EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Good Clinical Practice (E6/E8)

PCWP/HCPWP joint meeting

Presented by Fergus Sweeney on 3 March 2021
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ICH-E6(R3): Guideline for Good Clinical Practice EWG Meeting

Progress Update

Expert Working Group
November 12th, 13th, 16th, 17th, 19th, and 20th, 2020
Virtual meeting in place of the Athens EWG meeting

International Council for Harmonisation
of Technical Requirements
for Pharmaceuticals for Human Use

ICH-E6: An Important Global Standard for Clinical Trial Conduct

- **E6: Good Clinical Practice (GCP) – finalized in 1996**
- **Describes the responsibilities and expectations of stakeholders in the conduct of clinical trials**
- **GCP covers aspects of monitoring, reporting, and archiving clinical trials**
- **E6 (R2) – finalized in 2016**
- **Addendum to encourage implementation of improved and more efficient GCP approaches**
- **Updated standards for electronic records**

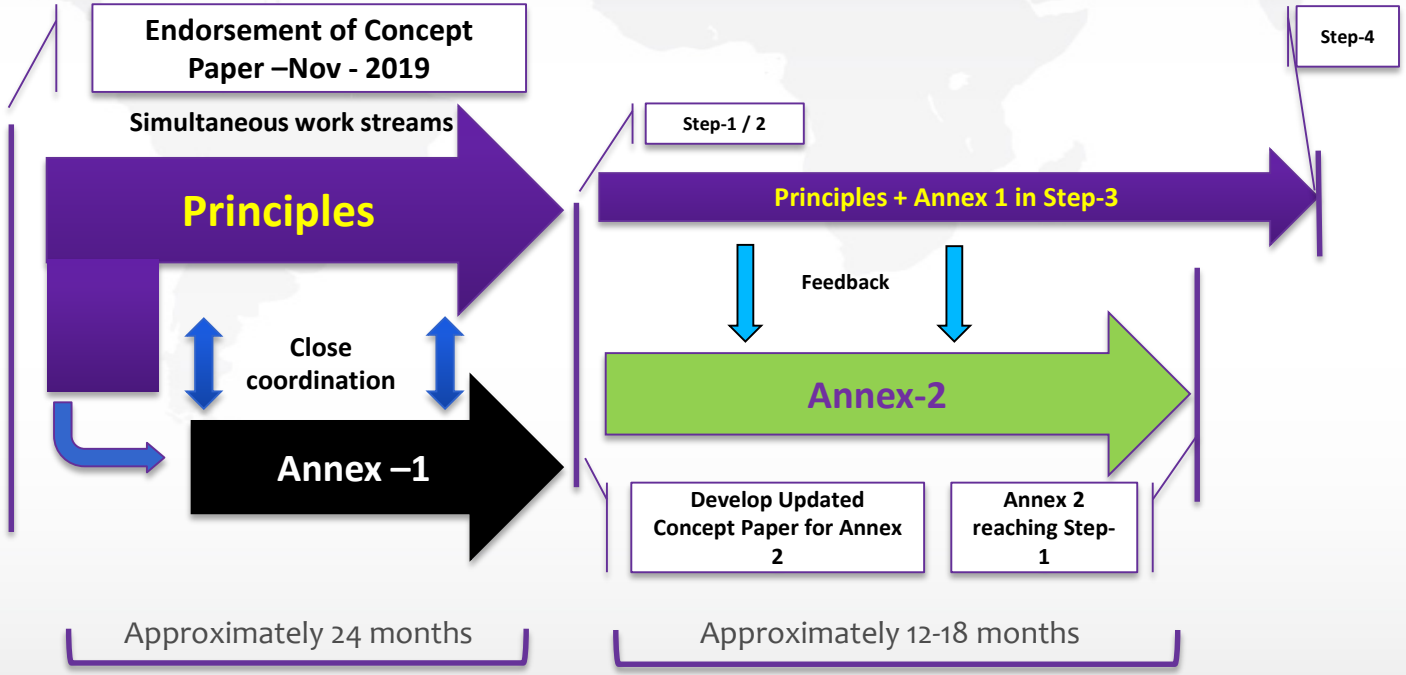
ICH E8 & E6
Connected Development

E8 clinical trial design principles

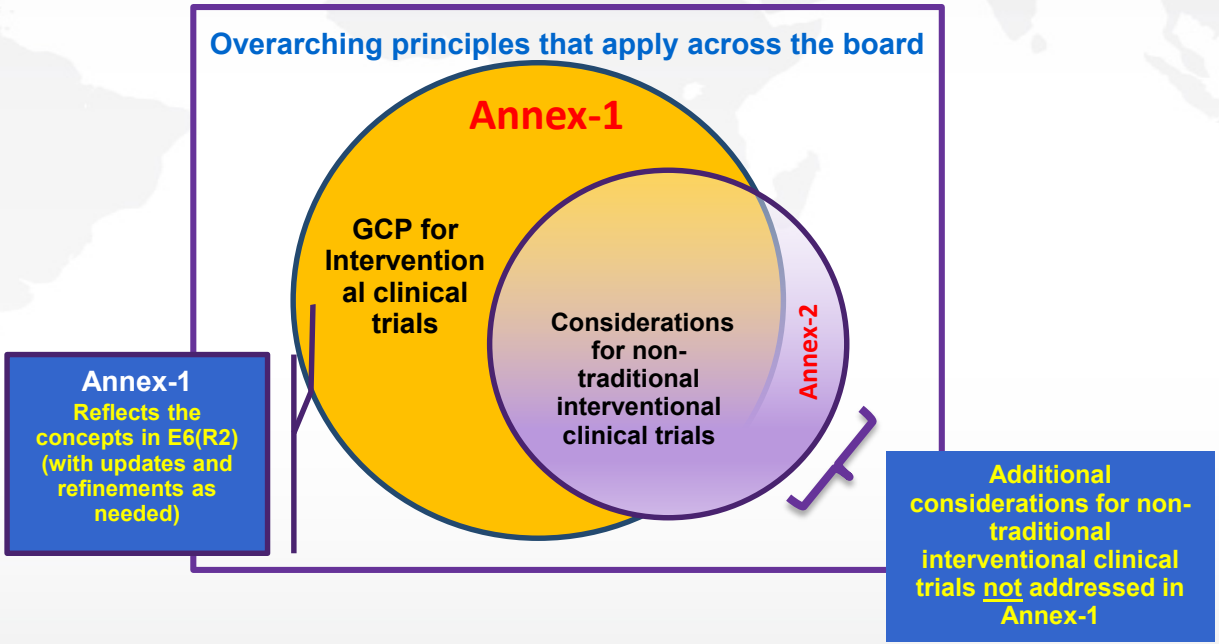
E6 GCP clinical trial conduct principles

Approach to E6(R3) Development

Simultaneous work on the principles & Annex-1



Conceptual Representation of the Approach to ICH E6(R3)



Annex 1 and Annex 2

- **Annex 1 – Interventional Clinical Trials**

  - Considers principles as they relate to the use of unapproved or approved drugs in a controlled setting with prospective allocation of treatment to participants and collection of trial data

- **Annex 2 – Additional Considerations for Non-traditional Interventional Clinical Trials**

  – Considers principles as they relate to the use of non-traditional clinical trial designs such as pragmatic clinical trials and decentralized clinical trials, as well as those trials that incorporate real world data sources

What is the difference between Annex 1 and Annex 2?

- **E6(R3) principles and Annex-1 will provide the details and address areas covered in the current version of E6(R2).**
  - E6(R3) principles and annex-1 are sufficient to provide GCP guidance for interventional clinical trials evaluating drugs/medicines and biologics, and will replace the current E6(R2).

- **Annex-2 will supplement the principles and annex-1 by providing further clarification to assist stakeholders in applying GCP principles across interventional clinical trials evaluating drugs/medicines and biologics that may include innovative design elements and those utilizing a variety of data sources. The scope of Annex-2 will be further clarified to determine what should be included, and will be described in an updated concept paper. This may include additional clarifications and discussions of:**
  - Designs that bring the trials to patients (e.g., decentralized clinical trials) that may include shipping the IMP to patients homes or local providers and data capture at home
  - Trials conducted within health care settings (e.g., trials with pragmatic elements), and
  - Trials that incorporate real-world data sources.

Engagement

- Many stakeholders are impacted by ICH-E6 GCP guidelines
- E6 stakeholder outreach approaches are approved by ICH and are ongoing.
- The knowledge gained by learning from stakeholder experiences and viewpoints will further enrich EWG discussions

- **ICH E6 Summary Engagement Plan - https://admin.ich.org/sites/default/files/2020-05/E6-R3_PublicEngagemenSummary_2020_0421.pdf**

ICH-E6(R3)

- Comprehensive principles that remain relevant as technology evolves and clinical trial design advances
- Risk-based approach and proportionality
- Thoughtful process throughout clinical trial conception, design, conduct and analyses

Progress

- EWG continued its work on the principles and introduction of ICH-E6(R3).
- Major principles are now outlined and explained.
- Unlike ICH-E6(R2), the draft principles for ICH-E6(R3) contain further explanations and important considerations.
- The ICH-E6(R3) principles are designed to be interdependent and should be viewed as a connected body.
- The EWG further refined the introduction of ICH-E6(R3) to serve stakeholders by providing details on how to read and utilize ICH-E6(R3).

Progress

- Principles of ICH-E6(R3) are meant to remain relevant as trial designs, methodology, and technology evolve.
- Principles address multiple key concepts including:
  - ❑ Focusing on critical to quality factors, such as the risks to participants and risks to trial results
  - ❑ Highlighting the importance of risk-based, proportional approach to determining trial processes and design elements
  - ❑ Encouraging the incorporation of innovations that are customized to fit the design and purpose of the trial
- Engagement with stakeholders

Progress

Stakeholder input

- Focus on-risk-based approach, proportionality, and fit-for-purpose. Minimize over-interpretation and avoid a “one size fits all approach.”
- Focus and clarify important aspects such as remote monitoring, quality and risk management.
- Accommodate new trial designs (e.g., decentralized trials, platform, and adaptive trials), and new data sources, such as real-world data (e.g., medical records, claims).
- Address trends in technology for trial conduct (e.g., bringing trials to participants, telehealth, e-Consent, remote training, IP shipment to participants).
- Input from investigators, academic research institutions, and trial participants is critical to inform trial design and conduct. Engage participants as partners in protocol design, trial conduct, and other aspects of clinical trials. Identify outcomes relevant to participants.
- Importance of doing adequate clinical trials, avoid wasting resources or time of participants and investigators.
- Others: scope, informed consent, GCP training, activity logs, drug accountability, data and information management, clear language-not jargon

Themes from the Principles (work-in-progress)

- **Declaration of Helsinki**
- **Rights, safety, and well-being of trial participants is paramount**
- **Consent and consent process are integral features of the ethical conduct of a trial. Should take into consideration:**
  - Relevant aspects of the trial (e.g., trials in emergency situations),
  - The potential use of technology to inform participants and obtain informed consent.
- **Independent ethics review – IRB/IEC**
- **Trials should be scientifically sound for their intended purpose**
- **Trials should be conducted by qualified individuals**
- **Clinical trial designs and processes should be proportionate to the risks inherent in the trial, including those to participants, and the importance, to the trial objectives, of the data being collected**

Themes from the Principles (work-in-progress)

- **Quality should be built into the design and conduct of the trial**
- **Clinical trials should be well-articulated in a concise and operationally viable protocol**
- **Clinical trials should be designed and conducted to generate reliable results**
- **Roles, tasks and responsibilities in clinical trials should be clear and documented appropriately**
- **Investigational products being studied in clinical trials should be:**
  - manufactured in accordance with Good Manufacturing Practice (GMP) standards and
  - stored, shipped, and handled in accordance with the product specifications and the approved protocol.

Work on Annex-1 - GCP for Interventional Clinical Trials

Gap Analysis

Gap Analysis

Stakeholder Comment Analysis

- **Academic Responses**
  - Open letter to EMA & ICH
  - Published articles
- **Responses to CTTI survey, comments, and interviews on "Informing the Renovations to the ICH E6" Project**
- **Regional Engagement Materials**
  - Americas Engagement Meeting (meeting transcripts and public comments)
  - Europe Engagement Meeting (meeting report)
  - Survey findings from Japanese academic investigators

ICH Guideline Analysis

- All Efficacy Guidelines + M11
- Peer-review publications

Purpose: to identify opportunities for improvement in E6 (R3) highlighted by external stakeholders and to provide EWG with information on where E6 (R3) modifications may be needed.

Next Steps:

- EWG determining changes needed in R3
- EWG determining potential structure and content in R3 Annex 1
- EWG to continue to refine the draft introduction and principles
- Continue the engagement with stakeholders

Any questions?

Further information

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