Reducing bureaucracy in clinical trials: now is the time!

Joint statement by medical societies and patient advocates

Over the last few years, clinical trials have become increasingly difficult and expensive to conduct, due in great measure to the disproportionate volume of bureaucratic demands involved. Direct consequences of the rising costs and complexity are the stagnation of clinical research in Europe, fewer academic clinical trials and limited accessibility to innovative treatments. [1] Crucially, excessive administrative demands limit the time that clinical researchers can dedicate to their patients, with potential negative consequences for the quality of studies and patient safety.

Medical associations and patient advocates across disciplines are calling for urgent actions to diminish bureaucratic burdens and move towards more patient-centered, risk-based, pragmatic, efficient and cheaper trials. In particular, solutions are needed for the following issues:

- **Inappropriate and counterproductive safety reporting**: conservative definitions of Suspected Unexpected Serious Adverse Reactions (SUSARs) and disproportionate reporting requirements – in particular by contract research organizations (CROs) – have led to an overwhelming volume of safety reports which prevents clinical researchers from identifying the truly important safety signals amid an unmanageable number of trivial queries and unfiltered notifications, thus posing a threat to patient safety.

- **Inadequate informed consent and re-consent:** Currently these documents are often lengthy, written in legal language and therefore difficult to understand. Instead, informed consent forms and re-consent procedures should be clear, accurate and limited to what is relevant for the patient. Ethics committees should see to it that consent forms serve their primary purpose – to inform the patient – and patients themselves should be involved in their design.

- **Overinterpretation of regulations and guidelines:** there is a pressing need to review and rewrite guidance documents (in particular ICH E6: Good Clinical Practice) to address textual ambiguity. Imprecise and vague texts leave the door open to overinterpretation of regulations, leading for instance to excessive on-site monitoring and increasing the cost of clinical trials disproportionately. There is widespread concern that potential overinterpretation of General Data Protection Regulation (GDPR) requirements will add to the administrative burden on researchers. Ultimately, GCP

[1] On the challenges facing clinical research see for instance Lacombe D et al., Clinical research in Europe: Who do we do all that for? *Journal of Cancer Policy*, March 2020 doi: 10.1016/j.jcpo.2020.100217; Rule S, LeGouill S. Bureaucracy is strangling clinical research, *BMJ*, March 2019 doi: 10.1136/bmj.l1097; Perez-Gracia JL, Awada A, Calvo E, et al. ESMO Clinical Research Observatory (ECRO): improving the efficiency of clinical research through rationalisation of bureaucracy, *ESMO Open*, May 2020 doi: 10.1136/esmoopen-2019-000662

guidelines need to be clear, concise, consistent and proportionate.[2]

To address these issues, a more flexible and adaptable regulatory environment is needed. It is unquestionable that safety and quality of clinical trials are paramount, yet this should not be used as an excuse to delay much-needed simplification measures.

A clear indication that quick and pragmatic adaptation of guidance is possible, without compromising either safety or quality, is the *Guidance on the Management of Clinical Trials during the COVID-19 (Coronavirus) pandemic* issued by European regulators on 31 March 2020[3]. The measures to make consent, (remote) monitoring and auditing easier and to facilitate the submission of large multinational trial protocols – although their impact may be offset in part by requirements to register each and every modification – have been widely welcomed by investigators and patients.

More structural and comprehensive measures are needed to overcome the disruption and deceleration of clinical research in Europe due to the accumulation of administrative demands that were visible long before the arrival of COVID[4]. We therefore welcome the plans for a thorough revision of the ICH E6(R3) guidelines on Good Clinical Practice. The involvement of patients and healthcare professionals from an early stage is promising, as are the signals that issues around safety reporting, informed consent, textual ambiguity and complexity will be addressed.

Europe's medical societies (many of them collaborating within the BioMed Alliance) and patient organizations stand ready and willing to assist the ICH and make this revision of GCP guidelines work.

Pushing back bureaucracy can only be done effectively if the rewriting of guidance is done in a way that reflects the broader need for advancing patient-centered, agile, risk-based clinical trials. Procedures and methods used to ensure GCP compliance should be proportionate to the risks and characteristics of a specific trial/treatment. Targeted guideline revisions need to contribute to a regulatory environment that puts the patient at the center of clinical research. Reducing bureaucracy and improving patient safety, trial quality, access and affordability go hand in hand.

This is a collective and urgent appeal by medical associations and patient advocates across disciplines to all involved – in particular, policymakers and regulators at EU and national levels, ethics committees and the pharmaceutical industry – to agree on risk-based pragmatic simplification measures to address the issues mentioned above. The shared goal must be a substantial reduction of bureaucratic obstacles in clinical trials, not (only) as a response to current exceptional circumstances, but on a permanent basis. What is at stake is the efficiency and affordability of clinical trials, and with it the quality of future health care and, ultimately and most importantly, patient safety.

[2] See also the objectives of the Good Clinical Trials Collaborative, https://wellcome.ac.uk/what-we-do/our-work/good-clinical-trials-collaborative

[3] European Commission, *Guidance on the Management of Clinical Trials during the COVID-19 (Coronavirus) Pandemic Version 3.* Available at https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-10/guidanceclinicaltrials_covid19_en.pdf (accessed 9 June 2020)

[4] Gribben J, et al. 'Reducing Bureaucracy in Clinical Research: A Call for Action', *HemaSphere*, March 2020 doi: 10.1097/HS9.0000000000000352

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*European Association of Nuclear Medicine (EANM)**

*European Association of Neurology (EAN)**

*European Association for the Study of the Liver (EASL)**

*European Association of Urology (EAU)**

*European Atherosclerosis Society (EAS)**

*European Cancer Organisation**

European Cancer Patient Coalition (ECPC)

*European League Against Rheumatism (EULAR)**

*European Organisation for Research and Treatment of Cancer (EORTC)**

*European Renal Association-European Dialysis and Transplant Association (ERA-EDTA)**

*European Respiratory Society (ERS)**

*European Society of Anaesthesiology (ESA)**

European Society for Blood and Marrow Transplantation (EBMT)

*European Society of Cardiology (ESC)**

*European Society of Endocrinology (ESE)**

*European Society of Intensive Care Medicine (ESICM)**

European Society for Medical Oncology (ESMO)

*European Society of Human Reproduction and Embryology (ESHRE)**

*European Society for Paediatric Gastroenterology Hepatology and Nutrition (ESPGHAN)**

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