Essential Records for the Conduct of a Clinical Trial

Proportionality

Critical Thinking

Risk-based approach

Fit-for-purpose

Susanne Nørskov, Novo Nordisk A/S – ICH E6(R3) EFPIA EWG Member

Disclamer

- The views presented are the views of the presenter, and not necessarily those of Novo Nordisk, EFPIA or the EWG
- These slides are intended for discussion purposes only and for the personal use of the audience. These slides are not intended for wider distribution outside the intended purpose without presenter's approval
- The content of this slide deck is accurate to the best of the presenter's knowledge at the time of production

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*

Definition of ‘Essential document’ changed

ICH E6R2:

1.23 Essential Documents

- Documents which individually and collectively permit evaluation of the conduct of a study and the quality of the data produced (see 8. Essential Documents for the Conduct of a Clinical Trial).

ICH E6R3:

Essential Records

- Essential records are the **documents and data (and relevant metadata),** in any format, associated with a clinical trial that facilitate the ongoing management of the trial and collectively allow the evaluation of the methods used, the factors affecting a trial and the actions taken during the trial conduct to determine the reliability of the trial results produced and the verification that the trial was conducted in accordance with GCP and applicable regulatory requirements (see Appendix C).

Principle 9
Clinical trials should generate reliable results (1/2)

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.**
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.
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.
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.**

Principle 9
Clinical trials should generate reliable results (2/2)

5. **Essential records should be retained securely by sponsors and investigators for the required period in accordance with applicable regulatory requirements. These essential records should be available to regulatory authorities, monitors, auditors and IRBs/IECs (as appropriate) upon request to enable appropriate evaluation of the trial conduct in order to ensure the reliability of trial results.**
6. The transparency of clinical trials includes timely registration on publicly accessible and recognised databases and the public posting of clinical trial results. Communicating trial results to participants should be considered. Such communication should be objective and non-promotional.

Annex 1 Requirements for Essential Records

This are requirements in the **Sponsor** section...

Maintain records... Investigators Product that document the identity, shipment, receipt, return and destruction or alternative disposition of the investigational product(s)

...transfer of ownership.....

Promptly inform..... Legal.. .....integrity and continuity.....

This are requirements in the **Investigator** section...

... Investigators Product .....retrain..
..... product's delivery, the inventory.. .....destruction or alternative disposition

...transfer of ownership.....

Promptly inform..... Legal.. .....integrity and continuity.....

.....

This are requirements in the **Data Governance** section...

Relevant metadata... .....to be archived.....

protected .....unauthorised access
.....
Protected from alterations .....throughout ... retention period

...

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	

*"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."

C.2 Management of Essential Records (1/3)

1. Records should be identifiable and version controlled (when appropriate) and should include authors, reviewers and approvers as appropriate, along with date and signature (electronic or physical), where necessary.
2. For activities that are transferred or delegated to service providers by the sponsor or investigator/institution, respectively, arrangements should be made for the access and management of the essential records throughout the trial and for their retention following completion of the trial.
3. These essential records should be maintained in or referred to from repositories held by the sponsor and by the investigator/institution for their respective records. These repositories may be referred to as a trial master file (TMF). The repository held by the investigator/institution may also be referred to as the investigator site file (ISF).
4. The sponsor and investigator/institution should maintain a record of where essential records are located, including source records. The storage system(s) used during the trial and for archiving (irrespective of the type of media used) should provide for appropriate identification, version history, search and retrieval of trial records.

C.2 Management of Essential Records (2/3)

5. The sponsor and investigator/institution should ensure that the essential records are collected and filed in a timely manner, which can greatly assist in the successful management of a trial. Some essential records should generally be in place prior to the start of the trial and may be subsequently updated during the trial.
6. The sponsor and investigator/institution should retain the essential records 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. Alteration to the essential records should be traceable.
7. The sponsor and investigator/institution should ensure the retention of the essential records required to fulfil their responsibility. The original records should generally be retained by the responsible party who generated them.
8. 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 (see sections 2.12.11 and 3.16.3(a)). The record location may vary during the trial depending on the nature of the record. For example, the investigator may access relevant essential records from the sponsor (e.g., suspected unexpected serious adverse reactions (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.

C.2 Management of Essential Records (3/3)

9. When a copy is used to permanently replace the original essential record, the copy should fulfil the requirements for certified copies.
10. Some records are typically maintained and retained only by the sponsor (e.g., those related solely to sponsor activities such as data analysis) or only by the investigator/institution (e.g., those that contain confidential participant information). Some records may be retained by the sponsor and/or the investigator/institution.
11. 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. For the sharing of essential records with service providers, see section C.2.2.
12. Certain essential records may not be specific to a trial but may be related to the investigational product, facilities or processes and systems, including computerised systems, involved in running multiple trials and retained outside the trial-specific repositories (e.g., Investigator's Brochure, master services agreements, standard operating procedures, validation records).

C.3 Essentiality of Trial Records

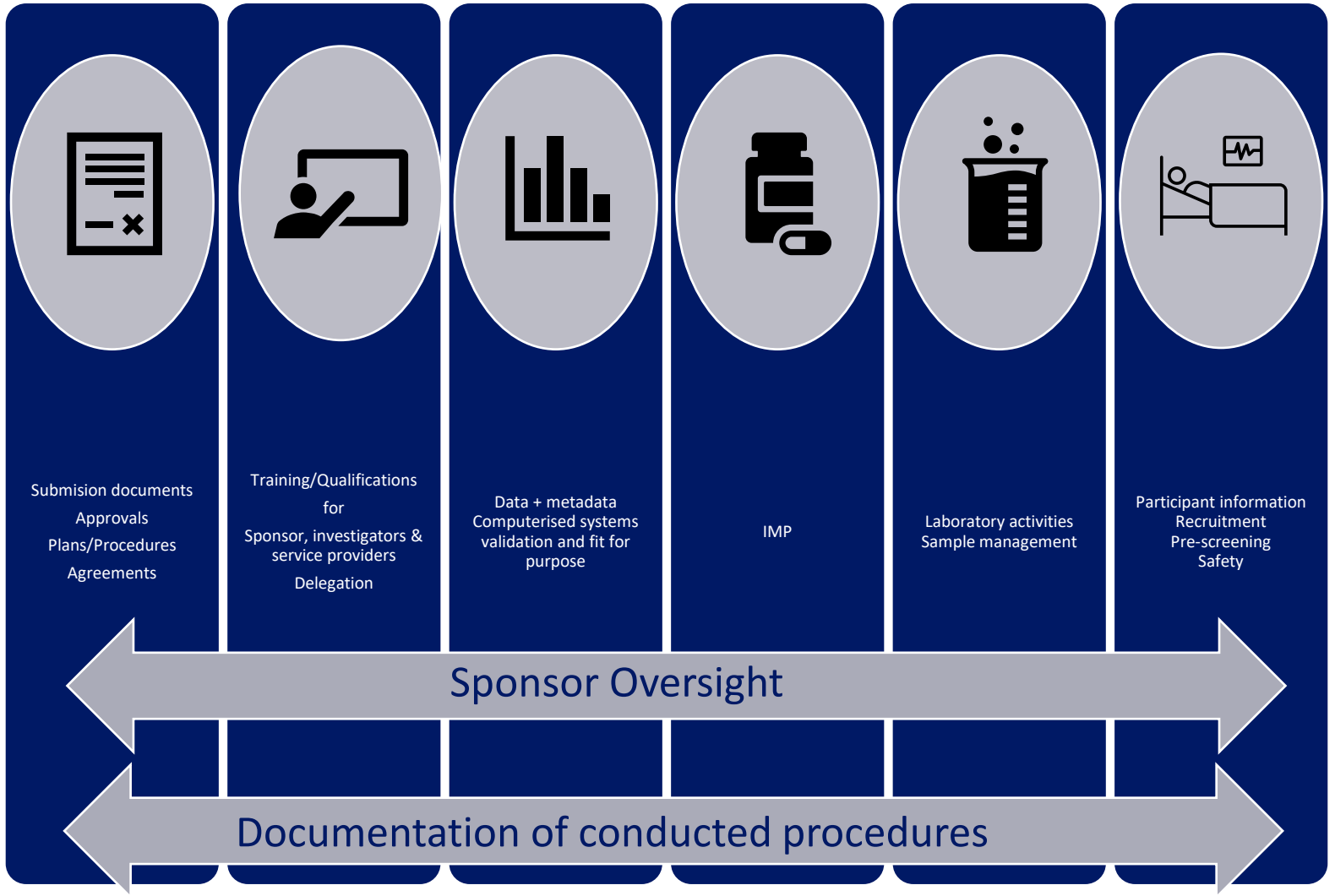
Requirements

- **Principles**
  - Information fit-for-purpose
  - Sufficient
  - Support good decision making
- **Annex 1**
  - retaining essential records specific to the trial

Guidance

- **Appendix C (C.3.1)**
  - Outlines an assessment to help deciding whether a record is essential and has to be retained.
  - Such an assessment needs not to be documented

C.3 Essentiality of Trial Records



Essential Records Table

ICH E6(R2)

8.2 Before the Clinical Phase of the Trial Commences

During this planning stage the following documents should be generated and should be on file before the trial formally starts

	Title of Document	Purpose	Located in Files of	
			Investigator/ Institution	Sponsor
8.2.1	**INVESTIGATOR'S BROCHURE**	To document that relevant and current scientific information about the investigational product has been provided to the investigator	X	X
8.2.2	**SIGNED PROTOCOL AND AMENDMENTS, IF ANY, AND SAMPLE CASE REPORT FORM (CRF)**	To document investigator and sponsor agreement to the protocol/amendment(s) and CRF	X	X
8.2.3	**INFORMATION GIVEN TO TRIAL SUBJECT** **- INFORMED CONSENT FORM** (including all applicable translations)	To document the informed consent	X	X
	- ANY OTHER WRITTEN INFORMATION	To document that subjects will be given appropriate written information (content and wording) to support their ability to give fully informed consent	X	X

ICH E6(R3)

Essential Records Table

If these trial records are produced, they are considered essential and should be retained (see sections C3.1 and C3.2).

Note: An asterisk (*) identifies those essential records that should generally be in place prior to the start of the trial (see section C2.5).

Investigator's Brochure or basic product information brochure (e.g., summary of product characteristics, package leaflet or labelling)*
Signed protocol* and subsequent amendments during the trial
Dated, documented approval/favourable opinion of IRB/IEC of information provided to the IRB/IEC*
IRB/IEC composition*
Regulatory authority(ies) authorisation, approval and/or notification of the protocol* and of subsequent amendments during the trial (where required)
Completed signed and dated informed consent forms
Completed participant identification code list and enrolment log
- Notification by originating investigator to sponsor of serious adverse events (SAEs) and related reports, where required - Notification by sponsor and/or investigator, where required, to regulatory authority(ies) and IRB(s)/IEC(s) of suspected unexpected serious adverse reactions (SUSARs) and of other safety information - Notification by sponsor to investigators of safety information, where required
Interim or annual reports to IRB/IEC and regulatory authority(ies) (where required)

Essential Records Table C.3.3

Essential Records Table

If these trial records are produced, they are considered essential and should be retained (see sections C3.1 and C3.2).

Note: An asterisk (*) identifies those essential records that should generally be in place prior to the start of the trial (see section C2.5).

Investigator's Brochure or basic product information brochure (e.g., summary of product characteristics, package leaflet or labelling)*
Signed protocol* and subsequent amendments during the trial
Dated, documented approval/favourable opinion of IRB/IEC of information provided to the IRB/IEC*
IRB/IEC composition*
Regulatory authority(ies) authorisation, approval and/or notification of the protocol* and of subsequent amendments during the trial (where required)
Completed signed and dated informed consent forms

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.

Thank you!