PIP AND MOM IMPLANTS:
WHAT SHOULD YOUR COMPANY DO NOW?

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James Pink and John Worroll look at what manufacturers can or should do to ensure that they are not next in the spotlight.

The ongoing controversies involving Poly Implant Prothèse (PIP) silicone breast implants and metal-on-metal (MoM) orthopaedic implants have combined to severely damage public confidence in the regulatory systems for medical devices and in the ability of the EU competent authorities to handle problems in this area.

Understandably, the PIP and MoM issues are having a significant impact on the redraft of the medical device directives, which is currently ongoing with the competent authorities and the European Commission. The regulation of high-risk medical devices, including implants, may move closer to the pharmaceutical regime. Whatever the changes, it is clear that in the medium term, manufacturers will have to come to terms with an increase in regulation.

There is also a short-term effect as competent authorities and notified bodies change the emphasis of their enforcement and audit activities to take into account the issues raised by PIP and MoM. This article focuses on what manufacturers can or should do now to ensure that they are not next in the spotlight.

Obviously, any actions should be risk-based. Manufacturers of high-risk implants are the most at risk themselves, particularly if they lack robust justifications for their products and demonstrably good follow-up and post-market surveillance.

We recommend several actions for companies wishing to strengthen their audit readiness.

Firstly, they should re-examine their technical documentation and take any necessary action to ensure that it fully justifies the risk/benefit of the medical device product on the market. Secondly, they should ensure that the post-market surveillance systems and processes fully meet current competent authority and notified body expectations and provide the manufacturer with early warning of any problems.

TECHNICAL DOCUMENTATION

Companies should ensure that their technical documentation demonstrates that there was a robust risk analysis and management system during the design and development of the product, including its accessories. For each product, the documentation should demonstrate that the benefits of the product justify the risks which could not be further reduced during the design phase, following the principles of the EN ISO 14971 medical device risk management standard. A common mistake is to omit or fudge this final conclusion, equally, to identify a risk and then fail either to demonstrate a linkage to the action taken or to justify the decision that no action is needed.

Companies need to check that the technical documentation demonstrates that all the essential requirements (ER) of the Medical Devices Directive (MDD) (93/42/EC as amended by Directive 2007/47) are properly addressed, and not just the most obvious aspects. For example, under ER7 Chemical, physical and biological properties, ER 7.1 states that:

The devices must be designed and manufactured in such a way as to guarantee… performances … particular attention must be paid to:

- *the choice of materials used, particularly as regards toxicity and, where appropriate flammability*
- *the compatibility between the materials used and biological tissues, cells and body fluids, taking account of the intended purpose of the device…*

Referring to EN ISO 10993-1:2003 (Biological evaluation of medical devices) is not enough, a careful reading of the ER will show that it refers to all performances, not just those affected by biocompatibility.

The most recent revision of the MDD placed much greater emphasis on clinical evaluation prior to placing a product on the market. This does not necessarily mean running a clinical investigation or trial for each new product. Ensure you document a robust justification for not undertaking an investigation, not doing so, in terms of the equivalence and relevance of the data used in the evaluation as derived from similar products (see EU guidance on clinical evaluation, MEDDEV 2.7.1), results in the confidence in the clinical benefit-risk conclusions made by the manufacturer being diminished and subsequently justifiably open to regulatory and scientific challenge.

Following the MDD and ISO 13485 (Medical Device Quality Systems) requirements should demonstrate that there is sufficient verification and validation to ensure manufactured products consistently meet the original design, and that the designed product actually works in practice. Commonly, manufacturers combine verification and validation into one without distinguishing between them. A good working definition is that verification confirms that the device meets the design specifications, while validation confirms that the device performs as intended. The US Food and Drug Administration places great emphasis on validation of products (and processes) and provides good guidance on these topics.

POST-MARKET SURVEILLANCE

As PIP and MoM have demonstrated, it is only when the manufacturer places the product on the market that the assumptions and calculations made during the design phase have their real collision with reality, in the shape of patients and users in all their variations. Once placed on the market, there must be a good feedback system in place to ensure the experience from use of the product on patients is fed back into a validation and risk management process. The situation is not as extreme as implied by the famous saying “No battle plan survives the first contact with the enemy”, but a manufacturer cannot get away with just putting the product out and then waiting by the telephone in case someone complains.

The 2007/47 revision of the EU device directives places greater emphasis on post-market surveillance via Annex X which states: “*The clinical evaluation and its documentation must be actively updated with data obtained from the post-market surveillance.”* A fundamental directive requirement is to have a defined post-market surveillance plan, which should have a proactive element. This means that the manufacturer should be actively seeking

information and not just waiting for it to appear. In the PIP example, there were significant issues with the flow of information back from the clinics to which the implants had been sold, as well as with the products that had been own branded by other companies.

High-risk products, including implants of all types, will need a post-market clinical follow-up (PMCF) programme, as per the EU PMCF guidance, MEDDEV 2.12/2.

For lower-risk products, especially those sold over the counter, manufacturers need to consider how they are going to obtain actual performance data and especially how to ensure that the data received does not just come from a few conscientious customers but is representative of all users in all markets; UK and elsewhere. Another guidance document, NBMED 2.12. Rec 1, provides guidance on how to achieve this.

The data received from post-market surveillance should be critically analysed. For example, if there is a cluster of incidents from one particular market, it is tempting to ascribe this to some user error or other peculiarity in the market, or even to a batch issue. However, there is always the possibility that this high rate of incidents is occurring because that particular market is particularly zealous in seeking out and reporting problems, and that the relative quiet from elsewhere is due more to non-reporting than to good product performance.

Then there is the vigilance system under which manufacturers report “serious” incidents to the competent authorities (see MEDDEV 2.12/1). Each manufacturer should have the criteria for making such reports, defined for their products based on the risk evaluation conducted during the design stage. In the event of a recall or advisory notice, the manufacturer will need robust processes that can be defended to the authorities.

Finally, the manufacturer’s internal processes must allow for good feedback of information received post-market back into the design process, the technical file and, most importantly, the risk management report.

There are many things manufacturers of medical devices can do to avoid becoming the next PIP or MoM, regardless of any changes in regulation. It is certain that the regulations will continue to emphasise the responsibility of the manufacturer to place safe and effective devices on the market. Therefore, the use of robust scientific, engineering, process and reliability tools should be in place now, and be reflected in the technical documentation and post-market surveillance plans of all existing products.

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