

Reducing Bureaucracy in Clinical Trials – An ongoing call for action

Origins of the campaign

In February 2020, a group of clinical researchers published an article discussing the issues resulting from the exponential growth of regulatory and administrative requirements for the conduct of clinical studies and its impact on investigators and patients. The article brought up challenges related to safety reporting, informed consent forms, and regulatory guidance. It pointed out that excessive administrative burdens affect the quality and efficiency of studies and ultimately pose a risk to the safety of patients that enter a clinical trial. The investigators called on regulators, medical societies, and patient organisations to ensure structural involvement of patients and clinical researchers in the development of a roadmap towards patient-centric, bureaucracy-light clinical research¹. At the initiative of the European Hematology Association (EHA) a cross-disciplinary coalition of medical societies and patient advocates was formed which, in September of the same year, released a Coalition Statement² followed by a series of consensus-based recommendations in November 2021³. These **Coalition Recommendations for Reducing Bureaucracy in Clinical Trials** aim to mitigate the risks identified by investigators and patients, proposing a number of actions grouped in four different clusters: I. Safety Reporting, II. Informed Consent, III. Regulatory guidelines, and IV. Harmonisation of requirements across the EU.

Over-reporting

The impact of accumulating administrative burdens is best described by the trial investigators who face them on a daily basis and by the patients who struggle with the ‘consent bureaucracy’ and whose safety may not be optimally guaranteed when their clinicians struggle to manage excessive volumes of safety reports which threaten to drown out the real risks. The investigator will receive notifications on safety issues from the clinical research organisations (CROs) on a daily basis. Reports listing all Suspected Unexpected Serious Adverse Reactions (SUSARs) and Serious Adverse Events (SAEs) need to be read and signed by the investigator, a requirement that becomes particularly burdensome if the investigator is part of multiple trials. Dr. Jeanette Doorduyn, hematologist: *“I would like to see some responsibility going to sponsor and CRO. Filter relative safety issues that need to be reported to investigators, the SUSARs, and only send a report on all reported SAEs every three months or so, with a special part for SAEs that have not been reported before.”* This would ensure that the investigator knows what to look for and minimize the multiple pages of documentation received daily. In the current situation, as Dr. Doorduyn points out, *“The CROs or sponsors make no difference at all in SAEs and SUSARs. This [filtering relative safety issues] should be the task of their safety departments”*.

‘Over-informed’ and inadequate consent

From the perspective of a patient who enters a clinical trial and places his trust in the principal investigator by signing off on the informed consent form, the burden of bureaucracy lies in the fact that these forms are too long and contain too many complex formulations. Privacy and security terms resulting from legislation such as the General Data Protection Regulation (GDPR), or overly scientific

¹ Gribben J, Macintyre E, Sonneveld P, Doorduyn J, Gisselbrecht C, Jäger U, Le Gouill S, Rule S, Dreyling M. Reducing bureaucracy in clinical research: A call for action. *HemaSphere*, 2020;4:2. <http://dx.doi.org/10.1097/HS9.0000000000000352>.

² The Coalition for Reducing Bureaucracy in Clinical Trials. Reducing bureaucracy in clinical trials : now is the time!2021; Published online September 2021. <https://bureaucracyincls.eu/statement/>

³ Dreyling M, Fajardo-Moser M, Gisselbrecht, C, Wanner C, Bolanos N, Collen S, Giles R, Badreh S. Recommendations of the Coalition for Reducing Bureaucracy in Clinical Trials. 2021; Published online Nov 2021. <https://bureaucracyincls.eu/recommendations-2/>

terminology in descriptions of the molecule, drug, and safety risks, often seem designed as an insurance policy covering the legal liabilities of trial sponsors rather than to ensure that the patient understands what he or she has agreed to.

As a patient advocate Richard Mindham illustrates: *“Consent forms tend to be long and repetitive, with an apparent bias towards legal aspects rather than having a focus on imparting information to the patient about their possible involvement in a trial. The goal must be to provide patients with the information they need to participate in a trial without burdening them with legal complexity.”* Of course, patients need to be aware of the protections available to them in law, but this should not cloud the purpose of the trial nor patients’ engagement in it.” Mr. Mindham goes on to explain that *“many patients will come to a trial following a conversation with an investigator. Whilst they wish to be kept safe when they participate in a trial, the primary purpose of the consent form should be to confirm their understanding of the trial and to have something to discuss with family members”.* Even for patients with a high level of education they [the informed consent forms] can be difficult to understand and the willing patient needs to put in a lot of work to understanding them and this can be a discouragement to many”.

Over-interpretation of regulatory guidelines

The Coalition for Reducing Bureaucracy in Clinical Trials has collaborated with the Good Clinical Trials Collaborative (GCTC) since the latter was established in 2020. As part of two-way consultations and feedback, the Coalition provided input for the guidance document developed by GCTC. The two collectives also aligned their participation in discussions with the European Medicines Agency (EMA) and The International Council for Harmonisation (ICH), influencing the revision of ICH E6 Good Clinical Practice guidelines which set the international ethical and scientific quality standards for designing, conducting, recording, and reporting trials that involve the participation of human subjects⁴.

The Coalition’s impact has also extended to the guidance documents developed by the European Commission (EC) and National Competent Authorities on implementation of the Clinical Trials Regulation (CTR). Although the CTR⁵ was adopted as far back as 2014, it only entered into application in January 2022, after EMA had delivered the Clinical Trials Information System (CTIS). The Coalition advised the European Commission during its development of a Questions & Answers (Q&A) document on implementation of the CTR, which describes how to best conduct clinical trials and report safety issues but leaves open many questions around implementation. This fruitful interaction has helped ensure that the updated guidance now has clear sections on how to report safety issues, which documents should be registered, and on interpretation of legal requirements that previously might have been too difficult to understand⁴.

The investigators and sponsor can now draft the protocol in a way that prevents excessive reporting, a first step towards helping investigators such as Dr. Doorduijn and Dr. Marcela Fajardo-Moser, an investigator at University Hospital Würzburg, push back administrative burdens. Dr. Fajardo-Moser: *“Reducing bureaucracy in clinical trials goes hand in hand with a re-orientation on two prerequisites for cost-effective and conclusive clinical trials: the quality of study protocols and – this is key – never letting the patient out of focus. Better education of sponsors and investigators is needed on how to design streamlined study protocols that always focus on the well-being of the patients.”*

⁴ European Medicines Agency (EMA). ICH E6 (R2) Good clinical practice – Scientific guideline. 2016; Published online Dec 15. <https://www.ema.europa.eu/en/ich-e6-r2-good-clinical-practice-scientific-guideline#current-version--revision-2-section>.

⁵ European Medicines Agency (EMA). Clinical Trials Regulation. 2022; Published online Jan 31. <https://www.ema.europa.eu/en/human-regulatory/research-development/clinical-trials/clinical-trials-regulation>

EU-level harmonisation

In January 2022, the European Commission, the Heads of Medicines Agencies (HMA) and EMA launched an initiative to transform how clinical trials are initiated, designed, and run referred to as Accelerating Clinical Trials in the EU (ACT EU). The strategy paper published by ACT EU listed ten priority actions for 2022-2023 including, notably, enabling innovative trial methods, establishing a multi-stakeholder platform, and supporting the modernisation of good clinical practice⁶. The Coalition Recommendations in combination with the Coalition's constructive engagement with regulators and guideline developers has already contributed to increased awareness on the need for harmonized and simplified safety reporting, less ambiguous regulatory guidelines, simplified informed consent forms and the urgency of decreasing bureaucracy in clinical trials. In the process, the Coalition has positioned itself as a key stakeholder in the implementation of the CTR and modernisation of clinical trials generally, as the voice of academic investigators and patient advocates in Europe.

⁶ Heads of Medicines Agencies, European Commission, European Medicines Agency. Accelerating Clinical Trials in the EU (ACT EU). 2022; Published online Jan 31. <https://www.ema.europa.eu/en/human-regulatory/research-development/clinical-trials/accelerating-clinical-trials-eu-act-eu>