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Review Article

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Modernizing Good Clinical Practice: Key Insights and Impact of ICH E6(R3) Guideline

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Abstract

An updated version of the Good Clinical Practice Guideline, E6(R3), has been made available by the International Council for Harmonization. This guideline places a strong emphasis on a more adaptable, risk-based method of trial supervision. Quality by Design (QbD) adoption, attention to Critical-to-Quality (CtQ) factors, participant safety enhancement, adoption of Digital Health Technologies (DHTs), decentralized trials, elucidation of sponsor, investigator roles and responsibilities are some of the major effects. The implementation of risk-based monitoring, updating SOPs, quality systems, bolstering data governance with technologies like audit trails and metadata are examples of operational impacts. These updates seek to minimize needless burden, safeguard the rights, safety, and well-being of trial participants, promote innovation in trial design and conduct, and assure data reliability.

Conclusion: This review article provides a comprehensive review of the major revisions to the GCP guidelines, offering insights into the E6(R3) framework, its key impacts, and the essential takeaways for modern clinical trial conduct.

Keywords: Good Clinical Practice; ICH E6(R3); Clinical Trial Innovation; Digital Health Technologies; Risk-Based Monitoring; Fit-for-Purpose

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1. Introduction

Clinical trials are defined as interventional investigations in human participant's aimed at discovering or verifying the clinical, pharmacological, and/or pharmacodynamic effects of an investigational product, identifying adverse reactions, and studying absorption, distribution, metabolism, and excretion to determine safety and/or efficacy. (1) The International Council for Harmonization (ICH) has guidelines for Good Clinical Practice (GCP), specifically version E6. Initially released in 1996 as E6(R1), it got updated in 2016 to E6(R2). This update was driven by the growing scale and complexity of clinical trials along with advancements in technology and risk management strategies. The E6(R2) revision made amendments to certain sections of the GCP guidelines to better align with modern clinical trial conduct. (2) However, given the rapid evolution of the clinical trial ecosystem towards decentralized trials, digital health technologies (DHTs), and participant-centric approaches, limitations of E6(R2) have become apparent. Specifically, concerns arose regarding the lack of proportionality in applying GCP requirements, a perceived "one-size-fits-all" approach, challenges in meeting GCP requirements in diverse situations like public health emergencies and pandemics, and the application of GCP requirements in contexts where they may not be applicable. This framework is expanded upon in E6(R3), which introduces a more adaptable, risk-based, and technologically driven framework. Informed consent (IC), quality management, data integrity, and investigational product (IP) management are among the main areas of update. Wider developments in clinical research, like the use of electronic systems, participant-centricity, and decentralized trial models, are reflected in these modifications. The GCP guideline transitioned from E6(R2 to E6(R3), the final version of E6(R3) was adopted on January 6, 2025, after the expert working group examined public consultation comments and made the necessary revisions to the draft, which was made available for public consultation by May 19, 2023. (1-3)

The updated GCP guideline has emphasized flexibility, risk-based approaches, and the integration of digital technologies. The E(6R3) guideline has expanded key concepts of quality by design (QbD) and trial conduct, discussed factors critical to the quality (CtQ) of the study, and described the management of risk to quality. The key changes to the GCP guidelines are discussed in this article along with the key lessons learned from the E6(R3) guideline.

2. Revisions of ICH E6 GCP guidelines and significance of ICH E6(R3) guideline

2.1 The revisions in the ICH E6 guidelines

The revisions in the ICH E6 guidelines with key updates described in table 1.

Table 1. The revisions in ICH E6 guidelines (1,4)

E6 (released in 1996)	E6(R2) (released in 2016)	E6(R3) (released in 2025)
1. **The** guideline outlines the expectations of interested parties involved in the conduct of clinical trial along with the responsibilities of sponsor and investigator. 2. The guideline provides guidance on essential documents, investigator brochure, and the aspects of monitoring, reporting and archival of the clinical trial data.	1. The guideline introduces an integrated addendum to support the adoption of enhanced and more efficient approaches to GCP. 2. Aim to improve trial processes while maintaining rigorous protection of human subjects. 3. Updated the standards for use and management of electronic records in clinical research. 4. Encouraged harmonized practices that facilitate smoother and more consistent trial execution. 5. Seen as one-size-fits- all.	1. Emphasizes QbD. 2. Involves critical thinking. 3. Use of proportionate, risk-based approaches 4. Recognises that a one size does not fit all. 5. Updated GCP definition. 6. Promotes transparency in trial conduct 7. Promotes risk mitigation strategies. 8. Focuses on operationally feasible protocol design, avoid unnecessary complexity. 9. Innovative design for diverse participant population, broadening trial outcome applicability. 10. Encourages integration of digital technologies.

2.2 Significance of ICH E6(R3) guideline (1,4)

2.2.1 Enhanced structure and scope

- Introduces a revised framework to improve readability, clarity, and more precised information on scope of GCP.
- Establishes realistic and practical expectations for sponsors and investigators within a dynamic clinical trial ecosystem.

2.2.2 Quality by design and risk-based approaches

- Emphasizes the integration of QbD principles to proactively identify CtQ factors, key processes and data essential for trial integrity and participant safety.
- Advocates for proportionate, fit-for-purpose, and risk-based strategies tailored to the significance of data, participant risk, and reliability of trial outcomes.
- Encourages operational feasibility and the avoidance of unnecessary complexity in trial designs.

2.2.3 Support for innovation in clinical trials

- Incorporates language to support innovative trial designs, technological advancements, and novel operational approaches.
- Reflects lessons learned from public health emergencies and pandemics, including adaptive and decentralized trial models.

2.2.4 Transparency and informed consent

- Reinforces the importance of clinical trial registration and results reporting to promote transparency.
- Enhances the informed consent process with additional guidance to ensure participant understanding and autonomy.

2.2.5 Quality culture and trial efficiency

- Builds upon concepts from ICH E8(R1) by fostering a culture of quality and embedding quality considerations into trial design.
- Recognizes variability in scale, complexity, and cost of trials, advocating for efficiency through targeted assessment of CTQ elements.
- Recommends risk mitigation strategies aligned with the importance of data, participant safety, and trial reliability.

2.2.6 Technology integration and participant engagement

- Encourages the exploration and integration of DHTs such as wearables and sensors to enhance trial execution.
- Stresses that technology use should be appropriate to the trial design and participant characteristics.
- Promotes inclusive trial designs that engage diverse populations, thereby improving the generalizability of outcomes.

2.2.7 Stakeholder perspectives

- Recognizes the value of stakeholder input, including participants, regulators, and healthcare providers to improve trial relevance, feasibility, and efficiency.

3. Significant changes in structure and content of ICH GCP guideline (1,4,5)

The revamped R3 version includes significant changes in the structure and the content of GCP guidelines. The summary of key structural changes and guidelines transition E6(R2) to E6(R3) are shown in figure 1 and table 2 respectively.

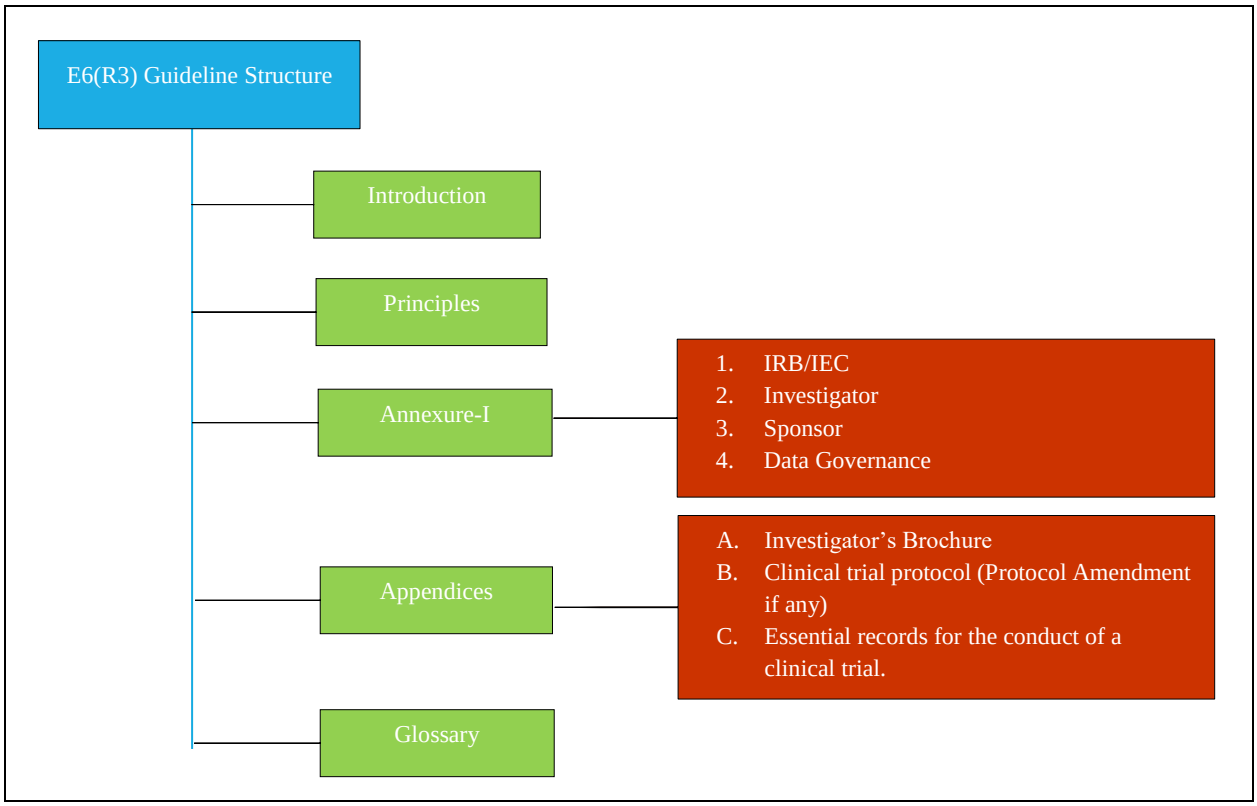

Figure 1. E6(R3) guideline structure (1)

Table 2. E6(R2) to E6(R3) guideline transition (1,2,4)

Section Description	ICH E6(R2)	ICH E6(R3)
Principles	2.1, 2.2, 2.3, 2.7, 2.11	1. Ethical principles
	2.9	2. Informed consent
	2.6	3. IRB/IEC review
	2.4, 2.5	4. Science
	2.8	5. Qualified individuals
	2.13	6. Quality
	NA	7. Risk proportionality
	2.5	8. Protocol
	2.1	9. Reliable results
	NA	10. Roles and Responsibilities
	2.12	11. Investigational product
IRB/IEC	NA	1.1 Submission and communication
	3.1	1.2 Responsibilities
	3.2	1.3 Composition, function and operations
	3.3	1.4 Procedures
	3.4	1.5 Records
Investigator	4.1	2.1 Qualifications and training
	4.2	2.2 Resources
	4.1, 4.2	2.3 Responsibilities

	4.4, 4.10	2.4 Communication with IRB/IEC
	4.1	2.5 Compliance with protocol
	4.12	2.6 Premature termination or suspension of a trial
	4.3, 4.11	2.7 Participant medical care and safety reporting
	4.8	2.8 Informed consent of trial participants
	4.3	2.9 End of participation in a clinical trial
	4.6	2.10 Investigational product management
	4.7	2.11 Randomisation procedures and unblinding
	4.9	2.12 Records
	4.13	2.13 Reports
Sponsor	5.0, 5.4	3.1 Trial design
	NA	3.2 Resources
	5.7	3.3 Allocation of activities
	5.3, 5.4	3.4 Qualification and training 3.4.1 Medical experties
	5.9	3.5 Financing
	5.1, 5.2, 5.6, 5.9, 5.23	3.6 Agreements
	5.6	3.7 Investigator selection
	5.10, 5.11	3.8 Communication with IRB/IEC and regulatory authority(ies)
	NA	3.9 Sponsor oversight
	5	3.10 Quality management
	5.1, 5.18, 5.19	3.11 Quality assurance and quality control
	5.2	3.12 Noncompliance
	5.16, 5.17	3.13 Safety assessment and reporting
	5.8	3.14 Insurance/indemnification/compensation to participants and investigators
	5.12, 5.13, 5.14	3.15 Investigational product(s)
	5.5, 5.15	3.16 Data and records
	5.21, 5.22	3.17 Reports
Data governance-Investigator and sponsor	NA	4.1 Safeguard blinding in data governance
	NA	4.2 Data life cycle elements
		4.2.1 Data capture
		4.2.2 Relevant metadata, including audit trails
		4.2.3 Review of data and metadata
		4.2.4 Data corrections
		4.2.5 Data transfer, exchange and migration
		4.2.6 Finalisation of data sets prior to analysis
		4.2.7 Retention and access
		4.2.8 Destruction
	NA	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
Appendix A (Investigator brochure)	7.1	A.1 Introduction
	7.2	A.2 General considerations
	7.3	A.3 Content of the investigator's brochure
Appendix B (Clinical trial protocol and protocol amendments)	6.1	B.1 General information
	6.2	B.2 Background information
	6.3	B.3 Trial objectives and purpose
	6.4	B.4 Trial design
	6.5	B.5 Selection of participants
	6.5	B.6 Discontinuation of trial intervention and participant withdrawal from trial
	6.6	B.7 Treatment and interventions for Participants
	6.7	B.8 Assessment of efficacy
	6.8	B.9 Assessment of safety
	6.9	B.10 Statistical considerations
	6.1	B.11 Direct access to source records
	6.11	B.12 Quality control and quality assurance
	6.12	B.13 Ethics
	6.4, 6.13	B.14 Data handling and record keeping
	6.14	B.15 Financing and insurance
	6.15	B.16 Publication policy
Appendix C (Essential records for the conduct of a clinical trial)	8.1	C.1 Introduction
	NA	C.2 Management of essential records
	NA	C.3 Essentiality of trial records

3.1 Significant changes in GCP principles

In table 4, presented the revised GCP principles, amongst these principles number 7 and 10 are new.

- Principle No. 7**:** This principle outlines that the trial processes should be proportionate to risks inherent in the trial and importance of information collected. Focus on managing risks to rights, safety, and well-being of participants, reliability of trial results, and CTQ factors should be managed proactively.
- Principle No. 10: This principle reflects that the clear roles and responsibilities in clinical trials should be documented. Even if tasks are transferred or delegated, sponsors retain responsibility for their activities, investigators retain responsibility for their duties, and agreements should clearly define roles and responsibilities.

These principles aim to ensure:

- **Risk-Proportionate Processes:** Minimizing risk to avoid unnecessary complexity and protecting the participants.
- **Clear Accountability**: Despite task delegation or transfer.

3.2. Key updates in content of GCP guideline and its Implications

The key updates in the GCP content with their implications are summarized in the table 3. (1,4,5)

Table 3. ICH E6(R3) guideline key updates and implications

E6R3 guideline section	Key updates	Implications
IRB/ IEC	• **Reporting:** Global language about reporting to IRB/IEC and regulatory authorities. • **Consent:** Reflects digitization and varied approaches to obtaining consent (if any), relevant information to be reviewed by IRB/ IEC. • **Compensation:** Clarifies potential for participants to be compensated for costs incurred to participate. • **Assent for minors:** IRB/IEC should review assent information considering the minor's age, maturity, psychological state, and applicable regulatory requirements. • **Records:** Guides on relevant records to be retained for specific duration with applicable regulatory requirement. (In E6(R2), it was for at least 3 years after the completion of trial).	• **Guide on communication:** Provide clarity and guidance on submission and communication with IRB/ ICE and applicable relevant regulatory. • **Modernized processes:** Accounting for digitization in consent. • **Clarify guidelines**: On compensation and assent for minors. • **Ensure retention of records**: For the duration in compliance with applicable regulatory requirements.
Investigator	• **Inform consent (IC):** The updated guideline provides the significant information on varied approaches of inform consent (paper or electronic e.g., text, images, videos, and other interactive methods) including remote consent, new information, re-consent, language and enrolment of minors. Clarity on presence of impartial witness (remotely or in-person) wherever applicable, along with this it is clarified that the reasonably foreseeable risk and inconvenience to the participant's partner (when applicable) to be included in inform consent (Participant partner-word was not observed in E6(R2) guideline). Listed in the guideline that the inform consent must include the data handling and follow-up procedure of the participant who is stop taking IP and withdrawal/discontinued from the study. • **Qualifications and training:** Flexible documentation for qualifications; trial-related training for staff should match their delegated activities beyond usual training/experience. • **Medical care:** Other qualified health professionals may be involved in trial participant care per local regulations. • **Safety reporting**: Include reporting unfavorable medical events before investigational product (IP) administration (e.g., during screening) to sponsor if protocol required. • **Sponsor-Investigator responsibilities:** Investigator retains ultimate responsibility for delegated activities via service providers. • **Investigator oversight:** Level of oversight should be proportionate to data importance and risks to participant safety/data reliability. • **Delegation documentation:** Requirements clarified. • **Important protocol deviations:** Clarity on explanation and implementation of preventive measures to avoid recurrence (where applicable).	• **Modern practice and clarity for consent:** Adapt to modern practices and provides clarity for consent along with ensuring IRB/ IEC compliance. • **Ensure adequate training:** For trial staff on delegated activities. • **Allow flexible medical care**: Involving qualified health professionals. • **Enhance safety reporting:** Including pre-IP administration events if protocol required. • **Ensure clear accountability**: Investigator responsibility for delegated tasks. • **Proportionate oversight**: Based on data importance and risks. • **Ensure the compliance:** Based on reviewing important protocol deviations and implementing preventive measures to avoid recurrence enhances the protocol compliance. • **Manage incomplete trial participation**: Follow-up and data archival. • **Ensure accountability**: For computerized systems and data management. • **Guide IP management:** With proportionate oversight and emergency preparedness.

	• **Participants not completing trial**: Appropriate follow-up per protocol required; instructions to avoid loss of collected data per regulatory requirements. • **Computerized systems**: Investigator responsibilities. • **Data and source records:** Expectations on identification, maintenance, and access. • **IP management:** Sponsor may facilitate aspects; a) Investigator oversight depends on IP characteristics, administration, safety knowledge, and marketing status. b) Alternative IP documentation for authorized products per regulations. • **Emergency unblinding:** Investigators should be prepared for emergency unblinding to protect participant's safety without delay/ hindrance.	• **Protect participant safety:** Ensure the investigator's preparedness and capability to emergency unblinding (wherever applicable)
Sponsor	• **Trial design:** Ensure throughout the clinical trial life cycle it is the responsibility of sponsor to implement risk-proportionate approach to protect participants' safety and wellbeing and trial data reliability. • **Agreements:** Have agreements with service providers before initiating the activities; date for significant changes. • **Sponsor oversight:** Tailor oversight to trial complexity/risks; implement QA/QC for investigators/service providers. • **Quality management:** Assess/manage CTQ factors impacting safety/result reliability; encourage proportionality. • **Monitoring:** Centralized monitoring/site visits (on-site/remote); strategy considers trial factors per risk-proportionate approach. • **Investigational product:** Alternative approaches for marketed products per local regulations. • **Computerized system**: Incorporates the concept of fit-for-purpose with computerized system, along with provide more précised information on blinding and unblinding with randomization.	• **Ensure the participant safety**: By implementing risk-proportionate approach and fit-for-purpose concept. • **Ensure trial quality and reliability of data**: Through QbD, CtQ oversight, and monitoring. • **Balance burden and safety**: Minimizing unnecessary burden while protecting participants. • **Ensure the data reliability**: By using monitoring (including decentralized, wherever applicable), electronic systems /electronic media in compliance with applicable regulatory.
Data governance	• **Data integrity management**: By investigators and sponsors for accurate reporting, verification, and interpretation. • **Key processes across data lifecycle:** Address data protection, computerized systems, essential elements (randomization, blinding), and decision-making processes. • **Proportionality and documentation**: Focus on data criticality; document appropriately. • Data lifecycle elements: From capture to destruction; clarifies metadata meaning. • **Computerized systems:** Fit for purpose; proportionate management based on importance to safety/reliability; clear/documented responsibilities; lifecycle management. • **System failure:** Focused on contingency procedures to prevent data loss or accessibility.	• **Ensure data integrity, traceability and security:** Accurate reporting, verification and interpretation of the clinical trial related information. • **Ensure quality and reliability of trial results:** Design and implementation of system and processes considering proportionate risks to participants. • **Guide computerized system use**: Fit for purpose with clear responsibilities. • **Ensure participant's safety and trial outcomes:** Contingency procedures.
Appendix A (Investigator's brochure)	• **Reference safety information (RSI):** List of adverse reactions (frequency, nature) as reference safety info should be included. • **Reorganization for clarity**: Language order reorganized. • **Removed examples**: Title page and table of contents examples removed as information is in guideline text.	• **Enhances safety information:** Including adverse reactions for reference. • **Streamline content**: Removing redundant examples.

Appendix B (Protocol and protocol amendment if any)	• **Importance of protocol:** Highlighting adaptability (e.g., acceptable ranges) to reduce deviations/amendments. • **Simplicity and clarity:** Encourage clear, concise, operationally feasible protocols minimizing complexity and risks to participants/data reliability. • **Withdrawal/discontinuation:** Address implications of consent withdrawal or investigator discontinuation. • **Statistical section:** Broadened to include statistical inference methodologies like Bayesian design and estimands.	• **Enhance protocol flexibility:** Through adaptability and simplicity. • **Protect participants and data**: Minimizing risks. • **Modernize statistical approaches:** Including Bayesian methods.
Appendix C (Essential records)	• **Definition of essential records**: Based on trial design, conduct, risk proportionate approaches, and record importance/relevance. • **Content and Maintenance**: Clarity provided on essential records content and maintenance. • **Examples of essential records:** One table with examples like protocols, investigator brochure, informed consent forms, approvals. • **Access to essential records:** Guidance on sponsor/investigator access to each other's records for responsibilities.	• **Clarify essential records:** Based on trial specifics and risk. • **Facilitate Access**: For sponsor/investigator responsibilities.
Glossary	• **Modified GCP definition:** E6R3 changes description of trial processes to "planning, initiating, performing, recording, oversight, evaluation, analysis, and reporting" with assurance of "reliable" data and protection of participants' "rights, safety, and wellbeing". • **Introduced source records definition**: Original documents or data (including relevant metadata) or certified copies of original documents or data, irrespective to the media used. (Trial participants hospital/ pharmacy/laboratory records, electronic patient-reported outcomes (ePRO), data generated from automated instruments e.g., wearables and sensors if any). • **Introduced essential records definition**: The documents and data (including relevant metadata), that allows evaluation of methods used, factors affecting a trial, and action taken during the trial conduct to determine the reliability of trial results produced and the verification that trial results are in compliance with GCP and applicable regulatory requirement. • **Terminology changes:** "Trial participant" replaces "subject"; "clinical trial" defined as any interventional investigation in human participant; "source records" replace "source documents and data"; "Essential records" replaces "Essential documents". • **New terms added:** Assent, data acquisition tool, computerized system validation, metadata, RSI, service providers, etc.	• **Update GCP standards:** Aligning with current trial conduct and oversight. • **Clarity in definitions**: Ensure understanding and application f terms across trials. • **Uniformity in terminology:** For consistency in trial documentation and reporting. • **Data integrity:** Reinforces data traceability, emphasizes robust system for reliable results.

Table 4. ICH E6(R3) revised principles (1,4)

Sr No.	Principle	Practice
1	Ethical principles	• Making sure not to unnecessarily exclude particular participant populations.
2	Informed consent	• Taking into consideration relevant aspects of the trial.
3	IRB/IEC review	• Periodic review according to applicable regulatory requirements.
4	Science	• Periodic review of scientific knowledge and approaches to determine whether modifications to the trial are needed.
5	Qualified individuals	• Individuals with different expertise and training may be needed across all phases of a clinical trial.
6	Quality	• The quality and amount of the information generated should support good decision making.
7	Risk proportionality (New)	• Focus on participant's safety and reliability of results. • Focus on the risks associated with trial participation. • Focus on risks beyond those associated with usual medical care for clinical trials involving patients.
8	Protocol	• A well-designed trial protocol is fundamental to the protection of participants and for the generation of reliable results. • The protocol and other documents (e.g., statistical analysis plan, data management plan) for trial execution should be clear, concise and operationally feasible.
9	Reliable results	• Trial processes should support the key trial objectives. • Clinical trials should incorporate efficient and well-controlled processes for managing records through appropriate management of data integrity. • The transparency of clinical trials should involve registration on publicly accessible databases and the public posting of clinical trial results.
10	Roles and responsibilities (New)	• Clarification of transfer of activities by the Sponsor and delegation by the Investigator. • Maintenance of appropriate oversight.
11	Investigational Product	• Investigational products should be carefully managed to align with treatment assignment and maintain blinding, where applicable. • The investigational product provided to the trial participant should retain its quality.

4. Insights

The updated GCP guideline E6(R3) featured significant changes, including a focus on technology, an emphasis on quality, an expansion of ethics, and enhanced responsibilities for investigators, sponsors, and ECs. It was also founded on new technological approaches to trial design and conduct. (6) The adoption of ICH E6(R3) guidelines, which place a strong emphasis on QbD, risk-based methodologies, and patient-centricity in clinical trials, represents a substantial change in GCP compliance. The modernization of GCP standards incorporates technological innovations such as electronic data collection, decentralized trials, and AI-driven analytics, which are in line with current clinical research practices. By emphasizing the early detection and mitigation of the risk to participant's safety and data integrity, the guidelines encourage a proactive approach to risk management. Since better recruitment, retention, and data quality result from participant engagement, there is also a greater focus on patient involvement in trial design. Digital technology adoption is anticipated to simplify adherence to contemporary data integrity standards.

5. Summary of key impact of ICH E6(R3) guideline

- **Risk-based approach:** Focuses on CtQ factors to guide trial design and oversight.
- **QbD:** Integrates quality into trial design and execution.
- **Enhanced participant safety:** Prioritizes safety and well-being with updated terms.
- **Technology integration:** Embraces DHT and decentralized trials.
- **Clear roles and responsibilities:** Clarifies expectations for sponsors and investigators.
- **Updated SOPs/quality systems:** Reassess legacy systems for compliance.
- **Risk-based monitoring:** Proportionate monitoring instead of routine visits.
- **Data governance**: Emphasizes integrity, validation and traceability using technology.

- **Flexibility in trial design:** Encourages adaptability based on risk and quality factors.
- **Participant-centric approaches:** Aligns with modern trial conduct focusing on participants.
- **Reduced unnecessary burden:** Minimizes burden while ensuring data quality and safety.
- **Encourages innovation:** In trial design and conduct with technologies like DHTs.
- **Proactive risk management:** Systems for real-time risk identification/management.
- **Importance of metadata:** For data traceability and validation in trials.
- **Harmonization with other guidelines:** E6(R3) refers to other ICH guidelines for trial design and conduct (including ICH E2(A), ICH E3, ICH E8(R1), ICH E9(R1) and. E19.

Uniformity in reporting: Updated and clarified the terminologies for consistency in documentation and reporting.

6. Conclusion

The evolving principles outlined in ICH E6(R3) reflect a transformative shift in clinical trial conduct, one that embraces innovation, prioritizes participant safety, and embeds quality at every stage. By adopting a risk-based approach and integrating QbD, sponsors and investigators are empowered to proactively manage risks, streamline operations, and enhance data integrity. The emphasis on technology, decentralized methodologies, and participant-centric strategies not only modernizes trial execution but also reduces unnecessary burdens while maintaining high standards of safety and compliance. Clear roles, updated SOPs, and harmonization with other ICH guidelines further ensure consistency and accountability across global trials. Ultimately, this framework fosters a culture of continuous improvement, adaptability, and ethical responsibility setting a new benchmark for efficient, high-quality clinical research.

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Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this article.

Abbreviations

AE: Adverse event; **CtQ**: Critical to quality;
DTH: Digital health technology;
E guideline: Efficacy guideline;
ePRO: Electronic patient-reported outcomes;
GCP: Good Clinical Practice;
IC: Inform consent;
ICH: International council for harmonization;
IEC: Institutional ethics committee;
IP: Investigational product;
IRB: Institutional review board;
NA: Not applicable;
No.: Number;
QA: Quality assurance;
QbD: Quality by design;
QC: Quality control;
Rn: Revision (n-number) of guideline;
RSI: Reference safety information;
SOP: Standard operating procedure.

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