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.

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Letter to the Editor

Re: Accelerating clinical trial implementation in the context of the COVID-19 pandemic by Diallo et al

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To the editors,

The European Commission appreciates the importance of large, multinational clinical trials to generate robust and reliable data to support rapid regulatory and public health decisions. In line with the ERA versus CORONA action plan [1], significant Horizon 2020 funding was mobilized for the establishment of a European Union (EU)-wide clinical trial network for coronavirus disease 2019 (COVID-19) therapeutics, including trial implementation.

In their commentary entitled "Clinical trial implementation in the context of the COVID-19 pandemic: Challenges, lessons learned and recommendations from DisCoVeRy and the EU SolidAct and the EU response group" [2], Diallo et al. list regulatory, legal, and financial hurdles that these trials have encountered. Additional information herein puts their concerns in perspective.

The authorization of clinical trials is a Member State competence, and the Commission's remit is to ensure the implementation of Clinical Trials Regulation (CTR) 536/2014 (applicable on 31 January 2022) and Clinical Trial Directive 2001/20. Reasons for delays in trial authorizations may be multiple, related to the assessment procedure, the completeness of the submission, and to regulatory and Good Clinical Practice compliance. Expedited approvals can only be given for high-quality and fully compliant submissions.

The CTR reinforces coordination by requiring a single decision, involving national competent authority and ethics committees within strict timelines. It also requires Member States to cooperate in the assessment of multicountry trial applications and increases the transparency of clinical trial data, thus facilitating public scrutiny and increased research efficiency. Cooperation among Member States will be required in safety assessments in further support of clinical trial participant and patient safety. The CTR recognizes the importance of noncommercial trials and contains provisions for fee waivers by Member States.

Low-interventional trials are a new concept in the regulation for trials with a minimal exposure of participants to additional risk and inconvenience, using the medicinal product in accordance with its marketing authorization, or in an evidence-based manner underpinned by scientific publications. Although the off-label use of repurposed medicinal products to treat COVID-19 may not fit this definition, risk adaptations can be requested. Although not considered a low-interventional trial, the main difference is that the sponsor is required to have insurance to cover compensation for any damage suffered from participation in the trial.

EU support for COVID-19 clinical trials

With the shared interest in making Europe more attractive for the conduct of clinical trials, in particular COVID-19 trials during the ongoing pandemic, Commission services have provided concrete and comprehensive support for European COVID-19 trials, including the DisCoVeRy and EU SolidAct trials.

Communication between national regulatory bodies and trial coordinators was strengthened to enable the exchange of information on trial design and protocol, in support of the preparation of high-quality applications and to highlight available support options for COVID-19 trials. Dedicated exchanges with concerned authorities were organized to facilitate the national authorization phase after the voluntary harmonization procedure assessment for EU-SolidAct and in support of the national authorisations for DisCoVeRy.

The Commission has published an EU-level harmonized guidance [3] with necessary regulatory flexibilities and procedural simplifications for the rapid authorization of COVID-19 trials. We cannot overemphasize the importance of direct communication

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between trial sponsors and regulatory bodies early on in the preparatory process to support the preparation of high-quality applications.

The European Medicines Agency emergency task force includes regulators from both the European Medicines Agency and national authorities of the Member States concerned. It provides expedited scientific advice free of charge for all COVID-19 trials. This will be extended when the Health Union [4] package becomes applicable.

In line with the COVID-19 therapeutics strategy [5] highlighting the importance of "ensuring access to and swift approval of large-scale clinical trials in the EU", a joint action under the EU4Health programme [6] will support national regulatory bodies for expedited assessments for fast-track authorization of COVID-19 therapeutic trials.

Regarding the legal hurdles encountered, we welcome concrete suggestions from sponsor organizations on the development of a harmonized European site contract template, considering the diversity of national funding programs for health care services, as well as the broad diversity of the health care providers involved in clinical trials.

Significant European funding has been mobilized to support the pandemic response early on; the pre-existing multicountry REMAP-CAP trial could rapidly pivot to COVID-19 patients with virtually no funding interruption. Once the interest in expanding the DisCoVeRy trial beyond France became clear, Horizon 2020 funding was rapidly mobilized to make this possible and to establish a truly EU-wide platform trial. Even if the processing of European funding decisions, entailing significant budgets, has never been so short, we agree with the authors that national seed funding mechanisms may be more reactive. However, proper accountability to European taxpayers remains fundamental, even in a pandemic context.

Transparency declaration

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Author contributions

Both authors contributed equally to the preparation of this work.

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