The breast implant scandal and European Medical Device Regulation

by Maria Donawa and Roger Gray

The recent silicone breast implant scandal in Europe has led to questions about whether or not European medical device regulations are sufficient to protect patients not only from unsafe breast implants, but unsafe medical devices in general.

What were the events that led to the discovery of substandard materials being used to manufacture the breast implants?

During the last quarter of 2009, the French Competent Authority for medical devices, the Agence française de sécurité sanitaire des produits de santé (Afssaps) noted an increasing number of adverse event reports of shell ruptures of silicone-filled breast implants manufactured by the French company, Poly Implant Prothese (PIP).

Following several unsuccessful exchanges with PIP, in March 2010, Afssaps conducted an inspection of the company, which revealed that from 2001 to the time of the inspection, most of the 400,000 implants manufactured by PIP contained a silicone gel different from the one it declared in the implant's design dossier and manufacturing files[1].

Afssaps immediately suspended the marketing and use of PIP implants, informed the European Commission of the events, and strongly advised other EU Competent Authorities to take all measures to verify that the implants were no longer distributed, used or exported[2]. The agency then began assessing whether or not there were increased risks of adverse events related to these implants. In March 2010, PIP filed for bankruptcy.

In September 2010, Afssaps reported that the analysis confirmed that the gel filling the tested implants was not as described in the PIP design file. The tests revealed that the gel was not of the level of quality required for breast implants. The implants showed a higher than average fragility in an elongation test, and a significant heterogeneity of mechanical properties among the implants was revealed.

A June 2011 report provides an overview of Afssaps activities and details of the tests conducted, a summary of the vigilance data analysed, and follow-up recommendations for women with PIP implants[3].

Despite the release of an expert report by French National Cancer Institute concluding there were no grounds for emergency removal unless there was the presence of clinical and/or radiological signs suggesting a change in the implant, the French Minister for Labor, Employment and Health, recommended explantation of the PIP silicone breast implants, even without any clinical signs of deterioration.

How are medical devices, specifically, breast implants regulated in Europe?

Breast implants are regulated by the Medical Devices Directive (93/42/EEC; MDD), covering the vast majority of medical devices, which became mandatory in June 19984. Directives must be transposed into European national laws in order for their requirements to be mandatory. Medical devices that comply with any national transposition of the Directive can be affixed with the CE mark and sold throughout Europe.

The European regulatory system for medical devices is risk-based. As the risks related to the use of a device increase, so does the level of regulatory control. The MDD requires that manufacturers determine the classification of their devices based on a set of rules found in Annex IX of the Directive. The four classes of devices under the MDD correspond to increasing levels of risk and therefore control: class I (lowest risk), class IIa (lower intermediate risk), class IIb (higher intermediate risk), and class III (highest risk).

The conformity assessment procedures, which are necessary for demonstrating compliance with the MDD, are carried out under the sole responsibility of the manufacturer for devices in class I. For devices in the higher risk classifications, the intervention of a third party conformity assessment body, called a "Notified Body" is required.

These bodies are designated by Member State Competent Authorities to carry out conformity assessment procedures. It is important to note that the medical device Competent Authorities have very limited pre-market responsibilities, and are not responsible for conducting CE marking conformity assessment procedures. The Notified Body responsible for conformity assessment activities for PIP was TÜV Rheinland®.

From 1998 to 2003, most breast implants were in class IIb; however, in September 2003, they were reclassified into class III. All existing designs of breast implant, including the PIP implants, had to be reassessed against the more extensive requirements for class III devices before they could continue to be marketed.

The MDD offers several means of demonstrating that class III devices comply with the Directive, which range from establishing quality systems to test programs. However, the vast majority of manufacturers select the conformity assessment procedure requiring the implementation of a full quality assurance system for the design, manufacture and final inspection of the device. This route was also chosen by PIP.

The full quality assurance system route to the CE mark for class III devices also requires the development of a design dossier containing detailed information on the device design, and this must be submitted to the Notified Body for approval and issuance of a design examination certificate. The Notified

Body must also conduct periodic surveillance quality audits to ensure continuing compliance.

An important feature of the European device regulatory system is that the directives contain only general requirements, whereas detailed technical specifications are contained in European harmonised standards. For example, EN 13485 is the harmonised standard for medical device quality management systems. In addition to general standards, those covering specific types of product have also been mandated. For example, EN 14607 specifies requirements for mammary implants.

In addition to harmonised standards, a series of European guidance documents have been developed to promote a common approach to compliance with the Directive. In the case of breast implants, the European guidance document, Guidelines for Conformity Assessment of Breast Implants According to Directive 93/42/EEC Relating to Medical Devices[5], was issued in 1998. The document provides important guidance on pre-market activities such as: the evaluation of hazards applicable to breast implants; review of clinical data by the Notified Body; requirements for post-market surveillance; and the need to provide information on the risks of surgery. Informative annexes include detailed guidance on pre-clinical tests that should be conducted, an example of a clinical evaluation plan and criteria of acceptability.

Once all applicable requirements of the MDD have been met and the Notified Body has approved the design dossier and certified the company's quality management system, the manufacturer issues a Declaration of Conformity, stating the device regulatory requirements have been met, and places the devices affixed with the CE mark on the European market. The MDD requires that the manufacturer implements a system of active post-market surveillance, which includes the obligation to report serious device adverse events to the Competent Authority. Vigilance procedures and records are routinely checked during Notified Body audits.

Did the European regulatory system function adequately?

Afssaps recognised an increase in PIP silicone breast implant rupture rates in the last quarter of 2009, conducted an inspection of PIP facilities in March 2010, discovered the use of substandard device materials, removed the devices from the market and conducted analytical testing to evaluate the health risks. In addition, from April 2010 to January 2012, fourteen publications were posted on the Afssaps website providing information on the events and advice to women who had been implanted with PIP silicone breast implants. On this evidence, it would appear that Afssaps met its responsibilities for post-market surveillance.

Although serious problems were not found until 2010, the fraudulent activity reportedly began in 2001, allowing hundreds of thousands of silicone breast implants of varying quality to be implanted in unsuspecting patients. Why were these problems not discovered by the Notified Body? A TÜV Rheinland® press release[6] states that its auditors were shown conforming silicone samples and corresponding documents during PIP quality system audits. The Notified Body stated that these materials must have been replaced with the substandard materials once the auditors left the premises.

In any case, to better assess why the use of unapproved materials during production of the PIP silicone breast implants was not identified during Notified Body audits, it would be necessary to examine the Notified Body audit reports and relevant PIP design and manufacturing documentation, discuss how the Notified Body audits were performed, be informed of whether or not Afssaps preannounced its inspection, and consider any differences between how the Notified Body audits and Afssaps inspection were conducted.

It was widely reported in the media that PIP personnel hid documentation on the actual materials used. Would unannounced audits have uncovered the deception? Perhaps – however, it is interesting to note that the US FDA conducted unannounced domestic device inspections for many years before changing to the current policy of pre-announced device inspections. Unannounced Notified Body audits may be introduced as a result of the PIP event, but the benefits of doing so must be seen to outweigh the disadvantages. It may prove much more useful to examine audit time constraints and the manner and depth to which audits are conducted.

What enforcement powers do regulators have regarding medical device compliance with the MDD?

The MDD contains four articles that Member States must transpose into national law that concern Member State enforcement powers. Readers should refer to the MDD for the complete provisions of these articles and to the national laws and regulations of each Member State to understand how they have transposed them.

What changes are being discussed regarding the European regulation of medical devices?

In 2008, the European Commission began considering a revision of the legal framework for the regulation of medical devices. Background information and the results of a public consultation can be found on the European Commission website, as well as a 'Roadmap'[7] on the changes being contemplated. According to the Roadmap, proposals will be made for a medical device regulation instead of a directive. The change from directive to regulation is important because a

regulation does not need to be transposed into national laws; regulations become law Europe-wide upon implementation. The use of directives has previously led to certain variations in implementation of some provisions among Member States, which the Commission is keen to limit in the future.

The Roadmap provides general information regarding the possible changes; however, draft proposed texts of the regulatory revision have been leaked, revealing the current thinking on features that the European regulatory system for medical devices should possess. For example, it is possible that Notified Bodies will be required to pay unannounced visits to manufacturers and that more stringent conformity assessment procedures for high risk medical devices will be required. The currently expected date of publication of the proposed regulation is June 2012, but it would not be surprising if this date slipped because of the PIP furor.

Need for careful analysis and effective decisions

The medical devices Directives were adopted to ensure that medical devices provide patients, users and third parties with a high level of protection and attain the performance levels attributed to them by the manufacturer. Such a regulatory system needs to be efficient as well as effective. It also needs to ensure that medical devices are available so we can benefit from the technological innovation that is the hallmark of the medical device industry.

A regulatory system to cover all medical devices, which range from the simple to the most complex technologies imaginable, is not easy to create or maintain and for this reason, it should be periodically analysed and modified to make needed improvements. This is what is occurring in the midst of the events surrounding the PIP scandal. Of course all reasonable measures should be taken to prevent such events from occurring in future, but at the same time, any changes should not jeopardise the availability of the medical devices that we need.

What immediate actions are being taken? A European Commission press release[8] lists the immediate actions being requested of Member States:

- Verify the designations of notified bodies to ensure that they are designated only for the assessment of medical devices and technologies that correspond to their proven expertise and competence.
- Ensure that all notified bodies in the context of the conformity assessment make full use of their powers given to them under the current legislation, including the powers to conduct unannounced inspections.
- Reinforce market surveillance by national authorities, in particular spot checks in respect of certain types of devices.
- Improve the functioning of the vigilance system for medical devices.
- Support the development of tools ensuring the traceability of medical devices as well as their long-term monitoring in terms of safety and performance.

Furthermore, it was announced that the European Commission is conducting a 'stress test' intended to identify any shortcomings that have come to light as a result of the PIP case. Thus far, it appears that careful analysis is underway, which will hopefully allow effective decisions to be made without jeopardising future innovation.

References

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3 Afssaps report, Topical report on PIP silicone gel-prefilled implants (29 June 2011); http://www.afssaps.fr/var/afssaps_site/storage/original/application/39acdab927235584ccfa340e4a9d3896.pdf

4 Council Directive 93/42/EEC of 14 June 1993 concerning medical devices (OJ L 169, 12.7.1993, p. 1) http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CONSLEG:1993L0042:20071011:EN:PDF

5 Guidelines for Conformity Assessment of Breast Implants According to Directive 93/42/EEC Relating to Medical Devices, MEDDEV 2.5-7 rev 1 (July 1998)

6 TÜV Rheinland® press release, Concerning latest media articles concerning Silicone-filled breast implants (29 December 2011) www.tuv.com/en/corporate/about_us_1/press/news_2/news_5.jsp

7 Regulatory Framework Revision Roadmap http://ec.europa.eu/governance/impact/planned_ia/docs/2008_sanco_081_proposal_medical_devices_en.pdf

8 European Commission Press Release, Medical devices: European Commission calls for immediate actions - tighten controls, increase surveillance, restore confidence (9 February 2012); http://europa.eu/rapid/pressReleasesAction.do?reference=IP/12/119&format=HTML&aged=0&language=EN&guiLanguage=en.

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