

6 March 2017

ICH Secretariat
9, chemin des Mines
1211 Geneva 20
Switzerland

**RE: ACRO Comment Submission:
*ICH Reflection on "GCP Renovation": Modernization of ICH E8 and Subsequent
Renovation of ICH E6 (January 2017)***

Dear Sir/Madam:

The Association of Clinical Research Organizations (ACRO) represents the world's leading, global clinical research organizations (CROs). Our member companies provide a wide range of specialized services across the entire spectrum of development for new drugs, biologics and medical devices – from discovery, pre-clinical, proof of concept and first-in-man studies through post-approval and pharmacovigilance research. With more than 130,000 employees engaged in research activities around the world (including 57,000 in Europe), ACRO advances clinical outsourcing to improve the quality, efficiency and safety of biomedical research. Each year, ACRO member companies conduct more than 7,000 clinical trials involving 1.3 million research participants in over 100 countries. On average, each of our member companies works with more than 700 research sponsors annually.

ACRO thanks the ICH organisation for seeking comments on the January 2017 Reflection Paper and is pleased to provide this response to the consultation exercise. ACRO notes that the Reflection Paper proposes revision of the ICH E8 and E6 guidelines to address three key concerns; these concerns and ACRO's responses are briefly summarised as follows:

- Revision of ICH E8 to provide updated guidance that is both appropriate and flexible enough to address the increasing diversity of clinical trial designs and data sources that are being employed to support regulatory and other health policy decisions. ACRO supports this proposal with some qualifications.
- Revision of ICH E6 to recognize variations in the level of risk for participants in different types of trials and allow corresponding flexibility in managing the risks. Again, ACRO supports this proposal with some qualifications.
- Revision of ICH E6 to expand its scope in order to address more holistically the planning and conduct of clinical trials to support regulatory and other health policy decisions. ACRO does not support this proposal, which would extend the role of ICH beyond its stated mission "to make recommendations towards achieving greater harmonisation in the interpretation and application of technical guidelines and requirements for pharmaceutical product registration".

ACRO's detailed comments on these three points are presented below.

1. Revision of ICH E8 to provide updated guidance that is both appropriate and flexible enough to address the increasing diversity of clinical trial designs and data sources that are being employed to support regulatory and other health policy decisions.

ACRO welcomes and supports the proposed modernization of ICH E8 in order to incorporate the most current concepts achieving fit-for-purpose data quality as one of the essential considerations for all clinical trials. ACRO also agrees that ICH E8 should be updated to reflect the current and future diversity of study designs and data sources in order to maintain the classification of different types of clinical studies according to their objectives. However, in line with the stated mission of ICH "to make recommendations towards achieving greater harmonisation in the interpretation and application of technical guidelines and requirements for pharmaceutical product registration", ACRO considers that the guideline should continue to focus on studies intended to support product registration (see also point 3 below). Consequently, it is ACRO's view that, in updating the guideline to address design or planning considerations for data quality, these considerations should be focused on those clinical trial designs that are required for product registration and those patients -- including, their safety, wellbeing and rights.

2. Revision of ICH E6 to recognize variations in the level of risk for participants in different types of trials and allow corresponding flexibility in managing the risks

ACRO supports the principle that an important tool for ensuring human subject protection and high-quality data is a well-designed and well-articulated protocol, and therefore agrees with the proposal that the renovated E6 guideline should refer to the proposed-to-be-revised E8 guideline for a more comprehensive discussion of study quality considerations and relevant discussion and guidance in other ICH E guidelines.

ACRO also welcomes and supports the proposal that the renovated E6 guideline would include a focus on overarching principles, including key elements of human subject protection and data quality, using a risk-based approach to study oversight and monitoring. In addition, ACRO welcomes the Reflection Paper's footnote noting that a detailed chapter describing standards for Ethics Committees/ Institutional Review Boards, a chapter describing in detail standards for sponsors when designing, conducting, evaluating and reporting clinical trials, and a chapter describing the structure and content of Investigator Brochures and Clinical Trial Protocol will be maintained, with revision, and that reference to the activities of regulatory authorities for clinical trials should also be included. These are fundamental responsibilities that are not altered by study design.

ACRO supports the concept of the use of annexes to provide clarification on the application of the overarching principles to specific types of study and data source. However, ACRO is not convinced that the three annexes proposed in the Reflection Paper support this objective, as their proposed contents would not be mutually exclusive. For instance, a traditional interventional clinical trial may include some data from novel data sources. Additionally, the alternative data sources mentioned in the Reflection Paper do not include several sources that are currently in use in clinical trials. It is

ACRO's view that the recent ICH E6(R2) revision does not sufficiently address the implications of developments in information technology such as the use of electronic signatures, electronic informed consent, increased use of cloud computing systems, and the development and use of mobile apps and the use of "bring your own devices" for the collection of clinical trial data. ACRO therefore recommends that annexes on individual topics such as these (and others mentioned in the Reflection Paper, e.g. use of electronic health records) would be more useful than annexes based on a relatively arbitrary distinction of traditional interventional trials, non-traditional interventional trials and non-traditional trial designs, in order to establish clarity on these important aspects of good clinical practice in the current clinical trials environment.

3. Revision of ICH E6 to expand its scope in order to address more holistically the planning and conduct of clinical trials to support regulatory and other health policy decisions

As noted earlier, the mission of ICH is "to make recommendations towards achieving greater harmonisation in the interpretation and application of technical guidelines and requirements for pharmaceutical product registration". It is ACRO's view, therefore, that it is not appropriate to extend ICH guidance documents to cover a broader scope than pharmaceutical product registration in the absence of a full revision of the governing ICH remit. As the Reflection Paper itself notes, in order to accommodate this broader application, ICH would anticipate engaging others with the appropriate expertise. This is clear recognition that an increased scope would not make best use of the resources and expertise immediately available to ICH, and ACRO therefore recommends that the organisation should remain focused on its core mission. It has long been recognised by sponsors and investigators that the ICH E6 guideline establishes good clinical practice for the conduct of clinical trials for product registration purposes and that other internationally accepted guidelines should be followed when clinical studies are used for other purposes, e.g. the Guidelines for Good Pharmacoepidemiology Practices published by the International Society for Pharmacoepidemiology (ISPE). It is ACRO's view, therefore, that it is neither necessary nor desirable for ICH to venture into areas where it has neither the required expertise nor the remit to do so.

ACRO thanks the ICH for the opportunity to provide this comment on Reflection on "GCP Renovation": Modernization of ICH E8 and Subsequent Renovation of ICH E6. Please do not hesitate to contact ACRO if we can provide additional details or answer any questions at all.

Respectfully submitted,



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