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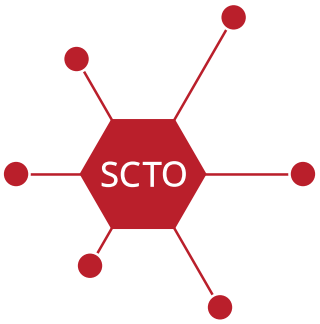

REGULATORY AFFAIRS WATCH

ISSUE 2, 15 OCTOBER 2019

Unique, credible, and regular updates on regulatory topics relating to human research

IN THIS ISSUE

EDITORIAL: A STORMY SEASON FOR MEDICAL DEVICES

Medical devices are experiencing the blustering winds of change – change that will have a considerable impact on Switzerland. Medical devices in Switzerland represent a CHF 15.8 billion business and hold a leading international position in terms of the country's economy (contributing 2.3% to the national Gross Domestic Product), with 1,400 dynamic, small, medium-sized, and multinational companies thriving in a highly innovative health environment.

With this stormy weather blowing in from the European Union (**EU**) and certain to sweep right across Switzerland, all players in this field need to get prepared as swiftly as possible. The deadline of May 2020 is around the corner. Those affected must build up strong capabilities to prepare the appropriate dossiers needed, so as to reassure the public and the authorities of the safety and usefulness of both existing and future medical devices. Organisations dealing with medical devices are being obliged to transform themselves. But how the Swiss authorities will manage their relationships with EU, concerning the harmonisation of rules and mutual recognition agreements, remains hazy.

The **DEEP DIVE** of this second issue of the *RA Watch* will help you understand better the regulatory changes coming from the EU and the ongoing revisions of Swiss laws regarding medical devices. You will find out how the clinical evaluations and investigations of medical devices in Switzerland will be affected. Key Swiss stakeholders, including the Swiss Clinical Trial Organisation (**SCTO**) and its network of Clinical Trial Units (**CTUs**), swissethics, the medtech industry, and patient associations have shared with our readers their **VIEWS AND OPINIONS** about this evolution. A concrete **CASE STUDY** – of an App used in clinical research – illustrates how demanding the new rules will be for investigators who may not even be fully aware that what they are using counts as a medical device.

There is no doubt that high tech will flourish in the future of healthcare. The public is dreaming of high-tech health-related devices and these aspirations create a market for it. However, the realisation of these high-tech dreams will depend heavily on trust, and Switzerland is extremely well equipped to face this challenge.

Several hundred readers have subscribed to our newsletter since its début issue in April. Such a flurry of interest confirms a need for the *RA Watch* and so we thrive on doing our utmost to satisfy you, our readers. We are very pleased to present to you this issue 2, with its fresh, appealing web and print formats. We trust you will find it enjoyable and enlightening, and wish you happy reading.

Bonne lecture!

Séverine Méance, *RA Watch* Editor, and Laure Vallotton, Coordinator of the SCTO Regulatory Affairs Platform

MEDICAL DEVICES: A MORE STRINGENT REGULATORY ENVIRONMENT FORECASTS MORE DEMANDING CLINICAL EVALUATIONS AND INVESTIGATIONS

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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 FocusTM

HOW TO DEFINE AND CLASSIFY A MEDICAL DEVICE?

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.

For "Classifying a medical device", see overleaf.

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 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.

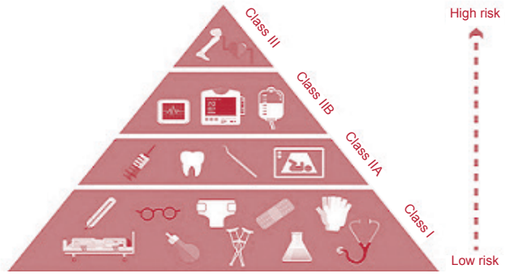

Image credit: CE Check, reproduced with permission

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.

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**")

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.

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.

CLINICAL EVALUATIONS AND INVESTIGATIONS OF MEDICAL DEVICES: WHAT CHANGES CAN BE EXPECTED UNDER THE NEW SWISS LAWS?

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The views expressed in this article are exclusively those of the authors and do not necessarily reflect those of Sidley Austin LLP, its partners, and its clients. This article has been prepared for informational purposes only and does not constitute legal advice.This information is not intended to create, and receipt of it does not constitute, a lawyer-client relationship. Readers should not act upon this without seeking advice from professional advisers.

Switzerland is about to roll out comprehensive new rules covering medical devices, aimed at providing greater clarity and harmonisation for the Swiss medtech industry. Some of these new rules are set out in the Ordinance on Clinical Trials with Medical Devices (**ClinO-MD**). Once adopted, the ClinO-MD will introduce many novel requirements regarding the conduct of clinical evaluations and investigations for medical devices in Switzerland. Many of the ClinO-MD's requirements mirror those set out in the Medical Devices Regulation (**MDR**). It is expected that the ClinO-MD will be adopted in its current draft format and become applicable simultaneously with the MDR, as of 26 May 2020.

The draft ClinO-MD is based on Chapter VI of the MDR. The text is largely in alignment with international standards for the conduct of clinical investigations with medical devices set out, inter alia, in ISO 14155:2011 and the Declaration of Helsinki. In the EU, the MDR leaves the Member States with a broad scope of discretion regarding the organisation of the assessment of clinical investigations and the applicable authorisation procedures.

Companies conducting clinical investigations with medical devices in Switzerland should be particularly aware of the following new requirements to become effective with the ClinO-MD, once adopted in its final form and applicable.

This article comments on changes that lie ahead relating to: clinical evaluations, in particular exceptions for equivalence; and to clinical investigations (focusing on: pre-market, post-market, monitoring, protecting personal data, and **Eudamed**).

Clinical evaluations

Today, a clinical evaluation of a device must be based on clinical data in relevant scientific literature and on any existing results of clinical investigations performed on the device. The new rules introduce the requirement for a clinical evaluation to consider also any "currently available alternative treatment option" (art. 44(2) of the draft Medical Devices Ordinance (**MedDO**), which states that art. 61 of the MDR is applicable in Switzerland). This requirement will place an additional burden on companies when evaluating the risks and benefits of their devices.

In particular, additional emphasis must now be placed on whether the clinical risks associated with a device being evaluated are comparable to other treatments for the disease in similar patient populations. Overall, the new requirements may appear burdensome at first. But once implemented, a well-executed clinical evaluation plan is likely to guide many companies through otherwise difficult conversations with their NB and competent authorities.

Exceptions for equivalence

Medtech companies have long used existing scientific literature and equivalent device statements in their clinical evaluation reports. This reuse of existing evidence can facilitate equivalence (as explained below), which saves the industry from conducting new and costly pre- or post-market clinical investigations to prove safety and performance.

Under the current rules, it is possible to claim equivalence from a given device with another similar device that another manufacturer has already placed on the market. However, that possibility has already been significantly reduced in the past few years with the EC's MEDDEV guidance on clinical evaluations as referred to MEDDEV 2.7/1 rev. 4, which, inter alia, introduced stricter expectations with respect to the demonstration of equivalence. Although the MEDDEV guidelines are not directly binding for devices placed on the Swiss market, they set the interim standard which should be respected by all manufacturers of devices in Switzerland until the new ClinO-MD is applicable.

The draft ClinO-MD is set to further diminish the chances of success for companies relying on data related to equivalent devices. Under the new rules, which further tighten the requirements set out in the MEDDEV guidance, a device for which equivalency is claimed must share the same technical, biological, and clinical characteristics. If, for example, a device, which is being compared to another device, has the same technical and clinical characteristics, but uses different materials or the materials are not intended for the same duration of contact with the skin, the devices will not be considered "equivalent".

The **EC** is meant to issue further guidance on the interpretation of "equivalence". This guidance will be indirectly applicable to the Swiss medtech industry as well.

Clinical investigations

PRE-MARKET: The draft ClinO-MD sets out new minimum requirements for pre-market clinical data with a reference to the MDR Annex XV, ch. II. The new requirements reflected in the ClinO-MD are much more detailed than the currently applicable guidelines set out in the EC's guidance to competent authorities for making a validation or assessment of a clinical investigation application MEDDEV 2.7/2, rev. 2.

POST-MARKET: The current standards require that the regulatory authorities be notified of pre-market clinical investigations. The new rules will require that manufacturers of medical devices also notify the competent authorities about the conduct of all post-market clinical investigations.

MONITORING: Another new requirement is that the sponsor of a clinical investigation must appoint a monitor to ensure that the investigation is conducted in compliance with the Clinical Investigation Plan, the principles of good clinical practice, and applicable law. The monitor must be independent from the investigational site draft new ClinO-MD art. 3, para. 1(b).

EUDAMED: Companies conducting clinical investigations in Switzerland will benefit from Eudamed (in addition to the data-processing systems set up in Switzerland), the new electronic registration of clinical investigations, which must still be set up by the EC. Eudamed will allow sponsors of clinical investigations conducted in more than one Member State of the European Economic Area or in Switzerland to submit applications for clinical investigations centrally. It will also feature a central location for vigilance reporting and submission of clinical investigation data.

Compliance with the new rules, which align Swiss legislation for medical devices to those of the EU, will benefit patients due to the higher standards that have to be met by Swiss manufacturers of medical devices, including the conduct of clinical investigations. Moreover, it is designed to ensure a continuing supply of devices to both the Swiss and EU markets. Medtech companies should familiarise themselves with the new requirements of the ClinO-MD to ensure a smooth transition to the ClinO-MD and to keep their products on the market.

PROTECTION OF PERSONAL DATA: One novel aspect of the new clinical investigation requirements is its strong focus on the protection of personal data. Companies should pay particular attention to the new data protection rules currently being introduced into the Swiss data protection legislation in order to align it with the EU General Data Protection Regulation EU 2016/679 (**GDPR**). (For a thorough overview of this topic, see the *RA Watch* Issue 1.)

The EC has issued several guidelines on the consent required by patients participating in clinical trials, for example, a **Q&A** on the interplay between the EU Clinical Trials Regulation EU 536/2014 (**CTR**) and the GDPR. In this Q&A, the EC has ruled that the current practice of obtaining the data subject's consent for the processing of their personal data is inappropriate in most circumstances, prompting companies to revise their informed consent forms and to indicate another legal basis for data processing. These considerations and guidelines are also relevant for companies conducting clinical investigations with medical devices.

VIEWS AND OPINIONS

STAKEHOLDERS' VIEWS ON THE SWISS DRAFT ORDINANCES ON MEDICAL DEVICES

To provide our readers with a good forecast of the changes ahead, the *RA Watch* editorial team asked different representatives – of the ethics committees umbrella organisation, the industry, and the SCTO network of CTUs – their views about the two ordinances proposed for consultation by the Federal Office of Public Health (**FOPH**). Their views and opinions refer to the drafted versions of the Medical Devices Ordinance (**MedDO**) and the ordinance on clinical trials for medical devices (**ClinO-MD**) as open to comments on 15 May 2019.

We asked the stakeholders to identify: **three crowning features** of the ordinances, **key modifications** they thought necessary, and **two central consequences** they would expect, as a result of the changing of the laws.

The SCTO and its network of CTUs commented only on the ClinO-MD.

Three crowning features

For your organisation, what do you believe will be the three most positive features of the draft ordinances currently underway?

swissethics

- The two new ordinances will be essential to keeping the equivalence with the EU Regulation.
- As for ClinO-MD, we believe it makes sense that not only the safety of medical devices be assessed, but that also their efficacy be systematically proven (as is the practice for investigational medicinal products), including in the post-market phase.
- The shift to full electronic systems will be warmly welcomed.

Swiss Medtech

- For both MedDO and ClinO-MD: Fortunately, both ordinances already contain many references to articles of the Medical Devices Regulation (**MDR**). These points provide the best guarantee of implementation equivalency with the EU.
- ClinO-MD: This ordinance has been designed specifically for the clinical trials of medical devices. It will thus enable Switzerland to fully harmonise its handling of clinical trials with EU laws – from the first application request, right through to the completion of a trial.
- ClinO-MD: This version released for consultation already provides Switzerland with the possibility of participating in coordinated assessment procedures for clinical investigations – one submission of an application of a clinical investigation to be conducted in more than one EU Member State. As a result, the Swiss competent authority is already able to establish the corresponding procedures – in good time, without needing so much time as to depend on the deadline of May 2027.

SCTO network of CTUs

- ClinO-MD: The future harmonisation with the EU is welcome. More rigorous clinical evaluations and investigations will be of benefit to the quality of medical devices and to patients' safety. Furthermore, harmonised rules will make it easier to run multicentre clinical studies, having sites in both the EU and Switzerland.
- ClinO-MD: We are in favour of the increased transparency guaranteed by the traceability of individual devices and the publication of information regarding clinical trials and their results.
- ClinO-MD: Having an ordinance specifically for clinical trials for medical devices will make it easier to identify and understand the given requirements.

Possible modifications

Can you mention three points of these ordinances that you believe should be modified?

swissethics

- swissethics and Swissmedic are working closely together to guarantee that the interfaces connecting Eudamed with the Swissmedic portal and with the Business Administration System for Ethics Committees (**BASEC**, the online platform for submitting research projects to Swiss ethics committees) will be ready on time and function smoothly.
- The cantons and the ethics committees will face additional costs. These are the current costs of building the interfaces, future costs for their maintenance, and those for the maintenance of the Swiss electronic portals. How these costs will be divided and borne needs to be addressed.

Swiss Medtech

- MedDO and ClinO-MD: Both ordinances should function, even without an MRA. If the MRA is not updated before the Swiss ordinances enter into force, individual passages of the regulations will:

  A be partially non applicable, e.g. ClinO-MD: category C1 or C2 clinical trials for CE marking purpose (conformity-related trials) may not be carried out in a legally binding manner,

  B contradict the MDR, e.g. the MedDO: the obligation to register a Swiss importer in Eudamed is not in line with the registration of the EU importer, as defined in the MDR, or

  C affect the current safety standards, e.g. MedDO: the obligation to report incidents and field safety corrective actions is now only applicable for Switzerland. As a consequence, Swiss manufacturers are no longer required to inform the Swiss competent authority about field safety corrective actions that are implemented in the EU.

- MedDO and ClinO-MD: The terminology in both ordinances must be fully aligned with the MDR. A respectable adaptation has already been carried out, but some terms still vary. For example, the differing usages of "supply" (termed "Abgabe" in the German version), appearing in the definition of "making available on the market", could lead to considerable uncertainty in Switzerland.
- ClinO-MD: Deadlines and trial procedures should be 100% aligned with **MDR**. Regarding deadlines, it would be sensible to align all the national options for deadline extensions with the EU regulation. Full compliance with the EU regulation should be the goal, with regard to trial procedures, too. For example, individualised time slot extensions to authorise "first-in-human trials" appears to be a national matter.

SCTO network of CTUs

- ClinO-MD: Several aspects bringing a worrisome complexity should be rethought: the proposed categorisation system which take into account both the current categorisation defined by the ClinO (A and C categories) and the **MDR**; the multiple data processing systems (BASEC, the Swissmedic system, and Eudamed); the multiple and short deadlines.
- ClinO-MD: The readability of the text should be greatly improved by incorporating important references (such as the ISO 14155:2011 standard or the applicable provisions) in the text itself.
- ClinO-MD: Before this new ordinance comes into force, the competent authorities will need to make available to researchers appropriate, easy-to-use, and interoperably robust processes, with good explanatory and supporting documents to ensure the transition is as smooth as possible.

Expected consequences

What are the two most likely consequences of the changing laws for your organisation?

swissethics

- The ethics committees will be required to carry out a more comprehensive review of the applications than they have done to date with the current legislation.
- The challenges are the new categorisation, which is not easy to convey in a simple and concise way, and to ensure that the members and the scientific secretariats of the ethics committees have the necessary expertise to handle these complex applications.

Swiss Medtech

- As an association, we share our findings together with other associations to receive remarkable support in extending the existing consultation drafts – to ensure their functionality, even without the MRA.
- As far as manufacturers are concerned, we inform them that the EU acceptance of conformity-related trials is uncertain at the moment – when applications are submitted to the Swiss competent authority.

SCTO network of CTUs

- ClinO-MD: Possibly the number of clinical trials to perform with medical devices in our CTUs will increase. More certain to increase will be their complexity and the associated administrative tasks with constraints in term of costs and resources. We must prevent the discouraging of investigator-initiated trials and of scientific innovation in Switzerland, more broadly.
- The SCTO, through its CTUs, will support academic researchers as they endeavour to apply this new ordinance to their work. We will consider providing training, regulatory guidance, and services for the running of clinical trials with medical devices.

PATIENT-TO-PATIENT: TALKING ABOUT MEDICAL DEVICES

How will the regulatory changes taking place for medical devices affect patients – those who carry the true risks or benefits of having them in or on their bodies?

For a down-to-earth patient perspective, European Patients' Academy (**EUPATI**) fellow Estelle Jobson met with Karen Topaz Druckman, President of the Swiss patient association (**HHT Swiss**) to ask her some questions. Karen's views represent years in patient advocacy including patient input.

Medical devices are so frequently associated with scandals and stories of patients who have suffered bad or even fatal experiences. How do you think the future harmonisation between Switzerland and the EU of the regulation of medical devices might affect safety?

I think that this harmonisation is likely to lead to more rigorous trials and investigations. This in turn should improve the safety of devices. Specifically, collecting and sharing complaints, feedback, and adverse events centrally (including long after a device has reached the market), will allow alerts about safety risks to be communicated swiftly all across Europe. When reporting is *ad hoc* and/or local, it can take a long time before any one community realises that an incident in that community is not isolated, but has also occurred elsewhere. Devices that appear harmful or dangerous must be pulled off the market everywhere, as quickly as possible, to spare patients unnecessary harm or even death.

The new European electronic registration system of clinical investigations with medical devices **Eudamed**, to be set up by the Commission, will facilitate centralisation. Perhaps even more important is the new requirement that failures, as well as successes, of trials be reported. Access to full information will help prevent unnecessary duplication of clinical trials, could save unnecessary costs, and give researchers the opportunity to build on actual trial results in the development and design of future trials. Such transparency also gives all stakeholders a chance to better evaluate the importance of any given study.

So safety and transparency are likely to improve. But is there a potential downside to the situation?

Some people believe there is risk that more stringent regulation (and the resulting costs) may cause some devices – particularly those produced by small to medium-sized companies – to be removed from the market resulting in patients losing access to these devices. I would hope that the expansion of the market for any such device would offset that risk.

Can you give an example of a medical device that your patient community would like greater access to?

Yes, an excellent example exists in my patient community (people affected by Hereditary Hemorrhagic Telangiectasia (**HHT**), also known as Osler-Weber-Rendu Syndrome): nasal packing.

HHT is an inherited disease that leads to malformations of the vascular system in multiple organs of the body; it typically begins with nosebleeds. When people with HHT suffer debilitating nosebleeds, they are forced to go to hospital emergency services simply to stop the bleeding. It can be stopped by using a medical device: bioresorbable nasal packing that can be inserted into the nasal cavities to apply pressure to stop the bleeding, as well as to help prevent adhesions between mucosal surfaces, and promote healing. The packing dissolves and clears away naturally thereby eliminating the need for painful removal, which can trigger bleeding again.

It is a life-changing event for HHT patients to be able to manage their disease themselves by learning to insert the nasal packing rather than having to be rushed to an emergency medical facility. Having easy access to this medical device can spare them traumatic, time-consuming hospital visits, and associated costs. In Switzerland, however, HHT patients are not currently allowed direct access to this device. It is only available to medical professionals.

In Germany, however, HHT patients are able to access this medical device themselves. It is now even approved (thus reimbursed) by the health system. We hope that mutual recognition between Switzerland and the EU will ultimately get more devices into patients' hands, so they can manage their conditions as independently (and economically) as possible.

Do you have any thoughts on how the changes underway may affect the research and development of medical devices?

Yes, R&D is crucial to rare disease patients. These changes should allow Swiss medtech companies inventing and developing these devices to help more patients, and access to the EU market will hopefully provide a better economic incentive. Harmonisation of rules between the EU and Switzerland regarding the clinical investigations of medical devices will facilitate cross-border clinical trials, on larger numbers of participants than would be available nationally.

And finally, what other patient needs or constraints related to medical devices do you think are particular to Switzerland?

In Switzerland, patients are subject to the conditions of their medical insurance, which varies considerably from one policy to another. Availability of additional medical devices is a good thing, but for these devices to be accessible to patients they must be affordable and, therefore, at least partly reimbursable. The next step for Switzerland will be to insure reimbursement under basic health insurance for the new devices.

We sincerely hope that greater harmonisation for devices will promote equal access, for all patients Europe-wide. If the regulations and controls are the same, once one country (such as Germany, in the example above) authorises a device, other countries can rely on that country's analysis and follow suit and authorise it. This could represent a sea-change for patients – as well as for industry. Will HHT patients here be able to access, use, and be reimbursed for the nasal packing, for example?

We hope government and insurance companies are listening attentively to patient requests and will be facilitating our access to the tools we need to live as well as possible, with our conditions.

CASE STUDY

WHAT ABOUT SOFTWARE USED IN HUMAN RESEARCH?

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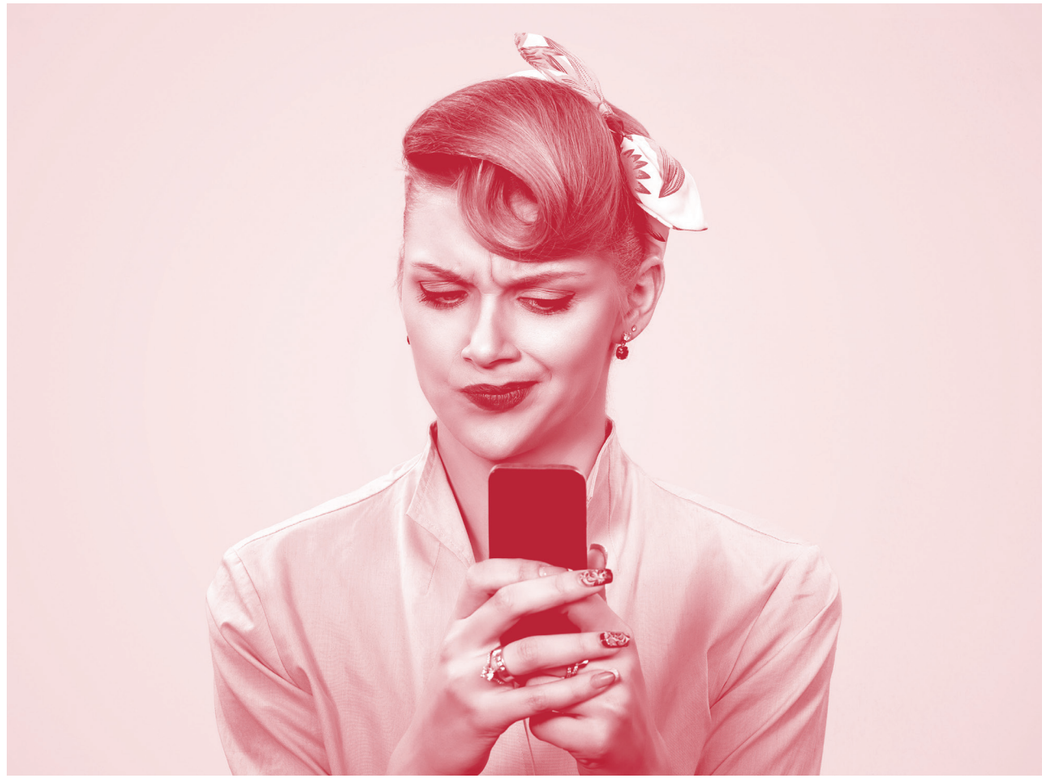
Face-to-face: investigator meets regulatory affairs specialist

Let's imagine a typical consultation at a CTU. An investigator is planning a trial using an App. So, they meet with a regulatory affairs specialist from the CTU who is helping the investigator to think through, prepare, and organise the necessary paperwork.

These are some of the questions that come up in such an interaction and some of the contextualising information.



CTU "So, you're planning to use an App in your trial?"

INVESTIGATOR "Yes, we are. Patients love typing on their phones and it is much easier for us to collect the necessary data, such as the patient's heart rate, digitally rather than in the traditional way. We have developed this App to give each patient the option of monitoring their own heart rate, independently."

CTU "What exactly does the App do with the patient data? Does it collect and transmit the data, primarily?"

INVESTIGATOR "Yes, but it does even more than that. After the data is collected, it is analysed by the software of the App. If the software detects that the patient's heart rate is out of the normal range, the patient will receive a message that they should see their family doctor. Finally, the recorded data is transmitted directly to the study site, where the trial is taking place."

CTU "You know, in this case, your App falls under the definition of a medical device."

Defining and framing medical devices in the EU

Next, in this kind of conversation, the regulatory affairs specialist often needs to explain that a medical device is not necessarily something "physical", like a hip prosthesis. A medical device can also be intangible, like an algorithm installed on a mobile phone.

The regulatory affairs specialist also explains the new regulatory context in the EU for medical devices, the Medical Devices Regulation (**MDR**), and the consecutive necessary adaptations of the legal texts in Switzerland: the drafted Medical Devices Ordinance (**MedDO**) and the Ordinance on Clinical Trials with Medical Devices (**ClinO-MD**) that should enter into force in May 2020 (see the **DEEP DIVE**). In the next part of this article, you will read about future scenarios facing medical devices in this new regulatory context.

Whether the software or App is defined as a medical device will depend on its intended use. For example, if the tool is programmed to monitor the heart rate of a person who is exercising in preparation for a marathon, but without any medical recommendation, then it does not count as a medical device. However, if the App analyses the heart rate and then gives feedback to the user (such as notification that one of their values is out of normal range, that the person should stop exercising and see their doctor to prevent their health from deteriorating), then the App carries a **medical purpose** MDR, art. 2.

If the App falls under the definition of a medical device, it should firstly be verified and validated, and, as a second step, be **clinically evaluated**. If this clinical evaluation then finds the device does not meet essential requirements relating to its safety and performance, the App should be tested in **clinical investigations** in order to prove these requirements.

CTU "Thus, if your App is able to modify participants' medical care and potentially impact their health status and not only capture and transmit data, then, you'll have to go through the medical device regulatory process..."

INVESTIGATOR "And how should we handle the paperwork?"

Defining the classification of expected risk and preparing for clinical investigation

Above all, you need to be clear about the definition of a "clinical investigation", as highlighted in the new ClinO-MD art. 2, para. 1(a) and defined in the MDR art. 2(45): "Clinical investigation means any systematic investigation involving one or more human subjects, undertaken to assess the safety or performance of a device."

Moreover, the investigator (and the sponsor) must perform the trial and provide relevant documentation in accordance with the MDR as detailed in Annex XV chs. 1–3, cross-referenced in ClinO-MD art. 4 and Annex I.

A risk–benefit analysis must be performed and precautions must be taken to address the identified risks MDR Annex XV, ch. 2, no. 2.5. In our example above of the App, the regulatory affairs specialist may raise the following questions, among others:

- Does the App run reliably on all possible devices available to study participants, i.e. on all operating systems?
- How is the support of the software regulated (e.g. after an update of the operating system)?
- What happens if the App does not have an Internet connection?
- Can the App be operated easily or does it require special training?

INVESTIGATOR "What happens when we have validated our App and it fulfils the criteria you just mentioned?"

CTU "You will need to then establish the specific risk classification of your App, which is made by considering the extent of the expected risk. Let me explain that to you in more detail."

The classification of the expected risk must be made MEDDEV 2.4/1 and MDR, Annex VIII and the new rule 11 MDR, Annex VIII, ch. 3, para. 6.3 is explained as following:

- Software intended to provide information which is used to take decisions with diagnosis or therapeutic purposes is classified as class IIa, except if such decisions have an impact that may cause:
  - » death or an irreversible deterioration of a person's state of health, in which case it is in class III; or
  - » a serious deterioration of a person's state of health or a surgical intervention, in which case it is classified as class IIb.
- Software intended to monitor physiological processes is classified as class IIa, except if it is intended for monitoring of vital physiological parameters, where the nature of variations of those parameters is such that it could result in immediate danger to the patient, in which case it is classified as class IIb.

All other software is classified as class I.

INVESTIGATOR "But why do I need this classification?"

According to the risk classification the App falls into, you'll need to take appropriate measures to mitigate the risks. You will need to include that information in the dossier that must be sent to Swissmedic and the responsible ethics committee, to apply for the authorisation required to conduct the clinical trial.

The area of review of the ethics committee is the same as the one referred in the ClinO art. 25.
Swissmedic reviews the aspects listed in the TPA:

- The risks associated with the devices are taken into account in clinical trials and whether the information provided on the devices is in line with scientific progress TPA, art. 54, para. 4, let. b.
- When used as intended, a medical device should not endanger the health of users, consumers, patients, or third parties TPA, art. 45, para. 1.

After approval, the investigator must perform their trial in accordance with the MDR Annex XV, chs. 1 and 3 (also in line with the international standard ISO 14155:2011 on good clinical practices for clinical investigations of medical devices for human subjects), which is directly cross-referenced in ClinO-MD art. 4.

Conclusion

- An App can be classified as a medical device if it does more than simply capture and transmit data.
- The development and use of clinical Apps is regulated by EU and Swiss laws.
- Considerable efforts must be made by the investigator, since the required documents represent an intense amount of work.

INVESTIGATOR "Ok, thank you. That sounds like a lot of work. I may consider using the App for data collection and transmission only, after all."

HEADLINES AND HAPPENINGS

IN SWITZERLAND

SCTO updates

• **JUNE 2019** 9th Symposium on "**Emerging methodologies and measures in clinical research**".

• **JULY 2019** **What's in a name? From "subject" to "participant"**. In The Advisor, special supplement to Issue 445, Estelle Jobson, from the SCTO and EUPATI CH, presents her thoughts on how the term "subject" became the most accepted term for individuals taking part in clinical trials and asks whether it is still appropriate. To contribute to the debate, send comments to info@brookwoodacademy.org, with the subject header "Participant debate".

source SCTO

swissethics

• **MAY 2019** Publication of an **Updated Guidance for providers of courses on Research Ethics and GCP**. Since 2014, GCP course providers can have their GCP courses for investigators and sponsor-investigators recognised by swissethics. Now swissethics has updated its guidance to include GCP refresher courses. The participation of investigators to refresher courses is generally voluntary, but the ethics committees retain the right to request the participation of an investigator in this course.

• **MAY 2019** Publication of a new document regarding the **professional qualifications of the investigators and project leaders of research projects** EN. swissethics specifies that the ethics committees will always make a decision on a case-by-case basis.

• **JUNE 2019** Publication of a new version (v3.5) of the **Template for study protocols for clinical trials** EN.

source swissethics

Swissmedic

• **AUGUST 2019** The agency announced news regarding its **eGov services**: Delegated user administration and new self-registration via CH-Login from 9 September 2019. Existing user accounts (including authorisations) will be automatically transferred to the new electronic environment.

Clinical trials of medicinal products

• **APRIL TO MAY 2019** Publications of updated documents:

- » **"FAQs on clinical trials with medicinal products"** EN
- » **"VO-Form: Submission of Changes to a Clinical Trial and Answer to Conditions"** EN
- » **"VO-Form: Reporting Related to a Clinical Trial"** EN
- » **"Checklist for applicants: Documents to be submitted to Swissmedic for clinical trials with transplant products, clinical trials involving somatic gene therapy or clinical trials with therapeutic products containing genetically modified organisms"** EN.

• **JULY 2019** Publication of recommendations for the submission of **Complex Clinical Trials** (e.g. Umbrella, Basket and Platform designs). There are differences between complex clinical trials and conventional clinical trials, particularly with regards to clinical trial applications and requests for substantial amendments. Swissmedic relies on the recommendation paper of the Clinical Trials Facilitation and Coordination Group Recommendation Paper on the Initiation and Conduct of Complex Clinical Trials published in February 2019.

Clinical trials of medical devices

• **APRIL TO JUNE 2019** Publication of updated forms:

- » "FO Clinical Trials with medical devices: application for authorisation" EN
- » "FO Clinical trials of research sequences on CE-marked MRI system" EN
- » "FO Clinical Trials with medical devices: submission for approved trial" EN
- » "FO Clinical trials with medical devices: serious adverse events and deficiencies in Switzerland" EN

• **JULY 2019** **Publication of a series of documents coming from the EU**:

- » MEDDEV 2.12/1 rev. 8 «Guidelines on a medical devices vigilance system»
- » Factsheet for **healthcare professionals and health institutions** based on the **MDR** and the **IVDR**
- » EC/MDCG Factsheets for **manufacturers**
- » Medical devices **nomenclature**

source Swissmedic

• **AUGUST 2019** Publication of a Q&A EN on the **Single Registration Number (SRN)**. Swiss manufacturers, European authorised representatives and importers will need to register in Eudamed. Once the registration has been validated by Swissmedic, Eudamed will assign an SRN to the economic operator.

Federal Office of Public Health (FOPH)

• **FIRST HALF 2019** Publication of several documents concerning departmental research projects on the HRA. The findings of these projects form the basis of the evaluation of the law.

• Statistics and survey on the implementation of the Swiss HRA

- » Costs of randomised clinical trials in Switzerland before and after enactment of the legislation on human research
- » Linguistic analysis of "**comprehensibility**" in research involving humans.

source FOPH

Swiss National Science Foundation (SNSF)

• **MAY 2019** Research funded by the public should be, as far as possible, publicly accessible and free of charge. SNSF, which is committed to the global project of Open science, published two noteworthy documents:

- » One article explaining the results of a large-scale survey showing that 75% of researchers are making their data accessible.
- » The second is the Swiss Biotech Report 2019 encouraging researchers to better support the evolving biotech sector.

source SNSF

eHealth Suisse

• **JULY 2019** The Electronic Patient Record: a revised ordinance published by the Federal Department of Home Affairs entered into effect mid-July DE FR.

Swiss Academy of Medical Sciences (SAMS)

• **FEBRUARY 2019** Publication of **"Translating academic discovery to patients' benefit: is academia ready to assume its key role?"** EN.

• **JUNE 2019** **"Are clinical trials too bureaucratic? Do the rules of Swissmedic and cantonal ethics committees hinder university clinical research?"**, an interesting debate published in *Horizons* magazine (pp. 8–9) DE FR.

• **JULY 2019** Publication of **"Open Science to foster scientific progress and to benefit society"**, a new Swiss Academies Factsheet containing recommendations to shape open access and open data, so that they foster scientific progress and benefit society in Switzerland EN.

• **SEPTEMBER 2019** Publication of **"Medical progress: Why is the translation of biological discoveries into new therapies so slow?"**. The articles explain the reasons for the well-known "valley of death" of research programmes DE FR.

Swiss Biobanking Platform (SBP)

• **MAY 2019** Publication of two key documents for researchers: SBP and Swiss Personalized Health Network have worked in close collaboration to deliver **Material Transfer Agreement** and **Data Transfer and Use Agreement** templates to facilitate material and data exchange in the context of academic research projects.

• **AUGUST 2019** Publication of an updated version of the **"Ethical, legal and professional compliance list for human research biobanks applicable in Switzerland"** EN.

source SBP News

HEADLINES AND HAPPENINGS ABROAD

IN EUROPE

European Medicines Agency (EMA)

• The agency has released draft guidelines for consultation purposes:
  - » **"ICH guideline E19 on optimisation of safety data collection"** EN. This document proposes harmonised guidance on when it would be appropriate to use a targeted approach to safety data collection in some late-stage pre-marketing or post-marketing studies. Deadline for comments was 29 September 2019.
  - » **"ICH guideline E8 (R1) on general considerations for clinical studies"** EN. ICH is proposing a modernisation of ICH E8 in order to incorporate the most current concepts achieving fit-for-purpose data quality as one of the essential considerations for all clinical trials. Deadline for comments was 30 September 2019.
  - » **"Quality requirements for drug-device combinations"** EN. Consultation ran until 31 August 2019. The EMA will finalise the guideline before the MDR comes into force in May 2020.

• **APRIL 2019** Senior executives of the EMA published a paper on "The role of regulators in establishing added benefit of novel therapies". The most fundamental proposals are to only authorise new medicines that have demonstrated added therapeutic benefit and to include the mandatory comparison of new therapies with the best available treatment at the time of authorisation. The paper is available through open access in Nature Reviews Drug Discovery.

• **JUNE 2019** Legal effective date for the "Guideline on the Content, Management and Archiving of the Clinical Trial Master File (paper and/or electronic)" EN.

source EMA

European Commission (EC)

• **MARCH 2019** Publication of a new **"Guidance on subgroups in confirmatory clinical trials"** EN. This guidance, which entered into force in August 2019, recognises the importance of subgroup analyses to explore the variability of treatment response between different subgroups of patients.

• **APRIL 2019** Publication of a Q&A on the **interplay between the CTR and the GDPR** EN.

• **JUNE 2019** Several publications:
  - » Draft standardisation request EN as regards the MDR and IVDR. This draft had a deadline for feedback on 25 July, and for each of the regulations, the EC presents two lists of existing standards needing revisions and two lists for the development of new standards.
  - » **Fact sheet** EN outlining the **impact that the MDR and the IVDR can have on healthcare professionals and health institutions** including new obligations and potential consequences in term of devices availability
  - » A **Q&A on the CTR** - Version 2 EN
  - » An update to the notification form EN for the declaration of the end of the clinical trial
  - » Updated list of fields contained in the "EudraCT" clinical trials database EN.

• **JULY 2019** The EC, EMA, and the Heads of Medicines Agencies have co-signed a letter reminding all sponsors of clinical trials conducted in the EU of **their obligation to make summaries of results of concluded trials publicly available in EudraCT** EN.

Medicines and Healthcare products Regulatory Agency (MHRA), UK

• MHRA revised the **Clinical Investigation Guidance** EN in line with the MDR. The first set of revisions points to the legislative provisions relating to biological safety evaluation under Annex XV of the MDR and introduces the need for ensuring that the "anticipated benefits to the patients enrolled in the clinical trial justify the foreseeable risks," in accordance with of MDR art. 62, and submitting sufficient data for review to "provide assurance that all necessary toxicological risks have been appropriately considered." Date of application: May 2020.

National Agency for the Safety of Medicines and Health Products (Agence Nationale de Sécurité du Médicament et des produits de santé, ANSM), France

• **SEPTEMBER 2019**, the ANSM launched **a pilot on clinical investigations** under the MDR. ANSM notes that MDR provisions relating to clinical investigations will result in new workflows among EU competent authorities and Member States' ethics committees. The first-of-its-kind pilot will allow for the simulation of new working methods per MDR's provisions "particularly with regard to the deadlines for the assessment of files and the organization of coordination." Participation is voluntary.
source RAPS Regulatory FocusTM

HEADLINES AND HAPPENINGS ABROAD

IN USA

US FDA

• **MARCH 2019** Final guidance document on **"Enrichment Strategies for Clinical Trials to Support Determination of Effectiveness of Human Drugs and Biological Products"** EN.

• **MARCH 2019** Publication of four draft guidance documents on **cancer clinical trial eligibility criteria** and one final guidance on including adolescents in adult oncology trials.

The four drafts, developed by the FDA with input from the American Society of Clinical Oncology and Friends of Cancer Research, focus on minimum age for pediatric patients, patients with HIV, hepatitis B or C viruses, patients with organ dysfunction or prior or current malignancies, and patients with brain metastases. source: Outsourcing-pharma.com

• **APRIL 2019** Draft guidance document on **"Adjusting for Covariates in Randomized Clinical Trials for Drugs and Biologics with Continuous Outcomes"** EN. This guidance provides recommendations for adjusting for covariates in randomised clinical trials with continuous endpoints that are appropriate for analysis with normal-theory methods, such as the two-sample t-test. Nonparametric methods, categorical outcomes, and survival methods, among others, are outside the scope of this document, although some of the same principles might apply to those methods as well.

• **JUNE 2019** Draft guidance document on **"Enhancing the Diversity of Clinical Trial Populations – Eligibility Criteria, Enrollment Practices, and Trial Designs Guidance for Industry"** EN. The purpose of this document is to encourage a broadening of eligibility criteria to allow more people to participate in clinical trials of drugs and biological products. The trials results should better represent those expected in the patient population.

• **JULY 2019** The delegation of the US raised "serious concerns" with several issues regarding the MDR and IVDR and called on the EU to delay their implementation by three years. In a statement to the World Trade Organization's Committee on Technical Barriers to Trade, the US said: "Our industry is worried about their continued access to the EU's USD 125 billion medical device market, USD 20 billion of which is supplied by US products."

The statement highlights two issues that specifically concern the implementation of the EU's new regulatory system: the ongoing lack of NBs and implementing acts to help ensure compliance with new product standards.
source: RAPS August Regulatory FocusTM

EVENTS AND PUBLICATIONS

Events

8-9 OCTOBER 2019

RAPS European workshops: on the MDR and on IVDR.
AMSTERDAM

10 OCTOBER 2019

RAPS European workshops: on Software as a medical device.
AMSTERDAM

5 NOVEMBER 2019

MEGRA StartUp DRA 2019-CH - Modul 10: Medical Devices und Abgrenzungsfragen
BRUGG

11–13 MAY 2020

RAPS Regulatory Conference Europe
BRUSSELS

Books and publications

- "Biobanques – Vers une harmonisation et un cadre règlementaire institutionnel" CRC info (Geneva), Bulletin n° 41 - June 2019 FR
- The Meddev Solutions Guidebook on the MDR, accompanied by a training course EN

ACRONYMS

BASEC: Business Administration System for Ethics Committees
CE: Conformité Européenne
ClinO: Ordinance on Clinical Trials
ClinO-MD: Ordinance on Clinical Trials with Medical Devices
CTR: Clinical Trials Regulation (EU) 536/2014
CTU: Clinical Trial Unit
EC: European Commission
EU: European Union
Eudamed: European Database on Medical Devices
EUPATI: European Patients' Academy
FOPH: Federal Office of Public Health
GDPR: General Data Protection Regulation (EU) 2016/679
HHT: Hereditary Hemorrhagic Telangiectasia
HRA: Human Research Act
HRO: Human Research Ordinance
IFU: Instructions For Use
ISO: International Organization for Standardization
IVDR: in vitro Diagnostic Medical Devices Regulation (EU) 2017/746
MDR: Medical Devices Regulation (EU) 2017/745
MEDDEV: guidelines on medical devices
MedDO: Medical Devices Ordinance
MRA: Mutual Recognition Agreement
NB: Notified Body
SCTO: Swiss Clinical Trial Organisation
SRN: Single Registration Number
TPA: Therapeutic Products Act

REGULATORY AFFAIRS WATCH

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Sources of information

- We gather news on regulatory topics linked to human research.
- We regularly read newsletters and visit the websites of relevant sources, including: the regulatory authorities in Switzerland, Europe, and USA; ICH and WHO; the major Swiss academic organisations and health associations; and professional associations.
- Additionally, we review major clinical research journals.

More on the Regulatory Affairs Platform

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