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Review Article

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Impact of New Medical Device Regulation in European Union

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ABSTRACT

The European Union (EU) is responsible for the proposing and implementation of new regulations in EU, the european commission put first medical device directive (MDD) into the place in June 1993 under the council directive 93/42/EC, which is the first attempt to harmonize the medical device regulation which is marketed across EU member states, the medical device manufacturers were attracted to the EU device market because of faster approvals, less strict and more innovation friendly than US and the shorter time to market for medical device, but the recent medical device controversy like PIP breast implant and MoM hip implant devices created controversy within the public because of its adverse effects and there should be need for the formalized regulation to stringent the requirements for approval of the medical device i.e., for class 3 devices biocompatibility testing requirements which is in the new medical device regulation 2017/745/EC is amended from directive to regulation in European Parliment.

Keywords: European union; Medical device; *In vitro* diagnostics; European economic community; Notified bodies

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INTRODUCTION

The medical device regulation was finally agreed after the prolonged difficult processes agreement has finalized the new European Union medical device regulation, which is approved in the parliament of Europe in April 5, 2017 and after the approval it is published in the official journal of European Union on 5 may 2017. The new regulation has lays down new rules concerning the placing the device on the market and checking the availability of the device in market, the new rules also applies to the clinical investigation concerning the medical device and accessories conducted in the EU.

The new regulation i.e. 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, will consolidate two existing legal provisions and

replace both the current medical device directive (93/42/EEC) and the active implantable medical device directive (90/385/EEC).

The MDR (medical device regulation) is a fundamental revision of the earlier directives is intended to establish a robust, transparent, predictable and sustainable regulatory framework for medical devices which ensures a high level of safety and health whilst supporting innovation.

The new regulation is a complex and lengthy document and the changes it embodies are significant, most of all it aims to provide practical steps that manufacturers should take as soon as possible to prepare for this substantial and unprecedented change in the European regulatory environment for medical devices.

The new regulations will ensure [1,2]:

- To ensure the high level health and safety protection for the European Union citizens using this products
- The products should be consistent and fair trade to market throughout EU region.

The EU's new Medical Devices Regulations (Figure 1) [3].

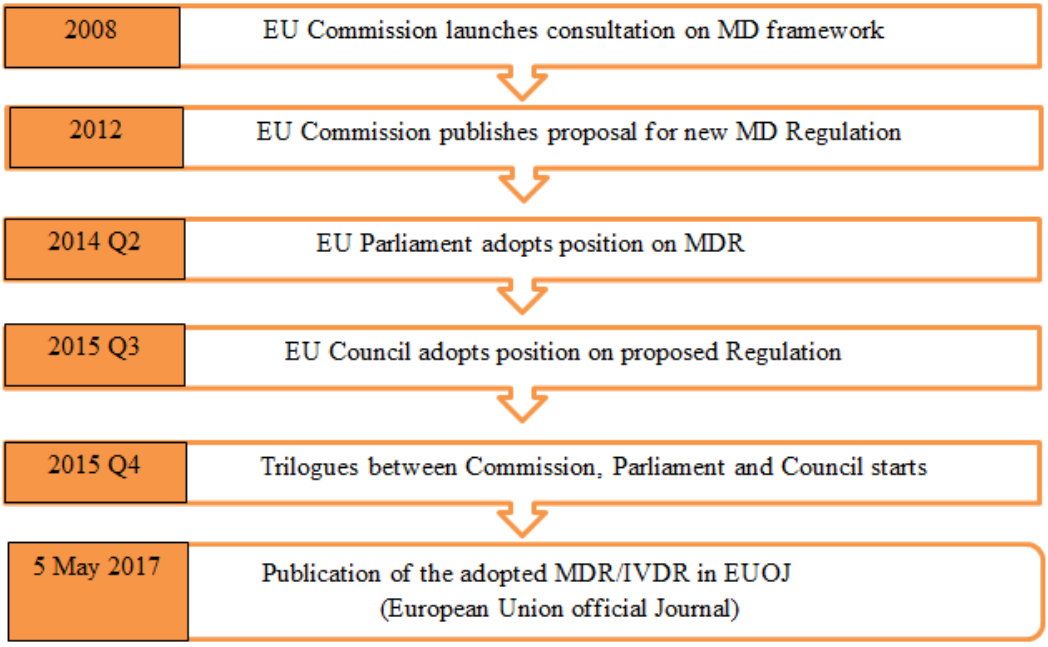

Figure 1. The EU's new medical devices regulations

OBJECTIVES

- To study out the potential impact of the new medical device regulation on industry
- The changes in the new regulation and the implementation for manufacturer to get through new changes and the new enforced quality management system to maintain a minimum quality in the device
- The practical impact consequences of changes to medical device directives to medical device regulation
- To know the transition period for medical device regulation to come into force.

LITERATURE REVIEW

In a recent survey of industry professionals on a new regulation:

- Most respondents are aware of coming changes to the European CE (European conformity) marking process as well as to the ISO 13485 quality system standard, but primarily on a high level.

- The majority of participants cited changing regulatory environments as their biggest challenge.
- A high proportion of firms based in Europe said they were already closely tracking proposed changes related to CE marking, compared to much smaller percentages of north American and Asian respondents

The quality management system should address the following aspects as per the new medical device regulation 2017/745/EEC [4].

(a) A strategy for requirements for regulatory compliance which including compliance with conformity assessment procedures and management of modifications to the devices covered in the system

(b) Identifying and comply with the applicable safety and performance requirements and exploration to address these requirements

(c) Management Responsibility

(d) Resource management including selection and control of suppliers and subcontractors

(e) Risk management as in post marketing surveillance and its risk assessment

(f) Clinical evaluation with reference to the article 61 (explains about the clinical evaluation of medical device and IVDs) including PMCF (post marketing clinical follow-up study)

(g) Product realization, including Planning, designing, development, production and service provision

(h) Verification of the UDI assignments made in accordance with article 27(unique device identification system and rules in official journal of union to all relevant devices

(i) Setup, implementing and maintenance of post market surveillance system

(j) The communication handling with competent authorities, notified bodies and the other stake holders

(k) Process for the reporting of adverse serious incidents and field safety report of corrective action in behalf of vigilance (l) Management responsibility for manage the corrective and preventive actions and verification of effectiveness (m) Processes and procedures for measuring and monitoring of output, data analysis and product improvement. The following list of the top ten hurdles that manufacturers will need to watch out for as the new MDR transitions into effect has been assembled [5,6].

Reclassification

Manufacturers need to pay close attention to the MDR classification rules to determine whether new conformity assessment routes are now applicable to their product portfolio. If so, they need to get in touch with their NB (notified bodies) to take steps to make sure that all requirements are met in the specific time frame.

The new classification of medical device on risk based classification of device (Table 1) [7].

Table 1. The class of medical devices increases, the risk of medical device increases

Class of Device	Risk of Device
Class I	Provided non-sterile or do not having a measuring cylinder (low risk)
Class I	Provided sterile and/or have a measuring cylinder (low/moderate risk)
Class II a	Medium risk
Class II b	Medium/high risk
Class III	High risk

The all medical devices fall into four basic categories:

- Non-invasive devices
- Invasive medical devices
- Active medical devices
- Special rules (which includes contraceptive, disinfectant).

Market Access of Legacy Products

The medical devices should be CE marked (confirmative marking) under the new regulation 2017/745. A comprehensive plan needs to be put in place to ensure that all products that are placed on the market are compliant with the new MDR. (This should also include products that are currently still in the development phase.)

A comprehensive plan needs to be put in place to ensure that all products that will be maintained on the EU market are CE marked in accordance with the full requirements of the new MDR. This should include products currently under development. This review may provide an opportunity for rationalization of the product portfolio and elimination of any marginal products (Figure 2).

Figure 2. Process of obtaining CE marking of medical device in European Union

Reprocessing of Single Use Devices

The uses of single use devices should only take place where permitted by national law which is specified in article 17 as Follows:-

- Risk management and analysis of the construction and materials used and related properties of the device (reverse engineering) and the procedures to detect in the design of the original device design as well as of its planned application after reprocessing
- The detailed validation of procedures for the entire process which includes cleaning steps
- The release of product and testing of performance
- The quality management system (QMS)
- The reporting of adverse incidents of the devices which have been reprocessed, and
- The reprocessed device should of traceable.

Technical Documentation

The MDR is going to be far more prescriptive about the required content of technical documentation, particularly as there are more detailed requirements for quality management systems.

Annex ii (Technical documentation) explains about new requirements for technical documentation. The technical documentation is to be organized in a readily searchable format and include in particular, the following elements:

- Medical device design description and specifications
- Labelling information supplied by the manufacturer
- Design and brief manufacturing information
- Requirements for clinical safety and performance
- Benefit vs. Risk analysis and risk management plan
- Product verification and validation (V&V) information which includes the data generated by preclinical and clinical data and if required additional information in specific cases

The specific instructions data related to the technical documents requirements on post marketing surveillance

The required technical file/design dossier documentation is heavily based on the current GHTF (global harmonization task force) Guidance document 3 reflecting the harmonization intent of global regulators.

Clinical Evaluation

The new MDR is much more specific about the need for clinical evidence proportionate with the risk associated with a given device. Following this, manufacturers may be required to obtain additional data from clinical studies manufacturers should look to review all their clinical evaluation reports (CER) if not reviewed within the last one to two years and guarantee that CERs include post market surveillance (PMS) data.

Clinical evaluations will be more closely aligned with clinical trials associated with medicinal products. This may require manufacturers to obtain additional clinical data from clinical studies. There will be Additional scrutiny of clinical evaluation reports (CERS) by notified bodies as outlined by new guidance (Med Dev 2.7.1 rev. 4)

Key changes in clinical Evaluation in new regulation are:

- More clinical data for high risk devices and less equivalence data
- Detailed safety and performance data published
- Details about Post market clinical follow up data.

Vigilance and Post Marketing Surveillance (PMS)

Under guidance of new regulation, medical device manufacturers will be required to collect post market clinical data as part of their on-going assessment of looming safety risks. Therefore, it is important that they review their procedures for PMS and ensure that the responsibility for the provision of this additional data and associated support is established clearly.

Additionally, reporting timeframes are tightened to the 15 days from 30 days for the reporting serious adverse incidents. There will be new electronic vigilance reporting (MDR article 92) and periodic safety update reports (PSUR) for all devices (MDR article 86) subject to differing frequency and submission requirements.

As of the date of application (new regulations), medical device manufacturers will be required to include a post-market clinical follow-up or post-market performance follow-up (for IVDs) in their post-market surveillance system in order to continuously update the clinical evaluation of the device. For implantable medical device and class III devices, a detail information of clinical and safety summary must be drawn up by manufacturers and validated by notified bodies before being made publicly available.

Key changes in PMS and vigilance in new regulation are:

• Central database and co-ordination

• Trend reporting

• Enforcement activities.

Mandatory Product Liability Insurance

It will be up to the manufacturer to guarantee responsible able to provide coverage sufficient for any potential liability. It is advisable that manufacturers rapidly seek legal counsel to assist with reviewing all product liability provisions.

Safety and Transparency

Transparency has been one of the key principles within the MDR and it is up to manufacturers to keep close watch on the European data bank on medical devices (EUDAMED) and to be ready to notify them of all products once it has been implemented.

EUDAMED [8] refers to then European Databank on Medical Device. The European Commission is required to establish this databank by 2020. EUDAMED will serve as a central, web-based portal for information about medical devices in the EU. The MDR and IVDR require manufacturers to submit specific information to EUDAMED. This information will be available to the competent member authorities and the European commission. Some information will also be available to the public, including details about the safety and performance summaries information for Class II and sterile implantable medical device

EUDAMED is a central European medical device database which is mainly used for collecting the information about medical device. Presently EUDAMED is accessed by the competent authorities and Notified bodies. The compliance to the EU MDR the functionality of database is expanded to include UDI registration requirements and also registration of information including medical device post market follow up, clinical and safety information, manufacturer's details and other relevant information.

The goal of EUDAMED is to improve the transparency of and access to information about medical devices in the EU

The key changes are:

• The device availability and economic operations registered centrally

• Unique device identification (UDI)

• Available of summary of safety and clinical performance (SSCP) and implant cards.

Labeling and the Supply Chain

Requirements for product labelling are more prescriptive under MDR than before. For example, the newly obtained information about the medical device should be made available on the manufacturer website and kept to be up to date.

There are requirements for:

- Specific details for labels and for sterile packages,
- The information should include about the use in the special population group (e g. children, pregnant women and aged persons) if applicable, and appropriate use instruction and precautionary measurements,
- Hazardous substances.

It will be the responsibility of each manufacturer to appoint the person responsible for regulatory compliance (PRRC). There are also more prescriptive requirements placed on EU authorized representatives (EUAR). Manufacturers should carefully review their current product labeling and precautionary statements.

UDI (Unique Device Identification)

The new MDR will require all devices to be fully traceable through unique device identification (UDI) system, which means detailed planning for UDI implementation in the EU will be required. Even though the details of the eu UDI system have not been finalized, it is thought it will not be too different to current systems in place in the United States.

The Medical Device UDI helps to manufacturer for better innovatory control, improved adverse event management, to reduce health care fraud, and to create transparency throughout the distribution chain.

A globally harmonized and consistent approach to UDI facilitates positive identification of medical devices and is expected to:

- Improve patient safety by reduction of medical errors,
- Provide public access to relevant data,
- Facilitate traceability of devices,
- Enhance vigilance and market surveillance,
- Fight counterfeiting and fraud,
- Support the downstream processes in the supply chain, and clinical and revenue management (Table 2).

Table 2. Practical consequences of changes to medical device directives to Medical Device Regulations [9]

	Change	Potential impact
Scope of devices regulated	In new regulation include the some cosmetic devices and the devices using non-viable human tissues	Mainly impacted on the industrial regulators and increased training and the consultancy works increases for newly included devices
Validation of notified bodies	Mainly on the selection of notified body (NBs) with detailed criteria and the monitoring to notified body about requirements	Shortage of the resourced validated notified bodies and strict requirements for present NBs and increased biocompatibility assessments and the increased costs and longer timelines for approval to manufacturer's
Device testing and inspection	Providing the more safety and performance details of the high risk devices and the supporting clinical investigation data and increased work for NBs for the providing data for EU reference laboratories which is validated for testing The second look by the NBs for the biocompatibility for high risk devices, and authorization to conduct the additional or conformatory testing, review of the data from reference laboratories by NBs, and the unannounced inspection of premises by NBs of the high risk devices premises (e.g. once in a year for class 3 devices)	The more importance on the test laboratory selection and increased release testing and must should be compliance to current standards and More need in biocompatibility /performance test training Increased interpretation of requirements and standards regarding information gaps and less tolerance for biocompatibility gaps and increased scrutiny on change controls
Surveillance	Robust requirements and increased post marketing surveillance, increased coordination in vigilance case analysis and reactions	Potential for increased costs/ litigation for manufacturers
Manufacturer staffing	The organization of a well-qualified person who will be responsible for regulatory compliance and increased manufacturer's responsibility	Increased in demand of qualified personnel and increase the resource needed and costs increases

SUMMARY AND CONCLUSION

- In order to assess the impact of these changes on the business and its commercial and R&D operating models, organizations will need to build a robust business case and strong project management capability

with effective cross-functional stakeholder management.

- In order to develop a regulatory strategy for implementation of new medical device regulation this will involve a multilevel approach like high-level impact assessment, planning, implementation and organizational alignment and communication and benefit realization
- The rules of medical device will apply after the transitional period namely after 3 years after entry into the force in spring 2020.

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