Overview of changes
Principles and Annex 1 (Step 4)
ICH E6 (R3)
Good Clinical Practice (GCP) GUIDELINE

HSA-SCRI Public Webinar

28 Feb 2025

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OUTLINE

- Overview
- Principles document
- IRB / IEC responsibilities
- Investigator responsibilities
- Sponsor responsibilities
- Data Governance – Investigator and Sponsor
- Essential Records
- Implementation timelines for Singapore
- Summary
- References

EVOLUTION OF ICH E6 GCP GUIDELINE

Revision 1: 1996

- Described responsibilities and expectations of stakeholders in the conduct of clinical trials.

Revision 2: 2016

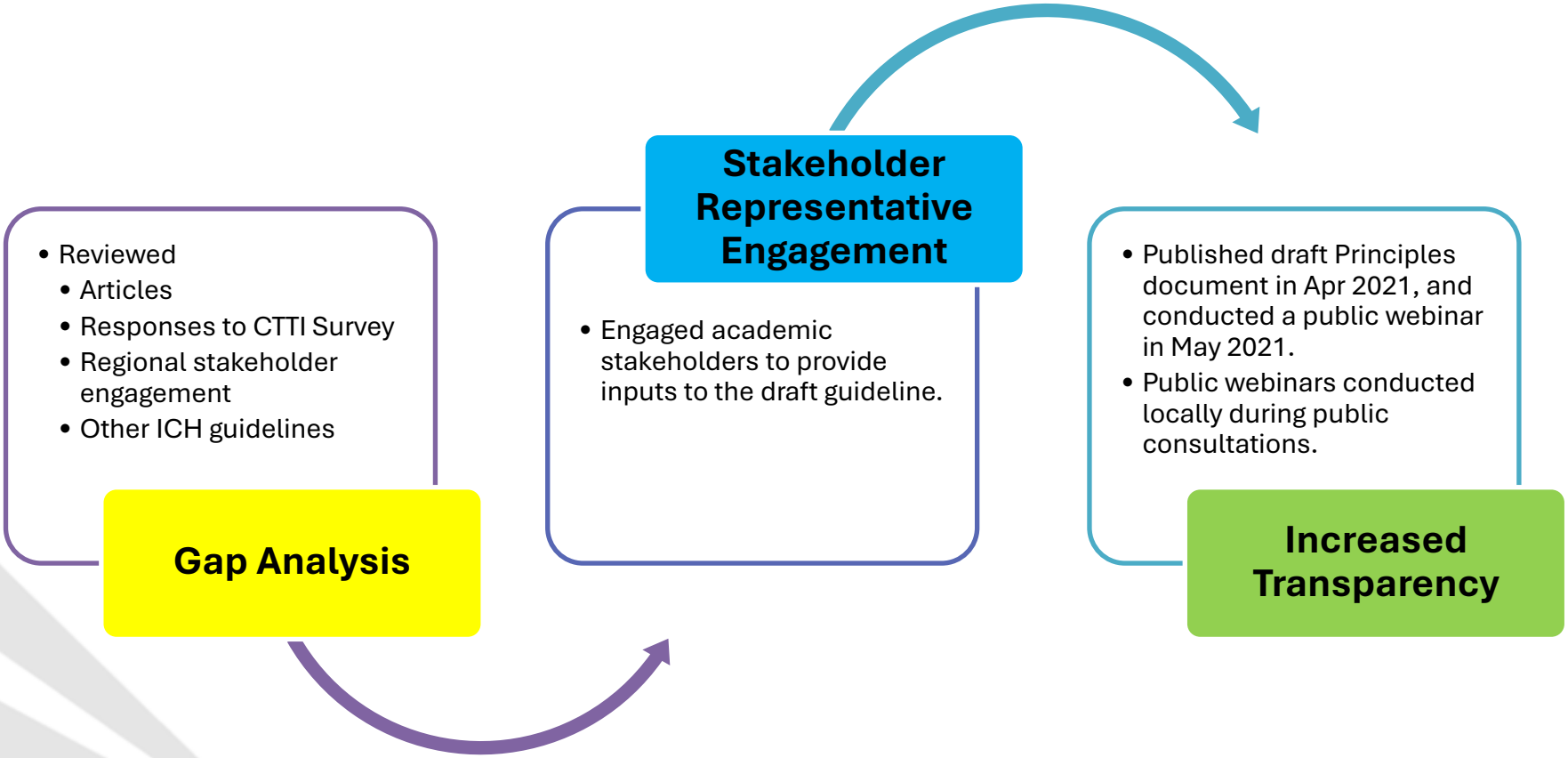
- Integrated addendum to encourage implementation of improved and more efficient approaches to GCP.

Revision 3: 2025

- Following the ICH Reflection Paper on GCP Renovation in Jan 2017,
  - There was a need to modernise ICH guidelines relating to clinical trial design, planning, management and conduct.
  - The scope of the proposed renovation included revising the ICH E6 and E8 guidelines.

NB:
- *ICH E6: Guideline for Good Clinical Practice*
- *ICH E8: Guideline on General Considerations for Clinical Trials*

ICH E6 (R3) DEVELOPMENT PROCESS



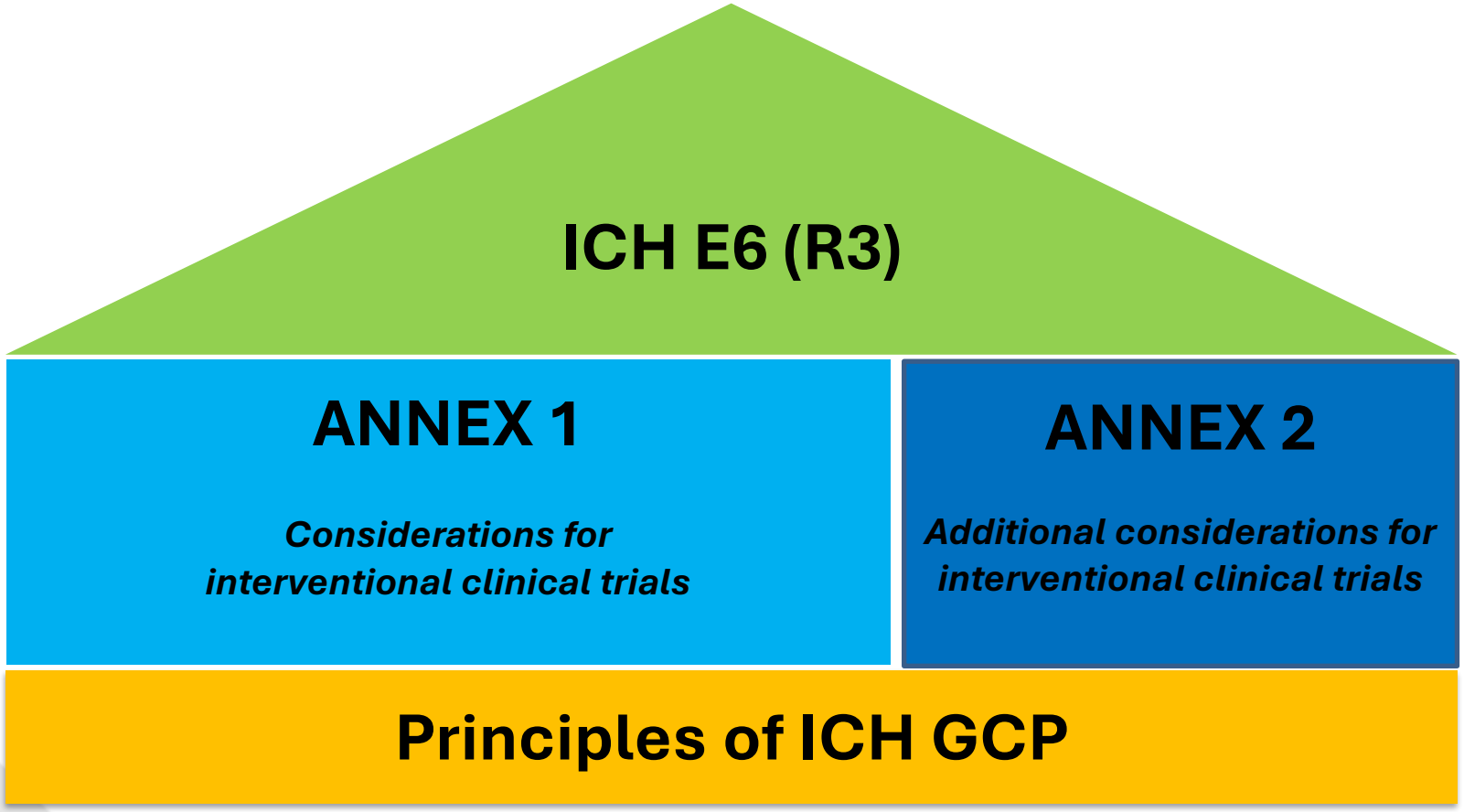
INITIAL TAKEAWAYS FROM FEEDBACK ON ICH E6 (R2)

- Rapidly evolving clinical trial ecosystem was not reflected.
- Academic community was concerned about the lack of proportionality.
- ICH E6 (R2) GCP guideline was seen as a ‘one size fits all’ approach to clinical trials.
- Challenge meeting all GCP requirements in different situations (e.g., public health emergencies)
- GCP requirements were applied where they were not applicable.

WHAT HAS BEEN ENHANCED IN ICH E6 (R3)?

- Clarity on scope
- Fitness for Purpose
- Quality by Design
- Proportionate, risk-based approach
- Innovations in clinical trial design, technology and operational approaches
- Engagement and inclusivity
- Revised structure

OVERVIEW OF ICH E6 (R3)



SCOPE

- **ICH E6 (R3) GCP guideline:**

Applies to **interventional clinical trials** of **investigational products** that are intended to be **submitted to Regulatory Authorities**.

Principles of GCP may be applicable for **other interventional clinical trials of investigational products** that are **not intended** to **support marketing authorisation applications,** in accordance with local requirements.

Annexes provide a basis for interpretation and application of GCP principles.

- Various approaches to the Annexes may be considered, provided they are justified and achieve the intended purpose of the application of the GCP principles.

KEY CONCEPTS (1)

- **FITNESS FOR PURPOSE**
  - **Quality** is defined as **fitness for purpose**.
    - Fitness for purpose: Ability to meet the intended purpose.
      - The **purpose** of a clinical trial is to **generate reliable information** to **answer the research question** and **support decision making** while **protecting trial participants**.

  - ***Examples of activities / processes which should be fit for purpose:***
    - *Protocols, data acquisition tools and other operational documents*
    - *Service Provider's quality management processes*
    - *Sponsor oversight*
    - *Data Governance*
    - *Essential Records*

KEY CONCEPTS (2)

- **QUALITY BY DESIGN (QbD)**
  - Ensures that the **quality** of a clinical trial is **driven proactively** by **designing quality** into the **protocol and processes**.
  - Focuses on **Critical to Quality factors (CtQ)** of the clinical trial in order to **maximise the likelihood of the trial meeting its objectives**.
    - **Prior to trial initiation** and **throughout the trial**.

Critical to Quality (CtQ) Factors

Attributes of a clinical trial that are fundamental to:

Protection of participants

Reliability and Interpretability of trial results

Decisions made based on the trial results

KEY CONCEPTS (3)

- **PROPORTIONATE, RISK-BASED APPROACHES**
  - Focuses on the **risks inherent in the clinical trial** and the **importance of the information** collected.
    - Risks include risks to:
      - Rights, safety and well-being of trial participants; and
      - Risks to the reliability of the trial results

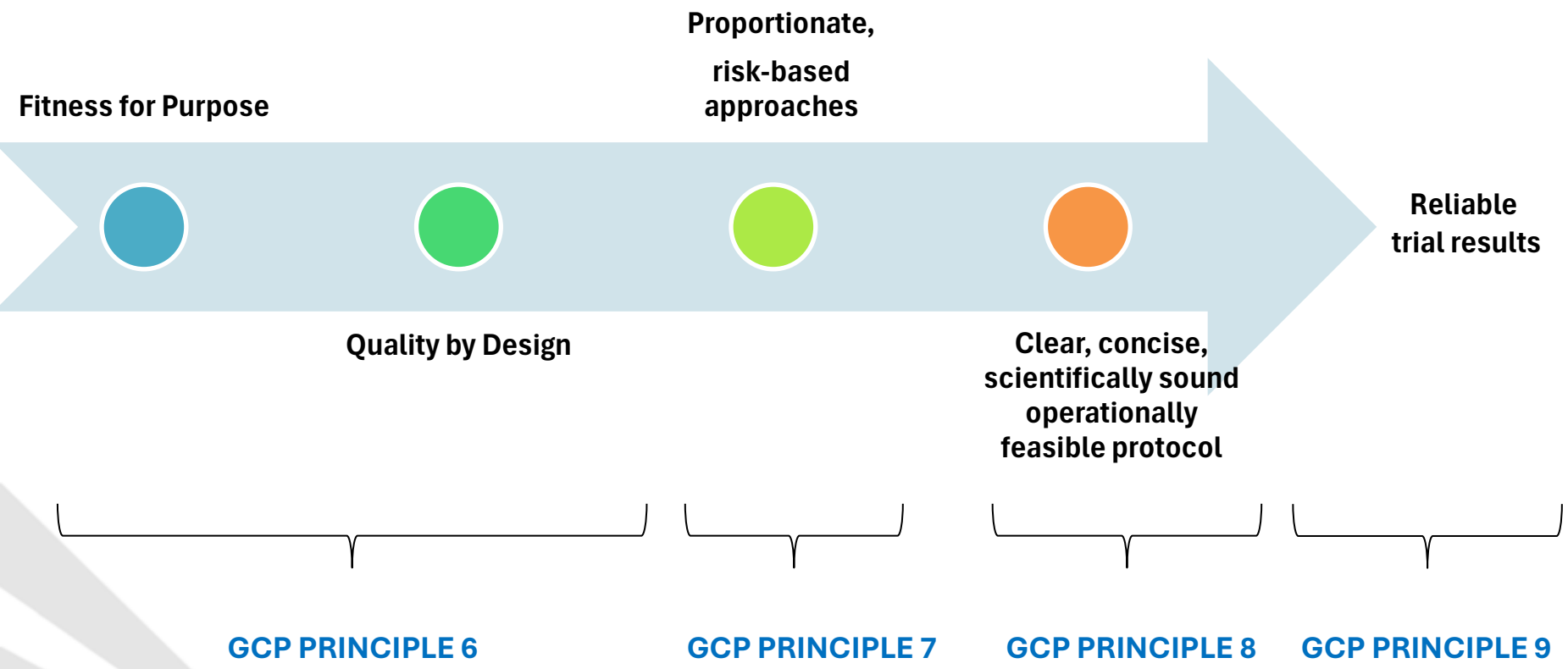
  - ***Examples where proportionate, risk-based approaches can be taken:***
    - *Delegation*
    - *Investigator Oversight*
    - *Quality Management*
    - *Audits*
    - *Data Governance*
    - *Essential Records*

KEY CONCEPTS (4)

- **Examples of risks to Critical to Quality (CtQ) factors:**

Critical to Quality Factors	Example of risk to Critical to Quality (CtQ) factors	Risk Mitigation Measures
Randomisation	Interactive Response Technology (IRT) system may not be validated.	Validate the IRT system.
Blinding	Investigator does not have access to IRT system to perform unblinding.	Provide timely access to IRT for the investigator.
Data Collection & Handling	Participant is unable to complete the Patient Reported Outcome (PRO) in English.	Use validated translations.

INTEGRATING THE KEY CONCEPTS



REVISED STRUCTURE

- **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**

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

- **ANNEX 2** – *under public consultation from Nov 2024 to Feb 2025 for HSA.*

SUMMARY OF CHANGES

Substantial changes

- **Principles of GCP**
- **Annex 1**
  - Investigator
  - Sponsor
  - Data Governance – Investigator and Sponsor **[NEW]**
- **Appendices**
  - Essential Records for the Conduct of a Clinical Trial
- **Glossary**

Other changes

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

PRINCIPLES OF ICH GCP

ICH E6 (R3) PRINCIPLE	TOPIC	ICH E6 (R2) Section
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) PRINCIPLE 1
Ethical Principles

Clinical trials should be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with GCP and applicable regulatory requirement(s). Clinical trials should be designed and conducted in ways that ensure the rights, safety and well-being of participants.

The safety of the participants should be **reviewed in a timely manner** as new safety information becomes available.

Scientific goal and purpose should be **carefully considered** so as not to unnecessarily exclude particular participant populations.

Participant selection process should be **representative of the population groups that the investigational product is intended to benefit, once authorised**, to allow for generalising the results across the broader population

A **qualified physician / qualified dentist / other qualified healthcare professionals (in accordance with local regulatory requirements)** should have the **overall responsibility for the trial-related medical care** given to, and **medical decisions** made on behalf of, participants.

ICH E6(R3) PRINCIPLE 2
Informed Consent

Informed consent is an integral feature of the ethical conduct of a trial. Clinical trial participation should be voluntary and based on a consent process that ensures participants (or their legally acceptable representatives, where applicable) are well-informed.

For participants who are unable to provide informed consent:

- Legally Acceptable Representative must act in the best interest of the participant.

- Participant should be informed in a manner that facilitates their understanding.

The **process and information provided** should enable potential participants to **evaluate the benefits, risks and burden of participating in the trial** and to make an **informed decision** on whether or not to participate in the trial. The information provided should be **clear and concise.**

The **informed consent process** should take into consideration **relevant aspects of the trial**.

In **emergency situations**, consent should be obtained from the **participant or their Legally Acceptable Representative** as soon as possible, and the processes **approved by the IRB / IEC.**

ICH E6(R3) PRINCIPLE 3
IRB / IEC Review

Clinical trials should be subject to an independent review by an IRB/IEC.

Periodic review of the trial by the IRB/IEC should also be conducted in accordance with applicable regulatory requirements.

ICH E6(R3) PRINCIPLE 4
Science

Clinical trials should be scientifically sound for their intended purpose and based on adequate and current scientific knowledge and approaches.

Periodic review of current scientific knowledge and approaches to **determine whether modifications** to the trial are needed, since new or unanticipated information may arise once the trial has begun.

ICH E6(R3) PRINCIPLE 5
Qualified Individuals

Clinical trials should be designed and conducted by qualified individuals.

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

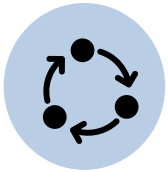
ICH E6(R3) PRINCIPLE 6
Quality

Quality should be built into the scientific and operational design and conduct of clinical trials.

- **Quality of a clinical trial** is considered as **fitness for purpose**.
- **Quality by design** involves focusing on **critical to quality factors** of the trial in order to maximise the likelihood of the trial meeting its objectives.
- **Strategies** should be implemented to **avoid, detect, address and prevent recurrence of serious noncompliance** with GCP, the trial protocol and applicable regulatory requirements.

ICH E6(R3) PRINCIPLE 7 [NEW]
Risk Proportionality

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.

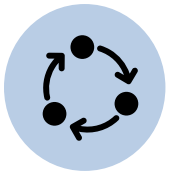


Trial processes should be **proportionate to the risks inherent in the trial** and the **importance of the information collected**.

- 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 8
Protocol

Clinical trials should be described in a clear, concise, scientifically sound and operationally feasible protocol.

A **well-designed trial protocol** is fundamental to the **protection of participants** and for the **generation of reliable results**.

The **scientific objectives of any trial** should **be clear** and **explicitly stated in the protocol**.

The clinical trial protocol and the **plans or documents for the protocol execution** should be **clear, concise and operationally feasible.**

ICH E6(R3) PRINCIPLE 9 Reliable Results (1)

Clinical trials should generate reliable results.

- **Quality and amount of information generated**
  - Fit for purpose;
  - Sufficient to provide confidence in the trial's results and support good decision making.

- **Systems and processes that aid in data capture, management and analyses**
  - Fit for purpose;
  - Capture the data required by the protocol; and
  - Implemented in a way that is proportionate to the risks to participants and the importance of acquired data.

- **Computerised systems**
  - Fit for purpose;
  - 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.

ICH E6(R3) PRINCIPLE 9 Reliable Results (2)

Clinical trials should generate reliable results.

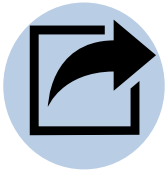
- **Efficient and robust processes for managing records (including data)**
  - Maintain record integrity and traceability;
  - Protect personal information.

- **Essential records**
  - Retained securely;
  - Available upon request to enable appropriate evaluation of the trial conduct in order to ensure the reliability of trial results.

- **Transparency of clinical trials**
  - Timely registration on publicly accessible and recognised databases;
  - Public posting of clinical trial results. Communicating trial results to participants should be considered.

ICH E6(R3) PRINCIPLE 10 [NEW] Roles and Responsibilities

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) PRINCIPLE 11
Investigational Products (IP)

Investigational products (IP) used in a clinical trial should be manufactured in accordance with applicable Good Manufacturing Practice (GMP) standards and be managed in accordance with the product specifications and the trial protocol.

Investigational products should be **manufactured in accordance with applicable GMP standards**.

IP should be **used** in accordance with the **protocol and relevant trial documents.**

IP labelling should **follow applicable regulatory requirements.**

Measures should be in place to ensure that the **IP provided to participants retains its quality**.

IP manufacturing, handling and labelling should be undertaken in a manner that **aligns with treatment assignment and maintains blinding,** where applicable.

Appropriate processes should be implemented for the **handling, shipping, storage, dispensing, returning and destroying or alternatively disposing of the IP.**

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*	NA
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 RESPONSIBILITIES

SUBMISSION

- Assent material;
- Informed consent process;
- Current scientific information (e.g., SmPC, package leaflet / labelling) and their updates;
- Other trial-related information to be provided to the trial participant(s), including a description of the media; and
- Ongoing updates to safety information

CONTINUING REVIEW

- At intervals appropriate to the degree of risk to participants.

MINORS

- Review the assent information, considering the age, maturity and psychological state of the minor, as well as applicable regulatory requirements.

PAYMENT

- Timely; and
- Reasonable reimbursement of participants' expenses, such as for travel and lodging, is not coercive.

IRB/IEC COMPOSITION, OPERATIONS, PROCEDURES & RECORDS

COMPOSITION

- At least one member whose primary area of interest is **not in medical sciences.**

OPERATIONS

- **Alternative processes** may be applicable **for expedited review.**
- **Investigator site staff and/or sponsor may provide information** on any aspect of the trial.

PROCEDURES

- **Communicate its opinion in paper / electronically.**

RECORDS

- **Retain records** in accordance with **applicable regulatory requirements.**

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 to 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 – Clinical Trial / Study Reports	4.13

SELECTED GLOSSARY TERM FOR INVESTIGATOR

ICH E6 (R2) GCP GUIDELINE	ICH E6 (R3) GCP GUIDELINE
Trial Site The location(s) where trial-related activities are actually conducted.	**Investigator Site** The location(s) where trial-related activities are conducted and/or **coordinated under the investigator's/institution's oversight**.

DELEGATION, TRAINING AND OVERSIGHT (1)

DELEGATION

- Maintain a **record of the persons and parties to whom the investigator has delegated trial-related activities.**
  - **Documentation of delegation** should be **proportionate** to the **significance of the trial-related activities.**
  - In situations where the **activities are performed as part of clinical practice, delegation documentation may not be required.**

TRAINING

- **Trial-related training** to persons assisting in the trial should **correspond to what is necessary to enable them to fulfil their delegated trial activities that go beyond their usual training and experience.**

OVERSIGHT

- Maintain **appropriate oversight** of the **persons or parties undertaking the activities delegated** to ensure the rights, safety and well-being of the trial participants and the reliability of data.
  - The **level of investigator oversight**:
    - 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.**

DELEGATION, TRAINING AND OVERSIGHT (2)

Example	Delegation Documentation	Trial-related training	Investigator Oversight
Phlebotomist draws blood for haematology and biochemistry tests	Not required, if there is nothing outside of routine clinical practice.	Not required, if there is nothing outside of usual training and experience.	Less
Phlebotomist draws blood for pharmacokinetic testing	Required	Required	More
Pharmacist dispenses a locally registered IP	Not required, if there is nothing outside of routine clinical practice. *(Alternative documentation recommended, as it is a significant trial-related activity)*	Not required, if there is nothing outside of usual training and experience.	Less
Pharmacist dispenses an unregistered IP	Required	Required	More
Research Nurse measures blood pressure	Not required, if there is nothing outside of routine clinical practice.	Not required, if there is nothing outside of usual training and experience.	Less
Research Nurse administers questionnaire	Required	Required	More

SERVICE PROVIDERS

Sponsor may assist with **identifying a suitable service provider** for the investigator (e.g., use of home nurses).

Investigator should **retain the final decision** on the **selection** of the service provider.

Agreements made by **investigator / institution** and **service providers** for trial-related activities should be **documented**.

- For e.g.,
  - Agreement between Sponsor and Service Provider; and
  - Agreement between Sponsor and Investigator, which specifies involvement of the service provider for the investigator.

Investigator should **maintain oversight** of the service providers.

PROTOCOL COMPLIANCE

Protocol Deviations

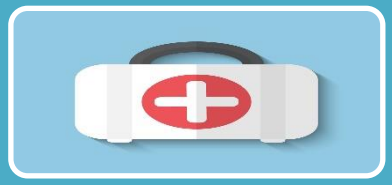
Review all protocol deviations.

Review protocol deviations notified by the sponsor that are relevant to their trial participants and their conduct of the trial .

For important deviations*, explain the deviation and **implement appropriate measures** to **prevent a recurrence.**

***NB: Important protocol deviations** are a **subset of protocol deviations** that **may significantly impact** the **completeness, accuracy and/or reliability of the trial data** or that **may significantly affect a participant's rights, safety or well-being**.*

MEDICAL CARE & SAFETY REPORTING



MEDICAL CARE

- **Other 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

- **Selected revised / new glossary terms for safety reporting:**
  - **Adverse Drug Reaction (ADR) [REVISED]**
    - ➢Clarification on the causal relationship between a medicinal product and an adverse event:
      - ➢The level of certainty about the relatedness of the adverse drug reaction to an investigational product may vary.
      - ➢If the ADR is suspected to be related to the medicinal product with a high level of certainty, it should be included in the reference safety information (RSI) and/or Investigator's Brochure (IB).
  - **Serious Adverse Event (SAE) [REVISED]**
    - ➢Extension of definition to include Important Medical Events.
  - **Suspected Unexpected Serious Adverse Reaction [NEW]**
    - ➢Suspected: There is a reasonable possibility that the drug caused the adverse drug reaction.
    - ➢Unexpected: An adverse reaction, the nature or severity of which is not consistent with the applicable product information (e.g., Investigator's Brochure or alternative documents according to applicable regulatory requirements; see RSI).

MEDICAL CARE & SAFETY REPORTING

SAFETY REPORTING

- May **delegate activities for safety reporting** to **qualified investigator site staff**, but **retains the overall responsibility for safety of the trial participants .**
- Consider **reporting unfavourable medical events occurring in participants before IP administration** (e.g., during screening) to the sponsor, if required by the protocol.
- **Assess the causality** of SAEs.
- Clarification on the **expectations of 'immediate' reporting of SAEs to the sponsor** i.e., after the investigator reasonably becomes aware of the event.
- **Supply the regulatory authority** of any **additional information** for **reported deaths**.

INFORMED CONSENT (1)

MODE

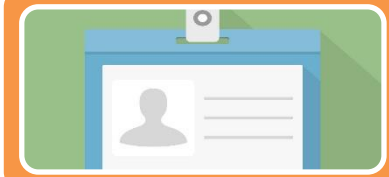
- **Electronic consent** may be used

Varied approaches

- **Text, images, videos and other interactive methods** may be used.
- The **characteristics of the potential trial population** and the **suitability of the method of obtaining consent should be considered.**
- **Paper format** should be **given as an option if electronic consent is used.**

Remote Consent

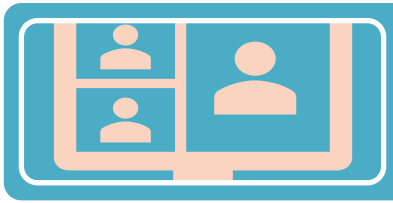
- May be considered.



Verification of identity

- Regardless whether informed consent process is conducted in **person / remotely, the identity of the participant / LAR should be verified.**

INFORMED CONSENT (2)



IMPARTIAL WITNESS

- May participate **remotely.**

SIGNATURE

- **Electronic signatures and dates** may be used.

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 approval in advance of use**.

Minors

- Provide **age-appropriate assent information** and **discuss** with the minor.
- Obtain **assent from the minor**, as appropriate**.**
- Consider **obtaining consent** during the course of the clinical trial, if the **minor reaches the age of legal consent**.

INFORMED CONSENT ELEMENTS

- Reasonably foreseeable risks or inconveniences to the participant's partner
- Participant may decide to stop taking the investigational product or completely withdraw from the trial at any time, without penalty or loss of benefits to which the participant is otherwise entitled
- The follow-up procedure for participants who stopped taking the investigational product, withdrew from the trial or were discontinued from the trial
- The process by which the participant's data will be handled, including in the event of the withdrawal or discontinuation of participation in accordance with applicable regulatory requirements
- Trial may be registered on publicly accessible and recognised databases, per applicable regulatory requirements
- That trial results and information on the participant's actual treatment, if appropriate, will be made available to them should they desire it when this information is available from the sponsor

INVESTIGATIONAL PRODUCT (IP) MANAGEMENT

SPONSOR

- **May facilitate** aspects of IP management (e.g., forms / technical solutions / supply).

INVESTIGATOR OVERSIGHT

- 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.

AUTHORISED MEDICINAL PRODUCTS

- **Alternative approaches to IP documentation** may be considered.

DECENTRALISED ELEMENTS

- The IP may be **shipped to the participant's location** or **supplied to/ dispensed at a location closer to the participant** (e.g., at a local pharmacy or a local healthcare centre).
- The IP may be **administered at the participant's location** by **investigator site staff**, the **participant** themselves, a **caregiver or a healthcare professional**.

END OF TRIAL PARTICIPATION

DISCONTINUATION / WITHDRAWAL

- Follow the **protocol / protocol-related** document.
- **Loss of already collected data should be avoided**.
- Consider if a **discussion** with the participant is necessary.

TRANSPARENCY

- Inform the participant about the **trial results and treatment received**, once available, **respecting the participant's preference to be informed.**

SOURCE RECORDS, DATA INTEGRITY, PRIVACY & CONFIDENTIALITY

SOURCE RECORDS LOCATION LIST

- Define **what is considered to be a source record**(s), the **methods of data capture** and their **location prior to starting the trial.**
- **Update** this definition when needed.

DATA INTEGRITY

- **Avoid unnecessary transcription steps** between the source record and the data acquisition tool.
- **Review data in a timely manner.**
- Ensure that **data acquisition tools** and **other systems deployed by the sponsor** are **used** as **specified in the protocol** or **trial-related instructions**.
- **Review** and **endorse** the **reported data** at **important milestones**.

PRIVACY AND CONFIDENTIALITY

- Ensure that **data reported to sponsor** are identified with an **unambiguous code** that can be **traceable.**

DATA SECURITY & RETENTION

DATA SECURITY

- **For systems deployed by investigator / institution that maintain and retain trial information, ensure that trial data are protected from:**
  - Unauthorised access;
  - Disclosure;
  - Dissemination / alteration; and
  - Inappropriate destruction / accidental loss.

RETENTION

- Implement measures to ensure **availability, accessibility and readability** and to prevent **unauthorised access** and **accidental or premature destruction** of these records.
- **Inform the sponsor** of the person responsible for **maintaining the essential records** during the retention period.

COMPUTERISED SYSTEMS

FOR SYSTEMS DEPLOYED BY THE INVESTIGATOR / INSTITUTION

- **Access** should be **secure and attributable**.
- 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** and **proportionate to the risks to participants** and to the **importance of the data**.

FOR SYSTEMS DEPLOYED BY THE SPONSOR

- **Notify the sponsor** when **access permissions** need to be **changed or revoked** from an individual.

EQUIPMENT FOR DATA ACQUISITION PROVIDED TO PARTICIPANTS

- **Traceability** maintained; and
- **Appropriate training** is provided to participants.

INCIDENT REPORTING

- **Report incidents** which may have a **significant and/or persistent impact on trial data** to the **sponsor and IRB**, where applicable.

SPONSOR

ICH E6 (R3) Section	ICH E6 (R2) Section
3.1 – Trial Design	5.0, 5.4
3.2 – Resources	NA
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	NA

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 – Non-compliance	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

TRIAL DESIGN, RESOURCES & AGREEMENTS

TRIAL DESIGN

- Incorporate sufficient **safety and efficacy data** to support human exposure.
- Incorporate **Quality by Design (QbD)** by identifying **Critical to Quality (CTQ) factors**, and managing the **risks** to CTQ factors.
- 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.**
- Avoid **unnecessary burden** on **participants and investigators**.

RESOURCES

- Ensure that **sufficient resources** are available to appropriately conduct the trial.

AGREEMENTS

- Ensure **agreements** are in place prior to initiating the activities.
- Update agreements to **reflect significant changes** in the activities transferred.

SERVICE PROVIDERS

- Ensure that **Agreements** are in place.
- Seek the **Investigator's agreement** about service providers who undertake activities on their behalf.
- Assess the **suitability** of the service providers.
- Provide a copy of the **protocol and other documents** to perform their activities.
- Ensure service providers provide **access to relevant information** to enable **selection and oversight by sponsor**.
- Ensure service providers implement appropriate **quality management**, and **report incidents that may impact participant safety and/or trial results**.
- Maintain **sponsor oversight** of service providers and **ensure GCP compliance**.

SPONSOR OVERSIGHT

- **Why is sponsor oversight important?**
  - To ensure that the **trial design**, **trial conduct**, **processes** and **information and data generated** are of **sufficient quality** to ensure:

Reliable trial results

Trial participants' safety

Appropriate decision making

- **Approach:**
  - The **range and extent of oversight** measures should be **fit for purpose** and tailored to the **complexity of and risks associated with the trial**.

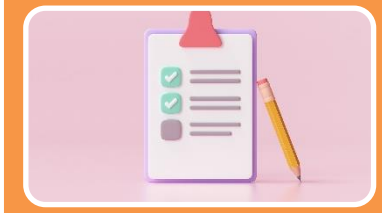
HOW CAN SPONSOR OVERSIGHT BE MAINTAINED? (1)

COMPLIANCE

- Ensure that trial processes are conducted in compliance with the trial protocol and related documents as well as with applicable regulatory requirements and ethical standards.
  - ❑*E.g.: Review policies, procedures and work instructions*

IMPORTANT PROTOCOL DEVIATIONS

- Determine the necessary **trial-specific criteria** for **classifying protocol deviations as important.**
  - *Subset of protocol deviations that may significantly impact the **completeness, accuracy and/or reliability of the trial data** or that may significantly affect a **participant's rights, safety or well-being**.*



SELECTION AND OVERSIGHT OF INVESTIGATORS AND SERVICE PROVIDERS

❑Implement Quality Assurance processes (including audits)

❑Implement Quality Control processes (including monitoring)

HOW CAN SPONSOR OVERSIGHT BE MAINTAINED? (2)

ISSUES

- Ensure **appropriate and timely escalation** and **follow-up of issues** to allow the implementation of appropriate actions in a timely manner.
  - NB:
    - *Risks – what could go wrong*
    - *Issues: what went wrong*

INDEPENDENT DATA MONITORING COMMITTEE (IDMC)

- Consider establishing an IDMC to **assess the progress of a clinical trial**, including the **safety data and the efficacy endpoints**, at intervals and to **recommend to the sponsor whether to continue, modify or stop a trial.**

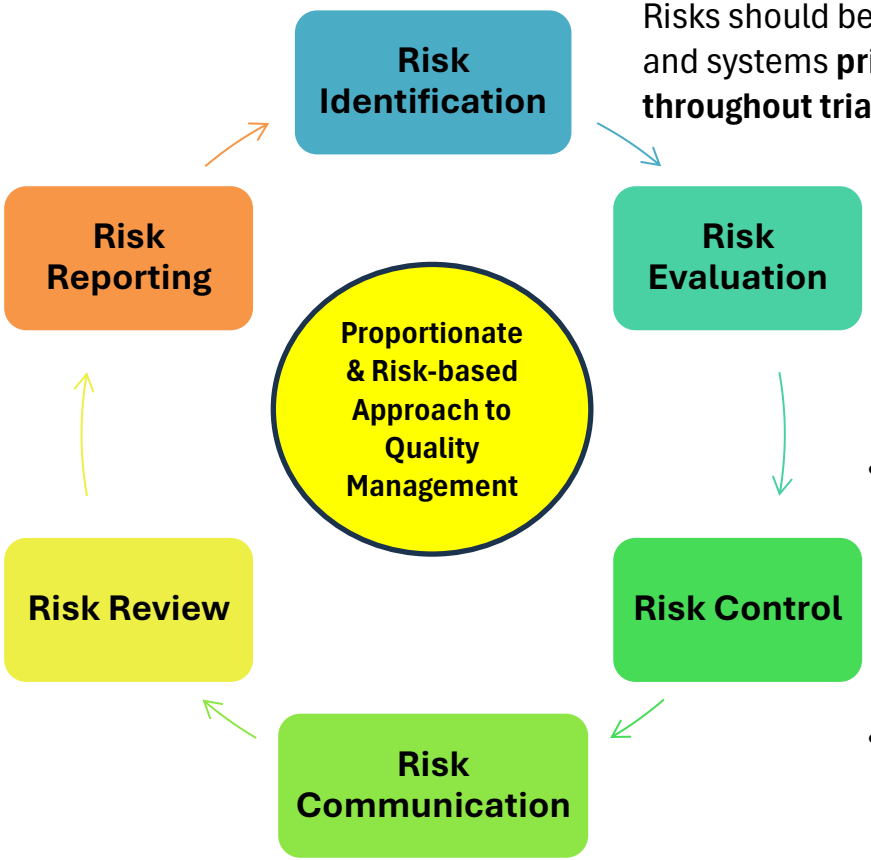
ENDPOINT ASSESSMENT / ADJUDICATION COMMITTEE

- Consider establishing an endpoint assessment / adjudication committee **to review endpoints reported by investigators** to **determine whether the endpoints meet protocol-specified criteria.**
  - *Such committees should be blinded to the treatment assignment to minimise bias*.

QUALITY MANAGEMENT

- Summarise and **report important quality issues** (including instances in which acceptable ranges are exceeded) and the **remedial actions** taken and document them in the clinical trial report.

- Implement **additional risk control measures**, as needed.



Risks should be identified across processes and systems **prior to trial initiation and throughout trial conduct**.

- Ensure that risk control is **proportionate to the importance of the risk to participants' rights, safety and well-being and the reliability of trial results.**
- Where relevant, set **pre-specified acceptable ranges** (e.g., Quality Tolerance Limits at trial level) beyond which **deviations could represent systemic issues.**

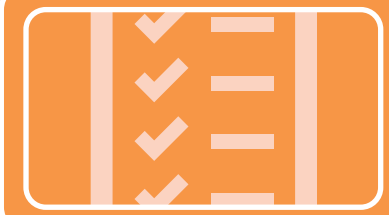
QUALITY ASSURANCE, AUDITS & QUALITY CONTROL

Quality Assurance

- Implement QA throughout the clinical trial.
- Implement risk-based strategies to **identify potential / actual causes of serious non-compliances** to enable their CAPA.

Audits

- Purpose is to evaluate whether the **processes put in place to manage** and **conduct the trial** are **appropriate to ensure compliance.**
- Conduct audits in a manner that is **proportionate to the risks** associated with conduct of the trial.
- Ensure that auditors are **independent** of the **clinical trial / processes being audited.**



Quality control

- Comprises **monitoring** and **data management** processes.
- Where appropriate, implement **quality control activities to facilities outside of investigator sites** (e.g., central image reading facilities).

MONITORING

SELECTION OF MONITORS

- Appoint persons **not involved in the clinical conduct** of the trial at the site being monitored.

SCOPE OF MONITORING

- Consider including the activities and services involved in the monitoring approach, including **decentralised settings**.

MONITORING STRATEGY

- The monitoring strategy should ensure **appropriate oversight of trial conduct** and consider **site capabilities** and the **potential burden**.

INVESTIGATOR SITE MONITORING

- Determine the **frequency of monitoring** based on **identified risks.**
- **Modify the monitoring activities** and **their frequency** as appropriate using **knowledge gained**.
- May be performed **on-site / remotely**, depending on the **nature of the activity** and its **objectives**.
- May include **remote and secure, direct read-only access**.
- Examine **data trends**.

CENTRALISED MONITORING

- Consider using **centralised data analytics** to identify **systemic or site-specific issues**, including protocol noncompliance and potentially unreliable data.

IMPORTANT PROTOCOL DEVIATIONS VS SERIOUS NONCOMPLIANCE VS SERIOUS BREACH

	IMPORTANT PROTOCOL DEVIATION	SERIOUS NON-COMPLIANCE	SERIOUS BREACH
Definition	**May significantly** impact: • The **completeness, accuracy** and/or **reliability of the trial data;** or • The **rights, safety or well-being of a participant.**	**Significantly** impacts: • The **reliability of trial results**; or • The **rights, safety or well-being of trial participants.**	**Likely to affect to a significant degree:** • The **scientific value** of the clinical trial; or • **The safety, or physical or mental integrity of any trial participant**
Reference	ICH E6 (R3) GCP guideline (sections 2.5.3, 3.9.3)	ICH E6 (R3) GCP guideline (section 3.12.2)	Health Products (Clinical Trials) Regulations (Regulation 11)
Additional ICH E6 (R3) GCP requirement	• Determine **the necessary trial-specific criteria** for **classifying protocol deviations as important**.	• **Verify the adequacy of the CAPA**, unless otherwise justified. • Notify the **IRB, RA and investigator,** as appropriate.	NA

- *A **protocol deviation** is any change, divergence or departure from the approved protocol.*
- *A **non-compliance** is failure to adhere to the protocol, GCP or regulations.*
- *A **breach** is a change, divergence or departure from the principles of GCP, approved protocol and clinical trials regulations.*

SAFETY ASSESSMENT & REPORTING

SPONSOR REVIEW OF SAFETY INFORMATION

- **Aggregate and review relevant safety information in a timely manner**, which may result in updates to study documents.
- Review the **available emerging safety information** to assess whether there is any **new data that may affect the trial participant's willingness to continue the trial, impact trial conduct, alter the approval / favourable opinion of IRB and RA**. Such information should be **communicated to the participants, investigator, IRB and RA** in a **timely manner**.

SAFETY REPORTING

- **Report SUSARs to investigators / institutions and IRBs** in a manner that **reflects the urgency or the action required** and consider the **evolving knowledge of the safety profile of the product**. In **some regions, periodic reporting of line listings with an overall safety assessment** may be appropriate.
- **Report urgent safety issues** requiring **immediate attention or action** to the IRB and/or RA and investigators **without undue delay** and in accordance with applicable regulatory requirements.
- **Alternative arrangements for safety reporting to RA, IRBs** and **investigators** and for **reporting by investigators to the sponsor** should be **prospectively agreed upon** with the RA and the IRBs/IECs, and **described in the clinical trial protocol.**

MANAGEMENT OF IMMEDIATE HAZARDS

- Take **prompt actions** to address immediate hazards to participants.
- Determine **causes** of the hazard to take appropriate **remedial actions.**
- **Notify the IRB and RA**, including any subsequent protocol amendment (if applicable).

IP MANAGEMENT

INFORMATION ON THE IP

- For **authorised medicinal products**, identify the **basic product information** to be used in the trial.

BLINDED CLINICAL TRIALS

- Develop a **mechanism to protect the trial blind if treatment assignment is unblinded for the purpose of safety reporting to IRB or RA**.

SUPPLY AND HANDLING OF IP

- May **directly supply IP to participants.**
- May **undertake various approaches for shipping and dispensing.**
- **May not require to keep retention samples** for **authorised medicinal products** used as an **IP, unmodified from its authorised state** in accordance with local regulatory requirements. In this situation, **samples are typically kept by the manufacturer**.

DATA HANDLING (1)

- Ensure the **integrity of data.**

Data Integrity

- Ensure the **confidentiality of data** generated.

Confidentiality

- Focus on **data of higher criticality** and **relevant metadata.**

QA & QC

- **Pre-specify data to be collected** and the **method of its collection** in the protocol.

Data Collection

- Where necessary, include a **data flow diagram** in a protocol-related document.

Data Flow Diagram

- Ensure they are **fit for purpose** and designed to capture the information required by the protocol.
- Ensure they are **validated prior to use.**

Data Acquisition Tools

- Ensure that documented processes are implemented to ensure the **data integrity for the full data life cycle.**

Documented Processes

- Implement measures to ensure the **safeguarding of the blinding.**
- Implement **procedures for unblinding.**

Blinding

EXAMPLES OF DATA OF HIGHER CRITICALITY

Personal data

Medical history

Informed Consent Date

IP dosing and administration

Safety and efficacy data

DATA HANDLING (2)

- Provide guidance on **expectations for data capture, data changes, data retention and data disposal.**

Guidance

- **Do not allow data changes,** unless justified, agreed in advance by investigator, and documented.

Data Corrections

- May allow data corrections, provided they are **justified and supported by source records around the time of original entry.**

Data Corrections

- **Provide investigator with timely access to data** for decisions on eligibility, treatment, continued participation and safety.

Access

- **Provide investigator with access to data** for retention purposes.

Access

- **Should not have exclusive control to trial data** in order to prevent undetectable data changes.

Exclusive Control

- Provide instructions on **navigating systems, data and metadata.**

Instructions

- Seek **investigator endorsement of reported data at predetermined milestones.**

Endorsement

DATA HANDLING (3)

- Determine the **data management steps** to be **undertaken prior to analysis** to ensure the data are of sufficient quality.

Data Analysis

- Manage the **ability to access and change data**, depending on the steps to achieve data of sufficient quality.

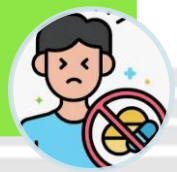
Planned Interim Analysis

- **Restrict edit access** to Data Acquisition Tools, and where applicable before unblinding the trial, prior to providing the data**.**

Final Data Analysis

- Describe the **process for handling participant's data** for withdrawal / discontinuation.

Participant Withdrawal



- Ensure that **data is protected** from **unauthorised access, disclosure, dissemination or alteration and from inappropriate destruction or accidental loss.**

Data Security

- Establish processes and procedures for reporting to relevant parties, including regulatory authorities, **incidents (including security breaches) that have a significant impact on the trial data.**

Incident Reporting

COMPUTERISED SYSTEMS DEPLOYED BY THE SPONSOR

Maintain a **record of important computerised systems used**.

Ensure that **requirements for computerised systems** (e.g., requirements for validation, audit trails, user management, backup, disaster recovery and IT security) are **addressed and implemented**.

Ensure that **documented procedures** and **adequate training** are in place to ensure the **correct development, maintenance and use** of computerised systems in clinical trials.

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

Ensure that **access permissions granted to investigator site staff are in accordance with delegations** by the investigator and **visible** to the investigator;

Ensure that there is a **process** in place for **service providers** and **investigators to inform the sponsor of system defects identified.**

COMPUTERISED SYSTEMS DEPLOYED BY THE INVESTIGATOR / INSTITUTION

ASSESSMENT

- Assess whether such systems (e.g., EHR), if identified as containing source records in the trial, are **fit for purpose** or **whether the risks from a known issue(s) can be appropriately mitigated**.
  - Assessment should be done during **investigator selection** and **documented.**
- **In situations where clinical practice computerised systems are used for clinical trials (e.g., EHR / imaging systems),**
  - These systems should be assessed for their fitness for purpose in the context of the clinical trial.
- Assessment should be **performed before being used in the clinical trial** and should be **proportionate to the importance of the data** managed in the system.
  - Factors such as data security (including backup measures), user management and audit trails should be considered as appropriate.

STATISTICAL PROGRAMMING & DATA ANALYSIS

- **Statistical Analysis Plan**
- **Quality control of statistical programming and data analysis** (e.g., sample size calculations, analysis results for IDMC review, outputs for clinical trial report, statistical or centralised monitoring)
- **Traceability of data transformations and derivations during data processing and analysis**
- **Criteria for inclusion or exclusion of participants from any analysis set is predefined**
- **Rationale for exclusion for any participant (or particular data point) should be clearly described and documented**
- **Deviations from planned statistical analysis or changes made to the data after the trial has been unblinded should be documented, justified, only occur in exceptional circumstances, authorised by the investigator, and reported.**
- **Statistical programming records that relate to the output contained or used in reports of the trial results should be retained.**

RECORD KEEPING & REPORTS

RECORD KEEPING

- Also **applies to service providers**.
  - Inform the investigator if sponsorship of the trial changes.

REPORTS

- **Premature suspension / termination of the trial**
  - **Provide the investigator with information** about **potential subsequent therapy(ies)** and **follow-up** for the participants, where appropriate.

- **Clinical Trial / Study Reports**
  - **Once the trial has been unblinded** and **relevant analyses/conclusions** have been **completed and finalised**,
    - Make **trial results publicly available**;
    - **Provide the investigator** with **information about the treatment taken by their participants for blinded trials**; and
    - **Provide investigators with the trial results**.

DATA GOVERNANCE

ICH E6 (R3) Section	ICH E6 (R2) Ref.
4.1 – Safeguard Blinding in Data Governance	NA – Major Revamp
4.2 – Data Life Cycle Elements	
4.3 – Computerised Systems	

SELECTED GLOSSARY TERMS FOR DATA GOVERNANCE

ICH E6 (R3) GCP GUIDELINE	Definition
Data Integrity [NEW]	Data integrity includes the degree to which data fulfil key criteria of being **attributable, legible, contemporaneous, original, accurate, complete, secure** and **reliable** such that **data are fit for purpose.**
Data Acquisition Tool [NEW]	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. The data originator may be a human (e.g., the participant or trial staff), a machine (e.g., wearables and sensors) or a computer system from which the electronic transfer of data from one system to another has been undertaken (e.g., extraction of data from an electronic health record or laboratory system). **Examples of DATs include but are not limited to CRFs, interactive response technologies (IRTs), clinical outcome assessments (COAs), including patient-reported outcomes (PROs) and wearable devices, irrespective of the media used.**
Metadata [NEW]	**The contextual information** required to **understand a given data element**. Metadata is structured information that describes, explains or otherwise makes it easier to retrieve, use or manage data. For the purpose of this guideline, **relevant metadata are those needed to allow the appropriate evaluation of the trial conduct.**
Audit Trail [REVISED]	**Metadata records** that allow the **appropriate evaluation of the course of events** by capturing details on actions (manual or automated) performed relating to information and data collection and, where applicable, to activities in computerised systems. **The audit trail should show activities, initial entry and changes to data fields or records, by whom, when and, where applicable, why. In computerised systems, the audit trail should be secure, computer-generated and time stamped.**

EXAMPLE OF METADATA

135

Metadata for Blood Pressure measurement:

1. Variable: Systolic Blood Pressure
2. Unit: mmHg
3. Type: Numeric (Integer)
4. Range: 70-250 mmHg
5. Method: Automated device, seated position
6. Frequency: 3 readings, 1 minute apart
7. Arm: Right (unless contraindicated)
8. Device: Omron HEM-907
9. Timing: Before study drug administration
10. Personnel: Research Nurse

IMPORTANT DATA GOVERNANCE REFERENCES IN ICH E6 (R3)

ICH E6 (R3) SECTION	INVESTIGATOR	SPONSOR
GCP PRINCIPLES	✓	✓
2.12 (Records)	✓	
3.16 (Data and Records)		✓
4 (Data Governance)	✓	✓

GENERAL REQUIREMENTS (1)

Responsible parties

- Sponsors
- Investigators

Appropriate management of data integrity, traceability and security

- Allowing **accurate reporting**, **verification** and **interpretation of the clinical trial-related information.**

Quality and amount of information generated

- **Sufficient** to address **trial objectives, provide confidence in the trial's results and support good decision making.**

Systems and processes that help ensure this quality

- **Proportionate** to the **risks to participants** and the **reliability of trial results.**

GENERAL REQUIREMENTS (2)

Key processes that should be addressed across the full data life cycle, with a focus on the criticality of the data

- 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

- Focus on the **criticality of the data**
- Implemented **proportionately**
- **Documented appropriately**

SAFEGUARDING BLINDING IN DATA GOVERNANCE

Integrity of blinding

- Maintain the **integrity of blinding** in system design, user management, delegation, data transfers, database review prior to planned unblinding, and statistical analysis

Roles, responsibilities and procedures

- **Define and document** roles, responsibilities and procedures for access to unblinded information.

Risk Assessment

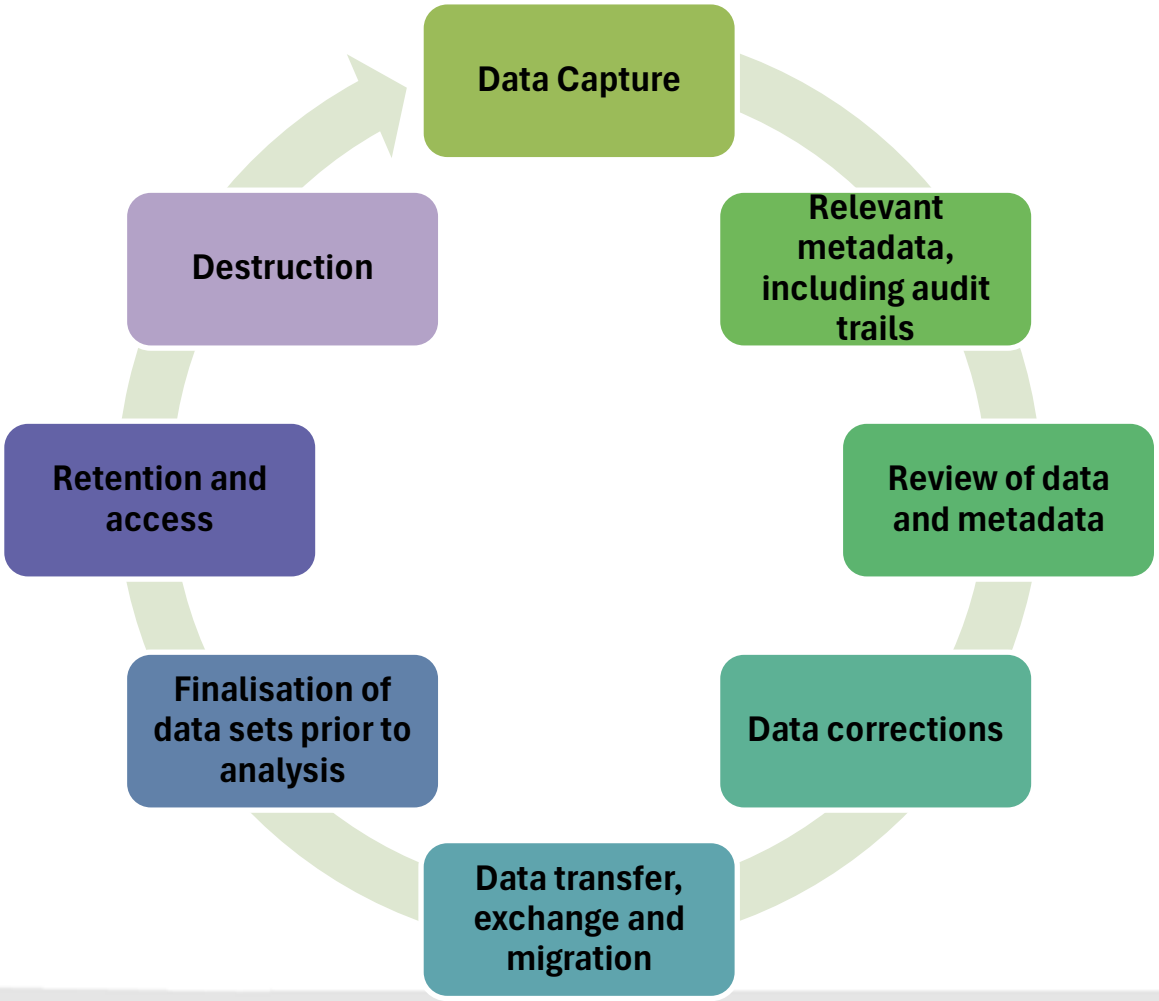
- Include potential for unblinding in **risk assessment**.
- Implement **suitable mitigation strategies** to reduce the risk of inadvertent unblinding of the blinded investigator site staff.

Planned / unplanned unblinding

- **Document** any planned or unplanned unblinding.
- Assess the **impact** of any unplanned unblinding on the trial results, and take **appropriate actions**.

DATA LIFE CYCLE ELEMENTS

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

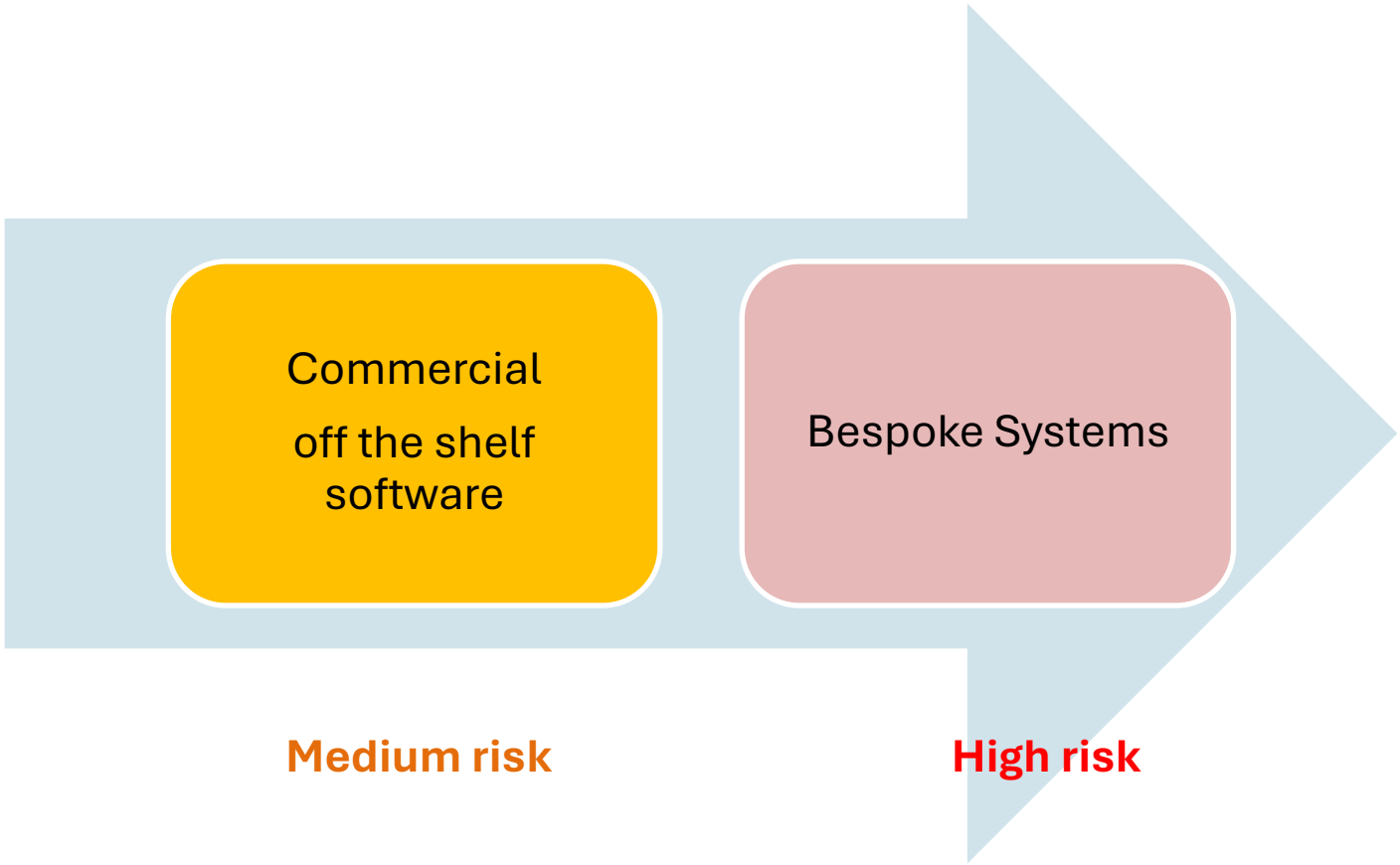


COMPUTERISED SYSTEMS

RESPONSIBILITY MATRIX FOR COMPUTERISED SYSTEMS

Responsibility Matrix	Systems deployed by Investigator/Institution	Systems deployed by Sponsor
System designed for clinical trial purposes	• e-Investigator Site File (eISF) • AI algorithm to screen patients or measure trial endpoints	• Bespoke systems [e.g., Interactive Response Technology (IRT), Electronic Patient Reported Outcomes (ePRO), Electronic Case Report Form (eCRF)] • Systems designed to be configured / managed (e.g., licensed eCRF)
System used for clinical trial, but designed for other purposes	• Electronic Medical Records (EMR) • Imaging equipment	• Systems where no alterations are needed (e.g., wearables or questionnaires not specifically developed for a clinical trial)

Which computerised system would you rank higher for Critical to Quality factors?



COMPUTERISED SYSTEMS

RESPONSIBLE PARTY

- Ensure that **responsibilities are clearly documented;**
- Ensure that those developing computerised systems for clinical trials are **aware of the intended purpose** and the **regulatory requirements** that apply to them.

ENGAGEMENT OF INTERESTED PARTIES

- Consider engaging interested parties in the **design of the system** to ensure that computerised systems are **suitable for use by the intended user population.**

DOCUMENTED PROCEDURES

- Maintain documented procedures to ensure the **appropriate use of computerised systems** in clinical trials for essential activities related to **data collection, handling and management.**

TRAINING

- Ensure that those using computerised systems are **appropriately trained in their use.**

SECURITY

- Manage security **throughout data life cycle**;
- Implement and maintain **security controls**;
- Ensure **adequate backup of data**; and
- Maintain **documented procedures** and perform **periodic testing**.

COMPUTERISED SYSTEM VALIDATION (1)

Throughout the life cycle of the computerised system.

Demonstrate that **the system conforms to its established requirements** for **completeness, accuracy, reliability**, and that its **performance is consistent with its intended purpose.**

Appropriately validated **prior to use.**

Periodic review may be appropriate to ensure that computerised **systems remain in a validated state throughout the life cycle of the system.**

Standard system functionality and **protocol-specific configurations** and **customisations**, including automated data entry checks and calculations, should be validated

COMPUTERISED SYSTEM VALIDATION (2)

Validation procedures for system design, system requirement, functionality testing, configuration, release, setup, installation and change control

Fitness for purpose

Requirements and **specifications** defined

Unresolved issues justified, and risks mitigated

COMPUTERISED SYSTEM VALIDATION (3)

System Release implemented for investigator sites after trial approvals

Contingency measures for system failure prevent loss or lack of accessibility to data essential to participant safety, trial decisions or trial outcomes.

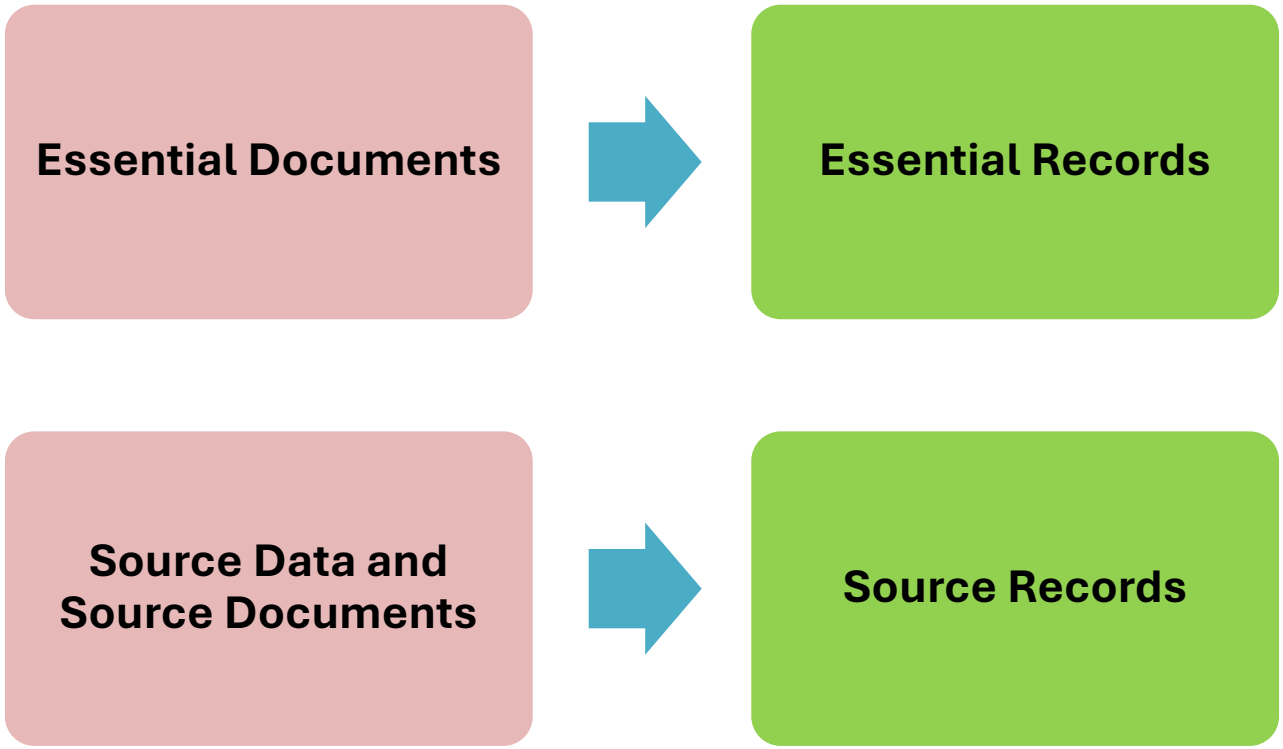
Technical Support for issue management, focusing on issues with higher criticality.

User Management, including user roles and access permissions

ESSENTIAL RECORDS

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

NEW GLOSSARY TERMS FOR ESSENTIAL RECORDS



PURPOSE, SCOPE & ACCESS

PURPOSE

- Permit and contribute to the **evaluation of the conduct of a trial** in relation to the **compliance of the investigator and sponsor with Good Clinical Practice (GCP)** and **applicable regulatory requirements** and the **reliability of the results produced**.
- Facilitate **investigator and sponsor oversight.**

SCOPE

- **Nature** and **extent** of essential records generated and maintained are dependent on:
  - Trial design;
  - Trial conduct; and
  - Application of risk proportionate approaches; and
  - The importance and relevance of that record to the trial.

ACCESS

- The **investigator/institution** should have **access to** and the **ability to maintain the essential records generated by the investigator/institution** before and during the conduct of the trial, and **retain them** in accordance with applicable regulatory requirements.

ESSENTIAL RECORDS MANAGEMENT (1)

Requirements

- Identifiable;
- Version Controlled (when appropriate);
- Authors, reviewers and approvers (as appropriate); and
- Dated and signed (electronic or physical), where necessary.

Activities that are delegated by the investigator or transferred by the sponsor

- **Arrangements** should be made for the **access, management and retention of essential records**.

Maintenance

- Maintained in / referred to from **repositories.**
- Collected and filed in a **timely manner**.
- **Retained** in a way that ensures that they remain **complete, readable and readily available** and are **directly accessible** upon request by regulatory authorities, monitors and auditors.
- **Alterations** to the essential records should be **traceable.**
- **Original essential records** should be **retained by the responsible party who generated them**.

ESSENTIAL RECORDS MANAGEMENT (2)

Access

- In order to fulfil their responsibilities in the conduct of the trial, the **sponsor and investigator/institution may need access to or copies of one another's relevant essential records before and during the conduct of the trial**. At the end of the trial, each party should retain their essential records.
  - **If the investigator has access to relevant essential records from the sponsor** (e.g., SUSAR reports) via a sponsor- provided portal, and **these essential records would need to be retained by the investigator/institution at the end of the trial**.

Blinding

- **Careful consideration** should be given to the **sharing of records** when there are **blinding considerations** and when the **records are subject to applicable data protection legislation**.

ESSENTIALITY OF TRIAL RECORDS

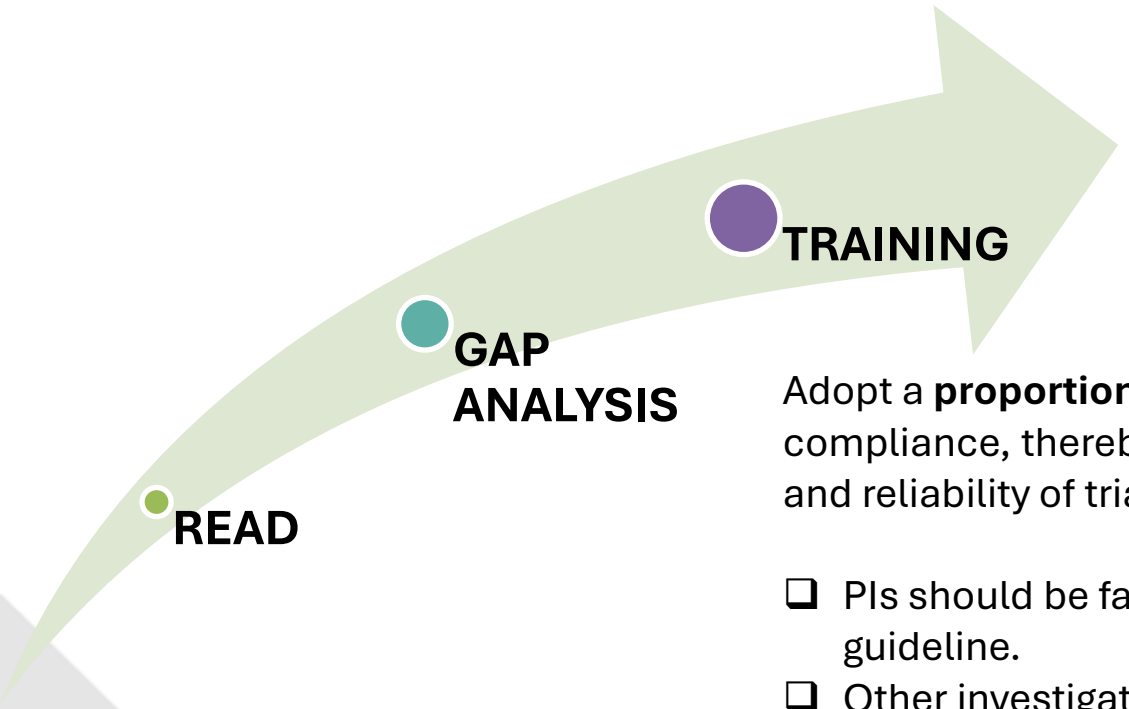
ASSESSMENT

- The **assessment of whether a record is essential** and **has to be retained** should **take into account the criteria provided.**
  - Such assessment, whilst important, is not required to be documented.
  - A structured content list for storage repository(ies) may be used to prospectively identify essential records.

ESSENTIAL RECORDS TABLE

- Essential records listed in the table **should be retained when produced.**
- The table is **not an exhaustive list.**
- For some trial records listed in the Essential Record Table, their **presence and nature** are dependent on the **trial design, trial conduct** and **risk proportionate management of the trial** and **may not be produced.**

ICH E6 (R3) GCP guideline Implementation timeline for Singapore



Adopt a **proportionate approach** to training to ensure compliance, thereby ensuring trial participant protection and reliability of trial results.

- ❑ PIs should be familiar with the revised ICH E6 (R3) GCP guideline.
- ❑ Other investigator site staff should be trained, depending on their delegated tasks.
- ❑ Training should be tailored to enable staff to fulfil tasks that extend beyond their usual training and experience.

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 (with use-cases) will be developed by the ICH E6 (R3) EWG to clarify or provide supplementary explanation to the application of the GCP guideline.
- **The implementation timeline for the Principles and Annex 1 document of ICH E6 (R3) GCP guideline for Singapore is 1 Jan 2026.**

REFERENCES

- ICH E6 (R3) – Guideline for Good Clinical Practice, 6 Jan 2025
- ICH E6 (R3) – Slide deck on Principles and Annex 1 document
- ICH E8 (R1) - Guideline on General Considerations for Clinical Trials, 6 Oct 2021
- MHRA GCP Symposium (11 Feb 2025)
- ACT EU workshop on ICH E6 R3 (principles and Annex 1) (19 and 20 Feb 2025)

Thank You!

We welcome your queries!

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