DEEP DIVE

REGULATORY DEVELOPMENTS IN THE MEDICAL DEVICES SECTOR: A LONG AND DIFFICULT JOURNEY

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doi: 10.54920/SCTO.2023.RAWatch.8.1

Because the development of medical devices, device users, and the devices themselves often cross borders, medical device regulations in Switzerland are closely aligned with those of the European Union. Therefore, the *Regulatory Affairs Watch* editorial team wanted to hear first-hand from a European stakeholder who has been involved in this matter since the events that triggered the changes to European medical device regulation. In this Deep Dive article, Catherine Simonin, MD, who is actively engaged in France's Ligue contre le cancer (**LCC**, league against cancer) and the overarching national patient organisation France Assos Santé, discusses some of the drivers of regulatory changes for medical devices. The LCC has long been advocating for medical device legislation to focus more on patient safety, and the effects of its advocacy efforts can be seen in the EU's changing legislative landscape. Using a Q&A format, Catherine Simonin also presents the perspective of patients and patient organisations on the EU's recent Medical Device Regulation.

European law has evolved to guarantee greater safety for patients who receive or use medical devices (**MDs**). The new EU Medical Device Regulation (**MDR**), which governs MDs and came into force on 26 May 2021, is an important step forward in making devices safer to use and thus in safeguarding patients' interests. In particular, the MDR upgrades the requirements for demonstrating that benefits outweigh risks and imposes stricter post-market surveillance.

Since the text was published in 2017, the French National Agency for Medicines and Health Products Safety (**ANSM**) has been supporting economic operators in understanding the new requirements, thus helping them get ready to apply them. Data on all European MDs are collected in the European Database on Medical Devices (**EUDAMED**), including follow-up on all reported incidents and transparent information on ongoing trials. The overarching aim of these requirements is to ensure MDs are safe to use while at the same time fostering innovation so that patients gain access to novel care solutions. The new MDR also includes provisions intended to improve collaboration in Europe.

REGULATORY CHANGE DRIVEN BY HEALTHCARE-RELATED SCANDALS INVOLVING MEDICAL DEVICES

These regulatory changes are the direct result of health scandals caused by defective medical devices that have severely affected people's health, as in the case of the breast implants manufactured by Poly Implant Prothèse (**PIP**). Instead of using medical-grade silicone, the PIP implants had been deliberately filled with industrial-grade silicone that did not meet the standards for implantable material. This large-scale fraud came to light in March 2010 during inspections by **AFSSAPS**, as ANSM was formerly known. The company did not meet the requirements governing certified procedures applicable to the production of implantable class III medical devices, the MDs that represent the greatest risk level for patients.

A total of 30,000 women received PIP breast implants – 9,000 of them after breast cancer surgery. Among all these women, some 3,000 breast implant ruptures were observed and 2,000 inflammatory reactions were reported. After a woman who had been fitted with a PIP implant died of lymphoma on 5 December 2011, France's director general for health (DGS, part of the French Ministry of Health) asked the French National Cancer Institute (**INCa**) to prepare recommendations for monitoring women at risk of developing lymphoma induced by the implants. French health minister Xavier Bertrand expanded the assignment after AFSSAPS reported a second adverse event involving a woman who had developed an adenocarcinoma of the breast in which a PIP implant had been fitted. Women with PIP implants who displayed abnormal clinical signs when consulting their doctor were told they had received a defective implant.

While this situation was bad enough for women who had received a defective implant during aesthetic surgery, it was a second blow to women who had undergone cancer surgery completed by breast reconstruction involving the insertion of PIP implants. It must be clearly understood that the reconstruction phase is not easy for women who have undergone cancer treatment, and some of them had considered it for several years before making their decision. They were not people who had light-heartedly hopped onto an operating table. Thanks to France's protective healthcare cost coverage system, patients who underwent post-cancer reconstructive surgery did not have to pay anything to have their PIP implants removed and new implants inserted, but they did have to pay any excess on the surgeons' fees. Furthermore, the traumatic nature of the experience resulted in some patients needing supportive psychological care, for which they did not receive any reimbursement.

From the moment the PIP scandal broke, the French Ligue contre le cancer (**LCC**, league against cancer) leapt to support the victims. It instituted civil proceedings and released emergency funding of 50,000 euros to provide material, psychological, and legal assistance to the victims. The French Supreme Court confirmed the conviction of the manufacturer of PIP implants in September 2018.

THE LCC PRESENTS PATIENTS' POINT OF VIEW

The awareness of the toxic risks of these implantable medical devices provoked by such harrowing experiences can be expressed as a set of questions and answers setting out the point of view of patients and patient organisations:

Thinking back on these harrowing experiences resulting from the PIP scandal, what happened and what triggered the necessity of better regulation for medical devices?

The PIP affair caused serious harm to the women who received those breast implants and to civil society in general. This harm took several forms: lasting anxiety among women who have or used to have a PIP implant and among their relatives; a feeling of injustice at having been deceived when in a situation of great vulnerability; and a climate of mistrust and doubt towards the health system, which results in a loss of confidence in the health messages issued by public and medical authorities.

Drugs, which are a class of therapeutic products, have long had to fulfil a series of scientific requirements to obtain marketing authorisation. In addition, clinical trials are required to demonstrate that drugs are both effective and safe before they can be placed on the market. According to the new regulation, medical devices – another class of therapeutic products – can now be certified only after clinical trials have been conducted. These trials must be approved by both an ethics committee and the competent national regulatory authority (ANSM in France). Nevertheless, the MDR still relies on certification by bodies, such as private certifying companies, whose impartiality vis-à-vis manufacturers is questionable. This is no substitute for marketing authorisation by a competent regulatory authority of the type required for drugs.

Do patient representatives view the new MDR as a milestone?

The MDR is a major step forward in improving the safety of the care pathways followed by people who receive or use medical devices. To obtain certification, manufacturers are required to draw up investigation plans under which they conduct a scientific evaluation of the toxicity of the materials chosen for a device. Nevertheless, the requirements imposed by the MDR are less stringent than those for drugs, which is questionable.

As a representative of the people who use the health system, the LLC demands the introduction of proper European marketing authorisation for those medical devices that pose the greatest risk. We also want to see impartial, independent monitoring and certification bodies so that health disasters can be avoided.

Does the new MDR address the concerns of the majority of patients?

The progressive implementation of the EUDAMED database will allow materiovigilance for medical devices by recording reports of adverse events identified by healthcare professionals and the people directly affected. This should help to identify weak safety signals early on and thus ensure that warnings can be issued and corrective action can be taken to safeguard device safety as quickly as possible.

Some operators in the medical device sector claim that the complex nature of the new MDR is likely to slow down the pace of new developments in a kind of backlash against the tightening of regulatory requirements. Would you agree with this?

It is certainly true that the new MDR will delay access to new medical devices because manufacturers now have to fund clinical trials for a longer period of time. However, patients' top priority is still to ensure safe care pathways, because when devices cause severe adverse events, the consequences for the people affected can sometimes be so severe that they include lasting after-effects and occasionally even disability.

All medical devices authorised in Europe will have to be recertified by May 2024. Given the large number of device dossiers, this deadline seems unrealistic, and there is a risk of patients being deprived of thousands of devices that are essential to their care. This risk of shortage should be analysed so that transitional measures can be introduced while recertification is in progress. Depriving patients of medical devices that they rely on in everyday life risks triggering another kind of public health crisis.

Do you think that the key to guaranteeing safety is to strengthen regulations or should we be focusing instead on follow-up and continual auditing to ensure shortcomings are identified at an early stage?

This MDR does increase patient safety, but it is the task of materiovigilance to undertake real-world monitoring and alert the authorities responsible for market surveillance, such as ANSM, to issues in the interests of providing long-term monitoring for medical devices on the same basis as medicines. Doing so would identify health scandals such as that caused by the PIP implants at an earlier stage and prevent them from affecting large numbers of people, who would in turn be spared the distress of having to fight for their health and for their legal rights. Issuing proper marketing authorisation for medical devices could be considered at the European level as a way of increasing the safety of care pathways. Whereas drugs can be discontinued quite easily if they provoke an adverse reaction, removing an implantable medical device involves surgery that takes longer to implement, which not only causes stress, anxiety, and pain but also increases costs for the people affected.

MEDICAL DEVICE SAFETY: THE JOURNEY CONTINUES

With any human activity, we must learn from our mistakes – a universal truth the medical device sector could not avoid. And even though the PIP breast implant scandal originated in France, it involved a German-based certifying body and impacted thousands of women in Europe, many of whom experienced this additional burden following breast cancer surgery. In its role as a of defender of cancer patients, the LCC filed in the PIP civil action for additional psychological care for patients, and the organisation continues to advocate on behalf of patients. The LCC acknowledges that the painful PIP experience has resulted in some progress, which is reflected in the new MDR and Swiss medical device regulations. Nevertheless, a few steps remain on this journey towards better medical device safety and thus patient safety.