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SCIENCE MEDICINES HEALTH

ICH guidelines and clinical research in Europe

ESMO Public Policy Webinar on the Clinical Trials Regulation

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An agency of the European Union

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Problem statement – GCP Renovation

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ICH Reflection on "GCP Renovation": Modernization of ICH E8 and Subsequent Renovation of ICH E6

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12 January 2017

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

E8 clinical trial design principles

E6 GCP clinical trial conduct principles and guidance

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ICH E8 General Considerations on Clinical Studies:

Finalised and published 6 October 2021

Key aspects linking to ICH E6 GCP

General Principles

- Protection of clinical study participants
- Scientific approach in clinical study design, conduct and analysis
- Patient input into study design

Designing Quality into Clinical Studies

- Quality by Design of clinical studies
- Critical to quality factors
- Approach to identifying critical to quality factors

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ICH E8 Quality of a clinical study

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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 participant. 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.

Identify attributes whose integrity is fundamental to study quality:

- use prospective, multidisciplinary approach to identify the key factors critical to the quality of the study,
- triage and focus on essential activities
- in a manner proportionate to the importance of the factors and the risks involved,
- clear communication of how this will be achieved.

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Involving Stakeholders in GCP Renovation

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Two-fold approach:

Stakeholder engagement during the **drafting process**:

- Global Workshop on ICH E8 – Oct 2019, Washington, D.C.
- 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 **guideline**:

- Foresees involvement of patients in study planning, anchored among E8 principles
- Stipulates including stakeholders across disciplines in study planning & design for identifying what is critical to study quality

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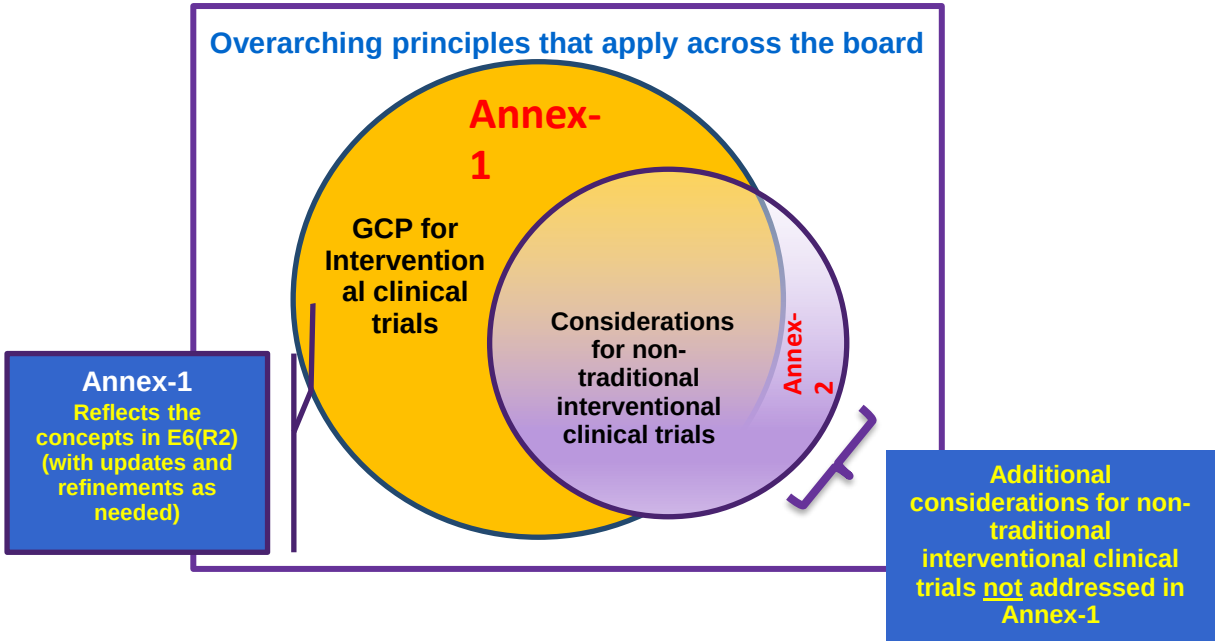
Conceptual Representation of the Approach to ICH E6(R3)



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Vision for ICH 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

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ICH GCP Draft Principles – some elements

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Draft ICH GCP Principles published 19 April 2021 as transparency measure.

- *"… **innovative digital health technologies may expand the possible approaches to trial conduct**. Such technologies can be incorporated in **existing healthcare infrastructures** and enable the **use of a variety of relevant data sources** "*
- *"… **trial designs that bring the trial to participants ..improve the representativeness of the participant population and enable wider participation.** The process of **building quality into the design of the trial ..**may include a broad range of stakeholders, **including patients** and treating physicians..**increase the likelihood of meaningful trial outcomes, which are relevant to both trial participants and future patients**. .."*
- *"The **principles** of GCP are designed to be **flexible** and **applicable to a broad range** of clinical trials."*
- *"Clinical trials should be designed to **protect** the rights, safety and well-being of **participants** and **assure** the **reliability of results**. Clinical trial designs and processes should **be proportionate to the risks** inherent in the **trial** and the **importance of the data** being **collected**. Trial **designs and processes should be evaluated to minimize unnecessary complexity and burden**."*

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ICH GCP Draft Principles

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- *"…the **participant selection** process should be **representative of the anticipated population** who are likely to use the medicinal product **in future clinical practice**. …. "*

- *"A **qualified physician** ….should have the **overall responsibility for the medical care** given to, and medical decisions made on behalf of, participants; however, the **practical interactions and the delivery of medical care and decisions** can be carried out by **appropriately qualified health care professionals**..."*

- *"The **informed consent** process should take into consideration **relevant aspects of the trial**……the potential **use of technology to inform** participants **and obtain informed consent**. "*

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ICH GCP Draft Principles

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*"8- Clinical trial **processes,** measures, and approaches should be **proportionate** to the **risks to participants** and to the **reliability of trial results**.*

- *8.1 Trial processes should be **proportionate** to the **risks inherent in the trial** and **the importance of the information** collected. ….*
- *8.2 **Risks beyond those of standard medical care** should be the focus of considerations; …*
- *8.3 .. **quality factors** should be **prioritized** ..identify those that are **critical to the trial***
- *8.4 Risks which have an impact on the quality factors considered critical to the trial should be managed."*

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ICH GCP Draft Principles

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*9.3 Trial processes should be **operationally feasible and avoid unnecessary complexity**, procedures, and data collection. Trial processes should support the study key objectives.*

*9.4 …**protocol** … **plans** or documents for the protocol execution … should be **clear, concise, and operationally feasible***

*10.7 The **transparency** of clinical trials in drug development includes **registration on publicly accessible and recognized databases**, and the **public posting of clinical trial results**.*

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Progress: Stakeholder input

- Focus on–risk-based approach, proportionality, and fit-for-purpose.
- Minimize over-interpretation and avoid a "one size fits all approach."
- 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.
- Importance of doing adequate clinical trials, avoid wasting resources or time of participants and investigators.
- Areas to address: Monitoring, use of technology, scope, informed consent, GCP training, activity logs, drug accountability, data and information management, safety reporting, clear language-not jargon

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E8 and E6 revision – goals and conclusion

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Facilitate objective-centered, yet flexible approach to clinical studies, including:

- Quality by design process & stakeholder engagement
- Enabling a broad range of study designs and different data sources
- Upfront assessment of risks specific to a study design, protocol and procedures
- Proportionate management of the risks and controls focusing on critical study elements
- Use of technology to ensure robust conduct, oversight, and reporting
- **Change management will be a key to implementation of E8 and E6 revision**.

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Next Steps

ICH E6 R3 GCP Principles and Annex 1 (rewrite of existing GCP) planned for release for public consultation mid 2022

Drafting of the full text has to integrate the principles including those of proportionality.

Ongoing discussion with Academic representatives recommencing this month

Drafting includes:

- Investigator and sponsor sections.
- Monitoring, recognising on-site, remote and centralised monitoring
- Data management

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Any questions?

Further information

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