Vision and Goals for the Work to Update E6(R3) GCP Guideline

The Continuum of Clinical Trial Design and Conduct

ICH E8 and ICH E6

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We Need to be Responsive to a Rapidly Evolving Ecosystem

Advancing Evidence Generation

Increasingly Digital World

Innovative Clinical Trial Designs
ICH E6 Good Clinical Practice: An Important Global Standard for Clinical Trial Conduct

ICH is inviting public review and comment on a reflection paper on Good Clinical Practice (GCP) “Renovation”, which contains the ICH proposal for further modernization of the ICH Guidelines related to clinical trial design, planning, management, and conduct. The scope of the proposed renovation includes the current E8 General Considerations for Clinical Trials and further revision to the E6 Guideline for Good Clinical Practice, which is already undergoing modernization with the recent production of ICH E6(R2).

The reflection paper is available for download via the following link:

- Reflection paper on GCP Renovation

The goal of the potential renovation is to provide updated guidance that is both appropriate and flexible enough to address the increasing diversity of study types and data sources that are being employed to support regulatory and other health policy decisions, as appropriate. The underlying principles of human subject protection and data quality would remain. ICH’s decision to invite stakeholder comment on the
Purpose of GCP Renovation

- Emphasise the role of achieving quality by good design and conduct
- Ensure that innovations in technology and design and facilitated and encouraged
- Ensure the involvement of all parties up front in study planning and conduct whenever appropriate (sponsors, patients, trial participants, investigators, healthcare professionals, regulatory agencies).
- Set the foundation for responsible and efficient clinical trial conduct
- Provide principles that remain relevant as technology, methods, and design evolve

This is about doing things differently – change –
We should not just add more to the status quo
Purpose of GCP Renovation (cont.)

- Establish a quality continuum throughout design and conduct
- Link to and emphasise ICH E8 focus on achieving quality by good design
- ICH E8 General Considerations on Clinical Trials and E6 GCP need modernising to prepare for the future –
  - future medicines, future trial designs, future technologies, future data sources
- Set the foundation for new study designs and conduct, technologies and data sources
ICH E8 General Considerations on Clinical Studies: Key aspects linking to ICH E6 GCP

• General Principles
  o Protection of clinical study participants
  o Scientific approach in clinical study design, conduct and analysis
  o Patient input into study design

• Designing Quality into Clinical Studies
  o Quality by Design of clinical studies
  o Critical to quality factors
  o Approach to identifying critical to quality factors
ICH E8 Quality of a clinical study

• Quality of a clinical study is … fitness for purpose.

• Purpose of a clinical study is to generate reliable information to answer the research questions and support decision making while protecting study participants. The quality of the information generated should therefore be sufficient to support good decision making.

• Quality by design … to ensure that the quality of a study is driven proactively by designing quality into the study protocol and processes.
  
  o use prospective, multidisciplinary approach to promote the quality of protocol and process design,
  
  o in a manner proportionate to the risks involved,
  
  o clear communication of how this will be achieved.
• Establishing a Culture that Supports Open Dialogue:
  - ... values and rewards critical thinking and open dialogue about quality ... beyond sole reliance on tools and checklists.

• Focusing on Activities Essential to the Study:
  - ... essential to the reliability and meaningfulness of study outcomes for patients ... safe, ethical conduct ... for study participants. Consider whether nonessential activities may be eliminated ... to simplify conduct ... improve efficiency ... target critical areas.
• Engaging Stakeholders in Study Design:
  o … best informed by input from a broad range of stakeholders, including patients and treating physicians. It should be open to challenge by subject matter experts and stakeholders from outside, as well as within, the sponsor organisation.

• Reviewing Critical to Quality Factors:
  o Build on accumulated experience and knowledge with periodic review of critical to quality factors to determine whether adjustments to risk control mechanisms are needed, since new or unanticipated issues may arise once the study has begun.
Involving Stakeholders in ICH GCP Renovation: Two-fold approach

- **Stakeholder engagement during the drafting process:**
  - Global Workshop on ICH E8 – Oct 2019
  - ICH E6 GCP stakeholder engagement plan
  - Regional Workshops on ICH E6 revision in June 2020
  - Regional Representatives of academic research engage with the ICH E6 GCP Expert Working Group – ongoing since August 2020

- **Stakeholder engagement is built into the revised ICH E8 – General Considerations on Clinical Studies guideline:**
  - Foresees involvement of patients in study design.
  - Including wide range of stakeholders in the design of the study and identification of what is critical to its quality.

Stakeholder involvement is essential, informative and enriching – it will lead to better guidance and better clinical trial designs, with better implementation of the processes and greatly improved results.
EWG is aware of the landscape

• Clinical trials are the cornerstone for evidence generation and ensuring that they are conducted responsibly and effectively is essential.

• It is a great responsibility to ensure that clinical trials are designed and conducted in a manner that respects the efforts and contributions of those participating in the trials, and in ways that address their needs.

• Clarity and focus on principles are important as innovative clinical trial designs are increasingly explored – decentralized trials and trials conducted in healthcare setting.

• Technology can be extremely helpful in making trials more efficient and it may enable those designing and conducting a trial to include relevant patient populations. However, the use of technology should be thoughtful and used to address specific issues. Such use should be customized to fit the purpose and design element of each trial.
Vision for ICH E6(R3) GCP

• GCP should be flexible to allow for and to encourage innovation, while helping ensure the protection of trial participants and reliability of trial results.

• GCP should help focus resources and efforts on what matters most for participant protection and the reliability of trial results – critical to quality factors.

• Focus on the intent and goal of GCP, and allow for the many ways these can be achieved.
Vision for ICH E6(R3) GCP (cont.)

- Comprehensive principles that remain relevant as technology evolve and clinical trial design advances
- Leveraging and facilitating an increasingly digital ecosystem
- Thoughtful process throughout clinical trial conception, design, conduct and analyses
Everyone involved in the conduct of clinical trials should read and understand these guidelines.

Change the way we all work – don’t add more to the status quo.

Change Management is the greatest challenge

– adjusting behaviors, attitudes – away from preconceived ideas and interests – and on to a new, better, way of working.

“Perfection is achieved not when there is nothing more to add but when there is nothing left to take away”  
Antoine de Saint-Exupéry

“Everything should be made as simple as possible but not simpler”  
Albert Einstein