Sponsor: main changes

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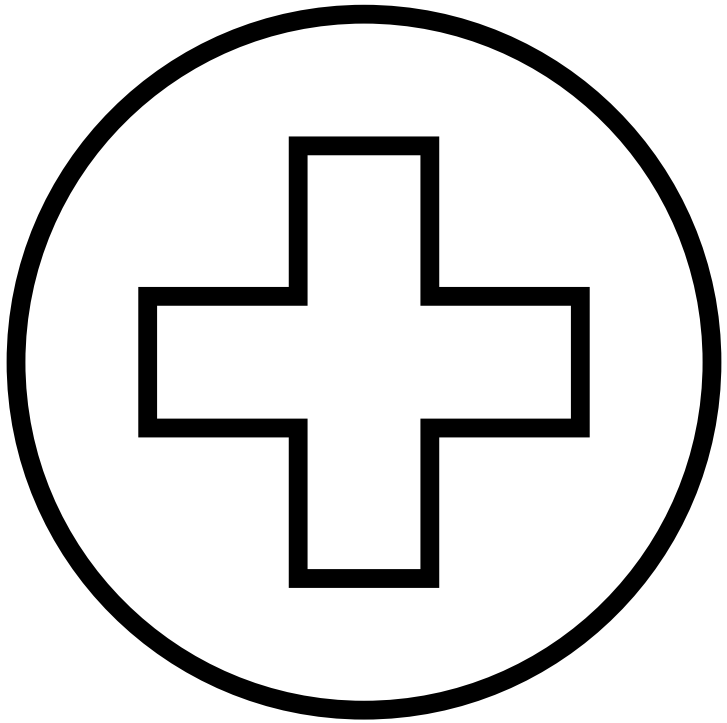
Agenda

- Overview of main changes for the sponsor.
- Changes from the draft to the final.
- Take home message.

Overview



- Overview of main changes for the sponsor

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ICH E6 (R3) Annex 1
Sponsor

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

ICH E6 (R3) Annex 1 *Sponsor*

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

Sponsor

- **Trial Design**

  Included language that the sponsor should:
  - Ensure that safety and efficacy data from non-clinical studies/clinical trials/real world sources are sufficient to support human exposure.
  - Implement QbD, including prospective identification of critical to quality factors and management of important risks.
  - Consider seeking inputs from interested parties (e.g., healthcare professionals, patients).
  - Ensure that protocols, data acquisition tools and other operational documents are fit for purpose, clear, concise and consistent.
  - Avoid unnecessary burden on participants and investigators.
- **Agreements**
  - Clarified that agreements with service providers and other parties (e.g., IDMC, adjudication committee) should be in place prior to initiating the activities.
  - Clarified that agreements should be updated to reflect significant changes in the activities transferred.

Sponsor (2)

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

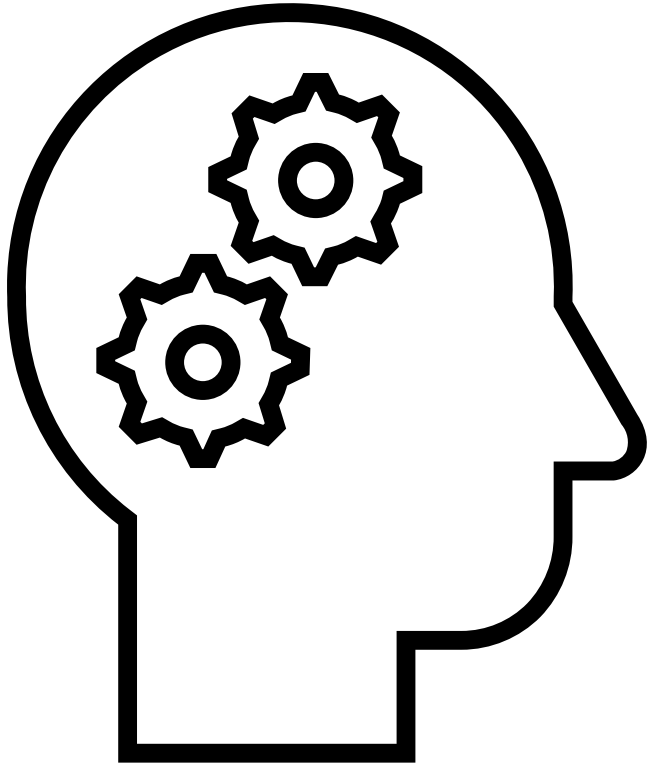
Sponsor (3)

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

Sponsor (4)

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

Changes from the draft to the final.



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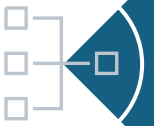
Changes from the draft to the final

Further emphasis on not placing unnecessary burden on participants and investigators.

Ensure that the retention of records clearly defined as in line with regulatory requirements.



Where service providers are used, they too should have appropriate quality management systems and report incidents with potential impact to participants or the trial results to the sponsor.

Important protocol deviations should be defined clearly in sponsor processes.

Adjudication/endpoint assessment committees should have data provided to them in a way to minimize bias.

Changes from the draft to the final (2)

Critical to quality factors should be assessed before initiation and throughout the trial conduct. Incorporate risk mitigation activities into protocol design, monitoring plans and agreements with parties clearly defining their roles and responsibilities.

Ensure you know the difference between remote monitoring and centralised monitoring.

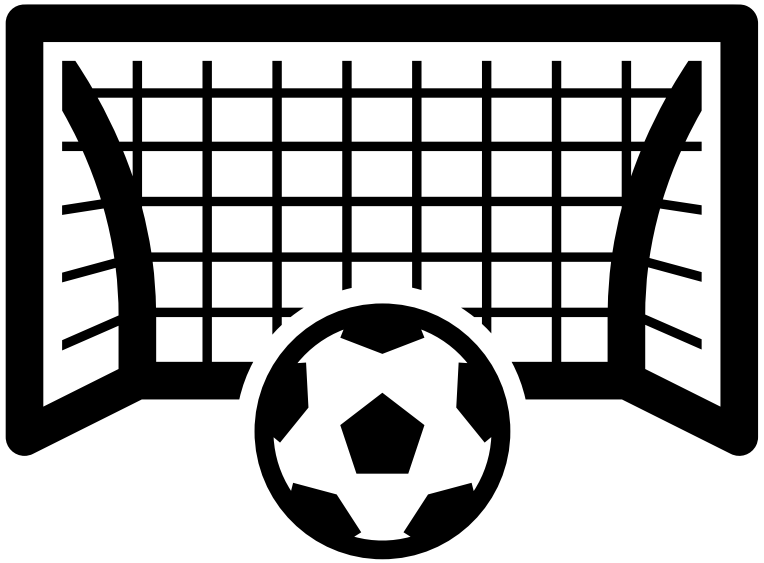
Control of unblinding when conducting an interim analysis.

Timely access to data for the investigator to be able to take medical decisions for their participants.

Timely and actional data, e.g., not millions of data points from a wearable device.

Not have exclusive control of data in order to prevent undetectable changes.

Summary



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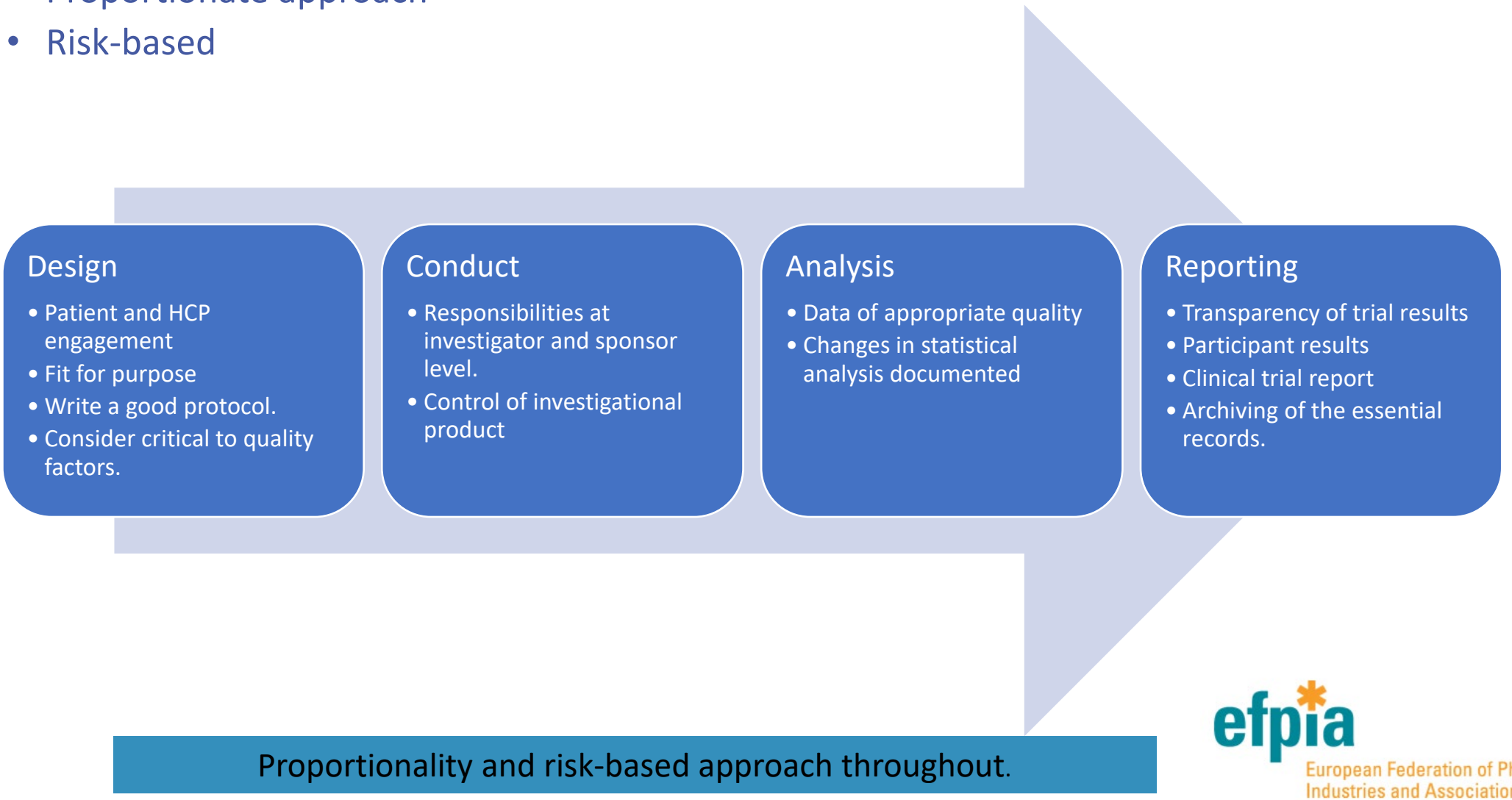
Take home messages for sponsors:

- Think – participant's rights safety and well-being and the reliability of results:
  - Proportionate approach
  - Risk-based



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