Patient First: Towards a New European Regulatory System for Medical Devices

By Paul Ranson and Indra Bhattacharya

The regulation of medical devices in Europe is currently undergoing a radical overhaul. The current regulatory system is now dated and the rules have not kept up pace with the rapid technological and scientific progress that the sector has seen in the last 20 years. In addition, differences in approach by different Member States have led to a lack of harmonisation across Europe. Many also question the current system’s ability to guarantee the safety of medical devices and preserve consumer confidence in the industry.

These perceptions have been reinforced by a number of recent high profile safety scandals, including the Poly Implant Prothèse (PIP) breast implants scandal which affected 100,000 women in Europe and 400,000 women globally and the issues with metal-on-metal hip replacement systems. These scandals are still making headlines; on Dec. 10, 2013, Jean-Clause Mas, a founder of the PIP company, was sentenced to four years in jail for fraud.

The recent scandals have highlighted a number of systemic flaws with the current system, such as the wide variations in the quality of Notified Bodies, and the lack of effective post-market vigilance and surveillance. Industry insiders have also highlighted that there needs to be greater sophistication in dealing with new technology platforms, such as Digital Health.

In this paper, the first in a series of articles looking at the current reforms, we provide an overview of the main aspects of the reform agenda. Subsequent papers will dig deeper into specific aspects of the reforms and consider what it means for the industry.

Toward a stronger, more sophisticated Notified Body system

Medical devices in Europe are regulated by a risk-based approach according to their classification. Class I devices (regarded as low risk) can be self-declared by the manufacturer as conforming to the “essential requirements” specified for that type of device, but must be registered with the relevant national body (in the UK, the MHRA) and CE-marked before being placed on the market. Class II and III (medium or high risk) devices are subject to extra conformity assessments by Notified Bodies before they can be CE-marked.

Notified Bodies (NBs) are organisations (typically private companies) that have been authorised in each European Union Member State to oversee implementation of the rules. There can be several NBs in each Member State, and a manufacturer can choose any NB in the EU to certify their products.

The safety issues surrounding metal-on-metal hip replacements highlighted the unevenness in the knowledge and sophistication held by NBs across the different Member States. A key part of the reform agenda is thus to achieve greater consistency amongst NBs whilst preserving the current decentralised regulatory structure.

Under the reforms, the NBs will be subject to tougher regulatory monitoring at regular intervals by Member

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States and could be issued with penalties if they fail to comply with the minimum standards laid out.

The proposals for stronger supervision of NBs by national authorities have been welcomed by industry, with industry bodies commenting that they want more competent NBs and that strengthening the NB system would be more effective in delivering improvements in patient safety and device quality than introducing a pre-market authorisation (PMA) system.

The system for designating NBs is also being toughened. Member States will now only be able to designate NBs after joint assessments have been conducted by Commission experts and other Member States (these reports will be made available to all Member States). In addition, NBs wishing to assess high-risk devices (such as implantable devices) will need special designations by the European Medicines Agency, which will assess whether they have the appropriate scientific expertise and knowledge to do so.

NBs will also be expected to perform more of a 'policing role' once the device has been placed on the market in an effort to remedy the weakness in post-market vigilance that the PIP scandal revealed. The new rules mean that NBs will be required to perform random, unannounced audits at manufacturing sites, inspect samples of products, and check the quantity of finished products against the amount of raw material produced. This aims to avoid the use of low-quality ingredients as occurred in the PIP scandal.

These changes were considered so important that they have been implemented ahead of the rest of the reform package through a Regulation and a Recommendation passed by the Commission in September 2013.

### A heated debate on pre-market authorisation

The Commission’s draft new Regulation, published in September 2012, proposed additional scrutiny by a central body before medical devices reach the market, but only in exceptional cases. The ENVI Committee in the European Parliament took this further, proposing a centralised PMA system for high risk devices on a case by case basis. This was a more involved system, potentially covering a wider class of devices than that proposed by the Commission.

The European medical technology industry association, Eucomed, was particularly vocal in denouncing the PMA proposals as expensive and a large administrative burden, which would substantially increase approval times for devices without any discernable safety benefits. Against industry lobbying, these proposals were watered down in the full Parliament debate in November 2013. The current proposal is that the central Assessment Committee for Medical Devices will only be involved where there are specified concerns. However, Eucomed was again critical of this, stating that not only will the Committee be unqualified to do the job, as it will have limited medical device expertise, but taxpayers will pay twice — once for the appointment of qualified experts to the Committee, and again for them to carry out a second assessment of medical devices, which Eucomed considers unnecessary.

The idea of a centralised marketing authorisation had been contentious even before the Commission’s original proposals in September 2012. Industry groups such as ABHI in the UK and Eucomed in Europe, along with some members of the European Parliament, argued that such a system would cause unnecessary regulatory delays, especially for small and medium-sized enterprises (SMEs). In contrast, those in favour of the PMA system contended that as NBs are mostly funded by medical device manufacturers, a more independent and central system of scrutiny is needed.

Currently, the non-centralised PMA system in Europe is highly cherished by industry. This is because the system allows devices to reach the market much faster than in jurisdictions that have a pre approval system (such as the US). However, the Medicines in Europe Forum has noted that the US system has not prevented it from maintaining its status as the leader in medical devices innovation.

### A ‘life-cycle’ approach to regulation

The concerns over the safety of metal-on-metal hip replacements demonstrated how difficult it is in the current system to trace medical devices back through the supply chain in order to identify the sources of defects. This problem stems in part from the uneasy combination of the borderless nature of the European market and the national fragmentation that characterises the regulatory structure.

To tackle this, under the new rules, it is proposed that each medical device will have a unique device identifier (UDI), so that it can be traced back to its supplier. Each company along the supply chain will have to keep records of who supplied it with the device, and whom it supplied the device to. There will also be a central European database of medical devices (Eudamed), which members of the public will be able to access. The database will give patients and healthcare professionals more information on the medical devices that they might use or purchase, such as registration details, relevant economic operators, certificates issued by NBs, clinical investigations, vigilance, and market surveillance information. Manufacturers and importers must register themselves and their European devices on this database.

A key feature of the reform proposals is the strengthening of post-market surveillance and vigilance, bringing the European system more in line with the ‘life-cycle’ approach taken by other jurisdictions such as the US and Australia. Manufacturers will be subject to heavier reporting obligations — for instance, they will have to produce trend reports relating to their devices, as regards safety and performance data and key elements of the supporting clinical data. They will have to ensure that this data is publicly available, as well as employing suitably qualified individuals responsible for regulatory compliance.

Distributors and importers will also face a heavier regulatory burden. They will be required to take active steps to ensure that all parties upstream of them in the supply chain are in compliance with regulatory requirements, and will be required to check, amongst other things, that the device bears a CE mark and a UDI and that it is labelled appropriately. They will also have to put their contact details on to devices, and monitor any complaints they receive as a result, taking autonomous corrective actions regarding safety where necessary. These requirements will more actively involve distributors and importers in post-market surveillance and vigilance, which has previously primarily been the responsibility of the manufacturer.
Manufacturers will also be required to take out appropriate liability insurance covering them from damages caused to users stemming directly from “manufacturing defects.” The level of coverage should be “proportional to the potential risk associated with the medical device produced.”

Adapting to technological change

The current regulations were drafted over 20 years ago and are increasingly viewed as ill-suited to today’s fast-moving technological landscape.

Products must be in compliance with the “essential requirements” specified for each type of device. It is often unclear how these requirements apply to novel forms of device. Software integration into devices, for example, has seen particularly fast development in the last two decades. The EU has sought to address this in part by issuing guidance on how software should be classified and how the essential requirements should apply to such products. However, given the non-binding nature of the guidance and the differing approach of Member States, the regulation of software in medical devices is still characterised by a lack of certainty and by a perceived lack of sophistication.

In addition, the current rules are based on three Directives which have been implemented and interpreted in slightly different ways across Europe. This has led to a lack of harmonisation in what is required for different kinds of devices. This can be particularly troublesome for innovative devices which already suffer from a lack of regulatory clarity.

The reforms thus represent an opportunity to provide clarity over the regulation of innovative devices and to produce new harmonised common technical standards to ensure greater consistency across Europe. The three Directives will be replaced with two Regulations, which will be directly enforceable in all EU Member States. New common technical standards should also reduce the need for piecemeal non-binding guidance to cope with areas of innovation.

Such harmonisation is also evident in the reforms to the regulation of in vitro diagnostic medical devices (IVDs). Whilst IVDs will still be covered by a separate law, the existing list of IVDs will be replaced by a new risk-based system that strongly resembles the system for other medical devices. Devices will be classified between Classes A (the lowest risk) to D (the highest risk) according to the risks associated with technical design and manufacture.

The rules governing the reprocessing of single-use medical devices are also being clarified. The current proposal is for a new list outlining those devices that can be reprocessed to be created, with a separate list indicating which devices are for single use only. If a device is not specifically listed as “single use,” it can be “reprocessed,” which means that it will be cleaned, disinfected and sterilised, and re-tested to ensure its technical and functional safety before being used again. Under the new rules, health bodies conducting this reprocessing would be liable for any consequences from it and, importantly, considered to be the manufacturers of reprocessed devices, which will mean they are subject to all the regulatory requirements, including conformity assessments.

The scope of the new Regulation on medical devices will also be extended to cover products manufactured using non-viable human tissue cells.

What next?

There have been delays to the various votes needed to progress the implementation of the new rules; for example, ENVI’s vote on the Commission’s proposals was delayed from July to September 2013. The European Council’s meeting on Dec. 10, 2013, also highlighted a lack of consensus between Member States on certain key issues like reprocessing and the need for PMA, so further delays are a real possibility. The Council is still discussing the proposals.

2014 will see the European Parliament and Council renegotiate on the text of the new rules, which take the form of Regulations. It is thought unlikely that an agreement will be reached before the Parliamentary elections due in May 2014. The Regulations are currently expected to be adopted in 2015, with the new regime to come into effect by 2019.

Conclusion

The key theme running through the debates that have marked the progress of the new Regulations so far is the need for a balance between increasing patient safety, so as to avoid the scandals that have gone before, and over-burdening the European medical devices industry with too much ‘red tape’ so that innovation is slowed and manufacturers struggle to place new devices on the market.

Although the initial reaction to the proposals was generally positive, especially with regard to increased transparency and harmonisation across the EU, the controversy relating to the proposed PMA system sparked a strong response from industry. This reveals how closely medical device manufacturers and others are following the progress of reforms.

Until the final text of the Regulations is agreed upon by the European Parliament and Council, it remains to be seen where the new rules will fall on the spectrum of a bureaucratic but safe system and a ‘light-touch’ approach.