Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

COVID-19 kick-starts a new era for clinical trials and pandemic preparedness in Europe

In their Personal View on the European clinical research response to COVID-19, Herman Goossens and colleagues[1] provide relevant recommendations for a future perspective for the pandemic research response. As a European public funder, we add complementary views below.

To address research questions posed by infectious disease threats more swiftly, the European Commission developed specific provisions in its annual work programmes for health research, allowing for mobilisation of research funds in case of public health emergencies. The first such call in response to the COVID-19 pandemic—guaranteeing fair competition for the award of public funds—was made on Jan 30, 2020.[2] Because researchers were given no more than 13 days to prepare proposals, they were allowed to be less elaborate than usually expected under Horizon 2020 rules. These challenging timelines reflect the urgency of the pandemic response. Project costs were eligible for reimbursement as of Feb 13, 2020. Grant agreements included dedicated provisions for open access to research data, in line with Horizon 2020 provisions for grants awarded in public health emergencies.

The ERAvsCORONA action plan[3] committed to support large EU-wide clinical trials for clinical management of patients with COVID-19. Therefore, Horizon 2020 funds were rapidly mobilised to increase funding for the REMAP-CAP trial, and two additional trials were funded through the EU-RESPONSE project. This enabled the European expansion of the French-initiated DisCoVeRy trial and the establishment of a new platform trial, EU-SolidAct.

Coordination of trials is essential and targeted mechanisms were successfully established for this purpose. The trial coordination board facilitates structural dialogue between coordinators of EU-funded and other adaptive platform trials to ensure cooperation and synergy. The joint access advisory mechanism ensures scientific assessment of candidate treatments with regard to their suitability for these EU-funded trials. Efforts are being made to overcome the hurdles encountered during the COVID-19 pandemic for the swift implementation of large-scale clinical trials of complex design across multiple countries.[4] It is hoped that this will improve preparedness for both future epidemic or pandemic waves of COVID-19 and other diseases.

The COVID-19 pandemic has opened significant opportunities for strengthened preparedness in Europe and beyond. Synergies between COVID-19 pandemic response initiatives and others—such as Ecraid—need to be sought.[1] Solutions are needed to enable complex and multicountry adaptive platform trials and to expedite their implementation or reorientation across the globe. Successful initiatives should be anchored sustainably in Europe's future pandemic preparedness. The European Health Emergency Response Authority and the European Research and Innovation Partnership for Pandemic Preparedness are intended to provide the suitable framework for this purpose for Europe, while remaining open to the world, including through other partnerships.

We declare no competing interests.

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Herman Goossens and colleagues[1] call for structures and partnerships to enable clinical research and identify regulatory hurdles among the challenges for clinical trials. As European regulators, we acknowledge the need to optimise the clinical trials environment in Europe. Here, we outline tools to address the challenges and highlight a new EU initiative, Accelerating Clinical Trials in the EU (ACT EU), that will enable faster, bigger, and more robust clinical trials.

From Jan 31, 2022, onwards, the way in which clinical trials are conducted in the EU will substantially change due to the application of the clinical trials regulation (CTR) number 536/2014.[2] The authorisation of clinical trials will remain a member state competence, but the new legal system sets up a robust and agile assessment procedure, increases transparency, and streamlines and reinforces safety monitoring.[3] The clinical trials information system will serve as a single entry point for applications. The CTR introduces the concept of low-intervention trials and includes further possibilities for risk adaptations, including no additional labelling for authorised medicines (Article 67 of the CTR) and targeted safety reporting.

In April, 2020, the European Commission, together with the European Medicines Agency (EMA) and Heads of Medicines Agencies (HMA), published a guidance[4] with regulatory flexibilities and simplifications for the rapid authorisation of COVID-19

For the **EU-RESPONSE project** see https://eu-response.eu/

trials and to support ongoing trials. Flexibilities include the possibility for remote monitoring and verification, and direct shipment of investigational medicines to patients.

The EMA emergency task force (ETF) was activated early in the COVID-19 pandemic. In addition to being responsible for the rolling review of marketing authorisation applications for COVID-19 vaccines and therapeutics, the ETF also provides expedited scientific advice free of charge for COVID-19 trials. In early 2022, the competence of EMA ETF will be extended[5] to include support for cooperation between sponsors to enable large-scale platform trials in public health emergencies.

As part of the global effort to deliver more effective clinical trials, European regulators are contributors to the ongoing revision of the International Conference on Harmonisation Good Clinical Practice and support the work within the International Coalition of Medicines Regulatory Authorities to facilitate the international acceptability of large-scale platform trials.

In January, 2022, the European Commission, EMA, and HMA launched ACT EU to transform how clinical trials are run.[6] Under ACT EU, we commit to modernise clinical trial methods and oversight and bring together the clinical research stakeholder community through a series of multi-stakeholder workshops that will focus on enabling more effective clinical trials involving researchers across Europe, benefitting from the EU's rich biomedical research potential. Working together, we believe we can invigorate the clinical trials environment in the EU for the benefit of patients and to improve knowledge and innovation.

We declare no competing interests.

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Defining post-COVID condition

Joan B Soriano and colleagues[1] proposed a clinical case definition for post-COVID-19 condition. We thank this WHO-led working group for their efforts to provide an operational definition for this emerging, challenging condition.

Similar to previous statements by the Centers for Disease Control and Prevention[2] and the National Institute for Health and Care Excellence,[3] the criterion "SARS-CoV-2 laboratory confirmation" was not included in the definition proposed by this working group. There are some compelling reasons supporting this perspective. A post-COVID-19 condition can affect people who have only minor, non-specific or even no symptoms during the acute phase of the infection. Such cases are not regularly tested for SARS-CoV-2. Additionally, there has been inadequate access to testing in low-income and middle-income countries (LMICs). People also avoid testing for fear of the consequences of a positive result. Furthermore, if done late, tests can become negative, making a retrospective diagnosis unfeasible.

Although a clinical definition without laboratory confirmation increases sensitivity (allowing more affected people to receive care), it comes with a trade-off with specificity. Hence, a stricter definition might be required for research purposes and comparison between different settings.

The WHO Delphi exercise had relatively few participants from Africa, South America, and southeast Asia. Although we cannot say that having a more global presence would have changed the definition, this underrepresentation of LMICs might be associated with the lack of ongoing research about this condition in low-income countries. We suggest that such research is urgently needed. For example, the COVID-19 pandemic caused an unprecedented amount of stress for people in LMICs.[4] Still, the full scale of mental health issues related to post-COVID-19 condition remains undetermined.

One of the criteria in the proposed definition is that "symptoms cannot be explained by an alternative diagnosis". Fulfilling the criterion might also be difficult in LMICs, where additional diagnostic testing might not always be available. Here, once again, health services might need to move on with diagnostic criteria, while rigorous studies inform and refine future definitions. The commission was open to consider such changes in the future. On behalf of the clinical epidemiology