Good Clinical Practice – ICH E6(R3)

Step 4 document – to be implemented

23 January 2025

Good Clinical Practice – ICH E6(R3)

Legal Notice

Good Clinical Practice – ICH E6(R3)

Background

- This guideline reached *Step* 2 19 May 2023 and was issued by the ICH Regulatory Members for public consultation.
- ICH E6(R3) Expert Working Group reviewed public consultation comments and revised the document as appropriate.
- This final document has been signed off as a *Step 4* document (6 January 2025) to be implemented by the ICH Regulatory Members.
- This document was developed based on a Concept Paper (approved 18 November 2019) and a Business Plan (approved 18 November 2019).

ICH-E6(R3): Background to this Revision

E8 – integrating QbD into study design and conduct

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E6 – Applying the foundation of E8 to the conduct of clinical trials

Do not read E6(R3) in isolation

- **E6: Good Clinical Practice (GCP) – finalised in 1996**
  - Described the responsibilities of investigators and sponsors and expectations of interested parties in the conduct of clinical trials;
  - Covered aspects of monitoring, reporting, and archiving of clinical trials; and
  - Included sections for essential documents and investigator brochures
- **E6(R2) – finalised in 2016**
  - Included integrated addendum to encourage implementation of improved and more efficient approaches to GCP, while continuing to ensure human subject protection; and
  - Updated standards for electronic records.
- **E6(R3) – finalised in 2025**
  - Grounded in the foundational principle of Quality by Design (QbD)
  - Involves critical thinking
  - Utilises proportionate, risk-based approaches
  - Recognises that a one size does not fit all.

E6(R3) Development Process

Gap Analysis: Utilising inputs from:

- Articles (including open letter to ICH & EMA)
- Responses to Clinical Trials Transformation Initiative (CTTI) survey
- Regional stakeholder engagement (such as public workshops, surveys)
- ICH guidelines

Stakeholder Representative Engagement

- E6(R3) EWG engaged with academic stakeholders in a series of meetings to seek input on the draft guideline.
- The EWG sought their views throughout the guideline development process.

Summary of Stakeholder Engagement to Support the Development of ICH E6(R3), 21 April 2020
https://database.ich.org/sites/default/files/E6-R3_PublicEngagemenSummary_2020_0421.pdf

Increased Transparency

- New approaches to enhance transparency (published draft principles in April 2021 and held a 2-day public web conference in May 2021).

Public Consultation - May to Nov 2023

- Over 7000 Comments received and reviewed.

Final Principles and Annex 1 document adopted - January 2025

Initial Takeaways from Feedback and Comments on ICH E6(R2)

Concerns about the following:

- The clinical trial ecosystem is rapidly evolving and this was not reflected in the guideline.
- The academic community were concerned about a lack of proportionality.
- The R2 guidance was seen as a “one-size-fits-all” approach to clinical trials.
- The ability of clinical trials to meet all GCP requirements in different situations (e.g., during public health emergencies).
- GCP requirements were being applied where they were not applicable.

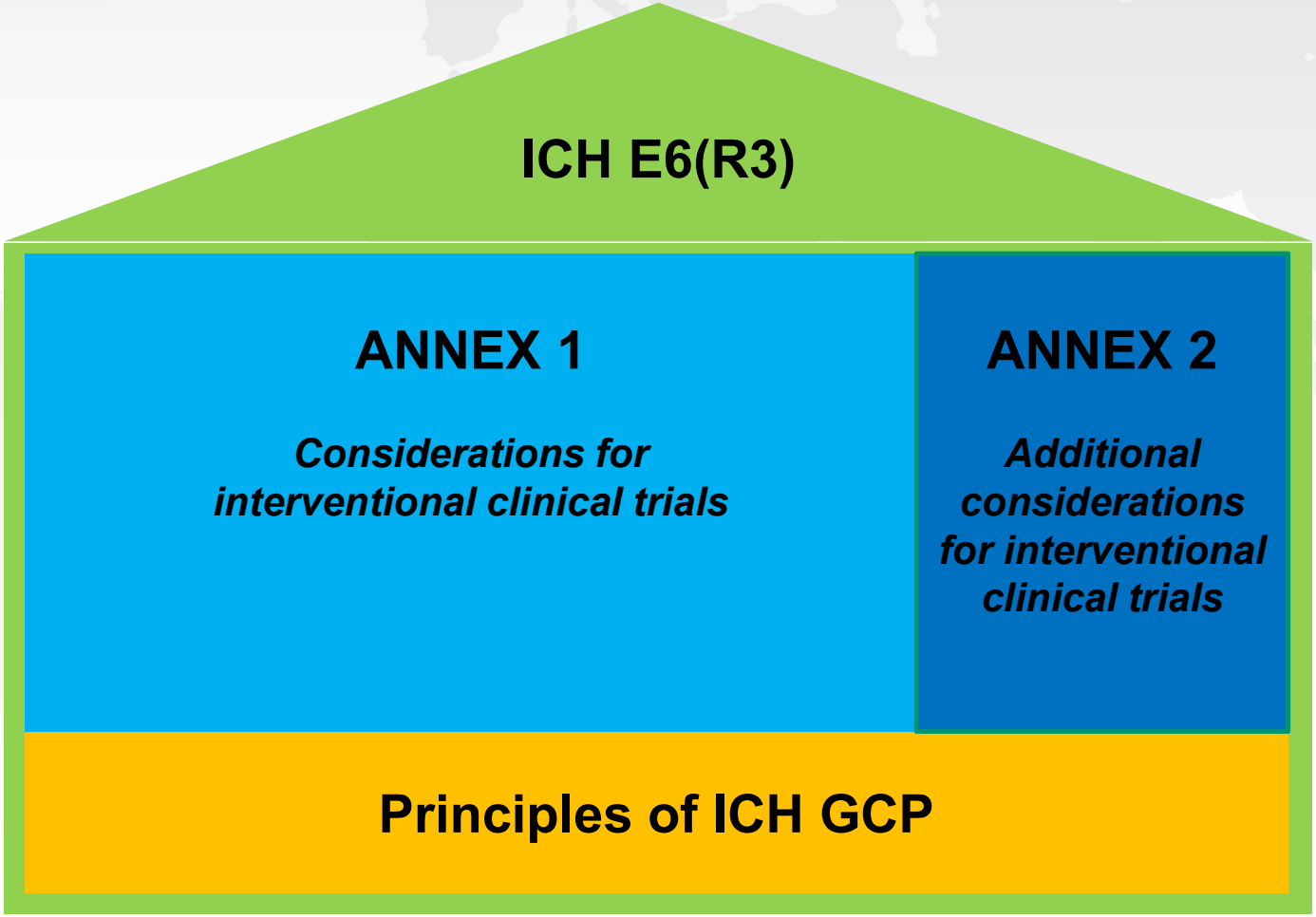
What is new about E6(R3) structure and content?

- New structure to provide clarity and better readability.
- Provide additional clarity on the scope.
- Included language to facilitate innovations in clinical trial design, technology and operational approaches.
- Set a foundation for practical/feasible expectations (through adoption of QbD and proportionate risk-based approaches) for responsibilities of sponsor and investigator in an evolving clinical trial ecosystem.

What is new about E6(R3) structure and content? (2)

- Encourage fit-for-purpose approaches.
  - Proportionality and risk-based approaches with a focus on the clinical trial's critical to quality factors (i.e., whose integrity is fundamental to safety of participants and the reliability of trial results);
  - Thoughtfulness in the design and conduct
- Incorporate learning from innovative clinical trial designs and lessons from public health emergencies/pandemics.
- Encourage transparency by clinical trial registration and result reporting.
- Provide additional language to enhance the informed consent process.

OVERVIEW OF ICH E6(R3)



Revised Structure

E6(R3) Guideline

E6(R3) Principles and Annex 1 replacing E6(R2)

I. INTRODUCTION

II. PRINCIPLES OF ICH GCP

III. ANNEX 1

1. Institutional Review Board/Independent Ethics Committee (IRB/IEC)
2. Investigator
3. Sponsor
4. Data Governance – Investigator and Sponsor

APPENDICES

Appendix A. Investigator's Brochure
Appendix B. Clinical Trial Protocol and Protocol Amendment(s)
Appendix C. Essential Records for the Conduct of a Clinical Trial

GLOSSARY

ANNEX 2 – *under public consultation from November 2024 to March 2025*

Scope

- This guideline applies to interventional clinical trials of investigational products that are intended to be submitted to regulatory authorities. The Principles of GCP in this guideline may also be applicable to other interventional clinical trials of investigational products that are not intended to support marketing authorisation applications in accordance with local requirements.
- The Annexes provide the basis for the appropriate interpretation and application of the principles and should therefore be appropriately considered; however, various approaches to the provisions in the Annexes may be considered provided they are justified and achieve the intended purpose of the application of the principles.
- This guideline encourages a risk-based and proportionate approach to the conduct of a clinical trial.

Focus on fit for purpose clinical trial quality (QbD and proportionate, risk-based approaches)

- This guideline builds on key concepts outlined in ICH E8(R1) General Considerations for Clinical Studies. This includes fostering a quality culture and proactively designing quality into clinical trials and drug development planning, identifying factors critical to trial quality, and engaging interested parties, as appropriate, using a proportionate risk-based approach.
- Clinical trials vary widely in scale, complexity, and cost. Careful evaluation of critical to quality factors involved in each trial and risks associated with the priorities will help ensure efficiency by focusing on activities critical to achieving the trial objectives.

Focus on fit for purpose clinical trial quality (QbD and proportionate, risk-based approaches) (2)

- QbD should be implemented to identify the factors (i.e., data and processes) that are critical to ensuring trial quality and the risks that threaten the integrity of those factors and ultimately the reliability of the trial results.
- Clinical trial processes and risk mitigation strategies implemented to support the conduct of the trial should be proportionate to the importance of the data being collected, the risks to trial participant safety and the reliability of trial results.
- Trial designs should be operationally feasible and avoid unnecessary complexity.

Innovation, Efficiency & Engagement

- Encouraging the exploration of technology:
  - The principles are intended to support efficient approaches to trial design and conduct. For example, innovative digital health technologies, such as wearables and sensors may expand the possible approaches to trial conduct.
  - Such technologies can be incorporated into existing healthcare infrastructures and enable the use of a variety of relevant data sources in clinical trials.
  - The use of technology in the conduct of clinical trials should be adapted to fit the participant characteristics and the particular trial design.
- Encouraging engagement and inclusivity:
  - The use of innovative trial designs and technologies may enable the inclusion of a wider and more diverse population of participants and thereby broaden the applicability of trial outcomes.
  - The design and conduct of the clinical trial may be supported by obtaining the perspectives of interested parties, such as patients and their communities, patient advocacy groups and healthcare professionals. Their input can help to reduce unnecessary complexity, improve feasibility and increase the likelihood of meaningful trial outcomes.

Summary of Changes

Substantial Changes

- **Principles of GCP**
- **Annex 1**
  - Investigator
  - Sponsor
  - Data Governance – Investigator and Sponsor **(New)**
- **Appendix C**
  - Essential Records for the Conduct of a Clinical Trial
- **Glossary**

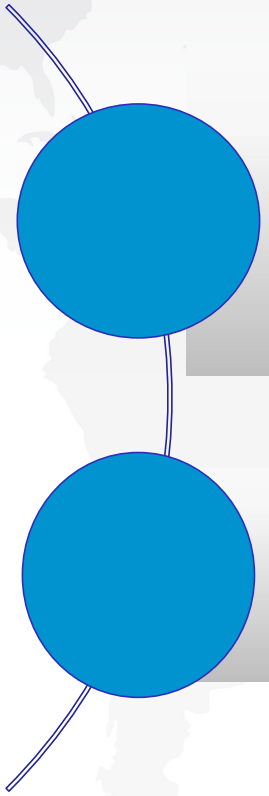
Other Changes

- **Annex 1**
  - Institutional Review Board/Independent Ethics Committee (IRB/IEC)
- **Appendices A & B**
  - Investigator's Brochure
  - Clinical Trial Protocol and Protocol Amendments

ICH E6(R3) Principle

ICH E6(R3) PRINCIPLE	TOPIC	ICH E6(R2) PRINCIPLE
1	Ethical Principles	2.1, 2.2, 2.3, 2.7, 2.11
2	Informed Consent	2.9
3	IRB/IEC Review	2.6
4	Science	2.4, 2.5
5	Qualified Individuals	2.8
6	Quality	2.13
7	Risk Proportionality	N/A
8	Protocol	2.5
9	Reliable Results	2.10
10	Roles and Responsibilities	N/A
11	Investigational Products	2.12

ICH E6(R3) Principles - New



Proportionality, risk-based

- Focus on participant's safety and reliability of results.
- Focus on the risks associated with trial participation.
- Focus on risks beyond those associated with usual medical care for clinical trials involving patients.

Roles and Responsibilities

- Clarification of transfer of activities by the Sponsor and delegation by the Investigator.
- Maintenance of appropriate oversight.

ICH E6(R3) Principle 7

Clinical trial processes, measures and approaches should be implemented in a way that is proportionate to the risks to participants and to the importance of the data collected and that avoids unnecessary burden on participants and investigators.

Trial processes should be proportionate to the risks inherent in the trial and the importance of the information collected.

- Risks to rights, safety and well-being of participants; and
- Risks to the reliability of trial results.

The focus should be on the risks associated with trial participation.

Risks to critical to quality factors should be managed proactively and adjusted when new or unanticipated issues arise once the trial has begun.

Trial processes should be operationally feasible and avoid unnecessary complexity, procedures and data collection.

ICH E6(R3) Principle 10

Roles and responsibilities in clinical trials should be clear and documented appropriately.

The sponsor may transfer or the investigator may delegate their tasks, duties or functions, but they retain overall responsibility for their respective activities.

Agreements should clearly define the roles, activities and responsibilities for the clinical trial and be documented appropriately. Where activities have been transferred or delegated to service providers, the responsibility for the conduct of the trial resides with the sponsor or investigator, respectively.

The sponsor or investigator should maintain appropriate oversight of the aforementioned activities.

ICH E6(R3) Principles - Revised

Ethical Principles

- Making sure not to unnecessarily exclude particular participant populations.

Informed Consent

- Taking into consideration relevant aspects of the trial.

IRB/IEC Review

- Periodic review according to applicable regulatory requirements.

Science

- Periodic review of scientific knowledge and approaches to determine whether modifications to the trial are needed.

Qualified Individuals

- Individuals with different expertise and training may be needed across all phases of a clinical trial.

ICH E6(R3) Principles – Revised (2)

Quality

- The quality and amount of the information generated should support good decision making.

Protocol

- A well-designed trial protocol is fundamental to the protection of participants and for the generation of reliable results.
- The protocol and other documents (e.g., statistical analysis plan, data management plan) for trial execution should be clear, concise and operationally feasible.

Reliable Results

- Trial processes should support the key trial objectives.
- Clinical trials should incorporate efficient and well-controlled processes for managing records through appropriate management of data integrity.
- The transparency of clinical trials should involve registration on publicly accessible databases and the public posting of clinical trial results.

Investigational Product

- Investigational products should be carefully managed to align with treatment assignment and maintain blinding, where applicable.
- The investigational product provided to the trial participant should retain its quality.

ICH E6(R3) Annex 1

Institutional Review Board/Independent Ethics Committee (IRB/IEC)

ICH E6(R3) Section	ICH E6(R2) Section
1.1 – Submission and Communication *In R3, added global language about reporting to IRB/IEC and regulatory authorities*	N/A
1.2 – Responsibilities	3.1
1.3 – Composition, Function and Operations	3.2
1.4 – Procedures	3.3
1.5 – Records	3.4

IRB/IEC

- Included global language about reporting to IRB/IEC and regulatory authorities.
- Updated to reflect digitisation and variable approaches to obtaining consent.
- Clarified the potential for participants to be compensated for costs incurred to participate in the trial.
- Clarified that the IRB/IEC should review the assent information, considering the age, maturity and psychological state of the minor, as well as applicable regulatory requirements.

ICH E6(R3) Annex 1
Investigator

ICH E6(R3) Section	ICH E6(R2) Section
2.1 – Qualifications and Training	4.1
2.2 – Resources	4.2
2.3 – Responsibilities	4.1, 4.2
2.4 – Communication with IRB/IEC	4.4, 4.10
2.5 – Compliance with Protocol	4.1
2.6 – Premature Termination or Suspension of a Trial	4.12
2.7 – Participant Medical Care and Safety Reporting	4.3, 4.11
2.8 – Informed Consent of Trial Participants	4.8
2.9 – End of participation in a clinical trial	4.3
2.10 – Investigational Product Management	4.6
2.11 – Randomisation Procedures and Unblinding	4.7
2.12 – Records	4.9
2.13 – Reports	4.13

Investigator - Informed Consent

- **Approaches to obtaining informed consent**
  - Varied approaches to the provision of information and the discussion about the trial can be used. This may include, for example, providing text in different formats, images and videos and other interactive methods.
  - The information should be as clear and concise as possible, use simple language and avoid unnecessary volume and complexity.
  - Informed consent is documented by means of a written (paper or electronic), signed and dated informed consent form.
  - Obtaining consent remotely may be considered when appropriate.
- **New information**
  - Considerations for re-consent, including stage of the clinical trial, whether the new information is relevant only to new / existing participants.
  - Revised informed consent materials require IRB/IEC approval in advance of use.
- **Enrolment of minors**
  - Where a minor is to be included as a participant, age-appropriate assent information should be provided and discussed with the minor as part of the consent process.
  - A process for consent should be considered if during the trial, the minor reaches the age of legal consent, in accordance with applicable regulatory requirements.

Investigator (2)

- **Qualifications and training**
  - Clarified expectations on evidence for qualifications: allow flexibility about documentation.
  - Clarified overall training requirements for trial staff: trial-related training to persons assisting in the clinical trial should correspond to what is necessary to enable them to fulfil their delegated trial-related activities that go beyond their usual training and experience.
- **Medical Care**
  - Clarified that other appropriately qualified health professionals may be involved in medical care of trial participants in line with their normal activities and in accordance with local regulatory requirements.
- **Safety Reporting**
  - Included language about the reporting of unfavourable medical events occurring in participants before IP administration (e.g., during screening) to the sponsor, if required by the protocol.

Investigator (3)

- **Responsibilities**
  - Clarified the expectations between the sponsor and investigator regarding service providers.
  - Confirmed that the investigator retains the ultimate responsibility for the persons or parties undertaking the activities delegated.
  - Clarified that the level of investigator oversight of the delegated activities should depend on the nature of the delegated activities and be proportionate to the importance of the data being collected and the risks to trial participant safety and data reliability.
  - Clarified the requirements for delegation documentation.

- **Considerations for participants who did not reach the routine end of the trial**
  - Clarified that appropriate follow up per protocol and/or other protocol-related documents is required.
  - Included language about the potential for instructions to avoid loss of already collected data, in accordance with regulatory requirements.

Investigator (4)

- **Computerised systems**
  - Clarified the investigator's responsibility for computerised systems.
- **Data and source records**
  - Clarified expectations regarding identification and maintenance of source records and timely data access and review.
- **Investigational product (IP) management**
  - Clarified that the sponsor may facilitate aspects of IP management.
  - Clarified that the level of investigator oversight will depend on a number of factors including:
    - Characteristics of the IP;
    - Route and complexity of administration;
    - Level of existing knowledge about the IP's safety; and
    - Marketing status of the IP.
  - Clarified that for authorised medicinal products, alternative approaches to IP documentation may be considered, in accordance with applicable regulatory requirements.
  - Included language that the investigators should be prepared and capable from the start of the trial to perform unblinding without undue delay and hindrance in the case of an emergency, to protect participant safety.

ICH E6(R3) Annex 1
Sponsor

ICH E6(R3) Section	ICH E6(R2) Section
3.1 – Trial Design	5.0, 5.4
3.2 – Resources	N/A
3.3 – Allocation of activities	5.7
3.4 – Qualification and Training	5.3, 5.4
3.5 – Financing	5.9
3.6 – Agreements	5.1, 5.2, 5.6, 5.9, 5.23
3.7 – Investigator Selection	5.6
3.8 – Communication with IRB/IEC and Regulatory Authority(ies)	5.10, 5.11
3.9 – Sponsor Oversight	N/A

ICH E6(R3) Annex 1
Sponsor

ICH E6 (R3) Section	ICH E6 (R2) Section
3.10 – Quality Management	5.0
3.11 – Quality Assurance and Quality Control	5.1, 5.18, 5.19
3.12 – Noncompliance	5.20
3.13 – Safety Assessment and Reporting	5.16, 5.17
3.14 – Insurance/Indemnification/Compensation to participants and investigators	5.8
3.15 – Investigational Product(s)	5.12, 5.13, 5.14
3.16 – Data and Records	5.5, 5.15
3.17 – Reports	5.21, 5.22

Sponsor

- **Trial Design**

  Included language that the sponsor should:

  - Ensure that safety and efficacy data from non-clinical studies/clinical trials/real world sources are sufficient to support human exposure.
  - Implement QbD, including prospective identification of critical to quality factors and management of important risks.
  - Consider seeking inputs from interested parties (e.g., healthcare professionals, patients).
  - Ensure that protocols, data acquisition tools and other operational documents are fit for purpose, clear, concise and consistent.
  - Avoid unnecessary burden on participants and investigators.

- **Agreements**
  - Clarified that agreements with service providers and other parties (e.g., independent data monitoring committee (IDMC), adjudication committee) should be in place prior to initiating the activities.
  - Clarified that agreements should be updated to reflect significant changes in the activities transferred.

Sponsor (2)

- **Sponsor Oversight**
  - Clarified that the sponsor should ensure that the range and extent of oversight measures are fit for purpose and tailored to the complexity of and risks associated with the trial.
  - Clarified that quality assurance and quality control processes should be implemented in oversight of investigators and service providers.
  - Included language about the oversight of facilities outside of investigator sites, e.g., central image reading facilities, as part of overall QC strategy.
- **Quality Management**
  - Further clarified the requirements for the assessment and management of critical to quality factors impacting participant safety or result reliability.
  - Encouraged proportionality and clarified acceptable ranges beyond which deviations could represent systemic issues.

Sponsor (3)

- **Monitoring**
  - Clarified that monitoring is one of the principal quality control activities.
  - Clarified expectations for centralised monitoring and visits to investigator sites (performed on-site or remotely).
  - Clarified that the monitoring strategy should consider factors such as the trial purpose, design, blinding, safety profile, and endpoints in line with the risk proportionate approach for that investigational product in that participant population.
- **Investigational Product**
  - Clarified that for product that has a marketing authorisation, alternative approaches may be considered e.g.:
    - The basic product information may be used in place of the investigator's brochure.
    - Alternative approach to investigational product accountability records may be applicable, in accordance with local regulatory requirements.

Sponsor (4)

- **Computerised Systems and Data Management**
  - Clarified the importance of certain processes, such as randomisation and blinding, and provided reasonable perspective on when unblinding may occur.
  - Clarified that the requirements for computerised systems should be fit for purpose and risk-based.
  - Clarified requirements of the sponsor's data management processes throughout the full data life cycle.
  - Included requirements related to finalisation of data sets, statistical programming and data analysis.

ICH E6 (R3) Annex 1

Data Governance

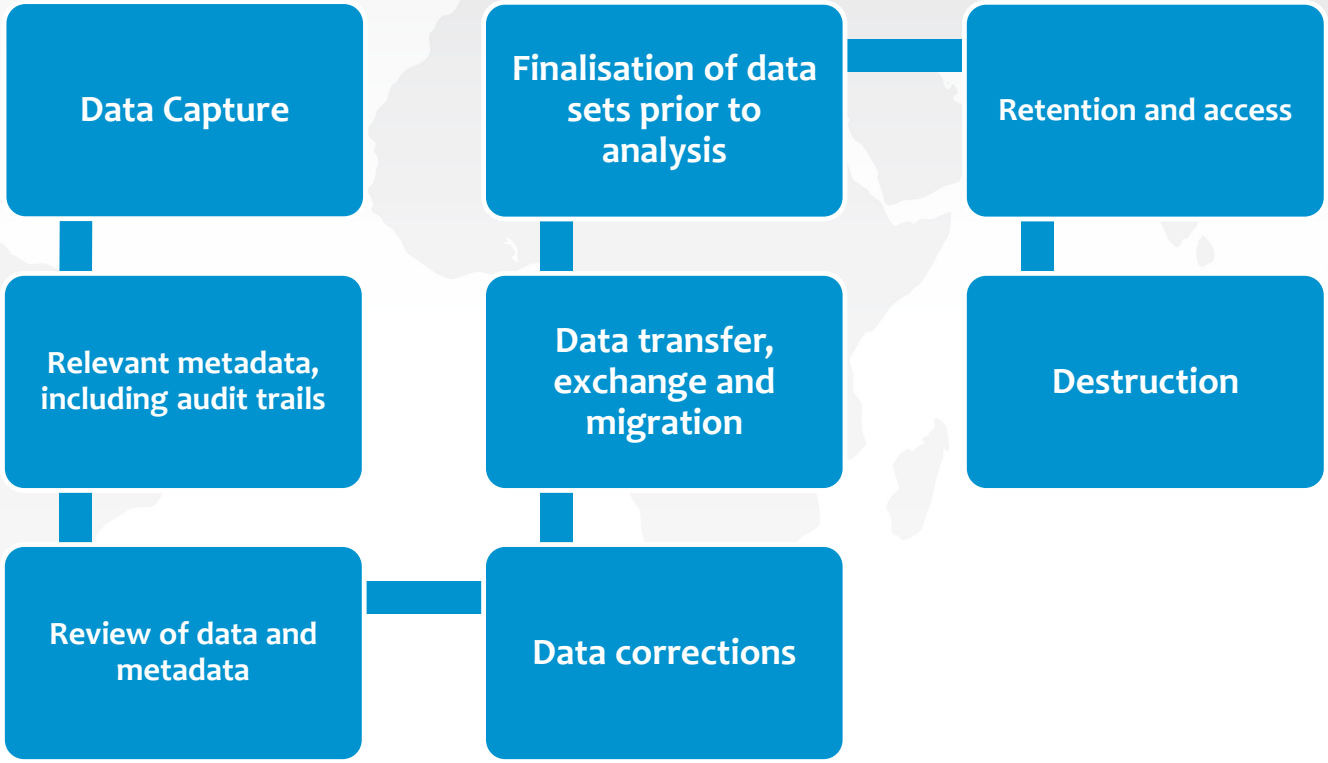
ICH E6(R3) Section	ICH E6(R2) Section
4.1 – Safeguard Blinding in Data Governance	N/A – Major Revamp For both investigators and sponsors
4.2 – Data Life Cycle Elements • 4.2.1 Data Capture • 4.2.2 Relevant Metadata, Including Audit Trails • 4.2.3 Review of Data and Metadata • 4.2.4 Data Corrections • 4.2.5 Data Transfer, Exchange and Migration • 4.2.6 Finalisation of Data Sets Prior to Analysis • 4.2.7 Retention and Access • 4.2.8 Destruction	
4.3 – Computerised Systems • 4.3.1 Procedures for the Use of Computerised Systems • 4.3.2 Training • 4.3.3 Security • 4.3.4 Validation • 4.3.5 System Release • 4.3.6 System Failure • 4.3.7 Technical Support • 4.3.8 User Management	

Data Governance

- Introduced a new section that provides guidance to the responsible parties (i.e., investigators and sponsor) on appropriate management of data integrity to allow accurate reporting, verification and interpretation of clinical trial-related information.
- Defined key processes that should be addressed across the full data life cycle:
  - data protection,
  - management of computerised systems,
  - essential elements such as randomisation, dose adjustments and blinding
  - processes to support key decision making such as data finalisation, unblinding and IDMC activities
- Specified that processes should focus on the criticality of the data and be implemented proportionately and documented appropriately.
- Described data lifecycle elements from data capture to data destruction.
- Clarified the meaning of metadata.

Data Governance (2)

Procedures should be established to cover the full data life cycle.



- Some activities may occur in a different order or in parallel, depending on the trial design, e.g., data transfer.

Data Governance (3)

- Clarified that computerised systems should be fit for purpose, depending on their specific use in the clinical trial.
- Specified that the approach to the management of computerised systems should be proportionate to their importance to participant safety and the reliability of trial results.
- Clarified that responsibilities for computerised systems should be clear and documented.
- Described the elements of computerised system life cycle to be addressed from design to decommissioning.

ICH E6(R3) Appendix A
Investigator's Brochure

ICH E6(R3) Section	ICH E6(R2) Section
A.1 – Introduction	7.1
A.2 – General Considerations	7.2
A.3 – Contents of the Investigator's Brochure • A.3.6 (b) – In R3, added frequency and nature of AEs should be included to determine expectedness of Serious Adverse Reactions.	7.3

Investigator's Brochure

- Added that a list of adverse reactions identified as the reference safety information, including information on their frequency and nature, should be included.
- Reorganised the order of language for clarification.
- Examples of title page and table of contents removed as same information can be read in the text of the guideline.

ICH E6(R3) Appendix B

Clinical Trial Protocol and Protocol Amendments

ICH E6(R3) Section	ICH E6(R2) Section
B.1 – General Information	6.1
B.2 – Background Information	6.2
B.3 – Trial Objectives and Purpose	6.3
B.4 – Trial Design	6.4
B.5 – Selection of Participants	6.5
B.6 – Discontinuation of Trial Intervention and Participant Withdrawal from Trial	6.5
B.7 – Treatment and Interventions for Participants	6.6
B.8 – Assessment of Efficacy	6.7
B.9 – Assessment of Safety	6.8
B.10 – Statistical considerations	6.9

ICH E6(R3) Appendix B

Clinical Trial Protocol and Protocol Amendments (2)

ICH E6(R3) Section	ICH E6(R2) Section
B.11 – Direct Access to Source Records	6.10
B.12 – Quality Control and Quality Assurance	6.11
B.13 – Ethics	6.12
B.14 – Data Handling and Record Keeping	6.4, 6.13
B.15 – Financing and Insurance	6.14
B.16 – Publication Policy	6.15

NB: E6 (R2) Section 6.16 on supplements relating to Final CSR removed.

Protocol

The guideline was updated to:

- Highlight the importance of the protocol, such as:
  - Building adaptability into the protocol, for example, by including acceptable ranges for specific protocol provisions, can reduce the number of deviations or in some instances the requirement for a protocol amendment.
- Encourage simplicity and clarity.
  - Clinical trials should be described in a clear, concise and operationally feasible protocol. The protocol should be designed in such a way as to minimise unnecessary complexity and to mitigate or eliminate important risks to the rights, safety, and well-being of trial participants and reliability of data.
- Address the implication for withdrawal of consent or discontinuation by the investigator.
- Broaden the statistical section to include statistical inference methodologies (e.g., Bayesian design and estimands).

ICH E6(R3) Appendix C

Essential Records for the Conduct of a Clinical Trial

ICH E6(R3) Section	ICH E6(R2) Section
C.1 – Introduction	8.1
C.2 – Management of Essential Records	N/A – Major Revamp
C.3 – Essentiality of Trial Records	

Essential Records

- Provided guidance on what makes a record essential.
  - Many records are generated before and during the conduct of a clinical trial. The nature and extent of those records generated and maintained are dependent on the trial design, its conduct, application of risk proportionate approaches and the importance and relevance of that record to the trial.
- Provided clarity on the content and maintenance of essential records.
- Developed one table of examples of essential records, e.g., protocols, investigator brochure or basic product information, informed consent forms, necessary approvals/opinions.
- Provided guidance about access by the sponsor and investigator/institution to one another's relevant essential records in order to fulfill their respective responsibilities.

ICH E6(R3) Annex 1 *Glossary*

New Glossary Terms

- Assent
- Computerised Systems Validation
- Data Acquisition Tool
- Data Integrity
- Metadata
- Reference Safety Information
- Service Provider
- Signature

Revised Glossary Terms

- Adverse Events and Adverse Reaction-related definitions
- Essential Records
- IRB/IEC
- Investigator
- Investigator Site
- Source Records
- Sponsor
- Trial Participant
- And Others…

Updating The Glossary (examples)

- Added terms that support advances in an evolving clinical trial ecosystem.
  - Data Acquisition Tool (DAT): A paper or electronic tool designed to collect data and associated metadata from a data originator in a clinical trial according to the protocol and to report the data to the sponsor.
  - Service provider: A person or organisation (commercial, academic or other) providing a service used during the conduct of a clinical trial to either the sponsor or the investigator to fulfil one or more of their trial-related activities.
- Provided more clarity on Adverse Events and Adverse Reactions.
- Updated some definitions (e.g., investigator site) to adapt for clinical trial operations in decentralised settings.
- Adapted definitions as needed to implement the media-neutral approach consistently.
- Revised subjects to participants.
- Removed confusing language and terms (e.g., non-therapeutic trials).

In Summary

- Various approaches to clinical trial design and conduct have the potential to streamline drug development and increase the convenience of clinical trials for participants.
- The intent of the revised guideline is to facilitate innovations in clinical trial design and conduct, while at the same time provide guidance to help ensure participant safety and that the clinical trial produces reliable results.
- Training materials are planned to be developed (with use-cases) that clarify or provide supplementary explanation to the application of the GCP guideline.

Thank You

- **The ICH E6(R3) Expert Working Group would like to thank our academic stakeholder representatives for their time and thoughtful consideration of the guideline. They were invaluable in providing their expertise in conducting clinical trials.**

Contact

- **For any questions, please contact the ICH Secretariat:**

admin@ich.org