Lessons learnt from the COVID-19 crisis: Regulatory aspects linked to human research and product authorisation

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The governmental measures instigated in connection with the COVID-19 pandemic have presented new challenges concerning the approval and conduct of clinical trials with medicinal products in Switzerland and the implementation of good clinical practice (GCP) and good pharmacovigilance practices (GVP) inspections. This article discusses various regulatory aspects of study approval, conduct, and inspections that have been affected by the pandemic and summarises lessons learnt in these areas.

Study applications and approval

Immediately after the Federal Council intensified measures to protect the public in March 2020 and declared that an “extraordinary situation” existed in Switzerland, Swissmedic offered sponsors the opportunity, as of 18 March, to submit study documents electronically in advance and then deliver the required paper documentation at a later date. In view of the need to extend the options to work from home for many of those involved, this step has created a framework not only for the submission of new studies, variation applications, and safety reports but also for the evaluation and approval of submitted applications during the pandemic situation.

Since the start of the pandemic, much focus has been placed on the evaluation and approval of trials to investigate the treatment of COVID-19 patients. These randomised trials – around 70% of the applications submitted in 2020 were investigator-initiated trials (IITs) – are processed by Swissmedic as a priority. In cases where applications are incomplete, Swissmedic specialists (clinical study reviewers) coordinate closely with the sponsors so that all the necessary documentation can be made available for prompt evaluation. As a result of these measures, it has been possible to approve most of the COVID-19 drug studies within a few days while maintaining compliance with quality requirements.

On the one hand, the approval process for clinical trials, the adaptations to established procedures required by the pandemic, and the review of subsequently submitted paper dossiers have posed a major challenge and increased the workload. On the other hand, this situation has created new options, such as electronic

advance submission, which sponsors have utilised in over 80% of all study applications. These adaptations and this flexibility have not only enabled people to work under pandemic conditions (i.e. from home), but they have also significantly accelerated procedures such as the prioritised approval of COVID-19 studies.

Study conduct

The measures to protect the public introduced in connection with the pandemic also affect the implementation of approved clinical trials. They affect trial participants, treating investigators, and study teams in hospitals and practices as well as the sponsors' responsibilities, for example in relation to monitoring.

The various interfaces involved in conducting studies were first addressed at the end of March 2020 in a joint publication produced by Swissmedic and swissethics entitled Joint Guidance of Swissmedic and swissethics on the Management of Clinical Trials with Medicinal Drug Products in Switzerland during the COVID-19 Pandemic. This guidance document describes the key recommendations concerning the conduct of clinical trials during the pandemic. These recommendations have since been adapted and extended several times (see the current version 2.4 dated 17 December 2020) and focus on how certain study-specific aspects (including the conduct of study visits, the delivery of investigational medicinal drug products (IMPs) directly to patients, the informed consent procedure, and monitoring) can be adapted on the basis of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use Guideline for Good Clinical Practice (ICH GCP) so that a study can be continued during the pandemic. Incidentally, these adaptations to the conduct of clinical trials, which are necessitated in part by the pandemic but which also have to comply with ICH GCP, are being identified not just in Switzerland but also by the European Medicines Agency (EMA) and other authorities.

Inspections

The pandemic situation has also raised the question as to whether inspections of clinical trials (GCP) and pharmacovigilance systems (GVP) can be carried out and, if so, under what conditions. While so-called "for-cause" inspections, based on the suspicion of an acute risk potential for patients, have continued, regular inspections of clinical trials in hospitals were suspended at the end of March 2020 to avoid imposing an additional burden on the responsible investigators and study teams.

Swissmedic has used the situation created by the pandemic to develop models that can be used to enable inspections of sponsors and marketing authorisation holders to be carried out remotely by video conferencing. Since July 2020, eight such remote inspections have been conducted, during which defined aspects relating to the management of clinical trials and the effectiveness of pharmacovigilance systems were reviewed. Moreover, for the first time since the start of the pandemic, a GCP inspection of a sponsor was carried out in October 2020 that was subject to a previously agreed safety and protection concept.

The initial experience with remote inspections has shown that the coordination workload involved before and during a remote inspection is relatively high. But this experience has also shown that remote inspections of sponsors and marketing authorisation holders offer a possible approach for effectively checking specific aspects. Therefore, remote inspections will continue to be used in future as a possible inspection model.

Summary of lessons learnt during the pandemic

Looking back on the experience acquired in 2020, it can be concluded that the COVID-19 pandemic has posed formidable challenges for all stakeholders regarding the approval, implementation, and inspection of clinical trials. Experience has also shown that the implemented measures are effective in maintaining the

quality of studies and guaranteeing the safety of participants even during the pandemic. Last but not least, this situation offers a great opportunity to build on the experience acquired from the implementation of clinical trials during the pandemic and to review how this can be exploited for the period after the pandemic. This will help to ensure that innovative clinical trials can continue to be carried out safely in Switzerland.