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Data Governance

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Disclaimer

The slides in this presentation are a mixture of official ICH E6 R3 slides produced by the Expert Working Group (in the official ICH template) and slides produced by me for the purpose of this or other meetings. The opinions expressed on the latter are my own.

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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*

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

Principle 9 (selected parts)

Clinical trials should generate reliable results.

9.1 The quality and amount of the information generated in a clinical trial should be fit for purpose and sufficient to provide confidence in the trial's results and support good decision making.

9.2 Systems and processes that aid in data capture, management and analyses, as well as those that help ensure the quality of the information generated from the trial, should be fit for purpose, should capture the data required by the protocol and should be implemented in a way that is proportionate to the risks to participants and the importance of acquired data.

9.3 Computerised systems used in clinical trials should be fit for purpose (e.g., through risk-based validation, if appropriate), and factors critical to their quality should be addressed in their design or adaptation for clinical trial purposes to ensure the integrity of relevant trial data.

9.4 Clinical trials should incorporate efficient and robust processes for managing records (including data) to help ensure that record integrity and traceability are maintained and that personal information is protected, thereby allowing the accurate reporting, interpretation and verification of the relevant clinical trial-related information.

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ICH E6 R3 – selected glossary terms

New glossary terms

Data integrity

Data Acquisition Tool (DAT)

Metadata

Revised glossary term

Audit trail

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Data Governance (Section 4)

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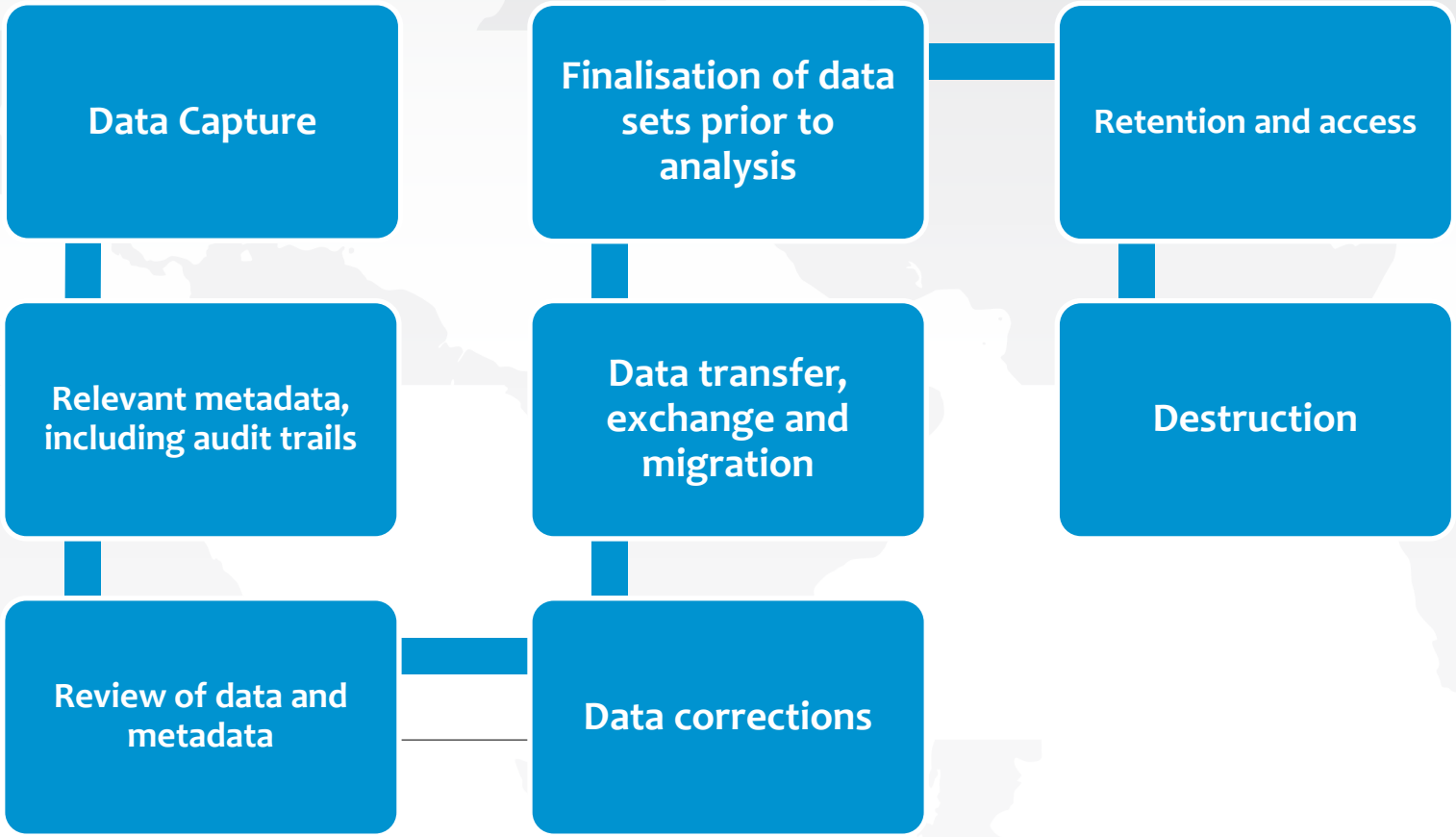
Data Governance

- 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 New section 4 - section overview

Definition of key processes (data protection, computerised systems, randomisation, blinding/unblinding, data finalisation (review, cleaning etc.), DMC activities)

4.1 Safeguard Blinding in Data Governance

4.2 Data Life Cycle Elements

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

Computerised systems responsibilities

NB! This is just a private visual aid to facilitate understanding on how responsibilitie s are divided in both the EU e-guideline and ICH E6 R3

Responsibility Matrix	Systems deployed by the investigator/Institution	Systems deployed by the sponsor
System designed for clinical trial purposes	Examples: • e-Investigator Site File • AI algorithm designed to screen patients or measure trial endpoints	Examples: • bespoke systems (Examples: sponsor-build CRF, ePRO or IRT) • systems designed to be configured or managed (Example: licensed eCRF)
System used for clinical trials but designed for other purposes	Examples: • electronic medical record • imaging equipment e.g. x-ray, DEXA	Examples: • systems where no alterations are needed (Examples: wearables or sensors or questionnaires not specifically developed for a clinical trial)

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Computerised systems responsibilities

Summary of responsibilities:

- The sponsor is responsible for ensuring that for computerised systems which they put in place, the expectations for computerised systems as described in this section are addressed in a risk proportionate manner
- The sponsor should review whether the systems used by the investigator/institution (e.g., electronic health records and other record keeping systems for source data collection) are fit for purpose in the context of the trial
- In the event that the investigator/institution deploys systems specifically for the purposes of conducting clinical trials, the investigator/institution should ensure that the expectations are proportionately addressed and implemented

Investigator section 2.12 (selected sections)

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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.

Investigator section 2.12 (selected sections)

2.12.1 In generating, recording and reporting trial data, the investigator should ensure the integrity of data under their responsibility, irrespective of the media used

2.12.3 The investigator should be provided with timely access to data by the sponsor (see section 3.16.1(k)) and be responsible for the timely review of data, including relevant data from external sources that can have an impact on, for example, participant eligibility, treatment or safety (e.g., central laboratory data, centrally read imaging data, other institution's records and, if appropriate, electronic patient-reported outcome (ePRO) data). The protocol may provide exceptions for access, for instance, to protect blinding

2.12.4 The investigator should ensure that data acquisition tools and other systems deployed by the sponsor are used as specified in the protocol or trial-related instructions.

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Investigator section 2.12 (selected sections)

2.12.7 The investigator/institution should implement appropriate measures to protect the privacy and confidentiality of personal information of trial participants in accordance with applicable regulatory requirements on personal data protection.

2.12.9 For systems deployed by the investigator/institution that maintain and retain trial data/information, the investigator/institution should ensure that such data are protected from unauthorised access, disclosure, dissemination or alteration and from inappropriate destruction or accidental loss.

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Investigator section 2.12 (selected sections)

2.12.10 When using computerised systems in a clinical trial, the investigator/institution should do the following:

(a) For systems deployed by the investigator/institution, ensure that appropriate individuals have secure and attributable access;

(b) For systems deployed by the sponsor, notify the sponsor when access permissions need to be changed or revoked from an individual;

(c) For systems deployed by the investigator/institution specifically for the purposes of clinical trials, ensure that the requirements for computerised systems in section 4 are addressed proportionate to the risks to participants and to the importance of the data;

(d) Where equipment for data acquisition is provided to trial participants by the investigator, ensure that traceability is maintained and that participants are provided with appropriate training;

(e) Ensure that incidents in the use and operation …may have a significant and/or persistent impact on the trial data or system security, are reported to the sponsor and, where applicable, to the IRB/IEC.

ICH E6 R3 Sponsor section 3.16 (selected sections)

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 Sponsor section 3.16.1 (selected sections)

The sponsor should (3.16.1 Data handling)

(a) The sponsor should ensure the integrity and confidentiality of data generated and managed.

(b) The sponsor should apply quality control to the relevant stages of data handling …focus…on data of higher criticality and relevant metadata.

(c) The sponsor should pre-specify data to be collected and the method of its collection in the protocol… additional details, including a data flow diagram, should be contained in a protocol related document (e.g., a data management plan).

(d) The sponsor should ensure that data acquisition tools are fit for purpose… validated and ready for use prior to their required use in the trial.

(e) The sponsor should ensure that documented processes… for the full data life cycle.

ICH E6 R3 Sponsor section 3.16.1 (selected sections)

(f) The sponsor should implement measures to ensure the safeguarding of the blinding…during data entry and processing.

(g) The sponsor should put procedures in place to describe unblinding…:

(i) Who were unblinded, at what timepoint and for what purpose they were unblinded;

(ii) Who should remain blinded;

(iii) The safeguards in place to preserve the blinding.

(h) The sponsor should provide guidance to investigators/institutions, service providers and trial participants, where relevant, on the expectations for data capture, data changes, data retention and data disposal.

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ICH E6 R3 Sponsor section 3.16.1 (selected sections)

(i) The sponsor should not make changes to data entered by the investigator or trial participants unless justified, agreed upon in advance by the investigator and documented.

(j) The sponsor should allow correction of errors to data, including data entered by participants, where requested by the investigators/participants. Such data corrections should be justified and supported by source records around the time of original entry.

(k) The sponsor should ensure that the investigator has timely access to data …including relevant data from external sources …

(l) The sponsor should not have exclusive control of data captured in data acquisition tools in order to prevent undetectable changes.

(o) The sponsor should seek investigator endorsement of their reported data at predetermined important milestones.

ICH E6 R3 Sponsor section 3.16.1 (selected sections)

(p) The sponsor should determine the data management steps to be undertaken prior to analysis… depending on the purpose of the analysis to be conducted… Completion of these steps should be documented.

(q) For planned interim analysis, the ability to access and change data should be managed depending on the steps to achieve data of sufficient quality for analysis.

(r) Prior to provision of the data for final analysis… edit access to the data acquisition tools should be restricted.

(t) The sponsor should implement appropriate measures to protect the privacy and confidentiality of personal information of trial participants, in accordance with applicable regulatory requirements on personal data protection.

ICH E6 R3 Sponsor section 3.16.1 (selected sections)

(u) In accordance with applicable regulatory requirements and in alignment with the protocol, the sponsor should describe the process by which the participant's data will be handled when a participant withdraws or discontinues from the trial.

(v) The sponsor should ensure that trial data are protected from unauthorised access, disclosure, dissemination or alteration and from inappropriate destruction or accidental loss.

(w) The sponsor should have processes and procedures in place for reporting to relevant parties, including regulatory authorities, incidents (including security breaches) that have a significant impact on the trial data.

ICH E6 R3 Sponsor section 3.16.1 (selected sections)

(x) When using computerised systems in a clinical trial, the sponsor should:

For systems deployed by the sponsor:

(i) Have a record of the important computerised systems used in a clinical trial…

(ii) Ensure that the requirements for computerised systems (e.g., requirements for validation, audit trails, user management, backup, disaster recovery and IT security) are addressed and implemented and that documented procedures and adequate training are in place …proportionate to the importance of the computerised system and the data or activities…

(iii) Maintain a record of the individual users who are authorised to access the system, their roles and their access permissions;

(iv) … in accordance with delegations by the investigator and visible to the investigator;

(v) Ensure that there is a process in place for service providers and investigators to inform the sponsor of system defects identified;

ICH E6 R3 Sponsor section 3.16.1 (selected sections)

For systems used or deployed by the investigator/institution:

(vi) Assess whether such systems…are fit for purpose or whether the risks from a known issue(s) can be appropriately mitigated. This assessment should occur during the process of selecting clinical trial sites and should be documented;

(vii) In situations where clinical practice computerised systems are being considered for use in clinical trials (e.g., electronic health records or imaging systems used or deployed by the investigator/institution), these systems should be assessed for their fitness for purpose in the context of the trial;

For all systems

(ix) Ensure that there is a process in place for service providers and investigator(s)/ institution(s) to inform the sponsor of incidents that could potentially constitute a serious noncompliance…

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ICH E6 R3 Sponsor section 3.16.2 (selected sections)

Statistical Programming and Data Analysis

Bridging to ICH E9 on Statistical Principles for Clinical Trials

(a) The sponsor should develop a statistical analysis plan …unless the approach to data analysis is sufficiently described in the protocol.

(b) The sponsor should ensure …appropriate and documented quality control of statistical programming and data analysis…

(c) The sponsor should ensure the traceability of data transformations and derivations during data processing and analysis.

(d) The sponsor should ensure that the criteria for inclusion or exclusion of trial participants from any analysis set is pre-defined (e.g., in the protocol or the statistical analysis plan). The rationale for exclusion for any participant (or particular data point) should be clearly described and documented.

ICH E6 R3 Sponsor section 3.16.2 (selected sections)

(e) Deviations from the planned statistical analysis or changes made to the data after the trial has been unblinded (where applicable) should be clearly documented and justified and should only occur in exceptional circumstances… should be reported in the clinical trial report.

(f) The sponsor should retain the statistical programming records that relate to the output contained or used in reports of the trial results, including quality control/validation activities performed. Outputs should be traceable to the statistical software programs, dated and time stamped, protected against any changes, and have access controls implemented to avoid inappropriate viewing of information that may introduce bias.

Some of the main changes in the approved version for sections 2.12, 3.16 and 4

- Clarified that criticality is a spectrum, not an either/or tick box
- Moving parts between section 3.16.1 and 3.16.2 (data management vs stat)
- Clarifying which requirements are valid for which types of systems
- Added that the investigator should inform the sponsor when access rights need to be changed or revoked for an individual
- Putting further emphasis on proportionality e.g. for clinical practice systems
- Clarifying that the sponsor should assess the computerised systems used by an investigator/institution prior to their use in the trial and added factors to be considered

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Some of the main changes in the approved version for sections 2.12, 3.16 and 4

- Clarifying why the sponsor should not have exclusive control of data
- Clarifying wording related to data management steps prior to statistical analysis, including interim analysis
- Included that the sponsor should develop a statistical analysis plan unless the approach to data analysis is sufficiently described in the protocol
- Adding an exceptional example on when an audit trail can be modified
- Added wording on missing steps in the data life cycle (retention and destruction)
- Added that a process for periodic review of the validated state and of users should be in place

Thanks for your attention

Useful links

ICH E6 R3: https://database.ich.org/sites/default/files/ICH_E6%28R3%29_Step4_FinalGuideline_2025_0106.pdf

ICH Step 4 release slides: https://database.ich.org/sites/default/files/ICH_E6%28R3%29_Step%204_Presentation_2025_0123.pdf

EU e-guideline: https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/guideline-computerised-systems-and-electronic-data-clinical-trials_en.pdf

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