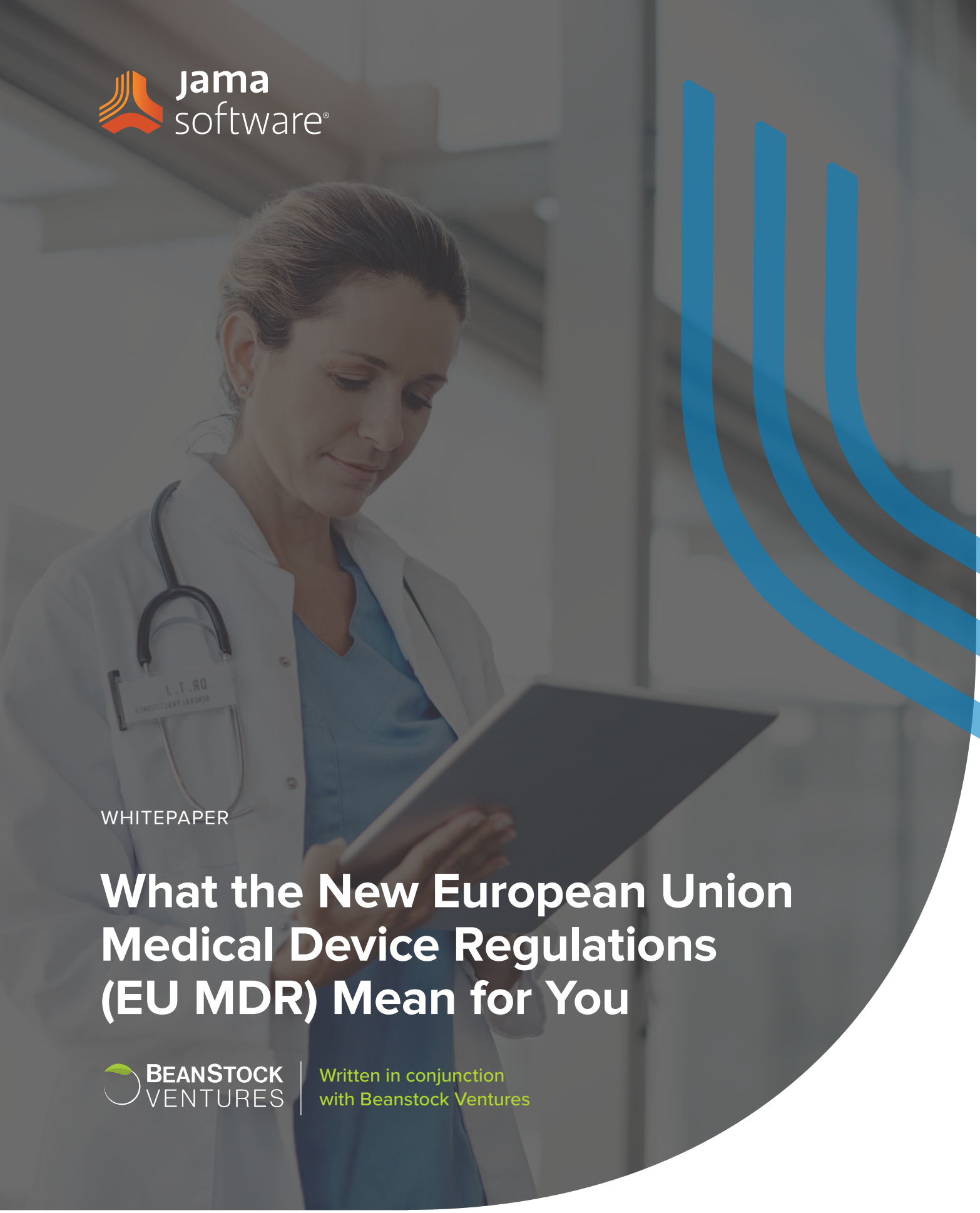

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WHITEPAPER

What the New European Union Medical Device Regulations (EU MDR) Mean for You

BEANSTOCK VENTURES

Written in conjunction with Beanstock Ventures

Introduction

As medical device technologies have rapidly advanced in recent years, regulations governing definitions, testing, and post-market activities have struggled to keep up. The pace of change and adoption of these technologies has made it difficult for governments and agencies to create the kind of inclusive and expansive rules that will ensure safety.

In response to this expanding market, the European Union released new guidance governing medical devices. With the release of Medical Device Regulation (MDR) 2017/745/EU, in 2017, the EU has issued the first updated regulations in more than 20 years. The new Medical Device Regulation (MDR) 2017/745/EU addresses software as a medical device [SaMD], as well as other products. It also places stringent requirements for compliance with post-market activities and post-market surveillance.

While enforcement of these new regulations was scheduled to begin in May 2020, it was postponed until May 2021 due to the COVID-19 pandemic.

What do these new regulations mean for the medical device industry? Experts from Beanstock Ventures explain what you need to know for EU MDR compliance.

Key Takeaways

- The EU Medical Devices Regulation (MDR) has replaced the EU Medical Device Directive effective 26 May 2021.
- The EU MDR is greatly expanded to cover more devices, including Software as Medical Device, implantable devices, contact lenses, and many digital health technologies. It also promotes a lifecycle approach to regulation.

- EU MDR requires improved device traceability by introduction of a unique identification system, or UDI (see section 05), for medical devices approved for use in the EU. To keep track of devices through every lifecycle stage, a device identifier (UDI) will be assigned, and all production series will be marked with a production identifier.
- The most important changes in the EU MDR include:
  - Increased scope of medical device definition;
  - New classification rules (including Rule 11 that specifically addresses software);
  - Increased scope of general safety and performance requirements, technical documentation, and clinical data and evaluation requirements;
  - Introduction of traceability and identification system and database; and
  - Increased post-market product surveillance.

SECTION ONE

The Impact of EU MDR on Digital Health Technology Manufacturers

EU Medical Devices Regulation (MDR), adopted by the European Parliament and Council as REGULATION (EU) 2017/745 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 5 April 2017, has replaced the former EU Medical Device Directive (MDD) and went into effect 26 May 2021. After this date, the MDR is applicable for all medical devices sold (developed or imported) in the European Union.

The MDR is significantly more comprehensive and detailed compared to the MDD. While the MDD was comprised of 23 Articles and 12 annexes over 60 pages, the MDR has 123 articles and 17 annexes over 175 pages. While MDD was focused on pre-approval stage (similar to the US FDA 510(k) submission checklist), the new MDR promotes a lifecycle approach to medical device regulation. The new MDR covers more types of devices, for example, Software as Medical Device, implantable devices, contact lenses, and more. Many digital health technologies will now fall into the scope of the new European MDR.

"Digital Health" is defined by the European Union as "tools and services that use information and communication technologies (ICTs) to improve prevention, diagnosis, treatment, monitoring and management of health-related issues and to monitor and manage lifestyle-habits that impact health. Digital health and care is innovative and can improve access to care and the quality of that care, as well as to increase the overall efficiency of the health sector." (ref: https://ec.europa.eu/health/ehealth/home_en)

European manufacturers and distributors of such digital health tools and services, medical web and mobile software applications, and wearable body sensors as examples must carefully consider the new rules and regulatory requirements set forth within the MDR. MDR contains much more detail on medical device software and introduces some key changes to the current European medical device regulation as it pertains to digital health and software in particular.

Key impacts of EU MDR on digital health technologies and medical device software include:

01

The definition of a medical device

"Medical device" is defined in Article 2 of EU MDR as:

> '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.

Recital 19 of MDR describes the approach to the regulation of medical device software:

> 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 lifestyle 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.

An analysis of these two definitions makes it clear that the intended use or intended purpose of a software will be a decisive factor in classifying the software as a medical device or not. In other words, not all software which is used in healthcare settings or interacts with medical devices will be classified as 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.

MDR has increased the scope of medical device definition by adding "prediction" and "prognosis" of disease to it. These new additions bring the advanced digital health care technologies capable of potentially predicting or providing a prognosis of possible future states

of disease identification into the range of medical devices. This means that software which is designed to predict a patient's likelihood of developing a particular disease or software providing healthcare professionals with a probability of individual outcomes of a certain therapy will now fall within the definition of a medical device.

So-called "wellness" software that is simply intended to provide information on or monitor general fitness and wellbeing should not be considered a medical device.

Some examples include:

MEDICAL PURPOSE	NON-MEDICAL PURPOSE
Software suggesting diagnoses based on test results	Software providing patient medical education such as general health tips
Software giving instructions to alleviate symptoms of a certain disease	Software used as physical exercise tracker

02

Software as an accessory to a medical device

If the software does not fall under the definition of a medical device, manufacturers of digital health technologies should also assess whether their product could be considered an "accessory" to a medical device.

Accessories to medical devices also fall under the scope of EU MDR as follows:

> The following products shall also be deemed to be medical devices:
>
> *'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).*

MDR has increased the scope of accessories to medical devices definition by adding "specifically and directly assist the medical functionality of the medical device(s)" to it. It means that accessories to medical devices are covered by MDR provisions and fall under the term "device" in the meaning of the MDR. Again, the manufacturers of digital health technologies should be aware that more products might be regulated in the foreseeable future.

03

Classification

EU MDR introduced new rules for determining the risk classification of medical devices, including a new Rule 11, which specifically addresses software.

Medical device classification is based on intended purpose and inherent risks, and it can range from a lowest-risk Class I (for example, adhesive bandage strip) up to highest risk Class III (for example, prosthetic heart valve). There are four risk classes: Class I, Class IIa, Class IIb, and Class III. The classification determines the conformity assessment route for the device in order to obtain Conformité Européenne (CE) markings. In general, the conformity assessment ranges from self-certification (for Class I) to a full review of the technical design and manufacture of the specific device by a notified body (for Class III). Self-certification includes compliance with general safety and performance requirements, performance of clinical evaluation, preparation of technical documentation, and the issuance of an EU Declaration of Conformity. In addition to Class I requirements, a Class IIa examination requires that a notified body examine the quality management system and the technical data of one representative product sample per product category. In Class IIb, examination is conducted per generic product group, and in Class III, the quality management system and technical data of every product must be examined.

According to Rule 11, which is applicable for digital health technologies and software as a medical device:

- Software intended to provide information that 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 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.

It seems that, based on Rule 11, the vast majority of digital health technologies and software as medical devices will be classified as Class IIa and up, meaning that self-certification is not sufficient in order to obtain EU marketing approval.

04

General safety and performance requirements and technical documentation

EU MDR outlines General Safety and Performance Requirements (GSPRs) in great detail for medical device designers and manufacturers. Annex I of MDR specifies the general safety and performance requirements for medical devices, including some new requirements which are specific to software.

The following new requirements were introduced in the EU MDR:

- Software referred to in this Section (i.e., Annex I) 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).
- Manufacturers shall set out minimum requirements concerning hardware, IT networks characteristics, and IT security measures, including protection against unauthorized access, necessary to run the software as intended.

These requirements must be addressed in the manufacturers' technical documentation as applicable. In addition, existing MDD software-related safety and performance requirements (SPRs) were expanded and include now "software that are devices in themselves" (e.g., SaMD); and "… software shall be developed and manufactured in accordance with the state of the art, taking into account the principles of … information security" (e.g., cybersecurity controls).

Existing MDD SPRs that were transferred to the EU MDR include "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, verification and validation."

In Annexes II and III, the EU MDR prescribes in detail the content of technical documentation. In comparison, the MDD previously did not specify much in terms of the content. Annex II lists six sections of the technical documentation from medical device description to verification and validation, while Annex III of the EU MDR requires several specific elements in the "Technical Documentation on Post Market Surveillance."

The following documentation must be provided in accordance with Annex II:

Software verification and validation (describing the software design and development process and evidence of the validation of the software, as used in 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).

Medical device manufacturers are required to create, maintain, and provide their technical documentation to competent authorities when requested.

05

Unique Device Identification (UDI)

EU MDR introduces a Unique Device Identification (UDI) system for medical devices approved for use in the EU. The purpose of this new requirement is to allow for clear and unambiguous identification of specific medical devices and to facilitate their traceability on the market. This will, of course, also apply to digital health technologies and medical device software.

According to Article 27 of the MDR, the UDI comprises of a Device Identifier (UDI-DI), which is specific to a manufacturer and a device, and the Production Identifier (UDI-PI), which identifies the unit of device production.

Annex VI provides UDI requirements for medical device software, specifically:

- 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.
- A new UDI-DI will be required if there is a significant modification which changes the original performance, the safety or intended use of the software, or the interpretation of data. Examples of such changes include new algorithms, operating platforms, or user interfaces. In addition, minor software revisions such as bug fixes, usability enhancements that are not for safety purposes or operational efficiency, or security patches, will require a new UDI-PI.
- If software is delivered on a physical medium (e.g., CD or DVD), every level of packaging needs to display the UDI in particular format. Software comprising a user interface must display the UDI easily accessible in plain-text format, while software without a user interface needs to be able to transfer the UDI by API.

Identifying Device Classification Under the New Regulations

Introduction of the now notorious Rule 11, which specifically addresses software, led to concerns among manufacturers of digital health technologies that the vast majority of software as medical devices are likely to be Class IIa, or even Class III (the highest risk category), where previously the majority were Class I. This up-classification will cause increased regulatory burden, involvement of a notified body, impeded innovation, and development of novel devices.

Rule 11 begins, "Software intended to provide information which is used to take decisions with diagnosis or therapeutic purposes is classified as Class IIa." It means that software providing temperature readings (e.g., thermometer) shall be classified as Class IIa. Since Rule 11 classification is based on the impact of decision making, multiple software devices shall be up-classified further to the highest risk, Class III. Incorrect decisions based on readings of patient's vitals may certainly lead to "death or an irreversible deterioration of a person's state of health." Does this rule mean that a thermometer shall be classified as Class III?

In order to answer multiple questions and concerns related to Rule 11, Medical Device Coordination Group (MDCG) released its "Guidance on Qualification and Classification of Software." The scope of this guidance is much broader than addressing Rule 11 only, but there is a dedicated section named "Rule 11 – Software for decisions with diagnosis or therapeutic purposes or software intended to monitor physiological processes."

The guidance explains that Rule 11 was introduced to mirror the regulatory guidance developed at the international level and, notably, in the context of the International Medical Device Regulators Forum (IMDRF). The IMDRF framework for risk categorization of software as a medical device (SaMD) classifies the risk of software based on the combination of the significance of the information provided by the software to the healthcare decision and the healthcare situation or patient condition. So, this guidance is trying to introduce more nuanced approach where patient condition is important. It suggests (the guidance is not legally binding) that only one combination will lead to Class III classification: significance of the information (High) and patient condition (Critical).

The table below, included in both IMDRF and MDCG guidance and intended for illustrative purposes only, may provide operators placing medical device software (MDSW) on the EU market with some useful indicative orientation on the risk class applicable to their products as a result of the application of Rule 11 of the MDR.

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

Table 1: Classification Guidance on Rule 11

Device Traceability Under the MDR

The EU MDR requires improved device traceability by introduction of an identification system for medical devices approved for use in the EU.

To keep track of devices through every lifecycle stage, a Unique Device Identifier (UDI) will be assigned, and all production series will be marked with a production identifier. These tracking measures satisfy the new mandate for UDI, which is entered into the European Databank on Medical Devices (EUDAMED) database.

The purpose of EUDAMED is to create a single European-wide accessible repository of device-related information for patients, regulators, notified bodies, and manufacturers to access data for medical devices being marketed in the EU and help improve overall post-market surveillance. Access to EUDAMED is free of charge.

Annex VI of EU MDR provides detailed requirements for a submission of UDI information to EUDAMED.

The European Medical Device Coordination Group (MDCG) has published a new "Guidance note integration of the UDI within an organization's quality management system." The guidance describes several QMS areas to be considered for integration with UDI requirements:

- Design and development
- Product documentation and retention
- Production and process
- Serious incidents and field safety corrective actions (FSCA)
- Purchasing controls
- Documentation and records
- Enterprise resource planning
- UDI data provided to the EUDAMED database

MDCG Guidance states that procedures should be implemented and documented in order to ensure that:

a. UDI/Device data as referred to in Annex VI MDR are provided to EUDAMED.

b. Where a change of a device affects the data attributes associated with a UDI-DI, the corresponding UDI data are updated in EUDAMED.

In addition, MDCG Guidance provides an example of a UDI implementation plan.

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Strategies to Ensure Adequate Clinical Data

Article 2(51) Definitions of the EU MDR defines clinical evidence as: “clinical data and clinical evaluation results pertaining to a device of a sufficient amount and quality to allow a qualified assessment of whether the device is safe and achieves the intended clinical benefit(s), when used as intended by the manufacturer.”

The requirements for clinical evaluation are outlined in Article 61 of the MDR (including Annex XIV).

Medical Device Coordination Group (MDCG) released its Guidance on Clinical Evaluation (MDR) / Performance Evaluation (IVDR) of Medical Device Software in order to provide a framework for the determination of the appropriate level of clinical evidence required for medical device software (MDSW) to fulfil the requirements set out in EU MDR and EU IVDR.

Just as in the case of clinical evaluations for medical devices other than digital health technologies and SaMD, clinical evidence is required to demonstrate continued device safety and intended clinical benefits and positive effects on patient health over the entire lifecycle of the software.

Manufacturers of digital health technologies and SaMD should follow the principles listed below while performing clinical evaluations:

- Establishment and maintenance of a clinical evaluation plan and criteria applied to generate the necessary clinical evidence based on the characteristics of the device.
- Identification of the relevant data pertaining to performance and/or safety of the device and any remaining unaddressed issues or gaps in the data.
- Appraisal of the relevant data in terms of quality and its contribution to the clinical evaluation.
- Analysis of the available data and its relevance with regard to demonstrating conformity with the relevant General Safety and Performance Requirements (GSPRs).
- Documentation of the relevant data, their assessment, and the clinical evidence derived therefrom in the clinical evaluation report.
- Update the clinical evaluation and its documentation throughout the life cycle of the MDSW concerned with data obtained from implementation of the manufacturer's Post-Market Clinical Follow-up plan.

Manufacturers of digital health technologies and SaMD are expected to provide sufficient clinical evidence to demonstrate conformity with relevant GSPRs under the normal conditions of the device's intended use. Clinical evidence should be sufficient and appropriate in view of the characteristics of the device, its clinical risks, and its intended purpose. The level of clinical evidence necessary should be specified and justified by the manufacturer.

When compiling the clinical data/evidence of medical device software, three key components should be considered:

1. **VALID CLINICAL ASSOCIATION / SCIENTIFIC VALIDITY**

   The extent to which the MDSW's output (e.g., concept, conclusion, calculations), based on the inputs and algorithms selected, is associated with the targeted physiological state or clinical condition.

   MDCG example: MDSW that detects heart arrhythmia by analyzing auscultation sound obtained by a digital stethoscope requires demonstrating VALID CLINICAL ASSOCIATION of the association between abnormal cardiac sounds and heart arrhythmia.

2. **TECHNICAL PERFORMANCE/ANALYTICAL PERFORMANCE**

   Demonstration of the MDSW's ability to accurately, reliably, and precisely generate the intended output from the input data.

   Evidence supporting TECHNICAL PERFORMANCE/ANALYTICAL PERFORMANCE can be generated through verification and validation activities, e.g., unit-level, integration, and system testing. In other words, TECHNICAL PERFORMANCE / ANALYTICAL PERFORMANCE confirms and provides objective evidence that the software was correctly constructed – namely, correctly and reliably processes input data and generates output data with the appropriate level of accuracy and repeatability and reproducibility (i.e., precision); and demonstrates that (a) the software meets its specifications and (b) the software specifications conform to user needs and intended uses.

3. **CLINICAL PERFORMANCE**

   Demonstration of a MDSW's ability to yield clinically relevant output in accordance with the intended purpose.

   Evidence supporting CLINICAL PERFORMANCE can be generated by testing the MDSW under evaluation, or an equivalent device, in the target population and for the intended use.

The level of the clinical data and clinical evidence required to demonstrate safety and performance and their adequacy are determined in accordance with the requirements documented within Article 61 MDR.

Guidelines for Post-Market Surveillance

One of the biggest additional changes in the EU MDR is related to post-market surveillance. Implementing and promoting the full lifecycle approach to medical device regulation, the EU MDR (Article 2 (60)) defines post-market surveillance as a proactive and systematic process which manufacturers implement and carry out (with other economic operators) in order to take corrective and preventive actions in accordance with information on medical devices and their performance. The surveillance and reporting of incidents involving medical devices allows identification of problems with the design, manufacture, or use of medical devices and, ultimately, enhances patient safety.

Article 83, "Post-market surveillance system of the manufacturer," clarifies expectations and states that the post-market surveillance system is an integral part of the manufacturer's quality management system:

> *For each device, manufacturers shall plan, establish, document, implement, maintain and update a post-market surveillance system in a manner that is proportionate to the risk class and appropriate for the type of device. That system shall be an integral part of the manufacturer's quality management system referred to in Article 10(9).*
>
> *The post-market surveillance system shall be suited to actively and systematically gathering, recording and analyzing relevant data on the quality, performance and safety of a device throughout its entire lifetime, and to drawing the necessary conclusions and to determining, implementing and monitoring any preventive and corrective actions.*

Manufacturers of Class I medical devices (Classes Is, Im, and Ir) are required to prepare a post-market surveillance report to summarize the results and conclusions of the data gathered as defined in the PMS plan. In addition to PMS Report, manufacturers of Class IIa, Class IIb, and Class III devices are now required to generate Periodic Safety Update Report (PSUR). The PSUR has to include the conclusions of the benefit-risk determination (when benefits of the product outweigh the risks or damages of its use), the main findings of the post-market clinical follow-up, rationale for corrective actions taken, and the volume of sales of the device together with information on the population using the device. The PSUR is part of the technical documentation and has to be updated regularly: at least every two years for Class IIa devices and annually for Class IIb and Class III devices.

Implications for US-Based and Other Global Device Development Companies

Because compliance with the EU MDR applies to any medical device that is imported to the EU, the standard has broad global implications, including for US-based companies that are already subject to United States Federal Drug Administration (FDA) regulations.

The US FDA is engaging with international regulatory agencies to promote alignment in regulations. One of these international engagements is via International Medical Device Regulators Forum (IMDRF). According to IMDRF's website: "IMDRF is a forum of voluntary medical device regulators from around the world who have come together to build on the strong foundational work of the Global Harmonization Task Force on Medical Devices (GHTF), and to accelerate international medical device regulatory harmonization and convergence."

The current IMDRF members represent medical device regulatory authorities from several countries and entities, EU included. EU is represented by European Commission Directorate-General for Internal Market, Industry, Entrepreneurship and SMEs and supported by advisory group MDCG (Medical Device Coordination Group).

IMDRF's Strategic Plan 2021 – 2025 states the following:

> *The IMDRF Management Committee (MC) is aware of the regulatory challenges within its global regulatory model for innovative devices. In order to manage these challenges and to achieve greater global regulatory convergence and consistency, development and review of regulatory guidance will be necessary.*
>
> *In order to facilitate timely access to safe medical devices for patients, achieving global regulatory convergence for these emerging areas is critical. IMDRF established the Software as a Medical Device (SaMD) working group that developed guidance on the appropriate regulatory controls for SaMD. The guidance has promoted international regulatory convergence as many countries who have finalized their SaMD regulatory approaches after this work item, have adopted or aligned with these IMDRF guidance. Some of the current IMDRF work items such as Medical Device Cybersecurity and Personalized Medical Devices are intended to promote convergence in regulatory requirements, support safe innovation and ensure better clinical outcomes for patients.*

To date, the SaMD WG has published the following documents:

- Software as a Medical Device (SaMD): Key Definitions (IMDRF/SaMD WG/N10FINAL:2013)
- Software as a Medical Device (SaMD): Possible Framework for Risk Categorization and Corresponding Considerations (IMDRF/SaMD WG/N12FINAL:2014)
- Software as a Medical Device (SaMD): Application of Quality Management System (IMDRF/SaMD WG/N23 FINAL:2015)

The group is currently developing guidance for the Clinical Evaluation and Evidence for Software as a Medical Device (SaMD) *(Software as a Medical Device (SaMD): Clinical Evaluation (SaMD WG (PD1)/N41R3)).* The group's objective is to provide detailed guidance and clarity on when and to what level clinical evaluation and evidence is necessary or acceptable for SaMD from a patient safety perspective with particular emphasis for those types of SaMD with diagnostic functionality.

IMDRF's provides a common definition of SaMD in the "Software as a Medical Device (SaMD): Key Definitions document" as "software intended to be used for one or more medical purposes that perform these purposes without being part of a hardware medical device."

IMDRF's "Possible Framework for Risk Categorization" is used in both EU and US. In the EU, Medical Device Coordination Group (MDCG) released its "Guidance on Qualification and Classification of Software" in order to explain how risk categorization network can be used to classify SaMD (Rule 11). US FDA uses IMDRF's risk-categorizations to apply a risk-based policy to its guidance (still in draft) of Clinical Decision Support Software.

IMDRF's "Application of Quality Management System" provides guidance on the application of existing standardized and generally accepted QMS practices to digital health technologies and SaMD. This document provides a mapping of applicable clauses, articles, and subsections of the regulations for a QMS for SaMD for the jurisdictions represented in the current IMDRF SaMD

working group members (US FDA and EU included). This document references both US Quality System Regulation (21 CFR 820) and ISO 13485 (the only QMS standard listed in the EU list of harmonized standards and as such the only reasonable way to implement a QMS according to the MDR).

Although still in draft, IMDRF's "Software as a Medical Device (SaMD): Clinical Evaluation" is already utilized in both EU and US. In the EU, Medical Device Coordination Group (MDCG) released its "Guidance on Clinical Evaluation (MDR) / Performance Evaluation (IVDR) of Medical Device Software" in order to provide a framework for the determination of the appropriate level of clinical evidence required for medical device software (MDSW) to fulfil the requirements set out in EU MDR and EU IVDR. According to the MDCG, "in order to promote global convergence, this document takes into account certain concepts outlined in International Medical Device Regulators Forum (IMDRF) guidance documents." In the US, the FDA released "Software as a Medical Device (SAMD): Clinical Evaluation." According to the FDA, "This guidance adopts the internationally converged principles agreed upon by the IMDRF."

Despite harmonization efforts listed above, significant differences in US and EU regulations remain. Here are a few key differences:

- In the EU, the term "SaMD" isn't used. Instead, they use the term "medical device software" or "MDSW." MDSW is defined as software that is intended to be used, alone or in combination, for a purpose as specified in the definition of "medical device" in the MDR.
- In the US, devices fall into three categories: Class I, Class II, and Class III. In the EU, the MDR distinguishes Class I, IIa, IIb, and III.
- In the US, a majority of the devices (some Class I and Class II) receive 510(k) clearance in order to be marketed. This regulatory pathway requires medical device manufacturers to present data demonstrating the functional equivalence of the device with a previously approved device, known as the "predicate." In the EU, a majority of the devices (Class I with medium risk and up to Class III) will need to undergo conformity assessments (assessment of a compliance with MDR requirements. These requirements are different for each class of devices) with notified bodies in order to receive CE markings to be marketed.

Certification Process with Notified Bodies

There are currently 22 notified bodies listed on the NANDO MDR database:

Notified bodies play a key role in supporting medical device manufacturers to place safe and compliant medical devices on the EU market. They are supporting the manufacturers by conducting conformity assessment procedures and grant conformity certificates to medical devices. There are certain expectations that a notified body must meet before being officially accredited by the EU Commission. A key aspect of the notified body's role is to audit the quality management system of the manufacturer and review the technical documentation of devices in Class Is/Im/Ir, IIa, IIb, and III. The scope of the conformity assessment depends on the risk classification of the medical device. Notified bodies will issue a conformity certificate upon completion of the assessment (if a medical device conforms to MDR requirements).

After receiving this certificate, the medical device manufacturer can label the product with the CE Mark, which is required for distribution and sale in the EU. Additionally, the EU member state accrediting the notified body will then inform the European Commission that the product complies with the MDR requirements.

Under the EU MDR, notified bodies will also play a new role in enforcing regulation through follow-up surveillance (including unannounced) audits of manufacturing processes and the quality management systems.

The EU MDR imposed stricter requirements on notified bodies. In order to assess whether notified bodies fulfil these stricter requirements, they have to be re-designated under the MDR. Among other things, stricter requirements have been included for impartiality, independence, staff expertise, and more detailed procedures which have to be followed when performing assessment work. As a result of stricter requirements, there are currently far fewer notified bodies under the MDR than there were under the now retired EU MDD (for example, there were 75 notified bodies in 2013).

Under the EU MDR, larger numbers of medical devices are expected to require notified body conformity assessment (medium risk Class I devices require conformity assessment now).

There are additional factors that led to the shortage of the notified bodies in the EU: Brexit, coronavirus pandemic, stricter requirements for subject matter experts that notified bodies must employ, etc.

Many medical device manufacturers with their products already on the market (certified under retired MDD) delayed the need for MDR certification until 26 May 2024. This extension was given by the EU because of the global COVID-19 pandemic. A survey conducted by The European Association Medical Devices - Notified Bodies found that **7,272 certificates (CE Marks) will expire in 2024**. The survey states: “Thus it is definitely a challenge to be taken into consideration if we want to avoid the risk of shortages of medical devices in 2024 which could lead to risks for patients.”

Conclusion

While the EU MDR is a necessary and long-awaited update to EU compliance standards for medical devices, it nevertheless presents new challenges for manufacturers. With expanded definitions of medical devices, increased requirements for documentation and traceability, and new guidance for post-market surveillance, the EU MDR will mean that manufacturers will have to improve processes at every step of development. However, using the guidelines and tips from Beanstock Ventures and Jama Software experts, global medical device manufacturers will be able to better position their products for compliance and long-term marketability.

Jama Software can help medical manufacturers create a closed-loop requirements management process that allows for real-time collaboration and decision-making. This enables organizations to keep up with the increasing pace of innovation as they drive new quality products to market, on time, while maintaining compliance with government regulations. To learn more about Jama Software's solutions, contact us.

BEANSTOCK VENTURES

HOW BEANSTOCK VENTURES CAN HELP

BeanStock Ventures is a project-based Software Development and Regulatory services with expertise in Digital Health including regulatory expertise in SaMD and Cybersecurity. With over 20 years of regulatory and software development experience, BeanStock Ventures has healthcare specific domains including but not limited to embedded devices, biotechnology, diagnostics, IoMT, the point of care, critical care, laboratory, automation, analytic, workflows, and connectivity.

The BeanStock Ventures service offerings include technical program management, software product development and regulatory compliance. In addition to the BeanStock Ventures domain expertise and experience in the medical device, biotechnology, and life sciences industry, it is also one of nine companies globally that has been approved as an FDA-Accredited 510(k) Third-Party Reviewer for the United States Food and Drug Administration (FDA).

For more information, please visit: www.beanstockventures.com or email marketing@beanstockventures.com.

Jama software®

ABOUT JAMA SOFTWARE

Jama Software is focused on maximizing innovation success. Numerous firsts for humanity in fields such as fuel cells, electrification, space, autonomous vehicles, surgical robotics, and more all rely on Jama Connect® to minimize the risk of product failure, delays, cost overruns, compliance gaps, defects, and rework. Jama Connect® uniquely creates Living Requirements™ that form the digital thread through siloed development, test and risk activities to provide end-to-end compliance, risk mitigation, and process improvement. Our rapidly growing customer base of more than 12.5 million users across 30 countries spans the automotive, medical device, life sciences, semiconductor, aerospace & defense, industrial manufacturing, financial services, and insurance industries. To learn more, please visit us at jamasoftware.com.