SCTO PLATFORMS

Medical devices: Regulatory environment forecasts

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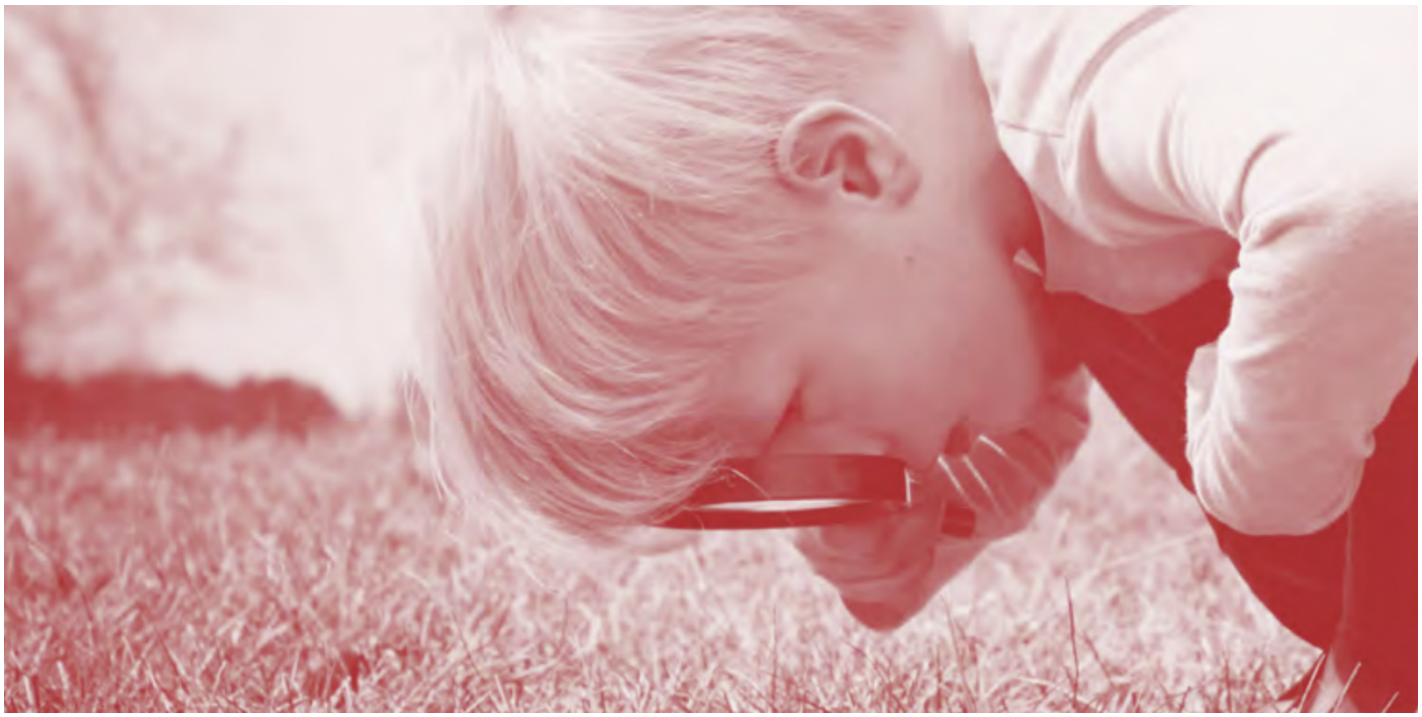

The regulatory landscape of medical devices is currently undergoing tremendous changes in the EU – changes that will directly affect Switzerland. Following numerous serious incidents resulting from medical devices (most notably, hip prostheses and defective silicone breast implants), a searchlight has been cast on the manufacturing, marketing, and surveillance of medical devices, as they stand in the EU. The systems in place contained many loopholes and shortcuts, which allowed some poor-quality and risk-compromising devices to be authorised. Consequently, the EU decided to tighten the regulatory procedures and two new EU regulations entered into force in 2017. They will apply, starting in 2020 and 2022, respectively. These changes set out in the regulations seek to improve medical device safety and performance and will carry consequences in terms of clinical evaluations and investigations on the devices, and how they are conducted.

Switzerland is currently adapting its legislation on medical devices, to ensure that Swiss-based patients will also benefit from the improvements made. At the same time, only by aligning its own legislation to EU developments, will Switzerland be able to maintain its position as an equal partner in the EU internal market for medical devices. Nevertheless, some issues still need to be solved urgently for a smooth transition to take place.

From May 2020: more stringent EU regulatory requirements for medical devices applicable

Regulation (EU) 2017/745 on medical devices (referred to throughout this newsletter as the Medical Devices Regulation, MDR) and Regulation (EU) 2017/746 on *in vitro* diagnostic medical devices (similarly, referred to throughout as IVDR) have replaced three existing medical device European Directives (93/42/EEC, 98/79/EC, and 90/385/EEC). The MDR and IVDR came into force on 26 May 2017.

A directive is a legislative act that sets out a goal that all EU member states must achieve, while leaving them the freedom to define their own laws on how to reach these goals. On the contrary, a regulation is a binding legislative act which must be directly applied across the EU. The two new regulations will come into full application on 26 May 2020 for the MDR and 26 May 2022 for the IVDR, following a transition period to allow all parties – including manufacturers, authorities, and Notified Bodies (NBs, organisations designated by a national notifying authority to assess the conformity of certain products before the products are placed on the market) – to comply with the changes.

With less than eight months left before the date of application of the MDR, as of October 2019, time has not provided solutions to all the challenges. Manufacturer representatives and some authorities, among others, recently raised concerns about the implementation aspects of the MDR, despite all the efforts made and support offered by the European Commission (EC) which published several guidance documents during the past months.

Critical considerations are: the number of NBs available and their capacity to treat the demands, the system requirements, and the implementation of legislation. In April 2019, MedTech Europe warned the EC of an “untenable” transition to the new regulations. In June, indeed, the EC cautioned health institutions that some devices may become temporarily unavailable (source: RAPS Focus™).

Key changes stipulated by the MDR

The new MDR imposes strict demands on both the medical device manufacturers and the NBs whom they must involve in the approval process of all medical devices, other than self-declaration class I devices (the classes of devices are further summarised below).

TÜV SÜD, a designated NB for the MDR with headquarters based in Germany, explains the most significant changes stipulated in the regulation, as compared to the old directives (source: TÜV SÜD):

- **Product scope expansion:** The definition of medical devices and active implantable medical devices covered under the MDR has been significantly expanded to include devices that may *not have an intended medical purpose* (such as coloured contact lenses and cosmetic implant devices). Also included in the expanded scope of the regulation are devices designed for the purpose of “prediction and prognosis” of a disease or other health condition.

- **Reclassification of devices according to risk, contact duration, and invasiveness:** Manufacturers need to take into account the updated classification rules and to update their technical documentation accordingly, by considering the fact that class III and implantable devices will carry higher clinical requirements and will require a regular process of scrutiny.
- **No "grandfathering" provisions:** All currently approved devices must be recertified according to the new requirements. Exemptions are under negotiation.
- **Implementation of the “Unique Device Identification”:** This requirement is expected to increase the ability for manufacturers and authorities to trace specific devices through the supply chain, and to facilitate the efficient recall of medical devices that have been found to present a safety risk. In addition, the European Database on Medical Devices (Eudamed) is expected to be expanded to provide more efficient access to information on approved medical devices.
- **Identification of a “qualified person”:** Device manufacturers are required to identify at least one person within their organisation who is ultimately responsible for all aspects of compliance with the requirements of the MDR. The organisation must document the specific qualifications of this individual, relative to the required tasks.
- **Rigorous post-market oversight:** The NB must take on an increased post-market surveillance role. Accordingly, unannounced audits, along with product sample checks and product testing will help to reduce risks from unsafe devices. Annual safety and performance reporting by device manufacturers will also be required in many cases.
- **Specifications:** The EC or expert panels must publish Common Specifications which shall be taken into account by manufacturers as well as the NB, together with the Harmonized Standards and the State of the Art.
- **Systematic clinical evaluation of class IIa and class IIb medical devices:** Manufacturers must perform a new clinical evaluation for their devices, by both considering the new wording of the regulation and by deciding if they can use an equivalence approach with other medical devices in order to be exempt from conducting a clinical investigation.
- **More rigorous clinical evidence for class III and implantable medical devices:** Manufacturers must conduct clinical investigations if they do not have sufficient clinical evidence to support the claims done on both the safety and performance of a specific device. Device manufacturers must collect and retain post-market clinical data as part of the ongoing assessment of potential safety risks.

The difference between a clinical evaluation and a clinical investigation

Clinical evaluation is a methodologically sound ongoing procedure used to to collect, appraise, and analyse clinical data pertaining to a medical device. This procedure enables manufacturers to provide their NB with sufficient clinical evidence to demonstrate that the device conforms with the Essential Requirements for Conformité Européenne (CE) marking according to the guidelines on medical devices (MEDDEV 2.7/1, revision 4 of June 2016). This process consists of collecting clinical data confirming the safety and performance when using the device according to the manufacturer’s Instructions for Use (IFU).

Clinical data can be sourced from:

- **clinical investigation(s)** of the evaluated device. Clinical investigations are clinical studies (trials) in one or more human subjects, undertaken to assess the safety or performance of a medical device
- clinical investigation(s) or other studies reported in scientific literature of an equivalent device
- published and/or unpublished reports on other clinical experience of either the device in question or an equivalent device.

As a general rule, clinical investigations of the device under evaluation are required for implantable and class III devices. However, as stated in the MEDDEV guidelines, the need for clinical investigations depends on the

ability of the existing data to adequately address the risk–benefit profile, claims, and side-effects in order to comply with the applicable Essential Requirements. Clinical investigations may therefore also be required for other devices, including for devices in class I and class IIa, and for class IIb devices that are not implantable.

How Switzerland is adapting its medical devices legislation

Although Switzerland is not part of the EU, it accepts certain EU legislation through bilateral treaties. To ensure that it can continue to participate as an equal partner in the EU market, the country needs to adapt its legislation. Currently, Swiss legislation on medical devices is amended gradually, in line with the transitional periods applicable in the EU Member States. The different steps are explained on the website of the Federal Office of Public Health (source: FOPH):

1. The **revision of the Medical Devices Ordinance (MedDO),** which was brought forward to 25 October 2017, allowed Swiss conformity assessment bodies to register as designated NBs according to the new regulations from 26 November 2017, and enables Swissmedic to participate in the EU expert groups that are created.
2. **Amendments to the acts:** The partial revisions of the Therapeutic Products Act (TPA) and of the Human Research Act (HRA) were intended to establish the necessary legal basis, in order to be able to amend the implementing legislation (complete revision of the MedDO and implementing provisions for *in vitro* diagnostics) to correspond to the MDR. On 30 November 2018, the Federal Council submitted the amended TPA to the Federal Parliament. The matter was adopted on 22 March 2019. The amendments are thus scheduled to come into force in the first half of 2020.
3. The **complete revision of the MedDO and the implementing provisions on *in vitro* diagnostics** take account of all provisions of the EU regulations and are likewise scheduled to come into force in the first half of 2020 and in 2022, respectively. On 15 May 2019, the Federal Council opened the consultation regarding the complete revision of the MedDO and the new Ordinance on Clinical Trials with Medical Devices (ClinO-MD). The consultation procedure lasted until 5 September 2019 (see **Views and Opinions**).
   Specifically, the definition of clinical investigation stated in the MDR covers both projects according to the Ordinance on Clinical Trials (ClinO) and those according to the Human Research Ordinance (HRO). The ClinO-MD will conveniently list in one legal text all the provisions relating to research with medical devices. Not surprisingly, the ClinO-MD project proposes that clinical trials with medical devices be carried out following rules of the MDR (arts. 72–82 and Annex XV) (see "Clinical Evaluations & Investigations**: Changes Ahead in Swiss Laws**").
4. **Adjustment of the Mutual Recognition Agreement (MRA) (ch. 4):** Alongside the current legislation revision projects, updates to the MRA need to be negotiated by the Switzerland–EU Joint Committee, in order to introduce mutual obligations for Switzerland and the EU at international treaty level. According to the Swiss Medtech Group, in a statement of April 2019, this aspect is problematic as uncertainties remain on whether the MRA will be updated early enough. Otherwise, Swiss manufacturers may have to meet the requirements imposed on third countries, in order to be permitted to export products to the EU.

Defining medical devices

According to the MDR (art. 2):

"'Medical device' means any instrument, apparatus, appliance, software, implant, reagent, material or other article intended by the manufacturer to be used, alone or in combination, for human beings for one or more of

the specific medical purposes:

- diagnosis, prevention, monitoring, prediction, prognosis, treatment or alleviation of disease,
- diagnosis, monitoring, treatment, alleviation of, or compensation for, an injury or disability,
- investigation, replacement or modification of the anatomy or of a physiological or pathological process or state,
- providing information by means of *in vitro* examination of specimens derived from the human body, including organ, blood and tissue donations,
- and which does not achieve its principal intended action by pharmacological, immunological or metabolic means, in or on the human body, but which may be assisted in its function by such means."

In Switzerland, a similar definition is provided by the MedDO (art. 1). In practice, medical devices include a great diversity of products, from simple and common household items (reading glasses, thermometers, and disposable gloves) to diagnostic instruments, like the stethoscope and blood-pressure gauge, to highly technical items like stents and cardiac valves inserted into the body. The feature common to all is that they carry *a medical purpose*. A flattened wooden stick used to inspect a patient's throat (a tongue depressor) is a medical device, whereas an identical, flattened wooden stick used for a non-medical purpose, like icing a cake, is not. Even if the item is fundamentally the same.

Classifying medical devices

The classification of medical devices is a **risk-based** system based on the vulnerability of the human body and the potential risks associated with the devices (including, for example, their intended purpose, time of contact with the human body, invasiveness, and failure or misuse risk). Medical devices can be subdivided in the following classes, according to MEDDEV 2.4/1, and classification rule(s) apply in accordance with Annex VIII of the MDR Classification:

- **Class I** (low risk): Devices that are non-sterile or that do not have a measuring function. Examples: wheelchairs, stethoscopes.
- **Class I** (low/medium risk): Devices that are sterile and/or have a measuring function.
- **Class IIa** (medium risk): Examples: magnetic resonance equipment, syringes for infusion pumps, dental fillings, surgical clamps, tracheal tubes.
- **Class IIb** (medium/high risk): Examples: condoms without spermicide coating, lung ventilators, urethral stents, plates for setting bones.
- **Class III** (high risk): Examples: spermicide-coated condoms, drug-eluting (-releasing) stents, intrauterine devices, pacemakers, heart valves, implanted cerebral simulators.

The MDR has added a few additional special rules, including one for nanomaterials.

In vitro diagnostics carry their own classification scheme (indicated in the IVDR, Annex VII) and although active implantable devices do not follow the same classification system as provided by the MDR, they are subject to similar requirements as class III devices.

In Switzerland, the classification of the medical device does not affect the categorisation of the clinical trial that is based only on the CE mark and the IFU of the product.

What is the CE mark?

Owing to bilateral agreements in place (mentioned in the MRA), medical devices must bear the **Conformité Européenne** (**CE) mark** of conformity, in order to be placed on the market in any EU member state and Switzerland. By contrast, the US FDA mark is not valid in Switzerland or Europe. Unlike medicinal products, medical devices do not undergo an official authorisation procedure. Almost all medical devices require the involvement of an NB, which provides the CE marking (with an exemption for class I medical devices without a measuring function and supplied in a non-sterile condition). Conformity to the International and European Standard EN ISO 13485 is voluntary.

NBs are independent private organisations designated by the given national competent authority. These NBs perform third-party conformity assessment activities of the devices, including the calibration, testing, certification, and audit. CE marking is only valid according to the IFU supplied by the specific manufacturer of a specific device.

Conclusion

Medical devices represent a wide range of products essential for the daily life of all people, not only patients. Current regulatory evolutions in Europe and Switzerland will certainly change the market significantly, since all manufacturers will be obliged to comply with new demanding requirements, including building dossiers that contain convincing clinical evidence for current products on the market and for others still in development. Subsequently, CTUs, ethics committees, NBs, authorities, as well as health institutions, all being affected will need to adapt their organisations promptly, as the deadline of the transition rapidly approaches.