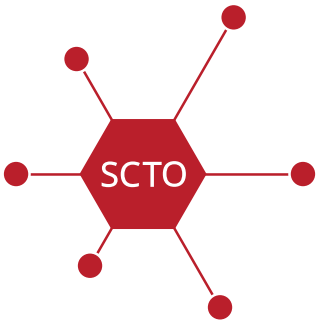
REGULATORY
AFFAIRS
PLATFORM



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

REGULATORY AFFAIRS WATCH

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EDITORIAL

11 MARCH 2021 – ONE YEAR OF COVID-19: REFLECTING ON LESSONS LEARNT SO FAR AS WE MOVE TOWARDS THE LIGHT AT THE END OF THE TUNNEL

In our last issue of *RA Watch* (published in October 2020), we flagged that the time will soon come to share the lessons related to the regulatory aspects of human research learnt from the COVID-19 pandemic. How optimistic! We did not imagine the pandemic would last so long … We are still in the tunnel, barely able to see the light at end of the second wave of the pandemic, tired, and worried that a third wave caused by new coronavirus variants could hit.

Yet one year after the pandemic was officially declared by the World Health Organization (on 11 March 2020), we have some good reasons for hope. The first vaccines have proven their high level of efficacy. Three vaccines are now approved for the Swiss market and are progressively being administered, starting with at-risk populations. In addition, 347 clinical trials and research projects on COVID-19 have been approved in Switzerland since the beginning of the pandemic (source: swissethics, updated on 4 March 2021) and most of them are still recruiting patients now. These glimmers of light have appeared thanks to the unprecedented collective efforts of the pharmaceutical industry, clinical researchers, regulatory authorities, politics, and – let's not forget – health professionals and the public.

So far, repurposed drugs have not been as successful as we had first hoped – except steroid dexamethasone and tocilizumab – and we will need to wait for effective, innovative treatments. Clinical research and authorisation processes for vaccines and treatments have never before been scrutinised so much by the medical community and the general population. Step-by-step scientific progress has never been the subject of so many public commentaries and controversies (e.g. chloroquine and hydroxychloroquine) – sometimes as the result of hope or fears of the unknown, "on air" reporting of the fragmented production of knowledge, scientific debate, and also fake news and unfounded plots that trigger a lot of scepticism. Despite all the debates and because a global pandemic calls for a global response, regulatory organisations have intensified their international cooperation: calls for larger studies, increased transparency, data sharing, common guidelines for vaccines, treatments, diagnostic device development, and new options for regulatory flexibility (e.g. early scientific advice, rolling submission, and fast-track authorisation). However, different approaches to hygiene measures, therapeutic options developments, and authorisations persist across regions (e.g. China, Russia, and Western countries).

In this *RA Watch* issue, we address various questions about the pandemic in the Swiss context:

How did we, the CTU network, support the clinical research effort and experience the regulatory aspects of this marathon?

How did our stakeholders respond to the pandemic: the Swiss National Science Foundation as a major source of funding for research and Swissmedic as the authority responsible for clinical trials with medicinal products approval, the adherence to good clinical practices, and inspections?

What kind of adapted support did swissethics and ethics committees provide to clinical researchers during the first phase of the pandemic, and how did they safeguard patients' rights in such a crisis context?

Will adapted operative innovations be opportunities to carry on in the post-COVID-19 future?

How has the "covidisation" of research affected patients?

In addition, we present two international initiatives in which our CTU network is involved. One initiative with Swiss participation is the World Health Organization's Solidarity trial, which is one of the largest international randomised trials for testing COVID-19 treatments. Another international initiative is the EU-RESPONSE project, which illustrates the cooperation and the innovation amongst European clinical research actors. Finally, we reflect on the pros and cons of human challenge studies, which can be used to more quickly test new medicinal products that protect against SARS-CoV-2 infection. Continuing research is vital because we may still have a ways to go until we reach the end of the COVID-19 tunnel …

Enjoy reading (likely at home) this issue of *RA Watch* and stay safe.

Séverine Méance, *RA Watch* Editor

DEEP DIVE

FIRST LESSONS LEARNT ABOUT THE REGULATORY ASPECTS OF HUMAN RESEARCH RELATED TO COVID-19: PERSPECTIVES FROM THE SCTO'S REGULATORY AFFAIRS PLATFORM

Author: **Séverine Méance** with input from all RA Platform members
Affiliations: CTU Lausanne, *RA Watch* editor, and RA Platform coordinator

This article summarises the findings of an internal survey, which was conducted at the end of the first wave of the COVID-19 pandemic by the Swiss Clinical Trial Organisation's (**SCTO's**) Regulatory Affairs Platform (**RA Platform**). The survey showed that the Clinical Trial Units (**CTUs**) and Swiss Group for Clinical Cancer Research (**SAKK**) centres received many requests to support academic human research on COVID-19 during the first wave of the pandemic. Local strategies to prioritise research projects had to be adopted, new practices were implemented, and ways of working from home were successfully developed. The established RA Platform network was considered helpful for sharing information and effective practices. Synergies among research projects were initially missing, and better coordination should be encouraged. At the same time, services provided by and interactions with Swissmedic, swissethics, and the cantonal ethics committees (**ECs**) were much appreciated. Swissmedic and ECs focused their resources on projects related to COVID-19 and adapted their procedures to allow studies to start quickly. Some practices have been effective and should continue. The pandemic has shown that Switzerland can be considered a competitive place to launch studies in an emergency situation.

INTRODUCTION

The SCTO's CTUs and SAKK centres provide services to clinical research units at university and cantonal hospitals in Switzerland. During the first wave of the COVID-19 pandemic, an avalanche of human research projects linked to COVID-19 arose. They were crucial to try to identify strategies to fight the SARS-CoV-2 virus by understanding its epidemiology, its pathophysiology, and its mechanisms of actions and by testing the first strategies of care and potential therapeutic products. The multiplicity of research questions and the urgency to start the studies put pressure on the individual CTUs/SAKK centres as well as on every link in the implementation chain. As a consequence, many studies were able to start in less than one month, compared to the average preparation time of 9 to 12 months for different steps: writing the study protocol and other documentation, securing funding, preparing investigation sites, and making submissions to the authorities (ECs and Swissmedic). Sharing how this was accomplished and the lessons learnt along the way should be of benefit to the human research community as a whole.

Internal survey and follow-up workshop

After the first pandemic wave, a calmer period followed before the start of the second wave. This allowed the SCTO's RA Platform, which includes regulatory representatives from the different CTUs/SAKK centres, to share their experiences and lessons learnt from the first wave (from March to the beginning of July 2020). A 21-question survey was sent to seven CTUs/SAKK centres in June 2020, and answers were provided in July 2020. Survey feedback was analysed and discussed during a half-day, in-person workshop held in September 2020. There were two main objectives of the questionnaire and workshop. The first objective was to understand the situation for each CTU/SAKK centre and share eventual best practices: the number of requests for support each CTU/SAKK centre received, internal organisational policies and practices put in place, and the advantages of participating in the CTU/SAKK network. The second objective was to share the experiences of the CTUs/SAKK centres when interacting with local ECs, swissethics, Swissmedic, and the Swiss National Science Foundation (SNSF) and to make recommendations for the future.

AN AVALANCHE OF REQUESTS MADE TO THE CTUS/SAKK CENTRES TO SUPPORT PROJECTS LINKED TO COVID-19

The CTUs/SAKK centres received 124 requests to support human research projects (all types) linked to COVID-19: 67 for observational studies, 36 for clinical trials, and 21 for registries (collections of health-related data for future research purposes) (**Figure 1**). One-third (41) of the projects asked for regulatory support mainly solicited for clinical trials (preparing documentation and making submissions for study authorisation to ECs and Swissmedic, participating in meetings with authorities, and entering information in study registries) (**Figure 2**). The most requests were received by the CTUs in Lausanne, Basel, and Geneva (**Figure 3**).

Figure 1: Number of requests made to CTUs/SAKK centres by human research project types on COVID-19 (from March to 10 July 2020)

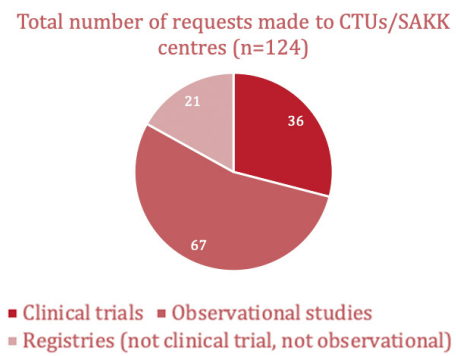


Figure 2: Number of requests for regulatory support made by human research projects on COVID-19

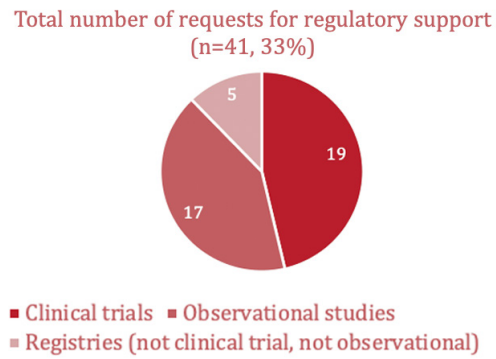
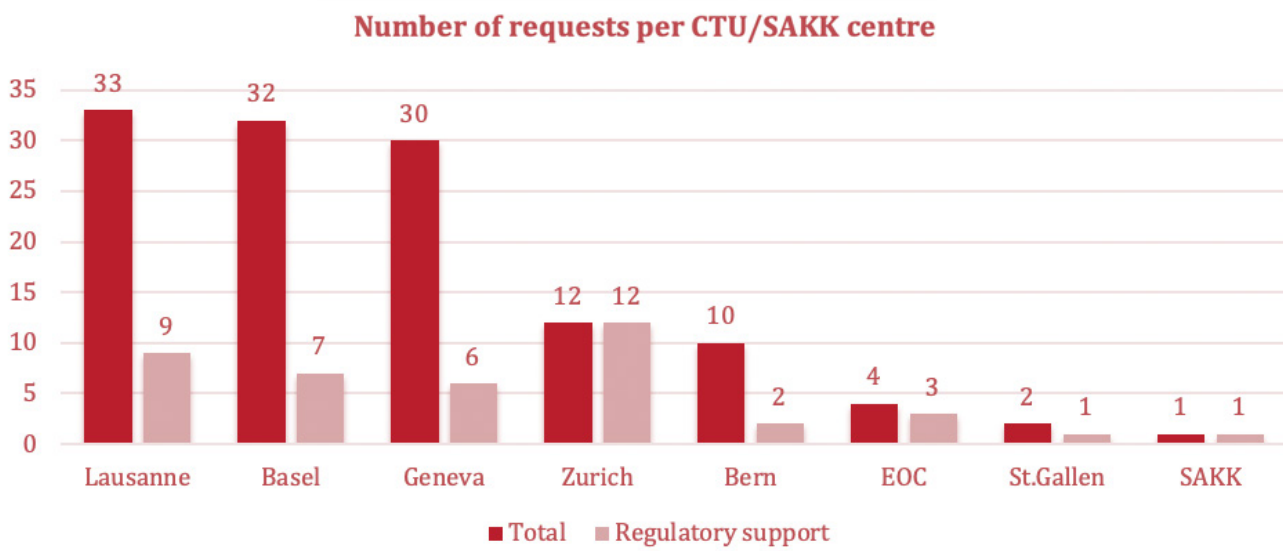


Figure 3: Number of requests made by human research projects on COVID-19 per CTU/SAKK centre



LOCAL STRATEGIES AT CTUS/SAKK CENTRES AND HOSPITALS TO PERFORM HUMAN RESEARCH ACTIVITIES

The incidence of infection was not homogenous in the different regions of the country. In order to manage research projects in view of the number of COVID-19 research requests, CTUs/SAKK centres and the institutions to which they belong followed different internal strategies (**Table 1**). The CTUs in Lausanne, Zurich, and Ticino decided to put the management of non-COVID-19 research projects on hold (with some exceptions) in order to focus on COVID-19 projects. The CTUs in Geneva, Bern, and St.Gallen prioritised COVID-19 projects but tried to continue with ongoing projects as much as possible. SAKK centres and the CTU Basel analysed non-COVID-19 projects case by case to determine if they could be put on hold. One illustration of a local strategy is the prioritisation committee put in place at Lausanne University Hospital (**CHUV**) to select COVID-19 projects to run at the institution (such committees were also put in place in other CTUs). Each COVID-19 project was evaluated in order to avoid harassing patients and staff with multiplicity and fragmented research initiatives and to consider ethical and practical issues – for example avoiding the enrolment of the same patient in many studies, reducing the use of multiple consent forms, and limiting blood spoliation with cumulated research-related samples. Such approaches were also taken to protect healthcare providers from an additional workload burden for research purposes and to indirectly limit the number of premature or infeasible projects submitted to ECs. Non-COVID-19 clinical trials projects were also affected by federal hygiene measures for protecting the public, such as limiting the visits of trial participants, delivering the investigational medical product to a patient's home, doing remote monitoring, etc. At the CTU Basel, a clinical research advisory board evaluated all studies to decide case by case if they could be continued or not; the evaluation was based on a justification prepared by each researcher.

Table 1: Local strategies for managing research projects in view of COVID-19 research requests made to the CTUs and SAKK centres during the first wave of the pandemic

COVID-19 studies prioritised, and other studies put on hold (with some exceptions)	Lausanne, Zurich, Ticino
COVID-19 studies prioritised, but other studies still continued	Geneva, Bern, St.Gallen
Case-by-case analysis of whether to stop non-COVID-19 studies	SAKK, Basel

LEARNING TO WORK FROM HOME

During the first wave of the pandemic, federal measures recommended working from home until the end of June. This applied to the regulatory teams as well as the rest of the centres' teams. A few people were allowed to go into the offices for specific reasons, for example to do filing or get signatures. There were initial fears that working from home could be a problem because it involved managing an increased workload – sometimes with children staying at home as well (until the beginning of May) – with inadequate equipment, and it required defining new ways to communicate within teams and with investigators (e.g. teleconferences, e-learning, a hotline, and online Q&A). But in the end, it turned out well, and teams were able to manage work demands in a very short amount of time while maintaining a high level of quality.

SCTO'S EXISTING RA PLATFORM WAS USEFUL

The RA Platform's members appreciated the positive communication within the network during the first wave of the pandemic, especially the monthly conference calls with representatives from each of the CTUs/SAKK centres, the special internal *RA Watch* COVID-19 weekly updates on regulatory developments in Switzerland and abroad, and the opportunity as a trusted partner to comment early on the joint guidance document written by swissethics and Swissmedic. The workshop held in September was also a good opportunity to share local experiences and best practices among the CTU/SAKK network. Examples of local best practices include the flexible reallocation of staff to urgent tasks, the possibility to quickly recruit manpower, compulsory good clinical practice (**GCP**) courses for all physicians and research staff to facilitate setting up research teams, a hotline for consultation services, regularly updated online Q&A resources for researchers, a crisis management approach to operating, and the aggregated reporting of study interruption and continuation to ECs, Swissmedic, etc. A detailed example of work practices at the CTU Basel is provided on p.10.

A TRUSTED NETWORK, BUT UPFRONT COORDINATION NEEDED

The feeling within the CTU/SAKK network was that the individual CTUs are reliable, service-oriented partners at the hospital institution level that help investigators to submit and run high-quality projects in a very short amount of time. The feedback received from researchers at individual CTUs was positive, especially the responses and advice received in such an unclear situation. An example of this appreciation (which can be listened to here) comes from the principal investigator of the CORON-ACT study, a multicentre trial that is being conducted at four Swiss hospitals. The CTU Bern provides support for CORON-ACT, and the CTU Zurich participates in the study as well. Another example of the CTU network's recognition is the involvement of both the CTU Lausanne and the CTU Bern in the World Health Organization's (**WHO's**) Solidarity trial in Switzerland (17 sites), which is one of the largest international randomised clinical trials for testing repurposed drugs for treating COVID-19. The lessons learnt so far from the Solidarity experience can be read on p. 22.

One main lesson learnt by the network is that the multiplicity of the demands significantly increased the workload of all teams involved. And despite all the efforts made, studies were not launched until the end of the first wave, which was too late to get enough patients enrolled (however, ongoing studies are recruiting during the second wave). The network's members observed a redundancy of sometimes small projects and lack of synergies. In the future, a more pronounced global coordination would be appreciated, including upfront discussions with the SNSF regarding funding key priority projects at the national level. More multicentre and multinational initiatives favouring platform studies should also be encouraged (an article on the EU-RESPONSE initiative can be read on p. 28). In addition, the "covidisation" of research has an impact on other research areas and consequently on patients affected by those other therapeutic fields. This aspect should be considered and mitigation plans should be proposed if other pandemics arise in the future.

INTERACTIONS WITH SWISSETHICS, LOCAL ECS, SWISSMEDIC, AND THE SNSF

The CTU/SAKK network appreciated the collaborative attitude and the initiatives of all stakeholders involved in the authorisation and conduct of human research projects during this crisis period. Survey respondents were highly satisfied with their interactions with Swissmedic, which received a mean score of 4.5 on a scale from 0 (not satisfied) to 5 (highly satisfied). There was also high satisfaction regarding interactions with local ECs (score of 4.2), with some local differences, and with swissethics (score of 4). The details of what was considered positive, what could have been better, and recommendations for the future were discussed during the workshop in September and are summarised in **Table 2**.

Fast research project authorisations

The main positive aspect was the rapid approval of COVID-19 projects, both by ECs and Swissmedic. The teams from the authorities were available for exchanges, responsive, and often pragmatic when evaluating projects. It was sometimes felt that some ECs insisted on unimportant aspects, and some ECs did not always review the projects enough. The pandemic situation exacerbated some pre-existing differences in practices, and harmonisation among ECs should be improved. The advance electronic submission to Swissmedic permitted an acceleration of the process. It would be appreciated if such a facilitative procedure could continue or even be transformed into an online submission portal. ECs should also consider fast-track authorisation processes.

Guidance

The initial situation was difficult for investigational teams who had questions regarding how to manage ongoing trials. swissethics published an initial version of a guidance document, which was a bit delayed due to circumstances surrounding the pandemic and was thus less applicable at the beginning of pandemic's first wave. In conjunction with what was already available at the EU level, the subsequent revised versions, which were aligned with Swissmedic, were much more useful.

Published lists

The initiative from swissethics to publish lists of projects that have been approved and projects that have been submitted but not yet approved provided useful information about ongoing research projects. This information should be used to set up collaborations on common objectives instead of launching projects in parallel or – even worse – in competition with each other.

Funding

The network also discussed recommendations for funders. They appreciated that the SNSF was very quick to fund some research projects. In the future, the SNSF could more quickly communicate postponed deadlines for project submissions. In order to minimise overlapping and small projects, the SNSF could also add more conditions for funding eligibility and promote national multicentre studies on key priorities by proposing more top-down calls.

Table 2: Experiences and recommendations from the CTUs/SAKK centres interacting with ECs, swissethics, and Swissmedic on COVID-19 projects during the first wave of the pandemic

	Experiences and recommendations		
Stakeholder	**Positive**	**Less positive/could be improved**	**Recommendations for the future**
ECs	• Helpful, available, supportive, fast, and pragmatic	• Sometimes some ECs insisted on unimportant questions; sometimes some ECs made inadequate/incomplete checks of studies • Initial unclear period with imprecise or contradicting information	• Harmonised work and improved communication among ECs • Possibility to implement fast-track authorisation during future crises
swissethics *Note: only half of the CTUs and SAKK centres were in contact with swissethics*	• Good and fast interactions • Joint guidance document: exchanges with the RA Platform allowed for an improved version • Online COVID-19 projects lists were helpful	• Guidance document: first version edited by swissethics was not aligned with Swissmedic and not as comprehensive as the EU guideline • Difficult management of the initial situation	• Possibility to reduce redundancy and loss of time and resources (for multicentre projects involving more than one EC) • Develop guidance for future crises
Swissmedic	• Very fast, helpful, available, informative • Joint guidance document: exchanges with the RA Platform allowed for an improved version • Electronic dossier submissions in advance accelerated the process	• Sometimes insisted on administrative details • Initially slow, first joint guideline was published a bit late • Communication was slow for ongoing non-COVID-19 studies, (repeated questioning was necessary to receive answers)	• Keep email/electronic submission possible or even switch to an online submission portal • Develop guidance for future crises

CONCLUSIONS AND FUTURE PERSPECTIVES

All the collective efforts to launch COVID-19 studies during the first wave of the pandemic are paying off now. Studies are recruiting patients from the second wave, which is unfortunately still ongoing in March 2021. These studies help to better understand COVID-19 and will hopefully contribute to slowing down the pandemic. The CTU/SAKK network has gained much experience on how to manage such a high demand for support during a pandemic situation and was a key partner for some ambitious projects. In general, there is a call for a better coordination from the beginning of a crisis in order to reduce the redundancy of sometimes small projects in the event of another extraordinary situation. The CTU/SAKK network acknowledges all the decisive efforts made by the authorities to adapt their resources, provide services, and modify their procedures. The pandemic has shown that Switzerland can be considered a competitive place to launch studies in an emergency situation. There is also an opportunity for some effective, innovative practices to be applied to regular research activities and thus help to decrease the commonly perceived regulatory burdens associated with human research.

COVID: 1–9 WORK PRACTICES AND LESSONS LEARNT AT ONE CTU

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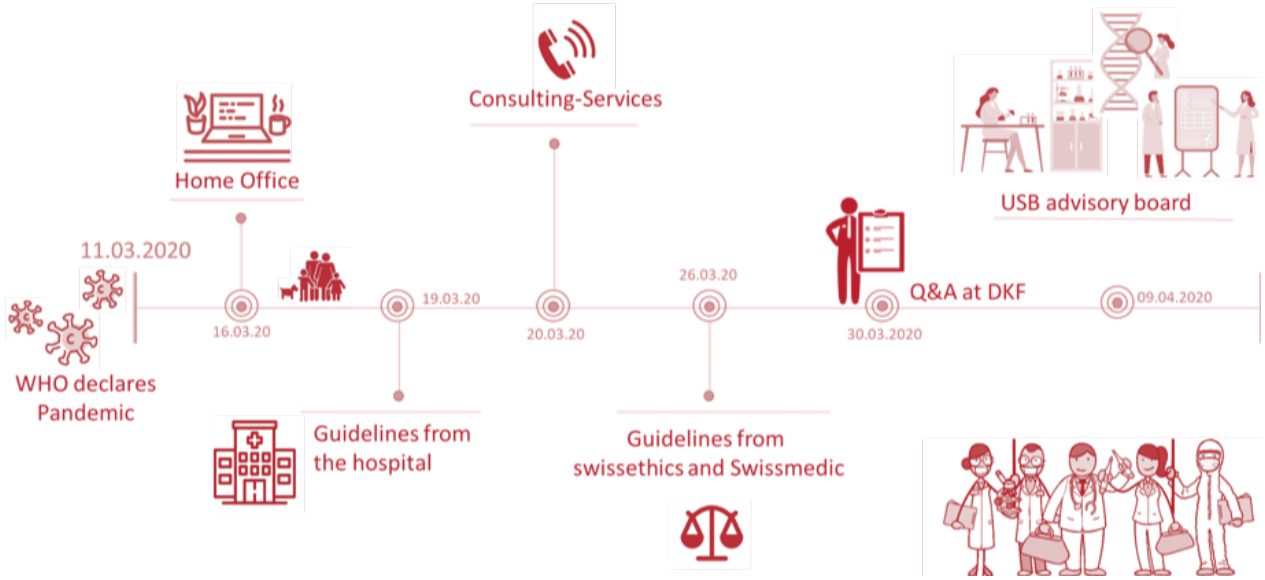
Affiliations: Department of Clinical Research (DKF), University Hospital Basel

The pandemic hit us all much faster and to a larger extent than we could have imagined. We have had to find strategies for adapting quickly to the circumstances on both private and business levels. The Department of Clinical Research (**DKF**) at the University Hospital Basel (**USB**) has developed work practices for how to reconcile home office and work, how to handle frequently updated guidelines, and how to respond to questions from researchers about their clinical trials. In this article, we summarise nine DKF work practices and discuss lessons learnt during the corona crisis.

DKF's corona crisis timeline



It was already clear to Churchill: *Never waste a crisis.* On 11 March 2020, the World Health Organization (**WHO**) declared the coronavirus situation a global pandemic – a crisis caused by the SARS-CoV-2 virus. The coronavirus has shown us that we have to adapt to this new situation as fast as the virus spreads. Therefore, at the DKF – the Clinical Trial Unit (**CTU**) at the USB – we started finding solutions to stay on track both in our personal lives and in clinical research from mid-March until mid-May 2020.

1 FROM THE OFFICE TO HOME

If a virus is able to travel around the world and connect people (in a negative way), we too should be able to connect with our colleagues and clients around the world (in a positive way). Using all possible virtual communication tools (which were surprisingly user-friendly) helped us see and hear our colleagues and study teams almost as well as in real life. Short questions, long discussions, and important meetings all took place in a virtual world and with hardly any problems. However, each situation also has its disadvantages: not only were we working from home, but schools and kindergartens were also closed. This forced many of us to face another difficult situation: 60% of our employees are women who had to take care of their kids and dogs (and husbands). The period we worked from home was relatively short due to the low case numbers in Basel.

2 CONSULTING SERVICES

All possible DKF services rapidly switched from physical to virtual operations. Our statistics and consulting team shifted to virtual meetings, and we also offered a consulting hotline. This hotline was used frequently, with the requested services providing direct support. In addition, we provided a contact form on the DKF's website, and the required service answered the corresponding question in a timely manner. We received much positive feedback on these remote services, and users very much appreciated that services were still being provided. It was, however, more challenging for our consulting team to coordinate and communicate complex research issues that involved several parties. On the other hand, existing partnerships were deepened since communication took place for a short time but more frequently.

3 GUIDELINES FROM SWISSETHICS AND SWISSMEDIC

It goes without saying that this situation caused researchers to despair and raised more questions than we had answers to. We struggled with a variety of questions: if researchers could still include new patients, if COVID-19 had to be reported as a serious adverse event (**SAE**), if physical visits could be replaced by phone calls, and if people had to re-consent when additional data were acquired and if sponsors needed to report a study interruption. Although swissethics and Swissmedic provided useful guidelines in April to answer almost all of these questions, the guidelines were published quite late and did not cover all aspects of the issues. Revised and expanded versions were later published.

4 QUESTIONS AND ANSWERS AT THE DKF

An example of a question not addressed by swissethics and Swissmedic was whether investigators were allowed to send medication to a patient's home. According to the guidelines, this was not allowed because the correct storage and temperature of the investigational medical product (**IMP**) could not be ensured. For one of our clients, IMP storage was at room temperature, so we submitted our request and received approval to send medication to the patient's home. This is why the Regulatory Affairs team created a questions and answers (Q&A) list on our website that summarised and supplemented all questions that arose. We adapted the corresponding answers to the latest guidelines from all institutions, such as the Federal Office of Public Health, swissethics, Swissmedic, and the USB. This Q&A list advised researchers on how they could handle certain situations. The final responsibility, however, always remained in the hands of the sponsor.

5 GUIDELINES FROM THE HOSPITAL

The USB provided additional institutional guidelines on how to handle (study) patients, remote working situations, and much more. Thus, not only did our Q&A list have be updated frequently, but our employees also had to react quite flexibly to new situations. However, in contrast to other hospitals, it was possible to continue specific studies. In order to organise the conduct of running studies at the USB, a specific advisory board for clinical research on COVID-19 was created. In addition, the DKF was involved in the USB's COVID-19 study task force, which coordinated all COVID-19-related studies according to their patient profile, research question, and/or data collection with the goal of using synergies.

6 USB ADVISORY BOARD

The clinical research advisory board decided which studies at the USB could be continued and which studies had to be interrupted. To help make this difficult decision, researchers had the opportunity to submit their application containing a justification for their study continuation (Did patients come for routine visits or extra study visits? Were patients undergoing important treatment for a life-threatening disease? etc.) and their protection concept. There were 116 studies that were evaluated, edited, and finally approved to be continued.

7 SITUATION FOR RESEARCHERS

Contrary to our expectations, the number of study applications did not decrease in the lockdown phase, but rather increased. Not only were new trials about COVID-19 set up, but dusty studies that may have been lying in the drawer for a while and waiting to be brought out were also submitted. One had the impression that researchers had time for their research again – which may have been due the fact that some clinical areas were put on hold.

8 SCTO NETWORK

Fortunately, the CTU Basel was not alone in dealing with this situation. We could always rely on the Swiss Clinical Trial Organisation's (**SCTO**'s) network to discuss regulatory questions, help us understand new guidelines, and give us tips on how to handle specific situations. However, we also realised that circumstances at the various CTUs differed. While the staff at most CTUs were still working from home and were not conducting any clinical studies, our CTU staff were already back in the office in May.

9 LESSONS LEARNT

Ultimately, what did we learn? We learnt to react fast and adapt to changes. And that changes are not necessarily bad. We learnt how to do interdisciplinary work, we started using virtual desks, we gained time because of shorter commutes, we enjoyed working at home as we became more efficient and focused, and we had national meetings without needing to sit in a train. However, we also missed several things: seeing our colleagues in person, running to the next office for a quick question, not having to prepare our own lunch, or getting a signature in a minute. Did we waste the crisis? Not at all. Because here we are in March 2021, back in home office (again) but fully operational.

NEWS FROM

This section highlights how clinical research stakeholders have responded to the pandemic: the Swiss National Science Foundation (**SNSF**) as a major source of funding for research and Swissmedic as the authority responsible for clinical trials with medicinal products approval, the adherence to good clinical practices, and inspections. There is also a short description of the support provided by swissethics and ethics committees to clinical researchers and a summary of patient organisations' concerns in such a challenging context.

Swiss National Science Foundation

SWISS NATIONAL SCIENCE FOUNDATION

SUPPORTING RESEARCH DURING THE PANDEMIC: HOW THE SWISS NATIONAL SCIENCE FOUNDATION HAS RESPONDED TO COVID-19

Authors: **Irene Knüsel**, **Stéphanie Wyss**, **Pascal Walther**, and **Marc Zbinden**
Affiliations: Swiss National Science Foundation (**SNSF**)

As the foremost research funding organisation in Switzerland, the Swiss National Science Foundation (**SNSF**) plays a key role in promoting scientific research in Switzerland. In 2019, the SNSF supported 18,900 researchers with over 1 billion Swiss francs in order to promote research that benefits society, the economy, and politics. All three of these areas have been dramatically affected by the COVID-19 pandemic – with profound national and international consequences. This article provides an overview of the SNSF's national and international responses to the pandemic, discusses the challenges the SNSF has faced during the pandemic, and highlights lessons learnt so far.

NATIONAL RESPONSE

In spring 2020, the SNSF launched two initiatives to respond to the COVID-19 pandemic:

1 Special call for research on coronaviruses An initial 10 million Swiss francs were awarded to 36 research projects. Financial returns recently allowed the SNSF to award an additional 1.9 million Swiss francs to nine more projects through this call.

2 National Research Programme "Covid-19" (**NRP 78**) A total of 28 research projects are being funded to find innovative solutions and develop public health recommendations for the COVID-19 pandemic. The NRP 78 operates with an overall budget of 20 million Swiss francs, and its research projects run for two years.

These projects, as well as those funded by Innosuisse and the European framework program Horizon 2020, are listed in the SNSF's COVID-19 project registry. More information on funded projects can also be found in the "News room" section of the SNSF's website.

In addition to the above-mentioned initiatives, the SNSF initiated other measures in spring 2020 to support researchers, including prolonging the call deadline for project funding, extending mobility fellowships, issuing grant extensions, and providing additional funding to bridge gaps. Furthermore, the SNSF has been invited by the State Secretariat for Education, Research and Innovation (**SERI**) to identify topics with societal, economic, and politically pressing challenges to the current pandemic and to formulate key questions associated with the thematic areas.

INTERNATIONAL RESPONSE

The SNSF's immediate responses to the pandemic were focused on national issues and challenges facing researchers in Switzerland (see measures outlined above). However, as a member of the Global Research Collaboration for Infectious Disease Preparedness (GloPID-R) network, the SNSF has communicated and aligned its activities related to COVID-19 with the other members of GloPID-R since the beginning of the pandemic. In addition to regular meetings and updates to coordinate funding activities, there have also been workshops with projects leaders who received funding for their COVID-19 research. The aims of these activities are to join forces, avoid redundancies, and share first data.

Both of the SNSF's initiatives listed above were open to international collaborators as co-applicants, thus allowing the best experts to develop a project together. The SNSF particularly promotes early and open access to data and publications for research activities related to COVID-19. In addition, the SNSF has financially supported the World Health Organization's global Solidarity trial, which produced conclusive evidence in record time on the effectiveness of repurposed drugs for COVID-19 (cf. article on Solidarity on p. 22).

CHALLENGES

The urgency to react to the pandemic and the associated time pressure have been the main challenges for the SNSF. Urgent timelines necessitated a novel approach to preparing and implementing the new special call on coronaviruses and the National Research Programme "Covid-19". Time pressure has also presented challenges for recruiting international scientists in the various projects' fields for their evaluation processes. During this global crisis, the vast majority of scientists are already involved in similar activities or initiatives, both in their own countries and internationally.

Responding to the pandemic required a significant amount of coordination. Although very useful, coordinating research activities with national and international partners under so much time pressure was also quite challenging from a legal and procedural perspective because the regulations of two different funders had to be taken into account. Despite reasonable intentions, not all of the partners' wishes or demands could be considered due to regulatory constraints. In addition, the time pressure and workload made it quite a challenge to optimise the coordination between the federal administration, the Swiss National COVID-19 Science Task Force, and the SNSF.

It was challenging to address the needs arising from the global pandemic and manage the SNSF's routine work at the same time. As a result, the SNSF's regular work suffered from some delays. Further challenges included the increased pressure on the SNSF's budget reserve as a result of all the special measures needed and the continuing efforts to maintain the SNSF's high quality standards throughout an accelerated evaluation procedure.

LESSONS LEARNT

Thanks to excellent cooperation – between divisions and across the organisation – as well as the enormous effort and dedication of everyone involved, the SNSF has been able to tackle the challenges related to the current COVID-19 crisis and also learn from them. Several of the newly implemented processes may become permanent procedures at the SNSF (e.g. the peer review process and virtual conference formats). And in the future, the SNSF can apply the following learnings from the pandemic: ensure a proper balance between rushing forward and careful, detailed planning; try to avoid a "covidisation" of research; and consider the long-term impact of immediate measures and needs (effects on the budget, immediate open access vs the protection of intellectual properties, etc.).

Swissmedic

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.

THE ROLE OF SWISSETHICS AND ETHICS COMMITTEES DURING THE COVID-19 PANDEMIC

swissethics has provided information and developed resources related to the COVID-19 pandemic on the "COVID-19" section of its website, which includes the following:

- a summary report published on 1 July 2020 outlining the work carried out by the seven Swiss ethics committees (ECs) from January to the end of May 2020 DE FR (see **Box 1**)

- regularly updated online lists of submitted and approved applications for clinical trials and projects on COVID-19 in Switzerland EN (see **Box 2**)

- a guidance document developed in collaboration with Swissmedic entitled Joint Guidance of Swissmedic and swissethics on the Management of Clinical Trials with Medicinal Drug Products in Switzerland during the COVID-19 Pandemic EN. This document contains specific guidance on risk assessment, the distribution of study medication, monitoring, study visits, informed consent procedures, safety reporting, protocol deviations, the resumption of clinical trial activities following the COVID-19 pandemic, and other relevant topics. This joint guidance is regularly updated; version 2.4 was published on 17 December 2020

- a list of links to relevant Swiss and international organisations and a wide variety of guidance documents related to COVID-19.

BOX 1:

swissethics published a report on 1 July 2020 DE FR summarising the most important issues for Swiss ECs in the first months of the COVID-19 pandemic until the end of May. The report shows how ECs supported researchers with extremely short processing times despite receiving significantly more research applications than usual. In addition, ethical standards are discussed in the report, particularly with regard to informed consent. It will be interesting to receive an updated analysis and figures for the whole period of the pandemic until now, including recommendations for measures that can be continued or adjusted after the pandemic and included in the revision of the Swiss Human Research Act (**HRA**).

Processing an unprecedented number of research project applications in record time

The summary report from swissethics also indicates that since the start of the pandemic in March 2020, Swiss ECs have experienced a large increase in the number of applications for research projects. Compared to 2019, project applications submitted to ECs in the months of March, April, and May 2020 increased by 57%, 94%, and 33% respectively. The urgency of the pandemic has increased the time pressure to process project applications. ECs have prioritised COVID-19 projects, and several ECs have even created special COVID-19 teams to handle these applications more expeditiously. Even while working remotely, ECs have been able to work extremely quickly. Between 1 January 2020 and 31 May 2020, the median processing time nationwide dropped significantly from 24 days (for pre-pandemic non-COVID-19 projects) to 6 days (for COVID-19-related projects). In terms of the type of request and categorisation, research projects involving people according to chapter 2 of the Human Research Ordinance (**HRO**) and further use projects as defined in chapter 3 of the HRO have dramatically increased (they more than doubled in April 2020 compared to 2019). Clinical trials have also seen some increases – for example, with almost 40% more in April 2020 compared to the previous year. Despite this significant increase in volume and the time pressure facing ECs, ethical standards remain their utmost priority; swissethics affirms in its summary report that ECs have maintained the quality of the review process throughout the pandemic.

Improving coordination and using innovative consent solutions

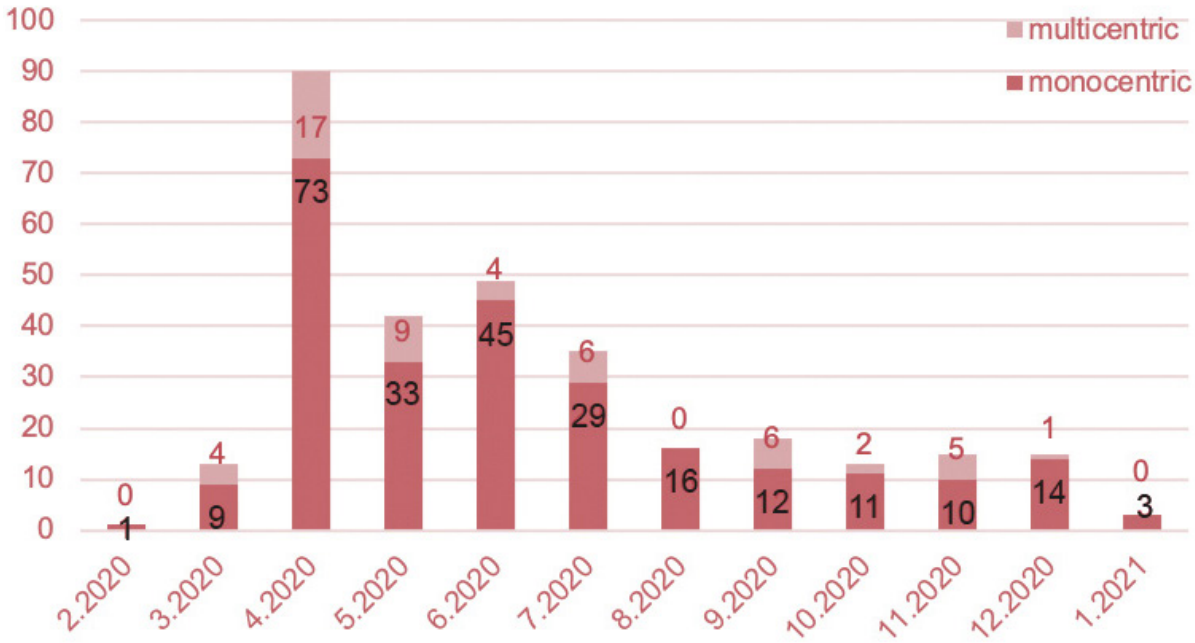
Another challenge, especially at the beginning of the pandemic, was the lack of coordination between the researchers of many COVID-19 projects. Even though multicentre projects might have been more beneficial, many of the initial applications were for monocentric projects. To improve coordination, swissethics began publishing and regularly updating lists of submitted and approved applications for clinical trials and projects on COVID-19 in Switzerland EN. As indicated in the summary report from swissethics, individual ECs also increased their local coordination efforts; the ethics committee in Vaud, for example, was able to reduce submitted applications by over 20%.

Moreover, ECs have worked with hospitals to find quick and pragmatic solutions to the COVID-specific challenges they have been facing – for example, obtaining informed consent and general consent. Obtaining consent was especially difficult at the beginning of the pandemic, when many of the patients affected were very ill and their relatives were not allowed in hospitals. Innovative consent solutions, such as getting an electronic signature on a tablet instead of paper or obtaining consent via SMS, have been used.

BOX 2:

In order to facilitate national coordination, swissethics began publishing two lists of submitted and approved clinical trials and research projects on COVID-19 in Switzerland [EN]. These lists are updated weekly. Detailed information about clinical trials on COVID-19 can be obtained on the Swiss National Clinical Trials Portal (SNCTP). **Figure 1** shows the evolution of the number of approved projects since the beginning of the pandemic. It can be seen that the majority of projects were approved during the first six months of the pandemic, and there were significantly more monocentric projects during the whole period. It is noteworthy that the second wave of the pandemic has not triggered a second wave of research projects.

Figure 1: Evolution of the number of approved clinical trials and research projects on COVID-19 in Switzerland since the beginning of the pandemic



Source: swissethics, Excel list of approved clinical trials and research projects on COVID-19 in Switzerland, extracted 11 Jan. 2021

PATIENT ORGANISATIONS: COVID-19 CONCERNS RELATED TO HUMAN RESEARCH

Patient organisations support and advocate for the patient communities they represent while also increasing the role of patients in improving and shaping healthcare practices, policies, and systems. During the coronavirus pandemic, patient organisations have provided their patient communities with relevant information on COVID-19 and have brought patients' perspectives into the dialogue around COVID-19. Moreover, they have advocated for patients' needs and concerns related to the pandemic's effects on human research and to coronavirus vaccine development and authorisation. This article summarises several of the issues facing patient communities during the pandemic and provides examples of patient organisations' responses to these issues.

PATIENTS' PERSPECTIVES

Patient organisations represent some of the most vulnerable patient groups in this pandemic: many have chronic conditions, are at a higher risk for illness and death from COVID-19, and may experience substantial disruptions to ongoing care and treatment due to the pandemic. Raising awareness of these issues is one focus of patient organisations during the pandemic. In December 2020, the Swiss patient organisation **SPO** wrote an open letter (in German) to the Swiss Federal Council and representatives of the cantons calling for more solidarity with ill and elderly people as well as healthcare workers. This was, however, one of the rare initiatives from Swiss patient organisations to our knowledge. Rare Diseases Europe (EURODIS), an alliance that gives voice to over 30 million Europeans affected by rare diseases, initiated a survey of almost 7000 people with rare diseases in 36 countries across Europe to ascertain how COVID-19 has impacted them. The survey shows that the pandemic has not only caused severe disruptions to care for people with rare diseases, but it has also increased their levels of uncertainty and anxiety. The survey also reveals positive developments, for example that the pandemic has resulted in more people using online health services.

THE SUSPENSION OR TERMINATION OF HUMAN RESEARCH DURING THE PANDEMIC

Patient organisations have been following and responding to the pandemic's effects on human research. As the result of COVID-19 becoming the focus of much research (i.e. the "covidisation" of research), attention and resources have been diverted from other research projects. Early on in the pandemic in May 2020, BioPharma Dive shared details on the disruption of clinical trials: three out of every four clinical trials worldwide had to be ended prematurely or put on hold. Later, studies performed in August 2020 identified the persistent impact of COVID-19, with over 60% reporting an "average" or greater level of impact on ongoing trials and the initiation of new trials. Respondents specifically highlighted challenges in patient enrolment and recruitment (see article in Applied Clinical Trials from October 2020). Those obstacles drove a discernible shift toward conducting decentralised trials and using telemedicine and mobile technologies in order to reduce contact with patients – and thus potentially lowering research costs.

Slowing down or stopping clinical research has resulted in both a disruption to care for patients receiving treatment in affected trials and a delay in the development and authorisation of the tested treatments for the whole group of patients. In an open memo to the health industry, the European Patients Forum (EPF), which represents patient organisations throughout Europe and over 150 million Europeans who are affected by chronic conditions, advocates for patients to be informed in a timely manner and supported if clinical trials are changed, suspended, or terminated. The EPF's memo also highlights the need for patients to continue receiving treatment if needed. In an open letter to policy makers, EURODIS draws attention to the fact that there are no effective treatments for most rare diseases and emphasises the importance of continuing research and clinical trials related to rare diseases, even during the pandemic. As a way to avoid prematurely ending non-COVID-19 clinical trials and to keep them from being put on hold, the clinical research service provider WIRB-Copernicus Group (**WCG**) proposes using independent sites that do not treat COVID-19 patients for clinical trials (see article on WCG's website).

CORONAVIRUS VACCINE DEVELOPMENT, TESTING, AND AUTHORISATION

The development, testing, and authorisation of coronavirus vaccines has occurred at an unprecedented pace. While there is a great urgency to develop and approve effective vaccines against the coronavirus, patient organisations have been advocating for patient safety to remain the top priority throughout all steps of the process. In a statement on patient safety as it relates to coronavirus vaccines, the EPF asserted that "regulatory 'shortcuts' must not lead to lowering standards of safety or efficacy that should remain under the strict control of **EMA** [European Medicines Agency]".

In addition to advocating for patient safety, patient organisations are calling for transparency in the vaccine development and authorisation processes in order to foster the public's trust in these processes, pharmaceutical companies, and the authorities. This trust will in turn increase the acceptance of approved vaccines. Together with the EPF, EURODIS successfully encouraged the EMA to hold public stakeholder meetings on the development and authorisation of COVID-19 vaccines and on the approval and roll-out of vaccines. During these meetings, the EMA provided the public and stakeholders with information on its processes and collected feedback from participants. The EMA also adapted its processes for more transparency.

Many of the patients represented by patient groups are at higher risk of becoming seriously ill or dying from COVID-19, so they are some of the first people who are able to receive coronavirus vaccines. Although these vaccines have gone through rigorous testing and approval processes, certain adverse effects may only become clear when the vaccines have been administered on a large scale for a longer period of time. In its statement on patient safety, the EPF calls for "an even greater level of vigilance and protection of patients' rights in case of adverse reactions". The EPF also asserts that coronavirus vaccines need to be subject to the same liability regulations as other vaccines and recommends creating a mechanism that ensures prompt compensation to vaccinated people who develop severe adverse reactions.

CONCLUSION

Throughout the coronavirus pandemic, patient organisations have made sure patients' voices and concerns are heard. In addition, they have drawn attention to the disruption to patient care resulting from the suspension or termination of research projects during the pandemic. And while patient organisations have welcomed the fast development and authorisation of vaccines, they have also emphasised the need for transparency and a focus on patient safety in those processes.

SWITZERLAND'S PARTICIPATION IN GLOBAL AND EUROPEAN COVID-19 INITIATIVES

SWISS PARTICIPATION IN THE WHO'S SOLIDARITY TRIAL: WHAT THE RESEARCH COMMUNITY HAS LEARNT SO FAR

Authors: **Loane Warpelin-Decrausaz** and **Aurélie Fayet-Mello,** national coordinators on behalf of the Solidarity trial's CTU Lausanne team*
Affiliations: CTU Lausanne

The World Health Organization's Solidarity trial is one of the largest international randomised clinical trials for COVID-19 treatments in the world and provides an excellent example of a global effort to fight the pandemic. When Switzerland was invited to participate in the trial, the Swiss research community gave a resoundingly positive response. Researchers, investigators, hospitals, ethics committees, and authorities all worked together and made extraordinary efforts – in the midst of the difficulties brought on by the pandemic – to get the trial up and running in Switzerland in a relatively short amount of time. Lausanne University Hospital (**CHUV**) and the Clinical Trial Unit (**CTU**) Lausanne coordinate these remarkable efforts. In this article, two national coordinators for the Solidarity trial provide an overview of the trial, address some of the challenges encountered and solutions found when preparing for and conducting the trial in Switzerland, and discuss some of the lessons learnt so far that can be carried into the future.

* *Solidarity trial's CTU Lausanne team: Yoanne Boulez, Monica von Brevern, Laurene Cagnon, Fady Fares, Aurélie Fayet-Mello, Marc Froissart, Isabelle Guilleret, Sara Mantero, Séverine Méance, Christiane Pellet, Laura Pezzi, Loredana Sene, Vassili Soumas, Laure Vallotton, Andreja Vujicic-Zagar, and Loane Warpelin-Decrausaz*

SOLIDARITY TRIAL

Solidarity is an international clinical trial launched by the World Health Organization (**WHO**) to help find an effective treatment for COVID-19 using repurposed drugs for this new indication. This platform trial is one of the largest international randomised trials for COVID-19 treatments, with an enrolment of almost 12,000 patients in 500 hospital sites in over 30 countries (latest update on 15 October 2020). An interim analysis in October 2020 showed that all four treatments evaluated up to that time (remdesivir (**RDV**), hydroxychloroquine (**HCQ**), lopinavir/ritonavir (**LPV/r**), and interferon beta-1a (**IFN B1a**) had little or no effect on overall mortality, the initiation of ventilation, and the duration of hospital stay in hospitalised patients compared to the standard of care (see related NEJM.org article from 2 December 2020). In July 2020, the WHO accepted the recommendation from Solidarity's International Steering Committee to discontinue the hydroxychloroquine and lopinavir/ritonavir trial arms (see the WHO's website). This decision was also supported by the results of the RECOVERY trial, which is another large trial on COVID-19 treatments based in the UK. The discontinuation of the interferon beta-1a arm in October 2020 meant that patients could only be included in the standard-of-care or remdesivir arms. Other treatments strategies are now being evaluated in order to continue the search for effective COVID-19 therapeutics. So far, only corticosteroids have been proven effective against severe and critical COVID-19 (see NEJM.org article from 17 July 2020).

SWISS PARTICIPATION IN SOLIDARITY

On 16 March 2020, a few days before the peak of the first COVID-19 wave in Switzerland, the WHO contacted the Swiss National Science Foundation (**SNSF**) and the Swiss Federal Office of Public Health (**FOPH**) in order to start a Solidarity feasibility study in Switzerland. Very rapidly, many Swiss investigators from university and non-university hospitals showed high interest in participating. This momentum resulted in the creation of a Swiss consortium of 17 clinical sites (see approved and activated sites in **Figure 1**) on 26 March 2020. The CTU Lausanne was approached by the national coordinating investigator Dr Oriol Manuel to collaborate and provide support on all aspects of coordination, including budget preparation, project management, monitoring, pharmacovigilance, and regulatory duties. One of the first tasks was to set up a study budget, which allowed the consortium to be rapidly granted funding from the SNSF. Another priority was to validate the distribution of study responsibilities among institutions (WHO, FOPH, SNSF, and CHUV) since the WHO was requesting governmental commitment into co-sponsorship of the trial. Lausanne University Hospital (**CHUV**) was to act as the sponsor's (WHO's) representative in Switzerland and the SNSF as the funding body. The trial's coordination was assumed by the CTU Lausanne, and close collaboration with the CTU Bern was set to ensure high-quality multilingual monitoring of German speaking sites. This collaboration between the two CTUs was established very rapidly since they experienced working together in the context of the Swiss Clinical Trial Organisation's (**SCTO's**) CTU network. The WHO independently mandated the CTU Bern to perform central data monitoring, data management, and statistics. At the end of March, a race against time started that resulted in successful ethical and regulatory authorisations four weeks later as well as the inclusion of the first Swiss patient in the trial on 21 April 2020. This remarkable feat was accomplished thanks to the extensive expertise, exceptional collaboration, and great dedication of all parties involved. **Table 1** summarises the main milestones in 2020 and at the beginning of 2021.

CHALLENGES, SOLUTIONS, AND SUCCESSES

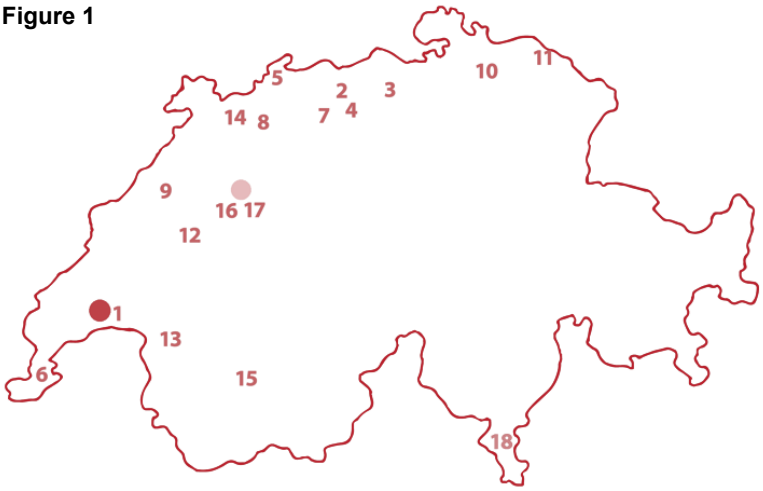
One major challenge was obviously time pressure. Reorganisation within the CTU Lausanne was essential since the staff had to be rapidly reallocated to new tasks. The strategy was to create a pool of persons fully dedicated to the trial (at least in April 2020) to handle the high workload that Solidarity generated, while other CTU staff continued with some routine activities (e.g. those trials not suspended during the pandemic) and at the same time remained involved in an institutional task force coordinating more than 75 COVID-19 research initiatives. Another high priority for CHUV was the initiation of other key research on COVID-19, which required the CTU to allocate significant resources, including study nurses, coordinators, data managers, and regulatory support. Finally, how staff worked had to be reorganised since almost all the staff who were normally in the office worked remotely during the first COVID-19 wave. During the first lockdown, the uncertainties on the incidence of COVID-19 infections pushed the team to move forward with preparations as quickly as possible. Preparing study documents for 17 sites in three different languages required the coordinating team to be well organised. In terms of the regulatory aspects of the trial, the team chose to concentrate first on the approval of the documentation for the national coordinating site in Lausanne (the country-specific addendum to the master protocol, informed consent documents, site agreements, etc.) and then adapt the documentation for the other 16 sites. Preparing and signing off agreements was especially challenging due to work-from-home requirements in most hospitals' administrative departments.

On the whole, the coordinating team's successful strategy ensured a very quick and easy review and approval process with the lead and local ethics committees (**ECs**) and a rapid initiation of the trial at all Swiss sites. As shown in **Table 1**, both Swissmedic and the Swiss ECs usually reacted to the submitted dossier within 24 to 48 hours, even though the standard timelines (as per law) are 30 days (or 45 days for multicentre trials). Close phone contact with the authorities and the possibility of electronic submissions – both exceptionally authorised by Swissmedic during the COVID-19 pandemic – greatly simplified exchanges. Grouped and remote site initiation visits, a novel approach for monitors, allowed the very rapid activation of all 17 sites. Even though these efforts to initiate the trial at all sites as quickly as possible were successful, the incidence of COVID-19 rapidly decreased in Switzerland, which resulted in the inclusion of fewer than 10 patients at the end of the first wave (**Figure 2**). However, all these efforts were not vain since sites were ready to enrol patients when the second wave arrived in autumn. As a result, in mid-December more than 200 patients were included in the trial. Unfortunately, the discontinuation of most of the trial arms and a shortage of the remdesivir drug provided by the WHO resulted in a temporary suspension in the inclusion of patients in the trial in Switzerland until new drugs to be tested in Solidarity are selected by the trial's International Steering Committee.

LESSONS LEARNT AND FUTURE PERSPECTIVES

Because the COVID-19 pandemic is unfortunately not yet under control and the Solidarity trial is still running worldwide, it is not yet time to discuss the final lessons learnt. However, an interim picture can be formed. Looking back at 2020, we can proudly state that Swiss participation in Solidarity has been a success, and it definitely demonstrates that Switzerland is an attractive country for running clinical trials in emergency situations. Investigators, CTUs, ethics committees, and regulatory authorities are all able to rapidly adapt together to reach the same objective without sacrificing quality. As representatives of investigators from all parts of Switzerland and the Swiss CTUs, the authors would like to thank the authorities in particular and encourage them to keep their much-appreciated collaborative attitude, which contributes to reducing the gap usually felt between researchers and ethics bodies/the authorities. Requesting feedback within a few days is clearly unrealistic in the long term after this pandemic is over since all stakeholders have accumulated massive amounts of overtime. However, the scientific community would definitely appreciate the possibility to continue to make electronic submissions to Swissmedic. Finally, the CTU Lausanne and the CTU Bern also demonstrated their synergetic collaboration, which was undoubtedly built on previous exchanges within the SCTO network and will pave the way for future collaboration on clinical trials within the CTU network.

Figure 1



APPROVED AND ACTIVATED SITES:

1 Lausanne University Hospital (CHUV) : **Sponsor's representative in Switzerland and the study's coordinating site**

2 Kantonsspital Aarau

3 Kantonsspital Baden

4 Hirslanden Klinik Aarau

5 University Hospital Basel

6 Geneva University Hospitals (HUG)

7 Solothurner Spitäler AG, Kantonsspital Olten

8 Solothurner Spitäler AG, Bürgerspital Solothurn

9 Réseau hospitalier neuchâtelois Neuchâtel

10 Spital Thurgau AG, Kantonsspital Frauenfeld

11 Spital Thurgau AG, Kantonsspital Münsterlingen

12 Hôpital fribourgeois Fribourg

13 Hôpital Riviera-Chablais Rennaz

14 Hôpital du Jura Delémont

15 Hôpital du Valais Sion

16 Insel Gruppe AG, Inselspital Bern

17 Campus SLB, Lindenhofgruppe Bern

APPROVED BUT NOT YET ACTIVATED SITE:

18 Clinica Luganese Moncucco Lugano

CLINICAL TRIAL UNITS INVOLVED

Clinical Trial Unit Lausanne

Clinical Trial Unit Bern

Figure 2

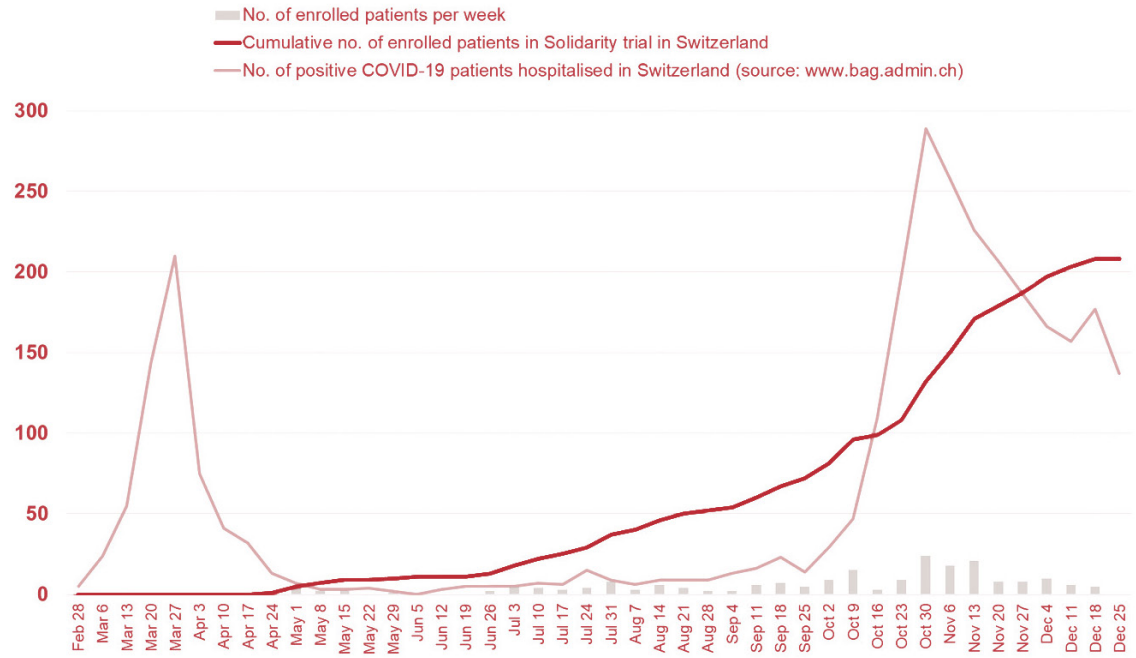


Table 1

Dates	Solidarity trial: Main milestones in Switzerland
16.03.2020	SNSF and FOPH contacted by WHO to initiate Solidarity feasibility study in Switzerland
25.03.2020	Teleconference organised by WHO to inform all interested Swiss investigators
26.03.2020	Dr Oriol Manuel (CHUV) chosen as national coordinating investigator; start of CTUs' involvement
02.04.2020	Study budget submission to SNSF
06.04.2020	Study budget pre-approval from SNSF
07.04.2020	Submission of Lausanne site to lead EC (EC Vaud)
08.04.2020	CHUV (Lausanne) designated as sponsor's representative in Switzerland according to FOPH–WHO agreement; initial submission to Swissmedic
09.04.2020	Official letter from SNSF granting budget for study conduct in Switzerland (*investigational medicinal products (**IMPs**) to be provided by WHO*); research service agreement involving CTU Lausanne signed
10.04.2020	Initial submission to Swissmedic; approval with conditions
14.04.2020	Submission of Lausanne site to lead EC; official feedback with questions
15.04.2020	Submission of Lausanne site to lead EC; final approval
21.04.2020	Initial submission to Swissmedic; final approval
21.04.2020	First patient enrolled (in Lausanne)
21.04.2020 to 28.04.2020	Submission of 16 additional local sites to lead and local ECs
23.04.2020 to 29.04.2020	Submission of 16 additional local sites to lead and local ECs; approval (with charges for some sites)
05.05.2020	Submission of 16 additional local sites to lead and local ECs; final approval
24.05.2020	Decision of WHO to suspend HCQ arm; communication to lead EC and Swissmedic on 24.05 and 25.05 respectively
04.06.2020	Decision of WHO to restart HCQ arm; request to restart with HCQ sent to Swissmedic (*which was not restarted, see below*)
18.06.2020 and 03.07.2020	Decision of WHO to definitively stop the three following arms: HCQ and LPV/r +/- IFN B1a; communication to lead EC and Swissmedic on 22.06 and 09.07 respectively
11.09.2020	Official submission to lead EC of amendment including two new arms: acalabrutinib (**ACA**) and IFN B1a (Lausanne first)
02.10.2020	Official submission to Swissmedic of amendment including two new arms: ACA and IFN B1a
15.10.2020	Decision of WHO to definitively stop the IFN B1a arm; communication to lead EC and Swissmedic on 20.10 and 22.10 respectively
26.10.2020	Official submission to lead EC of amendment including two new arms: ACA and IFN B1a (Lausanne first); approval of ACA only *(IFN B1a alone was never approved)*
11.11.2020	Official submission to Swissmedic of amendment including two new arms: ACA and IFN B1a; approval of ACA only *(IFN B1a alone was never approved)*
13.11.2020	Official submission to lead and local EC of amendment including ACA for all local sites plus one new site
13.11.2020	Decision of WHO to definitively stop ACA arm *(ACA was never started nor shipped to Switzerland)*; communication to lead EC and Swissmedic on 16.11 and 20.11 respectively
07.12.2020	Official submission to lead and local EC of one new site; approval with charges
18.12.2020	Patient recruitment put on hold due to RDV being sold out in Switzerland (208 enrolled patients); communication to lead EC and Swissmedic on 30.12.
07.01.2021	Official submission to lead and local EC of one new site; final approval
27.01.2021	Decision of WHO to definitively stop RDV arm

All treatments mentioned in this table were always submitted/approved in addition to the standard of care.

EU-RESPONSE

ECRIN'S AND THE SCTO'S ROLES AS COVID-19 FOSTERS INNOVATION AND CATALYSES COOPERATION AMONGST EUROPEAN CLINICAL RESEARCH ACTORS

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Uncoordinated and fragmented research activities were the scientific community's early reactions to the COVID-19 pandemic, with researchers planning and running many small stand-alone trials or observational studies of single-agent uses. In this article, we discuss actions that were taken by the European Clinical Research Infrastructure Network (**ECRIN**) and its national partner the Swiss Clinical Trial Organisation (**SCTO**) to address the issue of uncoordinated clinical research.

A LACK OF CLINICAL RESEARCH COORDINATION IN THE RACE FOR COVID-19 SOLUTIONS

One of the key instruments for addressing the COVID-19 outbreak is clinical research. At present, this includes clinical trials on drug repurposing and vaccines; in the future, it will focus on trials evaluating innovative treatments with novel designs. The clinical research community has shown tremendous activity over the past year and has initiated many repurposing trials supported by national and international funds.[1] It turns out that similar trials, addressing the same questions, are frequently run in parallel in multiple countries. This wastes time and resources that would be better used in well-designed multinational trials, and it raises ethical questions in respect of patients volunteering to participate.

Understandably, better coordination at the international level helps to avoid the fragmentation of clinical research capacity and leads to faster and more robust results. The world has reacted to the COVID-19 pandemic with calls for funding to accelerate research,[2] initiatives for coalitions for preparedness, the pursuit of cooperation across continents,[3] and – let us not forget – efforts to fast-track trial authorisation and publication as well as increase the transparency of research results.

ECRIN'S COVID-19 TASK FORCE

In March 2020, ECRIN established a COVID-19 task force with its national partners to ensure the preparedness of clinical trial units (**CTUs**) for COVID-19 trials and to combine and coordinate national initiatives to promote multinational rather than national trials. The task force continues to meet regularly and relies on actions carried out by members of ECRIN's national networks. Its efforts include networking with national funders, sponsors-investigators, and CTUs.

In addition, ECRIN launched the Clinical Research Metadata Repository to enable quick access to COVID-19 clinical research information and related data objects.[4] ECRIN's COVID-19 task force continues to update clinical trials literature reviews, COVID-19 funding calls, and databases on regulatory and ethical requirements, data protection, and fast-track approvals across Europe. Further outreach includes participating in the EU COVID-19 data hub operated by the European Molecular Biology Laboratory's European Bioinformatics Institute (**EMBL-EBI**) and assisting with the development of a COVID-19 clinical trial patient-level data-sharing platform (the European Open Science Cloud's EOSC-Life) that is compliant with the EU's General Data Protection Regulation (**GDPR**).

In the first half of 2020, hundreds of clinical trials were being conducted across Europe at the national level to test potential treatments of SARS-CoV-2; however, there was a marked absence of multinational clinical trials – except for the World Health Organization's (**WHO's**) Solidarity trial. ECRIN contacted the European Commission (**EC**) and promoted the idea of developing multinational, multi-arm platform trials to rapidly recruit patients and test multiple treatment options (see **Box 1**). This led to the EU-RESPONSE project, which is funded by the European Union and coordinated by the French National Institute for Health and Medical Research (**INSERM**).

EU-RESPONSE

In April 2020, the EC committed to developing instruments to help European countries and clinical researchers join forces, in particular by setting up a pan-European network for COVID-19 clinical trials to foster collaboration and coordination. In partnership with academic clinical research institutions across Europe, EU-RESPONSE (EUropean RESearch and Preparedness netwOrk for pandemics and emerging iNfectious diseaSEs) was approved for funding in July 2020 with funds from the EC's Horizon 2020 programme. The central activity in this network is the promotion of COVID-19 trial platforms in Europe that cover the various steps of disease progression. There is a growing consensus that multi-arm, multinational, adaptive platform trials[5] represent the most appropriate solution to test multiple interventions for a given medical condition and for disease outbreaks.[6]

EU-RESPONSE allows for the European expansion of ongoing studies, for example the DisCoVeRy and Solidarity trials, and the further expansion to many other European countries. Additionally, EU-RESPONSE allows a new multinational European adaptive platform trial to be built. This will be a flexible platform, providing a modular trial network that will enable most, if not all, European hospitals to participate at their preferred level of commitment. Hospitals will be able to run repurposing trials, assess combination strategies, and evaluate the efficacy and safety of new compounds on COVID-19.

The EU-RESPONSE project also includes a coordination module, led by ECRIN, with other EU-funded projects such as RECOVER and REMAP-CAP. This ensures complementarity and cooperation across all large European COVID-19 trials and improves their capacity to answer the needs of society through dialogue with the European Medicines Agency (**EMA**), national competent authorities, health technology assessment (**HTA**) networks, and industry partners. ECRIN will play a key role in reaching the objectives of the EU-RESPONSE project, and EU-RESPONSE complements the other tools available at ECRIN to help clinical researchers and national infrastructures in the battle against COVID-19.

THE SCTO'S CONTRIBUTIONS TO RESEARCH ACTIVITIES RELATED TO COVID-19

The EU-RESPONSE consortium brings together 21 partners from 13 EU countries, Norway, Switzerland, and Turkey. The SCTO is the project partner for Switzerland with observer status in ECRIN and plays a role in the realisation of the project's key objectives. The SCTO contributes to the project with expertise from its CTU network and with advice on trial design and protocol development, with statistical expertise, and with site support for the conduct of clinical trials. With its expertise in coordinating the WHO's Solidarity trial at 17 clinical sites in Switzerland, the SCTO's CTU network is in an excellent position. Moreover, the network is well-prepared to efficiently contribute to EU-RESPONSE and assure a smooth transition from current trials to upcoming EU-RESPONSE trials.

In addition to its participation in the EU-RESPONSE project, the SCTO's CTU network is actively supporting research activities related to the COVID-19 outbreak at CTU institutions. All CTUs in the network are either implementing changes for studies that are already underway, participating in COVID-19 tenders, or starting or supporting the performance of such studies.

BOX 1: WHAT ARE PLATFORM TRIALS?

Platform trials are a new type of clinical trial in which multiple interventions can be evaluated simultaneously against a common control group within a single master protocol. Platform trials are an extension of adaptive, multi-arm, multistage trial designs that allow for the evaluation of multiple interventions using interim evaluations and the addition of new interventions during a trial. Platform trials offer the flexibility of dropping ineffective arms early based on interim data and allow for the possibility of introducing new arms into a trial.

Based on a master protocol and subsequent amendments that open or close sub-protocols, platform trials allow continuous recruitment, randomisation, and the investigation of patients. Repurposed drugs, as well as new treatments or vaccines, can be tested without wasting time for trial approval and setup because just an amendment is needed. A common control arm lowers the number of patients who need to be recruited.

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[1] Janiaud P et al. (2020) The worldwide clinical trial research response to the COVID-19 pandemic – the first 100 days [version 2; peer review: 2 approved] F1000Research 9:1193. doi.org/10.12688/f1000research.26707.2
[2] See the EMA's press release from 19 March 2020 calling for pooling research resources.
[3] See the EMA's press release from 15 May 2020 on the need for international coordination to encourage large, relevant COVID-19 clinical trials.
[4] The Clinical Research Metadata Repository provides information on many other disease areas as well.
[5] Woodcock J and LaVange LM (2017) Master protocols to study multiple therapies, multiple diseases, or both. New England Journal of Medicine 377:62-70
[6] Dean NE et al. (2020) Creating a framework for conducting randomized clinical trials during disease outbreaks. New England Journal of Medicine 382:14

Can we speed up coronavirus vaccine development? A human challenge study, in which volunteers would be deliberately infected with coronavirus, could help in theory. In this article, two collaborators from the CTU Geneva explore the potential benefits and the risks associated with SARS-CoV-2 challenge studies.

HUMAN CHALLENGE STUDIES IN THE TIME OF COVID-19: PROS AND CONS

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COVID-19 poses an extraordinary global health menace for which new pharmacological therapeutics and vaccines are urgently needed. According to the World Health Organization's COVID-19 dashboard, as of 21 February 2021, severe acute respiratory syndrome coronavirus 2 (**SARS-CoV-2**) has led to over 110 million confirmed cases of COVID-19 and over 2.4 million deaths worldwide. Clinical trials have helped to find treatments, but just three therapeutics have been approved to treat COVID-19 so far: dexamethasone in the United Kingdom and Japan; Avigan (favilavir) in China, Italy, and Russia; and Veklury (remdesivir) in the United States, Japan, and Australia.[1] Since July 2020, Veklury has had a conditional marketing authorisation in Europe and it has also received a temporary authorisation in Switzerland, where the Swiss Agency for Therapeutic Products (**Swissmedic**) has decided to allow its temporary distribution to COVID-19 patients beyond those in clinical trials (see Swissmedic's website). However, none of these treatments are preventing people from getting sick and needing hospital care.

The best way to protect people's health is an effective vaccine. Among the hundreds of COVID-19 vaccines being developed around the world (Le et al. 2020), several have reported promising initial data, with some receiving authorisation for use and becoming available in some countries. But we are only at the beginning of vaccine development, and much work remains.

[1] See article posted on the Regulatory Affairs Professionals Society's website on 29 January 2021

COVID-19 HUMAN CHALLENGE STUDIES

In order to accelerate testing, researchers and institutions are exploring the feasibility and ethics of human challenge trials that could potentially support the development of vaccines and treatments to protect against SARS-CoV-2 infection. Human challenge trials deliberately expose healthy volunteers to infection in order to study diseases and test vaccines or treatments more quickly than a classical clinical trial. They have been used to understand and fight diseases such as influenza, malaria, typhoid, and dengue fever, and they have helped facilitate the licensing process of vaccines for cholera (Killingley et al. 2011; Haney et al. 2017).

One of the first COVID-19 human challenge studies will soon begin at the Royal Free Hospital in London since it has received final regulatory and ethical approval. In its first phase, researchers will try to identify a suitable dose of the virus SARS-CoV-2 that causes infection in healthy young people (aged between 18 and 30 years old). In a later phase, a vaccine candidate could be given to a group of healthy adults, who would then be exposed to the virus in a controlled environment. They would be closely monitored to see if the vaccine is successful in preventing infection and to identify any side effects (Kirby 2020).

PROS AND CONS OF HUMAN CHALLENGE STUDIES

Human challenge studies can speed up vaccine development, as it is easier to measure the effectiveness of a vaccine when participants are all exposed to the virus rather than waiting for natural exposure. A human challenge study takes months rather than years and involves fewer volunteers (usually around 25–100 people). In COVID-19 human challenge studies,[2] these rapid results will help researchers focus on the most promising vaccines, because it is not possible to conduct conventional large-scale phase 3 studies for all candidate vaccines.

Over 38,000 people have signalled their willingness to participate in COVID-19 human challenge studies,[2] and the UK government has invested 37.3 million euros to support such trials. However, purposefully infecting healthy volunteers with the virus SARS-CoV-2 raises ethical concerns, in part due to the unclear and developing risks of COVID-19. Previous human challenge trials involved diseases for which there was an extremely low risk of death or an approved rescue treatment. By contrast, COVID-19 has a significant mortality rate and there is no effective cure. Further, there is growing evidence that SARS-CoV-2 infection can cause long-term disabilities, as demonstrated by people experiencing "long COVID" (BMJ 2020). Some studies show that these sequelae can affect asymptomatic carriers and low-risk demographic groups. Based on these considerations, COVID-19 human challenges not only fail to provide any direct benefit for participants but also contradict the principle of non-maleficence. Besides objections for ethical reasons, scientific and practical limitations of the challenge model must also be considered. Since a challenge trial would include only young and healthy participants, the resulting data would not necessarily be generalisable to more vulnerable groups, such as older people or those with other health conditions.

Some vaccines, such as Oxford, Moderna, or Pfizer, have already received authorisation for use and vaccination has started in some countries. Therefore, challenge trials will not actually help accelerate the current vaccine development timeline. However, even if these trials do not accelerate the development of the first vaccines, they may be important for second-generation vaccines. Second-generation vaccines are important because they will be needed to vaccinate people in low- and middle-income countries. In addition, they could potentially be administered orally, not require a booster, have fewer cold chain requirements, and cause fewer side effects. Challenge studies could also be key to studying how long immunity lasts (both from a vaccine and natural infection) and the extent to which infection by one strain is protective against another.

CONCLUSION

In conclusion, COVID-19 human challenge studies could accelerate vaccine development by helping to test multiple candidate vaccines. However, further discussion is needed to address critical issues. Consultation with scientists, research ethics committees, regulators, and potential volunteers will help to determine what degree of risk is acceptable and compensated by the estimated benefits.

[2] Updated regularly on 1Day Sooner's website.

COMMENT

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There is perhaps an ethical and methodological argument to make for human challenge studies, but only under certain conditions. As outlined in the article, they should be employed for infections whose scope and duration of clinical manifestations are well established and for which highly effective rescue therapy exists. SARS-CoV-2 infection clearly does not fulfil these criteria. In addition, human challenge studies should be used only for infections that are expected to cause an actual clinical illness in volunteers and that are not already occurring at high frequency in the community.

The catch-22 of human challenge studies for SARS-CoV-2 is that, for ethical reasons, these trials must include volunteers who are relatively young and have no baseline medical conditions. These people are, however, the very ones in whom a SARS-CoV-2 infection is likely to be paucisymptomatic or asymptomatic. Therefore, clinical endpoints cannot be relied upon. While purely virological endpoints could be used instead (e.g. daily nasopharyngeal swabs for comparative viral kinetics), the vaccine's *clinical* effectiveness would remain poorly characterised. Regulatory approval requires more than virologic efficacy, as it should, given that severe COVID-19 appears to be driven primarily by the host's dysregulated cytokine responses and not upper respiratory viral replication per se.

There is a good deal of irony in performing a human challenge trial for a virus that is likely to produce few clinical events in its volunteers but is circulating and causing significant clinical morbidity and mortality in non-volunteers at the same time. Indeed, the high baseline prevalence of SARS-CoV-2 infections contradicts a key argument for human challenge trials: that induced infection is necessary because natural incidence is so low that thousands of trial participants would be necessary to observe just a few clinical events.

Given these paradoxes, recommending a human challenge study for SARS-CoV-2 remains a formidable challenge.

* The views expressed in this text are those of the author and do not necessarily reflect the position of the CTU Geneva.

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HEADLINES AND HAPPENINGS

SWITZERLAND

SWISS CLINICAL TRIAL ORGANISATION (SCTO)

- **DECEMBER 2020**
  - » **Federal government confirms 2021–2024 funding for the SCTO and its Clinical Trial Unit (CTU) network.** In its press release of 21 December 2020, the Department of Economic Affairs, Education and Research announced the government's funding contributions to research institutions of national importance for the years 2021–2024. The government's funding includes contributions to the SCTO's projects, including its CTU network and the Swiss Research Network of Clinical Pediatric Hubs (**SwissPedNet**) DE EN FR.

- **NOVEMBER 2020**
  - » **Update on COVID-19 and how the CTUs in the SCTO's network are involved** EN.

FEDERAL OFFICE OF PUBLIC HEALTH (FOPH)

MEDICAL DEVICES

- **NOVEMBER 2020**
  - » **Update on EU developments related to medical devices.** This report details the latest developments on implementing and delegated acts and guidelines, on the EUDAMED IT system, and on the designation of notified bodies EN.
    Source: FOPH

- **DECEMBER 2020**
  - » Publication of a summary of the annual reports of the **ethics committees** EN **and a statistical report on human research in Switzerland in 2019** EN on kofam's website.

SWISSETHICS

COVID-19

- **DECEMBER 2020**
  - » Publication of the **updated Joint Guidance of Swissmedic and swissethics on the Management of Clinical Trials with Medicinal Drug Products in Switzerland during the COVID-19 Pandemic (version 2.4)** EN.

- **FEBRUARY 2021**
  - » **Publication in *Jusletter* of an analysis of human research, further use, and informed consent.** In 2020, swissethics was mandated by the FOPH, Human Research Section, to prepare a structured analysis of the further use of health-related personal data and biological material and the application of article 34 of the Human Research Act (**HRA**). The study provides for the first time an in-depth insight into further use research in Switzerland since the introduction of the HRA DE.
  - » Publication of an article entitled **Research Projects in Human Genetics in Switzerland:** Analysis of Research Protocols Submitted to Cantonal Ethics Committees in 2018 EN.

- **DECEMBER 2020**
  - » Publication of **recommendations on gender-sensitive research** DE FR.
  - » Publication of a **guidance document on the use of foodstuffs and dietary supplements in research**. These products could be classified as investigational medicinal products (**IMP**) according to the Ordinance on Clinical Trials in Human Research (**ClinO**), in which case they would have to be made according to good manufacturing practice (**GMP**) and be submitted to an ethics committee and Swissmedic EN.

- **FROM DECEMBER 2020**

Updates to the following documents:

- » a template for the notification of the completion or discontinuation of a clinical trial or research project EN
- » a template for Human Research Ordinance (**HRO**) projects with persons, according to HRA/HRO chapter 2 DE FR IT
- » a template for writing the study information for relatives/parents/legal representatives according to ClinO DE FR IT
- » a template for writing the study information for relatives/parents/legal representatives according to HRO DE FR IT
- » a template for a patient information/informed consent for the collection of biological material according to HRA/HRO art. 8 DE FR IT
- » a summary of the annual reports of the ethics committees DE EN FR IT and a statistical report on human research in Switzerland in 2019 EN.

SWISSMEDIC

- **JANUARY 2021**
  - » Publication of a statement from the International Coalition of Medicines Regulatory Authorities (**ICMRA**) on "**regulatory reliance**". This statement encourages stakeholders to support each other in their activities. Swissmedic applies such reliance [EN].

CLINICAL TRIALS

- **DECEMBER 2020**
  - » **Notifications and reporting on ongoing clinical trials.** All correctly submitted notifications/reports (VO-Form Reporting Related to a Clinical Trial; ClinO art. 37, 38, and 43) on an ongoing clinical trial will be silently acknowledged with immediate effect. When making a trial submission, a red binder needs to be used [DE EN FR IT].

COVID-19

- **DECEMBER 2020**
  - » Publication of the **updated Joint Guidance of Swissmedic and swissethics on the Management of Clinical Trials with Medicinal Drug Products in Switzerland during the COVID-19 Pandemic (version 2.4)** [EN].
  - » Publication of a statement from the International Coalition of Medicines Regulatory Authorities (**ICMRA**). The ICMRA recommends **continued follow-up of study subjects in clinical trials of the SARS-CoV2 vaccine** [EN].
  - » **Updated statement from the Access Consortium on COVID-19 vaccines evidence**, including the United Kingdom's Medicines and Healthcare products Regulatory Agency (**MHRA**) [EN].

- **NOVEMBER 2020**
  - » **Publication of updated inspection aspects during the COVID-19 pandemic** in consideration of the strain that COVID-19 is placing on the healthcare system [DE EN FR IT].

- **OCTOBER 2020 TO FEBRUARY 2021**
  - » **Swissmedic started rolling reviews of COVID-19 vaccines and authorised two vaccines –** from Pfizer/BioNTech in December 2020 and from Moderna in January 2021. In order to educate people about COVID-19 vaccines, Swissmedic developed a series of explanatory videos. It also regularly published reports of suspected adverse reactions to COVID-19 vaccines.
    Source: Swissmedic

SWISS NATIONAL SCIENCE FOUNDATION (SNSF)

OPEN SCIENCE

- **NOVEMBER 2020**
  - » Publication of an **open science policy statement from the CHIST-ERA network**, in which the SNSF actively participates. This is the first multilateral declaration of its type in Europe [EN].
    Source: SNSF

SWISS ACADEMY OF MEDICAL SCIENCES (SAMS)

News from the Swiss Personalized Health Network (**SPHN**):

- **DECEMBER 2020**
  - » Publication of legal agreement templates for collaborative research [EN].

HEADLINES AND HAPPENINGS

EUROPE

EUROPEAN MEDICINES AGENCY (EMA)

- **JANUARY 2021**
  - » Publication of the document **Assent/Informed Consent Guidance for Paediatric Clinical Trials with Medicinal Products in Europe** EN.

- **DECEMBER 2020**
  - » Publication of the **EMA's network strategy for the next five years**. This document describes how regulators will continue to enabe the supply of safe of medicines in the face of developments in science, medicine, digital technologies, globalisation, and emerging health threats EN.

- **SEPTEMBER 2020**
  - » Publication of the **Big Data Steering Group's workplan for 2020–21** for making the best use of big data for public health EN.
  - » Publication of a **draft guideline on registry-based studies.** This guideline aims at improving the use of registry-based studies as a source of real-world evidence. The draft guideline was open for consultation until December 2020 EN.

COVID-19

The COVID-19 EMA pandemic Task Force is the main tool of the EMA and the European medicines regulatory network for enabling EU Member States and the European Commission to take quick and coordinated regulatory action during the pandemic. All developments can be seen on the EMA's website.

- **OCTOBER 2020**
  - » Publication of **extra transparency measures for COVID-19 vaccines and therapeutics** that have been approved or are under evaluation EN.

    Source: EMA's "COVID-19" web page

THE CLINICAL TRIALS REGULATION (EU) 536/2014 (CTR)

- **DECEMBER 2020**
  - » Announcement during an EMA Board meeting that the **EU Clinical Trials Information system (CTIS) will go live in December 2021**. The CTR will become applicable six months after the European Commission confirms the full functionality of the CTIS EN. The latest information on the CTIS can be found on the EMA's website.

EUROPEAN COMMISSION (EC)

- **DECEMBER 2020**
  - » Publication of a **valorisation policy making research results work for society** and engaging citizens to accelerate the use of research results to benefit all EN.

COVID-19

- **FEBRUARY 2021**
  - » Publication of the **updated Guidance on the Management of Clinical Trials During the COVID-19 Pandemic** (version 4). The key changes from version 3 are related to remote source data verification EN.
  - » Publication of **EU Research and Innovation Plan for Supporting Vaccine Development for COVID-19** EN.

- **NOVEMBER 2020**
  - » Publication of an updated document on EU research and innovation entitled **Preparedness and Response to Infectious Disease Outbreaks**. This document describes all EU initiatives that have been launched so far EN.

- **OCTOBER 2020**
  - » Update on the **EC's manifesto to maximise the accessibility of research results in the fight against coronavirus** EN.

    Source: EC's "Coronavirus research and innovation" web page

THE CLINICAL TRIALS REGULATION (EU) 536/2014 (CTR)

- **NOVEMBER 2020** Update of the CTR's draft Questions & Answers document to version 2.6.

THE GENERAL DATA PROTECTION REGULATION (EU) 2016/679 (GDPR)

- **FEBRUARY 2021** Publication of a study entitled Assessment of the EU Member States' Rules on Health Data in the Light of GDPR. The study reveals a fragmented approach in the way that health data processing for health and research is conducted in Member States. This can negatively impact cross-border cooperation for care provision, healthcare system administration, public health, or research EN.

HEADLINES AND HAPPENINGS

INTERNATIONAL

INTERNATIONAL COUNCIL FOR HARMONISATION OF TECHNICAL REQUIREMENTS FOR PHARMACEUTICALS FOR HUMAN USE (ICH)

- **NOVEMBER 2020**
  - » Publication of a reflection paper on advancing **patient-focused drug development.** This paper identifies key areas where incorporating the patient's perspective could improve the quality, relevance, safety, and efficiency of drug development and inform regulatory decision-making. Stakeholders were invited to provide comments by 7 March 2021, which the SCTO network has already done EN.

INTERNATIONAL COALITION OF MEDICINES REGULATORY AUTHORITIES (ICMRA)

During the COVID-19 pandemic, the ICMRA acts as a forum to support strategic coordination and international cooperation among global medicine regulatory authorities.

- **OCTOBER 2020**
  - » Collaboration among global regulators on the use during the COVID-19 pandemic of **observational studies and real-world data to understand the real-life benefits and risks of medicine**.
    Source: ICMRA's "COVID-19" web page

WORLD HEALTH ORGANIZATION (WHO)

The WHO is bringing together the world's scientists and global health professionals to accelerate the research and development process as well as to develop new norms and standards to contain the spread of the coronavirus pandemic. Regularly updated information on research developments and guidance can be found on the WHO's website, for example:

- » a draft landscape and tracker of COVID-19 candidate vaccines
- » COVID-19 living map of ongoing research
- » COVID-19 living synthesis of study results
- » regulatory updates on COVID-19.

- **DECEMBER 2020** Publication of the report Feasibility, Potential Value and Limitations of Establishing a Closely Monitored **Challenge Model of Experimental COVID-19 Infection and Illness in Healthy Young Adult Volunteers** EN and a report on human challenge studies EN.

US FOOD AND DRUG ADMINISTRATION (FDA)

- **FEBRUARY 2021**
  - » Publication of **FDA policies to guide medical product developers addressing virus variants** EN.

- **NOVEMBER 2020**
  - » Publication of the final **FDA guidance on research participants' certificates of confidentiality.** This guidance aims to protect clinical trial participants from whom sensitive information has been collected from disclosure EN.
  - » **Publication of the final FDA guidance entitled Enhancing the Diversity of Clinical Trial Populations** EN.

EVENTS AND PUBLICATIONS

Events

Symposium: Medical Devices: Lost in Translation?
Organised by the SCTO in collaboration with the Bern University Hospital, the University of Bern, and the Swiss Institute for Translational and Entrepreneurial Medicine.
Bern, 8 June 2021 (rescheduled)

D|A|CH Symposium
Tri-national congress on clinical trials in Germany, Austria, and Switzerland (in German only).
Salzburg, 20–21 September 2021 (rescheduled)

Note: Events might be rescheduled or cancelled due to developments in the COVID-19 pandemic.

Books and publications

- **Zaninelli M and Paarlberg R (2021 Jan 8)** Clinical trial disclosure and data transparency: Obligation or opportunity? Applied Clinical Trials online EN.
- **Mauri K (2021 Jan 5)** Clinical trial evolution: The drive to update ICH E6. Applied Clinical Trials online EN.
- **Guinchard M, Warpelin-Decrausaz L et al. (2021)** Informed consent in critically ill adults participating to a randomized trial. Brain and Behavior 11e01965 (first published 3 Dec 2020). doi:10.1002/brb3.1965 EN. The 2014 update of the Swiss law on research increases patients' protection. It adds specific requirements for emergency situations, implying an active search for patients' wishes regarding research participation. The possibility of consent waivers is not clearly stated. This article explores the law's practical impact in a randomised controlled trial (RCT) on critically ill adults.
- **Kadakia K et al. (2020 Oct 8)** US Food and Drug Administration support for oncology drug development during COVID-19. JAMA Oncology online. doi:10.1001/jamaoncol.2020.4975 EN. This article reviews which regulatory flexibiity measures applicable during the emergency period could be incorporated into a routine period.

ABBREVIATIONS

ACA: acalabrutinab
CHUV: Lausanne University Hospital
ClinO: Ordinance on Clinical Trials in Human Research
COVID-19: Coronavirus disease 2019
CTIS: Clinical Trials Information System
CTR: Clinical Trials Regulation (EU) 536/2014
CTU: clinical trial unit
DKF: Department of Clinical Research at the University Hospital Basel
EC: European Commission
EC: ethics committee
ECRIN: European Clinical Research Infrastructure Network
EMA: European Medicines Agency
EMBL-EBI: European Molecular Biology Laboratory's European Bioinformatics Institute
EOSC: European Open Science Cloud
EPF: European Patients Forum
EU-RESPONSE: EUropean RESearch and Preparedness netwOrk for pandemics and emerging iNfectious diseaSEs
EURODIS: Rare Diseases Europe
FDA: US Food and Drug Administration
FOPH: Federal Office of Public Health
GCP: good clinical practice
GloPID-R: Global Research Collaboration for Infectious Disease Preparedness
GDPR: General Data Protection Regulation
GMP: good manufacturing practice
GVP: good pharmacovigilance practices
HCQ: hydroxychloroquine
HRA: Human Research Act
HRO: Human Research Ordinance
HTA: health technology assessment
HUG: Geneva University Hospitals
ICH: International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
ICH GCP: International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use Guideline for Good Clinical Practice
ICMRA: International Coalition of Medicines Regulatory Authorities
IFN B1a: interferon beta-1a
IIT: investigator-initiated trial
IMP: investigational medicinal product
INSERM: French National Institute for Health and Medical Research
LPV/r: lopinavir/ritonavir
MHRA: Medicines and Healthcare products Regulatory Agency
NRP 78: National Research Programme "Covid-19"
RA Platform: Regulatory Affairs Platform (SCTO)
RCT: randomised controlled trial
RDV: remdesivir
SAE: serious adverse event
SAKK: Swiss Group for Clinical Cancer Research
SAMS: Swiss Academy of Medical Science
SARS-CoV-2: severe acute respiratory syndrome coronavirus 2
SCTO: Swiss Clinical Trial Organisation
SERI: State Secretariat for Education, Research and Innovation
SNCTP: Swiss National Clinical Trials Portal
SNSF: Swiss National Science Foundation
SPHN: Swiss Personalized Health Network
SPO: Swiss patient organisation
Swissmedic: Swiss Agency for Therapeutic Products
SwissPedNet: Swiss Research Network of Clinical Pediatric Hubs
USB: University Hospital Basel
WCG: WIRB-Copernicus Group
WHO: World Health Organization

REGULATORY AFFAIRS WATCH

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The *RA Watch*'s Readers' Corner is available online

We cordially invite all readers to send us comments and opinions on our selected topics and articles to share with our community of readers. Please submit your comments and suggestions to the *RA Watch* Editor, who reserves the right to review each comment prior to publishing it.

Read more about the Regulatory Affairs Platform https://scto.ch/en/network/scto-platforms/regulatory-affairs

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 regulatory authorities in Switzerland, Europe, and the USA; ICH and WHO; the major Swiss academic organisations and health associations; and professional associations.*
- *Additionally, we review major clinical research journals.*