Guide on Medical Device Regulation and App Certification

Medical Device Regulation (MDR) and App Certification as a Challenge

The **Medical Device Regulation (MDR)**[1] regulates the placing on the market, making available on the market or putting into service of medical devices for human use and accessories for such devices in the Union. It was planned to become fully applicable on May 26th, 2020. Due to the Corona crisis, the date of application was postponed by one year.[2] As the Regulation is still to become fully applicable, official guidance material by states and the EU regarding practical implementation is not yet fully available.

Medical devices (MD) make an essential contribution to healthcare in the EU for the benefit of European citizens. They are crucial in diagnosing, preventing, monitoring and treating illness, and overcoming disabilities (e.g. sticking plasters, X-ray scanners, dentures to hip joints and in-vitro diagnostic devices that monitor diabetes or identify infections) and are also important to the economy, providing €110 billion in sales and 675,000 jobs in Europe.[3]

A **Medical Device** is defined by the MDR as 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.[4]

An '**Accessory for a medical device'** is defined as 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.[5] It is possible that an app that is connected to a device that measures vital data is qualified as an accessory for a medical device.[6]

It is important to note that not all software used within healthcare is qualified as a medical device. Decisive is the intended purpose and functionality of the software/app. "Software which is intended to process, analyse, create or modify medical information may be qualified as a medical device software if the creation or modification of that information is governed by a medical intended purpose."[7] One needs to distinguish between software for medical purposes and software for general purposes. Software for general purposes even in a healthcare setting is not a medical device. Further criteria to distinguish between software for medical purposes and software for general purposes are still unclear.[8]

Classification: Regarding devices that are intended to be used in combination with another device, it has to be observed that the classification rules apply separately to each of the devices. Accessories for a medical device shall be classified in their own right separately from the device with which they are used. The same applies for software that is independent of any other device, it shall be classified in its own right. However, software, which drives a device or influences the use of a device, shall fall within the same class as the device.[9]

Importance of the MDR and Certification for Transforming and Supporting Person-centred Care

Generally, we consider as MD only hip prostheses or pacemakers, but their range is quite wide, ranging from contact lenses to bandages, X-ray scanners to in vitro diagnostic medical devices. Many of these devices are essential to health and quality of life, as well as to the European economy, and consumers expect them to be safe and effective.

In the Blueprint twelve personas have been developed, with different medical conditions and needs.[10] With the introduction of MD into their lives these personas can better manage symptoms, therapies, side effects and medical appointments and improve their quality of life.

The inclusion of MD within these Blueprint scenarios is important because it will allow evaluation of how different types of MD work together, and how different data from varied sources are analysed and shared among the users. This approach lays the foundation to better understand and demonstrate the clinical benefit with evidence of the use of MD.

Case Study using the Nikos Blueprint Persona

Nikos' lifestyle has changed drastically due to the diagnosis of metabolic syndrome that requires a different diet, multiple medications, and increased physical exercise. He is registered in a municipal-funded, basic periodic healthy lifestyle intervention programme, but he cannot afford the costs for further coaching afterthe programme is completed. The Greek NHS provides an Electronic Health Record (EHR) and on-line national e-prescription system allowing the multidisciplinary team (MDT) to have access to the patient's medical record including his prescribed medication. Unfortunately, the system is not available as part of routine care within the

Guide on Medical Device Regulation and App Certification

Greek NHS and is limited only to pilot projects and limited services. The MDT help Nikos with his new lifestyle and provide him with different medical devices (MD) which are able to monitor his chronic conditions (e.g. weight, diet, blood pressure, blood glucose and physical activity) directly connect with EHR and interoperable. To ensure that all the devices work and collect Nikos's data, and enable it to be shared among the MDT, a network data connection is needed. In this way the network connection allows Nikos to stay engaged with the MDT/or caregivers and the data is available to all of them. Wireless connections to smartphones or tablets enable smaller, easier to use or more comfortable to wear devices whereas connected devices can also be integrated with other medical devices or data sources to enhance treatment. Connecting all the device together provides the opportunity to perform clinical evaluations and figure out how to better manage the data. According to the MDR, it is necessary to carry out a clinical evaluation of a MD. Thus, a clinical evaluation will include not only Nikos' health data but also clinical follow-up of the MD in the market (Post Market Clinical Follow-Up, PMCF) and information about MDs's safety and performance.

ICT Solution	Medical Device Class	Medical Purpose
Measure weight and BMI	I (non invasive)	No
Dietary advice mobile app	I (non invasive)	No
Blood Pressure	I (non invasive)	Yes
Glucose	I (non invasive)	Yes
Education (gamification)		No
Physical training app	I (non invasive)	No
Social media		No

Key Issues[11]

- **Low evidence:** The lack of evidence to demonstrate the effectiveness of MD. This is linked to the difficulties of designing randomized controlled trials for medical devices, where blinding and proper randomization can be hard to implement.
- **Learning Curve Effects:** Clinical benefits may be reached only after an initial training/educational program for the end-users.
- **Organisational impact:** Medical devices have a greater potential to indirectly impact an organization. Improvements, especially from an economic standpoint, can be gained by improving patient pathways or hospital workflows.
- **Incremental innovation:** Innovation of MD often happens in small but fast steps like software upgrades or improved battery life. For this reason, it is important to understand whether and/or when it is necessary to revaluate these small improvements, and if so, in which degree new assessments are needed.
- **Diversity:** Medical devices cover a wide variety of products from small, single-use disposables (e.g., syringes), to high cost, long-term-use resources (e.g., magnetic resonance imaging machinery). This diversity creates an obstacle when trying to establish standard procedures for assessment and there is no solution for this problem
- **Dynamic pricing:** Complex medical devices can often involve a high up-front investment with benefits only showing after longer periods of use and list pricing, used for pharmaceuticals do not exist for MD.

Supporting Mechanisms and Tools that Help Address the Topic

Policies on different levels

World Health Organization (WHO)[12] has developed a guidance document which aims to raise the awareness of the importance of developing and implementing health technology policies – comprised of regulatory, health technology management, and health technology assessment components – within the context of a national health plan. It addresses the role of medical devices in global health care and the prioritization of needs within Member States and discusses the key components of an effective policy, the organisational systems necessary for implementation of the policy, and the methodology for measuring progress.

European Commission[13-14]***:*** MD are regulated by national competent authorities, a medicines regulatory authority in a European Union Member State, but the European Medicines Agency (EMA) is also involved in the assessment of certain categories of medical device under European Union (EU) legislation.

EU Member States: Example Italy[15-16]**:**

The work carried on from Italy on the managing of MDR has been appreciate in the European Union. Indeed, February 2019, the Medical Device Coordination Group (MDCG) of the EC has decided to revise and adopt the National Classification of Medical Devices (CND)[17] as nomenclator for the European database EUDAMED, named European Medical Device Nomenclature (EMDN), thanks to the peculiarities of structure, purpose, usability and updating methodology. The CND allows to classify MD into homogeneous product categories according to

criteria that allow a comparison between products belonging to the same classification group, also from an economic point of view. Moreover, it helps to monitor and assess the use of devices and accidents for individual types of MD for surveillance reasons.

Digital tools

The European Commission is working to provide its citizens access to safe and top-quality digital services in health and care. Transformation of healthcare in the Digital Single Market will benefit people, healthcare systems and the economy. They enable innovative approaches to independent living or integrated health and social care. Health data and advanced data analytics can help accelerate scientific research, personalised medicine, early diagnosis of diseases and more effective treatments.[18]

The **Digital Single Market**[19] aims to create the right conditions for digital networks and service. High speed, security and trustworthy infrastructure and service will be supported by the right regulatory conditions.

The ***Register of the Certified Defence-related Enterprises (CERTIDER)***[20] allow you to find information centrally about enterprises that are certified under Directive 2009/43/EC of the European Parliament and of the Council of 6 May 2009 simplifying the terms and conditions for the transfers of defence-related products within the EU.

The ***European Database for Medical Devices – EUDAMED***[21] is a secure web-based portal. It is a central repository for information on market surveillance exchanged between national competent authorities and the Commission. Its use is restricted to national competent authorities, it is not open for consultation and is not publicly accessible. The new MDR and on IVDR establish a much wider EUDAMED database than the existing one under the current directives (Eudamed2). Eudamed2, will function as a registration system, a collaborative system, a notification system, a dissemination system (open to the public), and will be interoperable.

The ***Basic Unique Device Identification (UDI) System***[22-23] is the main access key for device-related information in the EUDAMED database and it is referenced in relevant documentation [e.g. certificates (including certificate of free sale), EU declaration of conformity, technical documentation and summary of safety and (clinical) performance)].It identify and connect devices with the same intended purpose, risk class and essential design and manufacturing characteristics. It is independent/separate from the packaging/labelling of the device and it does not appear on any trade item.

CP-DS: Legislation on substances in construction products[24] is database designed to help all interested parties to identify all relevant regulations in the field of dangerous substances in construction products.

Main Stakeholders Concerned

There are many stakeholders involved in the medical device sector including manufacturers, regulators, healthcare providers, clinicians and patients. Involving representatives from all stakeholder groups is essential to produce standards that promote safety and result in enhanced patient outcomes.

World Health Organization (WHO)[25] is charged with providing leadership on global health matters, setting norms and standards, articulating evidence-based policy options, providing technical support to countries and monitoring, assessing health trends and participating in the work of Technical Committees.

The International Medical Device Regulators Forum (IMDRF)[26] is an organization of national regulatory authorities dedicated to promoting international requirements and practices. In particular, the IMDRF aims to promote harmonized regulation of the safety, performance, effectiveness and quality of medical devices and to serve as an information exchange through which countries with medical device regulatory systems under development can benefit from the experience of countries with established systems.

National Health Authorities: Every country has designated one or more governmental bodies with the authority to oversee and regulate aspects of its healthcare system. Their regulatory activities related to medical devices may include regulation of the development, manufacture and distribution of the medical devices, approval prior to commercial distribution, and post market surveillance of the safety and performance of the medical devices.

Examples, Good Practices and Evidence

InForMed project[27-28] - aims to establish an integrated pilot line for medical devices. The pilot line includes micro-fabrication, assembly and even the fabrication of smart catheters. The aim of the pilot line:

- to safeguard and consolidate Europe's strong position in "traditional" medical diagnostic equipment,
- to enable emerging markets - especially in smart minimally invasive instruments and point-of-care diagnostic equipment,
- to stimulate the development of entirely new markets, by providing an industrial micro-fabrication and assembly facility where new materials can be processed and assembled.

Protocols will be developed to ensure an efficient technology transfer between the different links in the value chain. Six challenging demonstrators' products will be realized that address societal challenges in: "Hospital and Heuristic Care" and "Home care and well-being," and demonstrate the trend towards "Smart Health" solutions.

eyePoC project[29] worked towards the clinical validation and market introduction of a device previously developed for ocular surface diseases (OSDs), named Tear Monitor, which allowed diagnosis and monitoring of Dry Eye and inflammation by measuring biomarkers in tears. Medical devices which are able to detect and measure biomarkers in human samples in a fast and non-invasive way can easily be introduced at the doctor's office, thus enabling better diagnosis of diseases in an objective manner and accurately monitoring treatments' effectiveness. Medical devices would allow objective diagnosis and accurate monitoring of a patient's condition and treatment efficacy to become a standard part of routine clinical protocols.

Potential Funding Sources

The procurement ecosystem should be aware that products certified under the old Directive 93/42/CEE[30] and products certified under the MDR[31] will coexist on the market until May 2025. During this period both types of certification will have equal status under the law and no discrimination in public tenders may take place.

Crowdfunding[32] is a way of raising money to finance projects and businesses. It enables fundraisers to collect money from many people via online platforms. Crowdfunding is most often used by start-up companies or growing businesses as a way of accessing alternative funds. It is an innovative way of sourcing funding for new projects, businesses or ideas. Exist different types of crowdfunding:

1. **Peer-to-peer lending:** The crowd lends money to a company with the understanding that the money will be repaid with interest. It is very similar to traditional borrowing from a bank, except that you borrow from lots of investors.
2. **Equity crowdfunding:** Sale of a stake in a business to a number of investors in return for investment. The idea is similar to how common stock is bought or sold on a stock exchange, or to a venture capital.
3. **Rewards-based crowdfunding:** Individuals donate to a project or business with expectations of receiving in return a non-financial reward, such as goods or services, at a later stage in exchange of their contribution.
4. **Donation-based crowdfunding:** Individuals donate small amounts to meet the larger funding aim of a specific charitable project while receiving no financial or material return.
5. **Profit-sharing /revenue-sharing:** Businesses can share future profits or revenues with the crowd in return for funding now.
6. **Debt-securities crowdfunding:** Individuals invest in a debt security issued by the company, such as a bond.
7. **Hybrid models:** Offer businesses the opportunity to combine elements of more than one crowdfunding type.

References and Guidance Documents

- Critical Review of European Health-Economic Guidelines for the Health Technology Assessment of Medical Devices (2019): https://doi.org/10.3389/fmed.2019.00278
- MDCG 2018-1 v3 Guidance on BASIC UDI-DI and changes to UDI-DI, European Commission (2020): https://ec.europa.eu/docsroom/documents/40322
- Unique Device Identification (UDI) System under the EU Medical Device Regulations, European Commission (2017): https://ec.europa.eu/docsroom/documents/36664/attachments/1/translations/en/renditions/native
- Medical Devices-Sector, European Commission: https://ec.europa.eu/growth/sectors/medical-devices_en
- European Innovation Partnership on Active and Healthy Aging; Blueprint Personas (2020): https://ec.europa.eu/eip/ageing/blueprint_en
- European Medicines Agency; Medical Devices (2020): https://www.ema.europa.eu/en/human-regulatory/overview/medical-devices
- Medical Device Establishment License (MDEL), government of Canada (2020): https://bit.ly/2W1M24l
- Ministero della Salute (2020): http://www.salute.gov.it/
- Ministero della Salute (2020): http://www.salute.gov.it/portale/temi/p2_3_dispositivi.html
- National classification of medical devices (CND), Ministero della Salute (2020): http://www.salute.gov.it/portale/temi/p2_6.jsp?lingua=italiano&id=328&area=dispositivi-medici&menu=classificazione&tab=1
- Development of medical device policies, WHO (2011): https://www.who.int/medical_devices/policies/en/

- Conformity assessment, Zentralstelle der Länder für Gesundheitsschutz bei Arzneimitteln und Medizinprodukten: https://www.zlg.de/index.php?eID=dumpFile&t=f&f=467&token=892121f7cd0a8573648a160c206f605eb26143a0
- InForMed project: http://www.informed-project.eu/index.php; https://cordis.europa.eu/project/id/662155
- eyePoC project: https://cordis.europa.eu/project/id/652132

Endnotes

1. EUR-Lex. (2017). *Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC (Text with EEA relevance.)*. Brussels: European Commission. https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32017R0745; not yet fully applicable.
2. European Commission. (2020). *Commission postpones application of the Medical Devices Regulation to prioritise the fight against coronavirus.* Brussels: European Commission. https://ec.europa.eu/commission/presscorner/detail/en/IP_20_589.
3. European Commission. (2020). *Medical Devices – Sector.* Brussels: European Commission. https://ec.europa.eu/growth/sectors/medical-devices_en.
4. Art. 2 (1) MDR.
5. Art. 2 (2) MDR.
6. Gassner, U. M. (2017). *Die neue Medizin Produkte Verordnung.* Aktueller Text mit Einführung, p. 26. Köln.
7. European Commission. (2017-2019). *MDCG, Guidance on Qualification and Classification of Software in Regulation (EU) 2017/745 – MDR and Regulation (EU) 2017/746 – IVDR.* https://ec.europa.eu/docsroom/documents/37581; *MDCG 2019-11, Guidance on Qualification and Classification of Software in Regulation (EU) 2017/745 – MDR and Regulation (EU) 2017/746 – IVDR.* Brussels: European Commission. https://ec.europa.eu/health/sites/health/files/md_topics-interest/docs/md_mdcg_2019_11_guidance_en.pdf.
8. Gassner, U. M. (2017). *Die neue Medizin Produkte Verordnung.* Aktueller Text mit Einführung, p. 26. Köln.
9. Medical Device Regulation. (2020). Cf. *Implementing Rules, Annex VIII, Chapter 2, Arts. 3.2,3.3 MDR.* https://www.medical-device-regulation.eu/2019/08/08/annex-viii/.
10. European Innovation Partnership on Active and healthy Ageing. (2020). *Blueprint Personas.* https://ec.europa.eu/eip/ageing/blueprint_en.
11. Blüher, M., Saunders, S. J., Mittard V., Torres R.T., Davis J.A., & Saunders, R. (2019). Critical Review of European Health-Economic Guidelines for the Health Technology Assessment of Medical Devices. *Frontiers in Medicine, 6,* 278. https://doi.org/10.3389/fmed.2019.00278
12. World Health Organization. (2020). *Medical devices.* https://www.who.int/medical_devices/policies/en/.
13. European Medicines Agency. (1995-2020). *Medical Devices.* https://www.ema.europa.eu/en/human-regulatory/overview/medical-devices.
14. European Commission. (2020). *Medical Devices – Sector.* https://ec.europa.eu/growth/sectors/medical-devices_en.
15. Ministero della Salute. (2020). http://www.salute.gov.it/.
16. Ministero della Salute. (2020). *Dispositivi medici e altri prodotti.* http://www.salute.gov.it/portale/temi/p2_3_dispositivi.html.
17. Ministero della Salute. (2020). *Classificazione Nazionale dei Dispositivi medici (CND).* http://www.salute.gov.it/portale/temi/p2_6.jsp?lingua=italiano&id=328&area=dispositivi-medici&menu=classificazione&tab=1.
18. European Commission. (2020). *Transformation of Health and Care in the Digital Single Market.* Brussels: European Commission. https://ec.europa.eu/digital-single-market/en/policies/ehealth.
19. European Commission. (2020). *Policies on Shaping the Digital Single Market.* Brussels: European Commission. https://ec.europa.eu/digital-single-market/en/policies/76026/3786.
20. European Commission. (2009). *Certified Defence-related Enterprises (CERTIDER).* Brussels: European Commission. https://ec.europa.eu/growth/tools-databases/certider/index.cfm.
21. European Commission. (2017). *Medical Devices – EUDAMED.* Brussels: European Commission. https://ec.europa.eu/growth/sectors/medical-devices/new-regulations/eudamed_en.
22. European Commission. (2018). *MDCG 2018-1 v3 Guidance on BASIC UDI-DI and changes to UDI-DI.* Brussels: European Commission. https://ec.europa.eu/docsroom/documents/40322.
23. European Commission. (2017). *Unique Device Identification (UDI) System under the EU Medical Device Regulations 2017/745 and 2017/746.* Brussels: European Commission. file:///C:/Users/merri/AppData/Local/Temp/faq_udi_en.pdf.
24. European Commission. (2020). *CP-DS: Legislation on substances in construction products.* Brussels: European Commission. https://ec.europa.eu/growth/tools-databases/cp-ds_en.
25. World Health Organization. (2020). https://www.who.int/.
26. International Medical Device Regulators Forum. (2011). http://www.imdrf.org/.
27. InForMed project. (2015-2018). http://www.informed-project.eu/index.php.
28. InForMed project. (2015-2018). http://www.informed-project.eu/index.php; https://cordis.europa.eu/project/id/662155.
29. eyePoC project. (2014-2015). https://cordis.europa.eu/project/id/652132.
30. EUR-Lex. (1993). *Consolidated text: Council Directive 93/42/EEC of 14 June 1993 concerning medical devices.* https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:01993L0042-20071011.

31. EUR-Lex. (2017). *Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC (Text with EEA relevance.)*. https://eur-lex.europa.eu/eli/reg/2017/745/oj/eng.
32. European commission. (2020). *Guide on Crowdfunding*. Brussels: European Commission. https://ec.europa.eu/growth/tools-databases/crowdfunding-guide_en.

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