

Revision of the medical devices and in vitro diagnostics regulatory framework

Designing a safer and more robust system is crucial to safety and innovation

Executive summary

Europe's highly innovative medical technology sector is a major contributor to the region's knowledge economy and renown healthcare. The evolution of technology has positioned the EU's medical devices industry among the most innovative sectors, but has also challenged Europe's medical devices and in vitro diagnostics regulatory framework.

AmCham EU strongly supports the revision of the regulatory system to ensure that it adequately improves patient safety while protecting innovation. AmCham EU outlines a number of elements that are key to ensuring that the system meets its dual objectives, as well as those that could hinder.

* * *

AmCham EU speaks for American companies committed to Europe on trade, investment and competitiveness issues. It aims to ensure a growth-orientated business and investment climate in Europe. AmCham EU facilitates the resolution of transatlantic issues that impact business and plays a role in creating better understanding of EU and US positions on business matters. Aggregate US investment in Europe totalled €2 trillion in 2014 and directly supports more than 4.3 million jobs in Europe.

* * *

American Chamber of Commerce to the European Union (AmCham EU)
Avenue des Arts 53, B-1000 Brussels, Belgium
Register ID: 5265780509-97
Tel: +32 (0)2 513 68 92 | www.amchameu.eu

Friday 20 November 2015

Introduction

Europe's highly innovative medical technology sector is a major contributor to the region's knowledge economy and renown healthcare. There are over 500,000 medical devices and diagnostic products (including 10,000 generic groups) on the European market. Products range from relatively simple tools such as bandages, wheelchairs, or self-care medical devices to highly-sophisticated products integrating many technologies, such as medical devices containing medicinal substances, pacemakers, defibrillators and various medical equipment. The European market for medical equipment is worth around €28 billion and 8% of revenues on average are reinvested into research and development (R&D) for advanced medical imaging and health information and communications technology (ICT) products. The evolution in technology has positioned the EU's medical devices industry among the most innovative sectors, with more than 10,000 patent applications filed with the European Patent Office (EPO) in 2013, equivalent to 7 % of the total number of application. Additionally, European eHealth and mHealth industries have leading positions in emerging fields such as remote patient monitoring and integrated care solutions. While technological advances have been extremely beneficial, they have also challenged Europe's medical devices and in IVD regulatory framework, which has resulted in proposed revisions to the framework.

Proposed revisions to strengthen the regulatory framework

On 26 September 2012, the European Commission adopted a [package of proposals](#) to revise the Medical Devices Directives (MD). The revised legislation aims to tighten controls around medical devices and IVD products and is the biggest regulatory change for medical devices in the European Union in the last 15 years. A regulation rather than a directive has been considered a more appropriate legislative measure to limit national deviations and will help ensure an equal level of patient safety across the EU. The proposed new regulatory framework consists of a regulation on medical devices and a regulation on IVD products.

The main elements of the proposals include:

Wider and clearer scope of EU legislation to include more products and clarify what is covered	Stronger supervision of Notified bodies	Transparency of data	Clearer rights and responsibilities Better coordination among Member States	Extended database on medical devices
Improved traceability	Stricter requirements for clinical evidence	Adaptation of the rules to technological and scientific progress	Regulation on re-use of single use devices	Alignment to international guidelines

The European Parliament adopted an opinion on 22 October 2013 which was confirmed by a first reading opinion on 2 April 2014. More recently, on 5 October 2015, after nearly three years of discussions, the Council of the European Union agreed on a general approach, leading to the start of the negotiations.

Key elements to consider in revised regulatory framework

The American Chamber of Commerce to the EU (AmCham EU) strongly supports negotiations towards the creation of a more modern and effective regulatory system for medical devices and in vitro diagnostics products and feels that the following elements are key to ensuring a robust regulatory system:

1. **Decentralised system/pre-market authorisation:** the European regulatory model on medical devices has been successfully exported around the world. But the current system can, and should, be further improved in order to better deliver the objectives of safeguarding patient safety and enhancing innovation. The revised regulatory system should continue to provide citizens access to innovative and cost-efficient medical technology while strengthening the oversight and the coordination of the Notified Bodies and regulatory authorities. AmCham EU does not believe pre-market approval by a central agency for medical devices would be an improvement; it would neither enhance patient safety nor prevent illegal activities (eg, the recent breast implant scandal).

The 'Scrutiny' procedure, as proposed by the European Commission, is essentially a random duplication of the Notified Body product assessment. As such, we consider that the 'Scrutiny' proposal from the Commission and the Parliament does not offer any substantive contribution to patient safety, nor does it make best use of competent authority and Commission resources. The procedure essentially adds layers of random duplication at several stages of the approval process and will increase red tape and unnecessary bureaucracy. However, if a 'Scrutiny' procedure would be introduced, the Council's suggested improvements to this procedure should be considered. This proposal integrates the 'Scrutiny' process further within the normal approval process and targets really innovative products (eg, new high risk implantable devices), which is a step in the right direction.

Furthermore, improving the quality and consistency of the assessment made by the Notified Bodies would be better carried out through a strengthening of their designation and monitoring procedures, in particular tackling the level of resources and expertise needed. Stricter and more harmonised criteria for designating and monitoring the quality of Notified Bodies is the best way to ensure equal levels of patient safety all over Europe.

None of the proposals foresee a clear path for the renewal of certificates after the device was first put on the market. We think that the conformity assessment procedure for the renewals path should focus on the additional information that has been gathered since the last certificate has been granted and should not automatically be a complete review of the dossier, which would be an unnecessary burden for the whole system.

2. **The reprocessing of single-use devices:** the Commission's proposal aims to regulate the reprocessing of single-use medical devices at the European level as a manufacturing activity covered by the Medical Devices Regulation, as is the case in other major jurisdictions such as the United States. This is an important step towards increasing patient safety throughout Europe by applying appropriate harmonised controls and allowing for the development of the reprocessing activity of single-use devices. This proposal maintains the possibility for Member States to allow or prohibit the reprocessing and reuse of single-use devices on their territory. AmCham EU supports the Commission's proposal as it guarantees a better level of patient safety combined with a better level playing field, subjecting all reproprocessors in the EU to the same rules.

In contrast, the proposal made by the Parliament to consider all devices as reusable by default is inconsistent and lacks clarity or appropriate safeguards for patient safety. It reverses the well-established safety principle that, in the interest of patient safety, devices should only be considered reusable if they have been developed and tested to be reusable. We welcome the Parliament's proposal to have a report on the reprocessing of single-use devices after five years, as this would allow for more informed decisions on devices that can be safely reprocessed.

The proposal from the Council is similar to the Commission's proposal in regulating the reprocessing of single-use device appropriately as a manufacturing activity. It falls short, however, in ensuring an equal level of safety for all patients as it provides for lower standards to be used by hospitals to reprocess single-use devices, and in particular with no reporting of incidents, no traceability and no transparency. Even more problematic is that these lower standards can be extended to external reproprocessors in case they are subcontracted by hospitals. This creates a loophole in the system and would disincentivise reproprocessors to apply the highest level of safety and comply with the full set of obligations of the regulation.

3. **More harmonisation:** there should be better coordination and harmonisation across Member States in Europe, in particular with regard to the designation and monitoring of Notified Bodies. Better coordination and harmonisation would also be beneficial to enhance legal certainty for manufacturers, in particular in the areas of classification and borderline decisions. AmCham EU welcomes the proposals to strengthen coordination and harmonisation in this area, as well as in other areas, such as the assessment of clinical trial applications and the shift from a directive to a regulation, which will limit national deviations across Europe.
4. **Increase transparency:** the revision of the regulatory system for medical devices is an opportunity to make the whole system more transparent and increase the availability of relevant information for patients and healthcare professionals, which would help restore trust among all the stakeholders in the system. To this end, AmCham EU welcomes the creation of the European Databank on Medical Devices (EUDAMED), to which patients and industry and healthcare professionals will have some level of access. However, transparency should be carefully balanced with the protection of intellectual property and commercially-sensitive information to secure a favourable environment for innovation. To this end, we would welcome a broad involvement of stakeholders in defining the technical and practical aspects of the database, including when defining the appropriate level of transparency by implementing acts.
5. **Better coordination in market surveillance:** the system would also benefit from stronger post-market safety and from more coordination between Member States in the market-surveillance area. This would be possible through broader stakeholder involvement, in particular in the reporting system, which would increase the efficiency of the vigilance system. Two examples of what is needed include an EU-coordinated system for unannounced visits to manufacturing sites and an EU-centralised reporting and surveillance system. However, improved coordination among Member States' regulatory authorities should not be used to justify disproportionate rises in national regulatory fees or charges to manufacturers. This would compromise European competitiveness.

AmCham EU also welcomes the introduction of provisions regarding economic operators within the proposed regulations on medical devices. A further clarification of the respective economic operators' tasks and responsibilities is needed and will benefit the functioning of the internal market while contributing to patient safety. In this context, consideration needs to be given to the delineation of the

tasks of the respective economic operators in order to take into account the specificities and the strengths of the current medical devices regulatory framework. In particular, the mandatory labelling obligation for importers has to be balanced with a good functioning vigilance system. The legal manufacturer and authorised representative should remain the single points of contact in the EU and importer labelling should not be made mandatory.

Potentially harmful elements in a revised regulatory framework

AmCham EU does have some concerns regarding portions of the proposals.

- 1. The clinical evidence requirements:** in an effort to restore the confidence of the public and the medical community in the Medical Devices Regulation, the proposal sets stricter requirements regarding clinical evidence. We believe a good balance should be found between pre-market and post-market requirements. In the medical devices field, post-market clinical evidence has proven to be effective and is critical for medical devices. We are concerned that some of the requirements introduced by the Parliament and the Council will have a negative impact on device innovation, while not improving patient safety.

The demonstration of efficacy is not a concept applicable to all medical devices (e.g. the efficacy of a syringe would be difficult to determine) and the text would benefit from a definition of efficacy that is appropriate for medical devices. The requirements to have clinical data for all medical devices is also a concept that is not applicable to all medical devices. What meaningful information would a clinical investigation on a medical bed provide?

Although a restriction of the definition of clinical equivalence is already included in the Commission's proposal, an amendment was introduced by the Parliament to further restrict its use for all Class III devices. As a consequence, clinical investigations would need to be performed for all Class III devices, even for modifications having no impact on the clinical performance of the device, thus strongly limiting incremental innovation and improvement of devices.

The proposal made by the Council goes even further by only allowing the use of peer-reviewed clinical data and by limiting the use of clinical equivalence for all Class III and implantable devices to modifications of existing devices from the same manufacturer. This would create a massive issue, as many available clinical data, like registry data, are not published in peer-review journals. The limitation of clinical equivalence will also have major consequences for Class III and implantable devices that have been used safely for decades or, in general, for which the clinical development has taken place before this regulation has been put in place. This may oblige manufacturers to perform clinical trials for these devices currently on the market and for which no safety concerns have been identified. This would also be contradictory with the general ethical principle from the Declaration of Helsinki which is to avoid unnecessary clinical trials.

An obligation to use Randomised Control Trials (RCT), which are not necessarily appropriate for medical devices, and a mandatory assessment by a third party will not only reduce the number of clinical trials performed in Europe but also the number of new CE-marked products introduced in the EU market.

Clinical trials are expensive and we might see fewer CE-marked devices with incremental innovation being introduced in the EU market. Combined with a more limited ability to rely on clinical equivalence, this will have a negative impact, in particular, on incremental innovations which are improving patients' quality of life.

We call upon the negotiators to carefully consider the consequences of such a restriction on the use of clinical equivalence for a broad range of devices and to balance this approach by introducing common specifications allowing for a broader use of equivalence by type of device and to limit unnecessary clinical trials for technologies that are well-established or for which the clinical development already took place in line with the applicable requirements, and for which no safety concerns have been identified.

2. **Disproportionate requirements on Class IIb implantable:** in its proposal, the Council foresees a further disproportionate increase in requirements for Class IIb implantable devices through introducing additional procedures in conformity assessment procedures, aiming to apply the same rules for high-risk implantable devices. This would have a disproportionate impact on medium-risk implantable devices and would be a negation of the risk-based approach system, as this would subject screws to the same requirements as internal cardiac defibrillators.
3. **Chemical substances:** the proposal from the Parliament to ban chemical substances classified as carcinogenic, mutagenic or toxic to reproduction (CMR) in medical devices is a proposal that will deprive European citizens from innovative products that do not pose any risk to patients or medical professionals and is unacceptable. Therefore, any regulatory option which ensures a streamlined, predictable and science-based risk assessment system for chemicals in medical devices is welcome. A regime that weighs the risks versus the benefits of chemicals in medical devices in order to achieve the best possible outcome for the patient is the most appropriate legislative solution. The Commission's proposal provides a suitable legislative framework to achieve this goal.

The Council's approach is closer to the original Commission's proposal, based on risk-management, where the manufacturer needs to minimise the presence of hazardous chemicals in alignment with the risk-benefit approach. The most significant change introduced by the Council is the broadening of the labelling requirement from applying only to phthalates (at >0.1% concentration in devices in direct patient contact), to covering all CMR substances Category 1a/1b, as well as endocrine disrupting chemicals (EDCs) identified as Substances of Very High Concern under the REACH legislation. Whenever these substances are used in products for maternal or child care, an additional justification for their use needs to be included.

The proposed increased labelling requirements are not intended to provide information on potential risks related to the use of these devices, but are aimed at informing the user about the presence of chemicals classified as hazardous due to their intrinsic properties, irrespective of their use in a medical device. Therefore, these requirements would not enhance patient safety in the EU, and they would not necessarily set a high standard of quality and safety for medical devices. Given the wide scope of the chemicals in question, the labelling requirement would not add more information to patients and could even put at risk the value of labels for patient safety.

4. **Changing the definition of a 'medical device':** the Parliament's proposals to change the Commission's definition of medical devices to bring products with unspecified 'indirect' medical purposes into the scope of the regulation is not helpful and could create more, rather than less divergence from globally agreed definitions. When it comes to software, for instance,

the new definition would unjustifiably qualify as medical devices a number of non-invasive, non-medical products such as mHealth applications that simply provide lifestyle and well-being advice. More generally, the very vagueness of the term 'indirect' runs the risk of triggering many new disputes about how to regulate borderline products. Many such disputes have taken place in the context of today's directive and the new regulation should aim to correct, rather than exacerbate, this situation.

5. Classification of medical devices

- **Nanomaterials:** AmCham EU does not support the proposed up-classification of products containing or consisting of nanomaterials in Class III, as this would unduly lead to the up-classification of many medical devices, such as all devices containing radio-opaque markers and almost 75% of all dental medical devices (such as tooth filling materials, dental crowns, bridges, impression taking materials) independently of the fact that the nanomaterials are intended to be released in the human body. The up-classification should be limited to products that are intended to release nanomaterials in the human body. The Parliament has acknowledged this point and has adjusted the classification criteria in its amendment 304. In its communication on the Parliament report in 2014, the Commission confirmed that it agrees with this proposed amendment.
- **Ingested products:** the Commission proposal for the systematic classification of devices composed of substances or combination of substances as high risk (Class III) is a matter of overregulation. Devices that are composed of substances or combination of substances primarily intended to be ingested, inhaled or administered rectally or vaginally and that are absorbed by and dispersed in the human body in order to achieve their intended purpose should be in Class IIa if they are intended for transient or short-term use, and in Class IIb if they are intended for long-term use (Rule 21 in Annex VII).
- **Devices coming into contact with the spinal column:** the Commission's proposal to up-classify spinal disc replacements and all devices coming into contact with the spinal column is a concern. Spinal disc replacements are designed to restore or maintain a spinal segment function, similar to hip, knee or shoulder replacements intended to provide a long-term functional articulation. They have a similar risk profile to joint replacement and therefore can be up-classified within Class III like the other joint replacements. However, this is not true for all devices entering into contact with the spinal column, which are used to fix and stabilise spine elements and should remain classified as Class IIb. We welcome the proposal from the Council to exclude from this up-classification some devices for which the risk profile is significantly lower than spinal disc replacement, like instruments or screws. However, we are concerned that this list would not be exhaustive and would still up-classify some lower risk products.

In vitro diagnostics: specific issues

AmCham EU welcomes the revision of the IVD regulatory framework and the move toward more global harmonisation: the proposed IVD Regulation promises widespread changes to the IVD landscape in Europe. Manufacturers and importers, Notified Bodies, Competent Authorities, reference laboratories and the Commission itself will have to adapt to significant changes to comply with the new requirements expected from the future Regulation. While the intended harmonisation of rules and checks across Europe is warmly welcomed by the IVD industry and will greatly benefit patient safety,

sufficient time needs to be allowed for all involved players to successfully implement the immense changes.

The Commission proposal regarding the classification for IVDs is based on the globally-developed and accepted Global Harmonization Task Force (GHTF) standard for classification, which aims to foster convergence of any international classification system. With manufacturers working globally, international standardisation is critical as manufacturers export their products for patients around the world and thus need to comply with various regulatory systems.

Australia, Canada, Saudi Arabia and other countries are already moving towards harmonisation with the GHTF standard for classification. There is huge potential for creating a new system that allows relevant data to be comparable globally and can greatly facilitate vigilance procedures. This is essential for patient safety and enhances the distribution of diagnostic technologies across markets and regulatory jurisdictions, promoting the European IVD sector on the global market.

The IVD industry strongly supports the introduction of a more harmonised classification system that is based on the international GHTF model, as reflected in the Commission text. European deviation from this model should be avoided to maintain the benefit of global harmonisation and bring IVD companies a return on investment.

However, there is a significant concern regarding the alignment of the IVD regulation with the MD regulation on aspects like post-market surveillance or clinical evidence requirements. Those requirements are not useful or relevant for IVD products. IVDs are fundamentally different from other medical devices as they are not intended to come into direct contact with the patient.

As a general rule, because of the unique nature of IVDs, their assessment and control and the regulatory process, the requirements applicable to other medical devices on clinical evidence and post-market follow-up are not transferrable to IVDs and should therefore be part of specific discussions leading to more appropriate requirements.

Regulatory convergence/harmonisation

The Presidency of the Council to the EU should take into consideration the ongoing US-EU discussions on transatlantic trade and the need for better harmonisation of regulatory and technical standards for medical devices. Further convergence would bring benefits to the medical devices sector, which operates globally, and to patients by lowering costs.