New EU Medical Device Regulations
Impact of New European Medical Devices Regulation

European Commission recently published a proposal on new regulation for medical devices on 29 September 2012. The concern raised in the PIP scandal is reason to expedite the publishing of new regulation on medical devices. New regulation is intended to maintain safety of the patient from high risk medical devices in Europe. The legislation includes new legislative framework and in particular, the economic operators (manufacturer, authorized representatives, distributors, and importers). The proposed regulation enforces clear and detailed rules which will become applicable in a uniform manner throughout EU and enhances innovation and competition of small and medium sized enterprises.

The new proposal outlines guidelines on Notified Bodies, electronic systems UDI (Unique identification number), registering of medical device clinical trials in ported database (EUDAMED), Post-Market Clinical Follow-Up (PMCFU / PMS), vigilance and market surveillance, Non compliance Levy fees & Penalties and the administrative burden of specific member state registration requirements and countries which have imposed traceability requirements on economic operators.

Key differences between OLD and NEW Regulation

The proposed regulation promotes a shift from the pre-approval stage (i.e. the path to CE-marking) to a life-cycle approach which is similar to US FDA. Differences between old and proposed new regulations on medical devices are summarized below:

<table>
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<tr>
<th>New Regulation</th>
<th>Old Regulation</th>
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<tr>
<td>Manufactures should fit their devices with Unique Device identification (UDI), so as to allow traceability.</td>
<td>No UDI system</td>
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<td>Manufacturer's authorized representatives and importers shall register themselves and devices they place on the EU market in a European central database</td>
<td>Manufacturer should register manually under the notified bodies</td>
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<tr>
<td>Every clinical investigation must be registered in public accessible electronic system (EUDAMED)</td>
<td>Clinical investigation reports to be submitted manually</td>
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<td>The sponsor or CRO carrying the trial should submit an application confirming that there is no health and safety or ethical aspects which would oppose it</td>
<td>The sponsor or CRO carrying the trial should submit the trial details manually, including that there is no risk or any opposition to ethical or health issues</td>
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<td>Introduction of an EU portal where manufacturers must report serious incidents and corrective actions they have taken to reduce the risk of recurrence.</td>
<td>Not specified</td>
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Quality management should focus more on high risk system rather than low risk systems

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<th>Notified bodies to periodically inspect the manufacturer regarding the quality and production process</th>
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Adverse effects can be reported by Patients, healthcare professionals and public, directly in the portal (EUDAMED)

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<th>Not specified</th>
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New launch of medical devices in market to be updated in the portal

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<th>Public access towards awareness of new devices was not available</th>
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### Initiatives in New Regulation:

#### UDI and EUDAMED Database

New regulation mandate to use UDI (Unique Device Identification) system allows medical device traceability, market surveillance and also addresses a combination of mandatory inputs by Notified Bodies, Economic Operators and Member States (Member States into EUDAMED and other databases).

Unique Device Identification (UDI) system will enhance the effectiveness of the post-market safety of medical devices due to improved incident reporting, targeted field safety corrective actions and better monitoring by competent authorities. It should also help to reduce medical errors and to fight against counterfeit devices. Use of the UDI system should also improve purchase-policy and stock-management by hospitals.

The Manufacturers of high-risk devices should make publicly available summary of safety and supporting clinical data. This allows further development of the European databank on medical devices (EUDAMED), which will contain integrated electronic systems on a European UDI, on registration of devices, relevant economic operators and certificates issued by notified bodies, on clinical investigations.

Class III medical device manufacturers must generate a summary of safety and clinical performance (Article 42). The establishment of a central registration database will provide a high level of transparency, diverging national registration requirements and contribute to reducing the administrative burden on manufacturers.

#### Benefits of Unique Device Identification

When fully implemented, the UDI system may:

- Allow more accurate reporting, reviewing and analyzing of adverse event reports so that problem devices can be identified and corrected more quickly
- Reduce medical errors by enabling health care professionals and others to more rapidly and precisely identify a device and obtain important information concerning the characteristics of the device.
New EU Medical Device Regulations

- Enhance our analysis of devices on the market by providing a standard and clear way to document device use in electronic health records, clinical information systems, claim data sources and registries
- Provide a standardized identifier that will allow manufacturers, distributors and healthcare facilities to more effectively manage medical device recalls
- Provide a foundation for a global, secure distribution chain, helping to address counterfeiting and diversion and prepare for medical emergencies
- Lead to the development of a medical device identification system that is recognized around the world

Notified Bodies

According to the proposed Regulation, NBs will be placed under a strict regimen of supervision, although it remains unclear whether the intended sanctions could be implemented against the will of a Member State, should the need occur. In case Class I devices, a notified body must verify the aspects related to the measuring function or to the sterilization process. For devices of Classes IIa, IIb and III, an appropriate level of involvement of a NB is compulsory to the risk class. Class III Devices requires explicit prior approval of the design or of the type of the device and of the quality management system before they may be placed on market. In case of Class IIa and IIb devices, notified body checks quality management system and the technical documentation. After initial certification, notified bodies must regularly conduct surveillance assessments in post-market phase.

In addition, the proposal introduces the obligation for notified bodies to notify an expert committee of new applications for conformity assessment of high-risk devices. On scientifically valid health grounds, expert committee will have the power to request the NB to submit a preliminary assessment on which the committee can issue comments within a deadline of 60 days, before the NB can issue a certificate. This scrutiny mechanism empowers the authorities to have a 'second look' at individual assessments and make their views heard before a device is placed on market.

Clinical evaluation and clinical investigation

This section lays down the key obligations of manufacturers on their performance of clinical evaluation needed to demonstrate safety and performance of devices. This addresses the pre-market clinical evaluation and post-market clinical follow-up that together constitute a continuous process during the life cycle of a medical device.

The scope of the proposal, however, remains restricted to clinical investigations carried out for regulatory purposes, i.e. for obtaining or confirming regulatory approval for market access. Non-commercial clinical investigation that does not pursue a regulatory purpose is not covered by this Regulation.

Every clinical investigation must be registered in a publicly accessible electronic system. Before commencing a clinical investigation, the sponsor must submit an application to confirm that there are no health and safety or ethical aspects which would oppose it. A new possibility will be opened up for sponsors of clinical investigation to be conducted in more than one Member State. In future, they may
submit a single application through the electronic system to be set up by the Commission. The clinical investigation should be in line with major international guidance such as ISO 14155 on good clinical practice for clinical investigation of medical devices for human subjects and the most recent (2008) version of the World Medical Association Declaration of Helsinki on Ethical Principles for Medical Research Involving Human Subjects.

**Vigilance and market surveillance**

Complications with medical devices that are designed to be implanted or to operate for many years or even decades might come to light only after a certain period of time. The main progress which the proposal will bring in this field is the introduction of an EU portal where manufacturers must report serious incidents and corrective actions they have taken to reduce the risk of recurrence. The information will be automatically forwarded to the national authorities concerned. When the same or similar incidents have occurred, or where a corrective action has to be taken, in more than one Member State, a coordinating authority will take the direction in coordinating the analysis of the case. Coming to market surveillance, the main objective of the proposal is to reinforce the rights and obligations of national competent authorities, to ensure effective coordination of their market surveillance activities and to clarify the applicable procedures.

**Levy fees & Penalties**

The Member States shall lay down the provisions on penalties applicable for infringement of the provisions of this Regulation and shall take all measures necessary to ensure that they are implemented. The penalties applied for must be effective, proportionate, and dissuasive. The Member States shall notify those provisions to the Commission [3 months prior to the date of application of the Regulation] and shall notify it without delay of any subsequent amendment affecting them.

**New themes in the Regulation**

The new regulation on medical devices created a vast change by implementing the electronic submission. Various databases for clinical investigations, product registration, and vigilance are introduced under the guidelines of EU Commission. This new regulation introduces the Qualified Person (QP) who is highly educated, experienced and intended to safeguard the regulatory compliance within the manufacturer. Mandatory Unique Device Identification (UDI) introduced with the intention to facilitate the traceability of devices and manufacturer. This allows the notified bodies to easily access data specific to the device through UDI system.

The high risk devices and implantable devices are to be overseen with high quality management along with providing clear and detailed clinical trial reports. New devices been placed in the market are updated in the portal for public access, which helps in public awareness regarding the device including the adverse effects. If any complication regarding the device conformity or any adverse effect observed would be posted by anyone in the public access portal maintained by EU Committee. The surveillance and vigilance of the product is made easy through new regulations. Analysis of the adverse effect and filed safety corrective actions can be ensured easily. Manufacturers shall update their technical documentation with information on incidents received from healthcare professionals, patients, users and make this documentation available to their notified bodies to assess the impact of the vigilance data on the conformity.
The roles of clinical evaluation, clinical investigation and the regulatory pathway to study approval are well defined in new regulation. This emphasized on clinical data collection through database and Post Marketing Clinical Follow-Up (PMCFU) studies. Inclusion of MEDDEV 2.7/1 and parts of ISO 14155 is appreciated.

The safety and health risk should be maintained by notified bodies and hence there is a huge responsibility laid on such notified bodies by the member states. This includes regular audits to the manufacturer and auditing the regular manufacturing process. The member states have also taken the initiative, by regularly shuffling notified bodies to maintain the standards. The economic operators shall ensure that appropriate corrective action is taken for all concerned devices that they have made available on the market throughout the Union. In case of Class III devices and implantable devices, manufacturer shall prepare a summary of safety and clinical performance and submit to notified bodies.

The new Regulation effort to make transparent the time frames for review by various parties for different activities and concentrate the harmonization between the Member States by means of a new regulatory body called the Medical Device Coordination Group (MDCG). The objective of the MDCG would be to foster cooperation between the Member States while at the same time increasing the Commission’s power to act as needed in acute cases.

Conclusion

The objective of this Regulation is to ensure high standards of quality and safety for medical devices, as a result ensuring a high level of protection of health and safety of patients. An electronic system at Union level will help in to ensure every clinical investigation is registered in a publicly accessible database and protect the right to protect personal data.

Healthcare professionals and patients should be empowered to report suspected serious incidents. The national competent authorities should inform manufacturers and share the information with their peers when they confirm that a serious incident has occurred in order to minimize recurrence of those incidents. This new approach would drastically minimize all the noncompliant devices in the market and providing safe and quality medical devices to the patients and definitely creates a faster approval of the device while ensuring all standards.

Expansion is always exciting, but it usually comes with a lot of unanswered questions. MakroCare is here to provide answers to these questions.

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