The Changing Landscape of Medical and In Vitro Diagnostic Device Regulations in the European Union
Prompted by rapid advances in medical device technologies and in part by recent findings of safety issues with previously approved devices, the regulation of medical devices in the European Union (EU) is undergoing a sweeping transformation. Current changes include an expanded scope of regulated devices, greater oversight and control of notified bodies, unannounced audits of suppliers and more. For most medical device manufacturers, these changes will directly impact the product review and certification process, and are likely to increase the investment of time and resources required for product approval.

The proposed regulatory changes are likely to have the greatest impact on manufacturers of in vitro diagnostic medical devices. In vitro diagnostics, which include chemicals and reagents, consumables and analyzers used in the evaluation of human specimens such as blood and urine, represent an annual global market value of approximately $50 billion (USD),¹ and are projected to exceed $22 billion (USD) in Western Europe alone by 2018.² Under the proposed changes, nearly 80% of in vitro diagnostic medical devices sold in the EU could be subject to notified body approval, up from just 20% currently.

This UL white paper offers an overview of the recent and proposed changes to regulations applicable to medical and in vitro diagnostic devices sold in the EU. The paper begins with a brief summary of the EU’s original regulatory structure and the motivations behind the proposed changes. The white paper then provides a summary of the proposed changes, as well as their possible impact on device manufacturers. The paper also discusses new regulations regarding auditing and assessment activities by notified bodies, and important changes to their appointment and oversight. The paper concludes with some suggestions to effectively navigate the changing EU regulatory landscape.
Challenges with the EU’s Medical Device Regulatory Framework

For more than two decades, the framework regulating medical devices in the EU has been based on three separate directives, addressing requirements for medical devices, active implantable medical devices and in vitro diagnostic medical devices. Unlike the pre-market authorization scheme administered by the U.S. Food and Drug Administration (FDA) for medical devices marketed in the U.S., compliance with these “New Approach” directives is generally based on conformity assessments conducted by notified bodies, independent third-party certification organizations appointed by competent authorities within EU member states. Manufacturers whose medical devices receive notified body approval may then apply the CE mark to their products, and legally market, sell and distribute them throughout the EU.

The medical device industry is driven by scientific research and characterized by rapid and continuous technological innovation. As the global population ages and the demand for healthcare services expands, regulations covering medical and in vitro diagnostic devices must necessarily evolve to account for new technologies while continuing to protect the safety of patients. The directives underlying the EU’s regulatory framework for medical and diagnostic devices were originally implemented in the 1980s. Although new regulations have been periodically issued in an effort to address the introduction of new technologies, the resulting patchwork of regulations has actually made the business of compliance even more challenging for manufacturers.

Efforts to address this challenge have also identified inequities in the administration of medical device regulations in individual EU member states. Directives lack the force of law throughout the EU. Instead, individual member states are responsible for passing national legislation that implements the requirements of EU directives within their respective boundaries. In addition, competent authorities in member states have employed different criteria in the appointment and oversight of notified bodies. This has resulted in variations in assessment rigor, potentially impacting the competitive dynamic in the marketplace and exposing patients to uneven levels of protection and safety.

In addition, localized oversight of medical devices and enforcement actions against noncompliant products means that competent authorities in EU member states may react differently to health risks that are identified in connection with certain devices. This issue is further exacerbated by the absence of uniform electronic registration or traceability requirements across the EU. These variations ultimately compromise the effective safety level of medical devices and the protection of patients throughout the EU.

Concerns about the effectiveness of the EU’s regulatory framework and market oversight activities were dramatically illustrated in late 2011 with the recall of breast implants produced by French manufacturer Poly Implant Prothèse (PIP). Investigators found that the company used industrial silicone in the manufacture of implants for as long as 10 years, rather than medical-grade silicon evaluated and approved during the product’s conformity assessment process. At least 100,000 women in Europe and 400,000 women globally were reportedly impacted by the subsequent product recall. In France, health authorities reported in 2012 that nearly half of the 30,000 women with PIP-manufactured implants had had them removed.

Responding to the Challenges

In a Communication issued in 2011, the EU Council noted the importance of an updated regulatory framework in supporting continued innovation in the medical device industry. “A suitable, robust, transparent and sustainable regulatory framework ... is central to fostering the development of safe, effective and innovative medical devices for the benefit of European patients and healthcare professional,” wrote the Council. The Council called on the EU Commission to develop a “sustainable legislative framework for medical devices which ensures safety and promotes innovation.”

In fact, the Commission had already been considering a fundamental revision of the existing regulatory framework for medical devices prior to the Council’s Communication in 2011. It launched a
public consultation in May 2008 designed to seek the views of stakeholders, and received some 200 responses and comments. The Commission launched a separate public consultation in June 2010 on technical aspects of a proposed revision to the EU’s directive on in vitro diagnostic medical devices that produced more than 180 responses.

Ultimately, in September 2012, the Commission released a Communication outlining its plan for the restructuring of the EU’s medical device regulatory framework. According to the Commission, the primary goals of the restructured framework would be: 1) to ensure a high level of protection of human health and safety; 2) to ensure the smooth functioning of the internal market; and 3) to provide a regulatory framework that is supportive for innovation and the competitiveness of the European medical device industry.

Concurrently, the Commission also published a proposed regulation for medical devices and active implantable medical devices (2012/0266), and a separate proposed regulation for in vitro diagnostic medical devices (2012/2067). The proposed regulations are expected to replace the three existing directives covering medical devices, active implantable medical devices and in vitro diagnostic medical devices. Further, when adopted, the proposed regulations will have the force of law throughout the EU and will not be subject to interpretation or transposition into national laws by individual EU member states.

As of this writing, the proposed regulations are moving through the EU’s extensive and complex deliberation and review process. Final regulations could be published as early as 2015, although some are predicting that regulations may not be finalized until 2017. Also uncertain is the length of the transition period applicable to devices with existing approvals, with estimates of anywhere from three to five years following the issuance of the final regulations.

Proposed changes to EU Medical and In Vitro Diagnostic Device Regulations

Although specific aspects of the EU’s proposed medical device regulations are subject to further modification prior to their final publication, the proposed regulations do provide some insight into changes likely to affect manufacturers, importers and distributors of medical devices once the new regulations take effect. While some of the anticipated changes will affect the approval and post-market surveillance of all medical devices, the largest impact is expected to fall on manufacturers of in-vitro diagnostic medical devices.

Each of the proposed medical device regulations includes a number of annexes that detail general health and safety requirements, classification rules, clinical evidence requirements, and the role of
The Changing Landscape of Medical and In Vitro Diagnostic Device Regulations in the European Union

notified bodies. Some of the specific, anticipated changes from the current medical device directives include:

- **Extension of regulatory scope** —Both 2012/0266 (medical devices and active implantable medical devices) and 2012/0267 (in vitro diagnostic medical devices) will extend the scope of medical and in vitro diagnostic devices currently regulated by the EU. Newly regulated products are expected to include implants for aesthetic purposes, genetic testing products, dedicated medical software and some high-risk devices manufactured for use within a single health institution.

- **Implementation of classification structure for in vitro devices** —In vitro diagnostic medical devices will now be subject to classification rules that allocate products to one of four risk classes, similar to the classification structure that already exists for medical devices in the EU. Notified body approval will be required for the majority of in vitro diagnostic devices, with the exception of those that pose a low risk to patients.

- **Reinforced regulations covering clinical investigations** —2012/0267 will require manufacturers to provide a summary of safety and clinical performance in support of pre-market applications for in vitro diagnostic medical devices posing medium to high risk or high risk to patients, and to maintain post-market data for continuous assessment of potential safety risks.

- **Implementation of unique device identification requirements** —Both 2012/0266 and 2012/0267 propose requirements regarding the use of unique device identification (UDI) mechanisms to increase traceability of devices through the supply chain, and to facilitate effective product recalls in the event of safety concerns.

- **Role of “qualified persons”** —Manufacturers will be required to have within their organization at least one individual responsible for all aspects of regulatory compliance. This “qualified person” must possess the experience and/or skills appropriate to this task.

- **Expanded registration database of devices** —Both regulations propose to expand the use of the European Databank on Medical Devices (Eudamed) to provide a centralized repository of information on approved medical devices for regulators and consumers. This change is expected to increase EU-wide access to product information, thereby increasing transparency and improving overall safety.

- **Increased regulation and oversight of notified bodies** —Notified bodies will be granted increased authority to conduct post-market product testing and sample checks, including unannounced factory inspections at manufacturing locations. Increased vigilance issues, reported field complaints or other product concerns may result in additional unannounced audits.

- **Greater coordination of regulatory efforts** —The proposed regulations call for the formation of a medical device coordination group (MDCG) composed of members representing national authorities. The goal of the MDCG is to facilitate coordination between EU member states of medical device regulation and surveillance, with scientific, technical and logistical support provided by the EU Commission.

- **Other changes** —Both proposed regulations clarify key definitions and terms used to avoid confusion or misinterpretation. The regulations also clarify the legal responsibilities of medical device distributors and importers as well as those who sell or market medical devices via the Internet.

**Recent Changes in Notified Body Audits and Assessments, and Notified Body Oversight**

As noted previously, EU member states are responsible for transposing the essential requirements of directives into national law, leaving open the possibility for interpretive differences. In addition,
The changing landscape of medical and in vitro diagnostic device regulations in the European Union

Competent authorities in member states can apply different criteria in the appointment and operation of notified bodies. The gaps between individual member states in the transposition of product requirements and the criteria applied to notified bodies can ultimately compromise the goal of achieving uniform levels of patient safety across the EU.

To help narrow these gaps, the EU Commission has also issued a Recommendation addressing the performance of audits and assessments by notified bodies. Commission Recommendation No 2013/473/EC clarifies the current Directives in terms of conducting product assessments, assessments of a manufacturer’s quality system, and unannounced audits. Specific guidelines are detailed in the Recommendation’s three Annexes, with product assessments addressed in Annex I, quality system assessments addressed in Annex II, and unannounced audits addressed in Annex III.

The Commission’s guidance on unannounced audits has been the focus of much of the attention being given to this Recommendation. It calls on notified bodies to carry out unannounced audits at least once every third year. More frequent unannounced inspections are recommended in cases involving high risk devices, if devices of the type in question are frequently found to be non-compliant, or when specific information gives cause for concerns regarding a product’s safety. The guidance also specifies the length of unannounced audits (at least a day), and the minimum number of auditors (at least two).

The Commission’s Recommendation on audits and assessments is applicable to the Commission’s current medical device regulatory framework and is not dependent on the approval of the Regulations discussed earlier in this paper. Although the guidance has been published as a Recommendation only, it is expected that notified bodies will comply with the guidelines regarding audits and assessments. Failure to do so could be interpreted by national authorities as a derogation by the notified body of the essential requirements of current directives and regulations, potentially resulting in the loss of its notified body designation.

Further changes can be found in Commission Implementing Regulation No 920/2013, which came into force at the end of 2013. The Implementing Regulation establishes EU-wide criteria for the designation of notified bodies, as well as provisions governing the extension and renewal of notified body designation. The Regulation also requires designating authorities in EU member states to monitor the performance of notified bodies within its jurisdiction through file reviews, on-site assessments and audits. Finally, under the terms of the Regulation, the Commission reserves the right to investigate individual cases of notified body competence.

**Anticipated Impact on Manufacturers**

The recent and proposed changes to the EU regulatory framework for medical devices will be applicable to all devices sold or marketed within the EU, regardless of where they are manufactured. For that reason, these changes will have a number...
of significant impacts on manufacturers, importers and distributors of medical devices and in vitro diagnostic medical devices. The impacts include:

- **Broader applicability of regulatory requirements**—The number and type of medical devices that fall under the provisions of Regulations 2012/0266 and 201/0267 are significantly greater than those covered under the current medical device framework. For example, UL estimates that nearly 80% of all in vitro diagnostic medical devices on the market will be subject to notified body review and approval, compared with approximately 20% under the current framework. This means that more diagnostic devices and device manufacturers will now be regulated.

- **More exacting requirements for device safety and performance**—The current framework relies on New Approach directives, with specific safety and performance requirements based on international standards. The proposed regulations incorporate all applicable requirements and do not rely on the transposition of Essential Requirements into national laws. As such, deviations in compliance requirements are less likely to occur.

- **Increased inspection rigor and post-market surveillance**—Commission Recommendation 2013/473/EC regarding audits and assessments will lead to more rigorous product assessments and more frequent post-market inspections. Notified bodies will have less discretion in the assessment of compliance with safety and performance requirements. Unannounced post-market inspections will require a commitment to the implementation and maintenance of effective quality management systems.

- **Greater provisions for traceability and transparency**—The adoption of UDI requirements and the expansion of the Eudamed device database will make it easier for the market to quickly identify defective or unsafe medical devices. These new traceability and transparency tools will require manufacturers to respond more quickly to remove defective products from the market to minimize adverse publicity and other consequences.

As for the timing of the implementation of the new regulatory framework for medical devices, it is anticipated that Regulations 2012/0266 and 2012/0267 could be published as early as the beginning of 2015. With a three year transition period for medical devices that have been approved under the current framework, the final transition to the new framework could be completed as early as 2018. However, regardless of when the final regulations are published, it is unclear whether the actual implementation of the regulations might be delayed to allow manufacturers of new medical devices additional time to achieve compliance.

Despite calls from some EU legislators for the establishment of a central authority for the approval of medical devices, similar to the U.S. FDA, the proposed regulatory framework for medical devices does not currently reflect that approach. Because the regulatory process in the EU is also a political one, further changes in the proposed framework may be in the offing. Nonetheless, given the investment of time and resources required to bring new medical devices to market, manufacturers are well-advised to thoroughly investigate the potential impact of the new EU regulatory framework on their current and planned product lines, and to identify the steps necessary to achieve compliance with the anticipated requirements within the current expected timeframes.
Summary and Conclusion

Now more than two decades after its initial implementation, the EU’s regulatory framework for medical devices, active implantable medical devices and in vitro diagnostic medical devices is undergoing significant changes. While work on final framework is still underway, its eventual shape is already evident from extensive communications from the EU Commission regarding its objectives, and from the regulations and recommendations that have been proposed or released. Manufacturers can take important steps in advance of the EU’s final published regulations to prepare for the transition, thereby avoiding delays in bringing new and innovative medical devices to market.

For additional information about the EU’s new regulatory framework for medical devices, and how UL notified body experts can support you during the transition, contact Medical.Inquiry@ul.com.
The Changing Landscape of Medical and In Vitro Diagnostic Device Regulations in the European Union

1. "Strategic Analysis of the Global In Vitro Diagnostics Market," Frost & Sullivan, July 2010. Web. 1 April 2014. http://www.frost.com/sublib/display-report.do?searchQuery=IVD&ctxixpLink=FcmCtx15&ctxixpLabel=FcmCtx16&id=N7C4-01-00-00-00&bdata=aHR0cDovL3d3dy5mcm9zdC5jb20vc3JjaC9jYXRhbG9nLXNlYXJjaC5kbz9wYWdlU2l6ZT0xMiZxdWVyeVRleHQ9SVZEJnNvcnRCeT1EJnBhZ2U9MTBAfkBTZWFyY2ggUmVzdWx0c0B%2BQDEzOTY4OTI5ODMzNTY%3D.


©2014 UL LLC. All rights reserved. This white paper not be copied or distributed without permission. It is provided for general information purposes only and is not intended to convey legal or other professional advice.