'interoperability' is the ability of two or more devices, including software, from the same manufacturer or from different manufacturers, to:* *(a) exchange information and use the information that has been exchanged for the correct execution of a specified function without changing the content of the data, and/or*	

	(b) communicate with each other, and/or *(c) Work together as intended.*	

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Annex I (Essential requirements) II. Requirements regarding design and construction 12. Requirements for medical devices connected to or equipped with an energy source 12.1a *For devices which incorporate software or which are medical software in themselves, the software must be validated according to the state of the art taking into account the principles of development lifecycle, risk-management, validation and verification.*	**Annex I (general safety and performance requirements)** **Chapter I (general requirements)** 14.2. *Devices shall be designed and manufactured in such a way as to remove or reduce as far as possible:* *(d) the risks associated with the possible negative interaction between software and the IT environment within which it operates and interacts;* 17. *Electronic programmable systems — devices that incorporate electronic programmable systems and software that are devices in themselves* 17.1. Devices *that incorporate electronic programmable systems, including software, or software that are devices in themselves, shall be designed to ensure repeatability, reliability and performance in line with their intended use. In the event of a single fault condition, appropriate means shall be adopted to eliminate or reduce as far as possible consequent risks or impairment of performance.*	Annex I of the MDD which covered the essential requirements of a medical device has been replaced by Annex I of the EU MDR now called the general safety and performance requirements (GSPR) which is much more extensive and covers more criteria and definitions. In relation to software, the GSPR section covers the following: 1. Regulations for removal/reduction of risks associated with interaction between software and its intended environment 2. Regulations for the design, development and manufacture of devices that incorporate electronic programmable systems, including software, or software that are devices in themselves and the consideration of the specific features of any mobile

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	17.2. *For devices that incorporate software or for software that are devices in themselves, the software shall be developed and manufactured in accordance with the state of the art taking into account the principles of development life cycle, risk management, including information security, verification and validation.* 17.3. *Software referred to in this Section that is intended to be used in combination with mobile computing platforms shall be designed and manufactured taking into account the specific features of the mobile platform (e.g. size and contrast ratio of the screen) and the external factors related to their use (varying environment as regards level of light or noise).* 17.4. *Manufacturers shall set out minimum requirements concerning hardware, IT networks characteristics and IT security measures, including protection against unauthorised access, necessary to run the software as intended.* 23.4. Information in the instructions for use: (f) *where applicable, information allowing the healthcare professional to verify if the device is*	computing platform the software is used on. 3. What information should be included in instructions for use such as minimum hardware requirements and IT security measures Strong similarities between 12.1a of MDD Annex 1 and 17.2 of EU MDR Annex 1 the main differences being: 1. Devices that incorporate software are to be 'validated' (MDD) vs 'developed and manufactured' (EU MDR) according to the 'state of the art' 2. EU MDR includes 'information security' as a factor that needs to be considered in the development of a medical device with no mention of 'information security' in the MDD

	suitable and select the corresponding software and accessories; (ab) *for devices that incorporate electronic programmable systems, including software, or software that are devices in themselves, minimum requirements concerning hardware, IT networks characteristics and IT security measures, including protection against unauthorised access, necessary to run the software as intended.*	

	Annex II (Technical documentation) 1.1. Device description and specification (j) *A general description of the key functional elements, e.g. its parts/components (including software if appropriate), its formulation, its composition, its functionality and, where relevant, its qualitative and quantitative composition. Where appropriate, this shall include labelled pictorial representations (e.g. diagrams, photographs, and drawings), clearly indicating key parts/components, including sufficient explanation to understand the drawings and diagrams;* 6. Product verification and validation 6.1. Pre-clinical and clinical data (b) *detailed information regarding test design, complete test or study protocols, methods of data analysis, in addition to data summaries and test conclusions regarding in particular:* *— Software verification and validation (describing the software design and development process and evidence of the validation of the software, as used in*	The EU MDR coves much more information regarding the requirements of the technical documentation. Two annexes of the EU MDR are dedicated to technical documentation: 1. Annex II (technical documentation) 2. Annex III (technical documentation on post-market surveillance) In the MDD technical documentation is covered under: 1. Annex II section 3 (particularly 3.2(c)) 2. Annex VII section 3 In the new EU MDR the technical documentation must also include all the detailed information regarding software verification and validation in accordance with Annex II 6.1(b)

	the finished device. This information shall typically include the summary results of all verification, validation and testing performed both in-house and in a simulated or actual user environment prior to final release. It shall also address all of the different hardware configurations and, where applicable, operating systems identified in the information supplied by the manufacturer); *— Performance and safety.* *Where applicable, conformity with the provisions of Directive 2004/10/EC of the European Parliament and of the Council (1) shall be demonstrated. Where no new testing has been undertaken, the documentation shall incorporate a rationale for that decision. An example of such a rationale would be that biocompatibility testing on identical materials was conducted when those materials were incorporated in a previous version of the device that has been legally placed on the market or put into service;*	

	Annex VI, Part C (UDI system) 1. Definitions *UDI-PI The UDI-PI is a numeric or alphanumeric code that identifies the unit of device production.* *The different types of UDI-PIs include serial number, lot number, software identification and manufacturing or expiry date or both types of date.* 3. The UDI 3.5. *If a lot number, serial number, software identification or expiry date appears on the label, it shall be part of the UDI-PI. If there is also a manufacturing date on the label, it does not need to be included in the UDI-PI. If there is only a manufacturing date on the label, this shall be used as the UDI-PI.* 6. Rules for specific device types 6.5. Device Software 6.5.1. UDI assignment Criteria	A new addition to regulations in the EU MDR not previously covered by the MDD is the introduction of a Unique Device Identification (UDI) system as specified in: 1. Article 27 (Unique Device Identification system) 2. Article 28 (UDI database) 3. Article 27 (registration of devices) 4. Annex VI In the EU MDR, Annex VI, Part C, 6.5 outlines the rules for the UDI of standalone software and of software that is a medical device in its own right.

	The UDI shall be assigned at the system level of the software. Only software which is commercially available on its own and software which constitutes a device in itself shall be subject to that requirement. The software identification shall be considered to be the manufacturing control mechanism and shall be displayed in the UDI-PI. 6.5.2. *A new UDI-DI shall be required whenever there is a modification that changes:* *(a) the original performance;* *(b) the safety or the intended use of the software;* *(c) interpretation of data.* *Such modifications include new or modified algorithms, database structures, operating platform, architecture or new user interfaces or new channels for interoperability.* 6.5.3. *Minor software revisions shall require a new UDI-PI and not a new UDI-DI.* *Minor software revisions are generally associated with bug fixes, usability enhancements that are not for safety purposes, security patches or operating efficiency.* *Minor software revisions shall be identified by a*	

	manufacturer-specific form of identification. 6.5.4. UDI placement criteria for software *(a) Where the software is delivered on a physical medium, e.g. CD or DVD, each packaging level shall bear the human readable and AIDC representation of the complete UDI. The UDI that is applied to the physical medium containing the software and its packaging shall be identical to the UDI assigned to the system level software;* *(b) the UDI shall be provided on a readily accessible screen for the user in an easily-readable plain-text format, such as an 'about' file, or included on the start-up screen;* *(c) software lacking a user interface such as middleware for image conversion, shall be capable of transmitting the UDI through an application programming interface (API);* *(d) only the human readable portion of the UDI shall be required in electronic displays of the software. The marking of UDI using AIDC shall not be required in the electronic displays, such as 'about' menu, splash*	

	screen etc.; *(e) the human readable format of the UDI for the software shall include the Application Identifiers (AI) for the standard used by the issuing entities, so as to assist the user in identifying the UDI and determining which standard is being used to create the UDI.*	

	Annex VII (requirements to be met by notified bodies) 3. Resource requirements 3.2. Qualification criteria in relation to personnel 3.2.1. *The Notified Body shall establish and document qualification criteria and procedures for selection and authorisation of persons involved in conformity assessment activities, including as regards knowledge, experience and other competence required, and the required initial and ongoing training. The qualification criteria shall address the various functions within the conformity assessment process, such as auditing, product evaluation or testing, technical documentation review and decision-making, as well as the devices, technologies and areas, such as biocompatibility, sterilisation, tissues and cells of human and animal origin and clinical evaluation, covered by the scope of designation.* 3.2.2. *The qualification criteria referred to in Section 3.2.1 shall refer to the scope of a notified body's designation in accordance with the scope description used by the Member State for the notification*	MDD covers notified bodies in the following sections: 1. Article 16 (Notified bodies) 2. Annex XI (criteria to be met for the designation of notified bodies) The EU MDR introduces more information and regulations governing notified bodies with the addition of strict criteria detailing the requirements to be met by notified bodies and their certification which can be found in EU MDR: 3. Chapter IV (Notified bodies, Articles 35 to 50) 4. Annex VII (requirements to be met by notified bodies) 5. Annex XII (certificates issued by a notified body)

	referred to in Article 42(3), providing a sufficient level of detail for the required qualification within the subdivisions of the scope description. Specific qualification criteria shall be defined at least for the assessment of: *— the pre-clinical evaluation,* *— clinical evaluation,* *— tissues and cells of human and animal origin,* *— functional safety,* *— software,* *— packaging,* *— devices that incorporate as an integral part a medicinal product,* *— devices that are composed of substances or of combinations of substances that are absorbed by or locally dispersed in the human body and* *— the different types of sterilisation processes.* 3.2.5. The personnel responsible for carrying out product-related reviews (product reviewers), such as technical documentation reviews or type examination, including aspects such as clinical evaluation, biological safety, sterilisation and software validation, shall have all of the following proven qualifications: — successful completion of a university or a technical college degree or equivalent qualification in relevant	According to Annex VII 3.2.2 of the EU MDR, software is one of the categories requiring specific qualification criteria to be defined for its assessment and 3.2.5 defines the qualifications required by personnel carrying out the software validation. This was not previously defined in specifics in the MDD.

	studies, e.g. medicine, pharmacy, engineering or other relevant sciences; —four years' professional experience in the field of healthcare products or related activities, such as in manufacturing, auditing or research, of which two years shall be in the design, manufacture, testing or use of the device or technology to be assessed or related to the scientific aspects to be assessed; — knowledge of device legislation, including the general safety and performance requirements set out in Annex I; — appropriate knowledge and experience of relevant harmonised standards, CS and guidance documents; — appropriate knowledge and experience of risk management and related device standards and guidance documents; — appropriate knowledge and experience of clinical evaluation; — appropriate knowledge of the devices which they are assessing; — appropriate knowledge and experience of the	

	conformity assessment procedures laid down in Annexes IX to XI, in particular of the aspects of those procedures for which they are responsible, and adequate authorisation for carrying out those assessments; — the ability to draw up records and reports demonstrating that the relevant conformity assessment activities have been appropriately carried out.	

Annex IX (classification criteria) I. Definitions 1. Definitions for the classification rules 1.4. Active medical device *Any medical device operation of which depends on a source of electrical* *energy or any source of power other than that directly generated by the*	**Annex VIII (Classification rules)** **Chapter II (Implementing rules)** 3.3. *Software, which drives a device or influences the use of a device, shall fall within the same class as the device. If the software is independent of any other device, it shall be classified in its own right.* **Chapter III (Classification rules)** 6.3. *Rule 11 Software intended to provide information which is used to take decisions with*	Annex IX of the MDD and Annex VIII of the EU MDR deal with classification and the classification rules. According to EU MDR Annex VIII Chapter II and MDD Annex IX, II 2.3: 'Software, which drives a device or influences the use of a device, shall fall within the same class as the device' The addition to the EU MDR is: 'If the software is independent of any other device, it shall be classified in its own

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human body or gravity and which acts by converting this energy. *Medical devices intended to transmit energy, substances or other elements between an active medical device and the patient, without any significant change, are not considered to be active medical devices.* *Stand-alone software is considered to be an active medical device.* II. Implementing rules 2.3. *Software, which drives a device or influences the use of a device, falls automatically in the same class.*	*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.*	right' Rule 11 of Annex VIII, Chapter III outlines the way in which software should be classified according to its function and the risks associated with it.

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	Annex XIV Part A (Clinical evaluation) 3. *A clinical evaluation may be based on clinical data relating to a device for which equivalence to the device in question can be demonstrated. The following technical, biological and clinical characteristics shall be taken into consideration for the demonstration of equivalence:* *— Technical: the device is of similar design; is used under similar conditions of use; has similar specifications and properties including physicochemical properties such as intensity of energy, tensile strength, viscosity, surface characteristics, wavelength and software algorithms; uses similar deployment methods, where relevant; has similar principles of operation and critical performance requirements;*	Clinical evaluation in the MDD is covered by Annex X and in the EU MDR by Annex XIV. According to both the MDD and the EU MDR, clinical evaluation can be based on data obtained from a device that can be demonstrated to show equivalence to the device in question. The EU MDR specifies similarities in software algorithms between devices (could be a SaMD) as a property to be considered in terms of demonstrating equivalence between the two devices and to justify the use of data derived from it for clinical evaluation.

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	Annex XV (Clinical investigations) **Chapter II (Documentation)** 2. Investigator's Brochure *The investigator's brochure (IB) shall contain the clinical and non-clinical information on the investigational device that is relevant for the investigation and available at the time of application. Any updates to the IB or other relevant information that is newly available shall be brought to the attention of the investigators in a timely manner. The IB shall be clearly identified and contain in particular the following information:* *2.3. Pre-clinical evaluation based on relevant pre-clinical testing and experimental data, in particular regarding in- design calculations, in vitro tests, ex vivo tests, animal tests, mechanical or electrical tests, reliability tests, sterilisation validation, software verification and validation, performance tests, evaluation of biocompatibility and biological safety, as applicable.*	According to the new EU MDR, Annex XV, Chapter II, 2, 2.3 the Investigator's brochure must clearly identify and contain (among many other things) information on pre-clinical evaluation regarding software verification and validation as part of documentation required for clinical investigation.