Hosted by GHC Global Harmonization Center
National Institute of Food and Drug Safety Evaluation Republic of Korea
Operated by KONECT Korea National Enterprise for Clinical Trials

## 2025 Global Harmonization Center Clinical Trials Webinar
## Implementing ICH E6(R3)

# Operationalizing ICH E6(R3): Practical Site Strategies for IRBs, RWD, etc.

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# Operationalizing ICH E6(R3): Practical Site Strategies for IRBs, RWD, etc.

## Overview

# ICH E6(R3): Modernized GCP

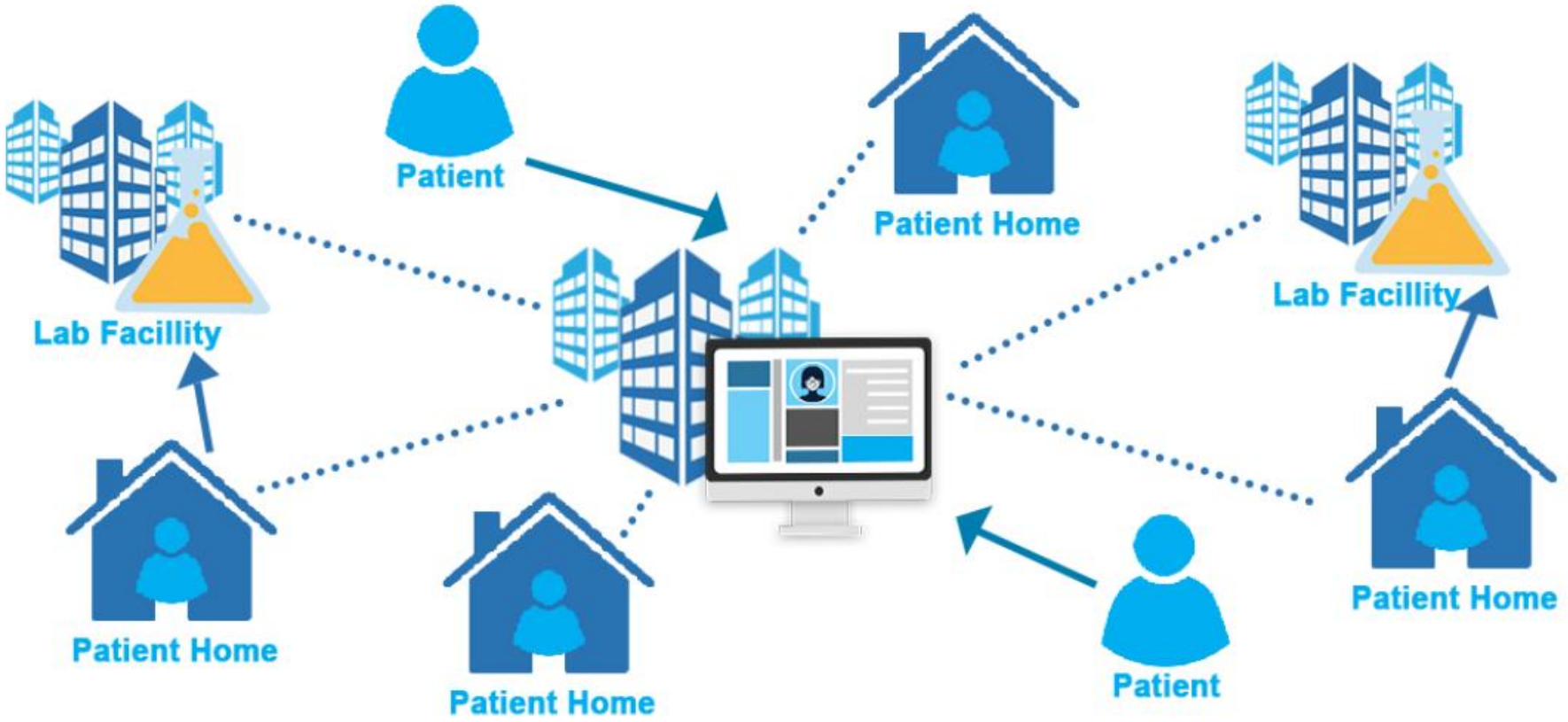
- What is ICH E6(R3)?
  - Adopted in January 2025 as the Step 4 Final Guideline
  - Revision of Good Clinical Practice (GCP) standards
  - Successor to ICH E6(R2) (2016)

- Why a New Revision?
  - Clinical research environment rapidly evolving
  - Need to address digitalization, decentralization, and real-world data (RWD)
  - Stronger emphasis on patient-centricity and risk-based quality management

# Technical Background

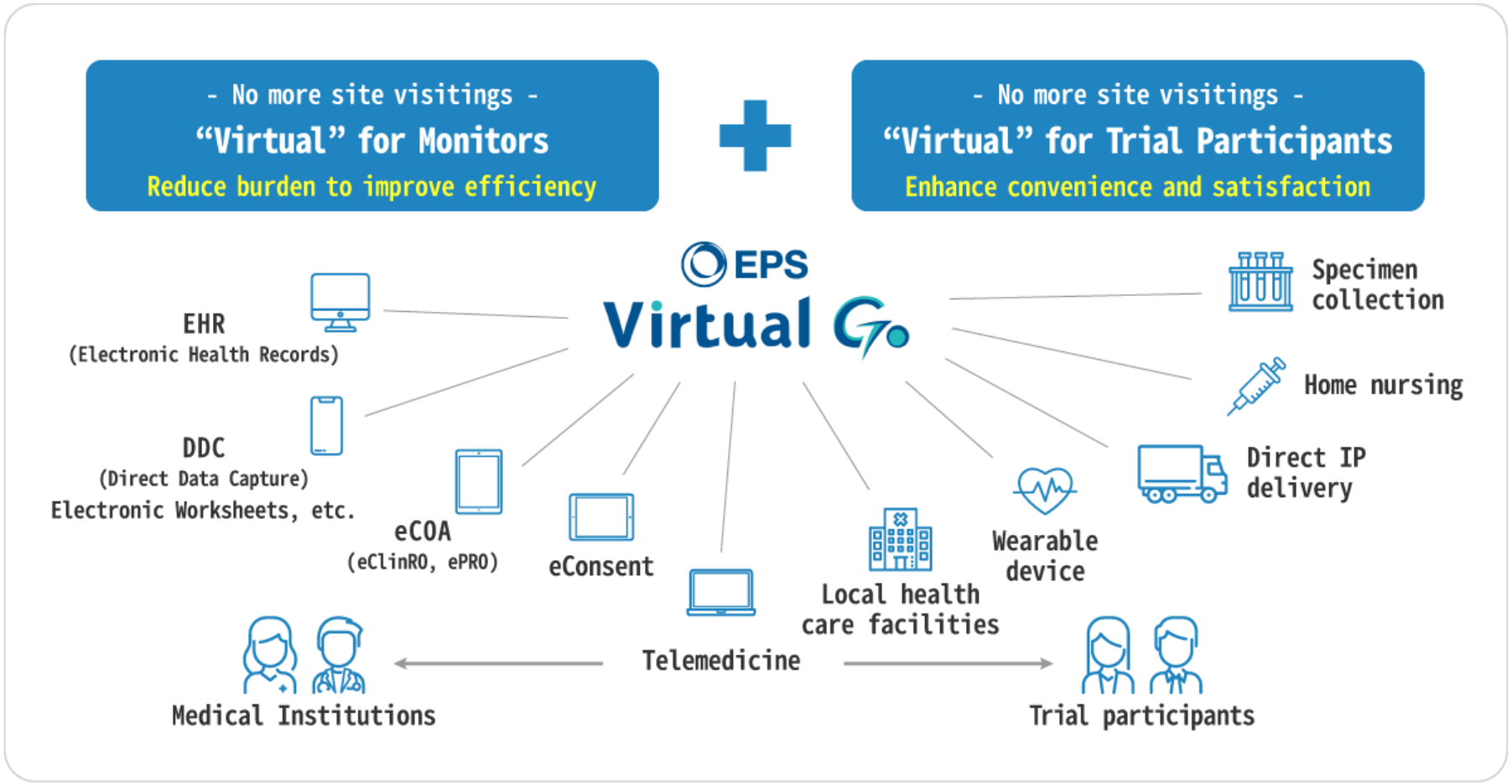
- 1. Changing Clinical Trial Environment
  - Digital Transformation:
    Rapid adoption of EHRs, wearable devices, and remote monitoring created new data collection pathways, which were not adequately addressed in ICH E6(R2).
  - Decentralized Clinical Trials (DCTs):
    The COVID-19 pandemic accelerated the use of remote and hybrid trials, highlighting the need for formal ethical and operational guidance.

# Technical Background




https://www.florencehc.com/blog-post/decentralized-clinical-trials-what-the-future-holds/

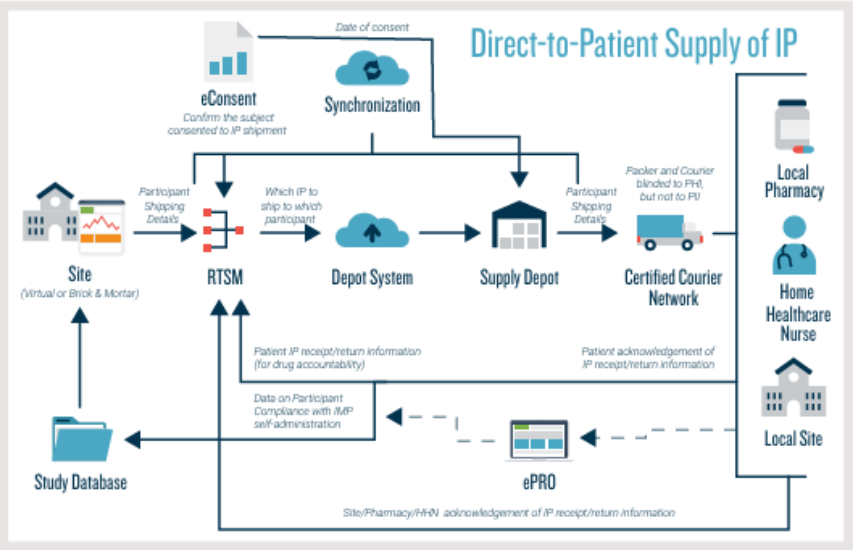
# Technical Background

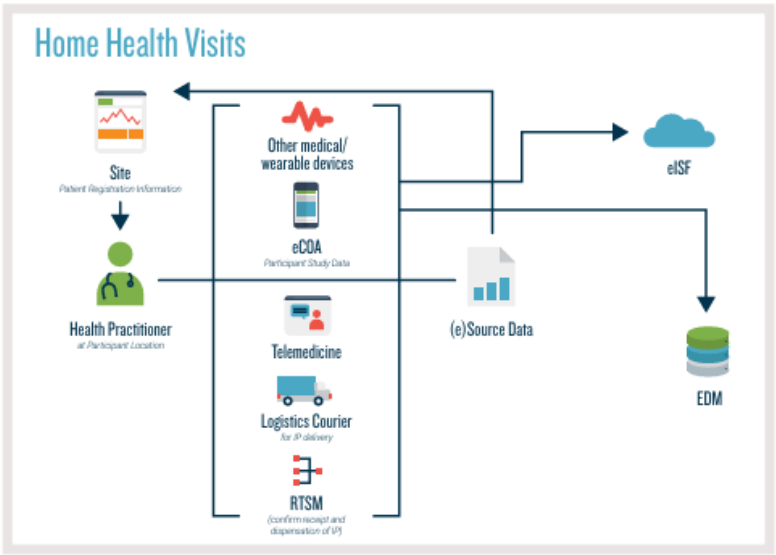


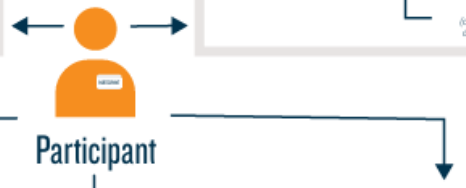

*Virtual go is not a software/application

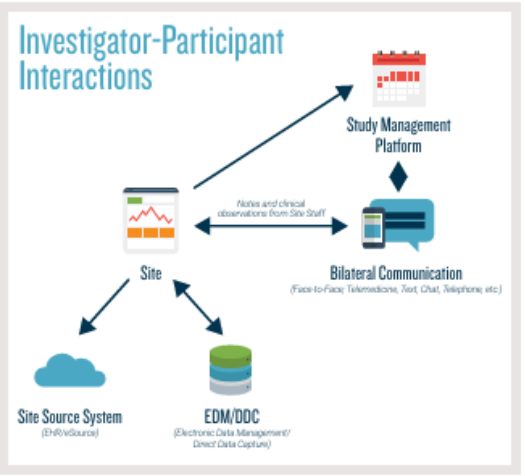
https://www.epsi-global.com/services/dct.html

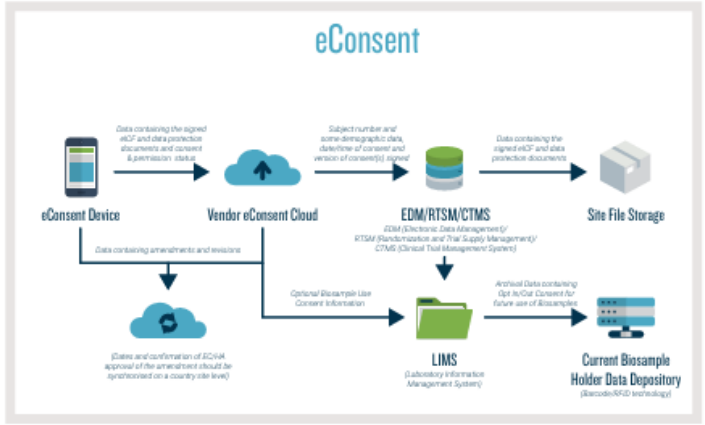
# Technical Background

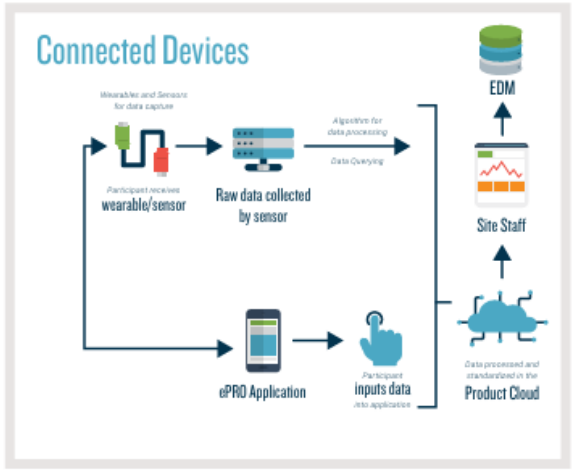



Decentralized Clinical Trials
Data Flow Maps

from ACRO Decentralized Clinical Trials Working Party July 2021

# Technical Background

- 2. Strengthening Patient-Centric Approaches
  - Improving Participant Experience:
    Patient-centric trial design, focused on minimizing participant burden and broadening access, became a global expectation.Reframing
  - Informed Consent:
    The traditional one-time consent process evolved into ongoing, continuous consent—supported by digital solutions such as eConsent.

# Technical Background

- 3. Diversity of Data and Use of RWD/RWE
  - Increased Role of Real-World Data (RWD):
    Integration of data sources such as EHRs, registries, and insurance claims into clinical research required clearer governance principles.
  - Data Integrity Needs:
    With digitalization came heightened demands for security, validation, and audit trails to ensure trustworthy evidence generation.

# Technical Background

- 4. Risk-Based Quality Management
  - From Monitoring to Design:
    While E6(R2) introduced risk-based monitoring, E6(R3) expanded the concept into a full Quality by Design (QbD) framework.
  - Critical-to-Quality (CtQ) Factors:
    Sponsors and investigators are now expected to identify and manage trial elements that most directly impact patient safety and data reliability.

# Technical Background

- 5. Global Consistency and Regulatory Alignment
  - International Requirements:
    Increasing reliance on multi-regional clinical trials (MRCTs) demanded harmonized GCP standards across jurisdictions.
  - Regulatory Expectations:
    Agencies such as FDA, EMA, PMDA, and MFDS highlighted the limitations of E6(R2) in addressing modern trial designs, prompting a comprehensive update.

# New & Emphasized Terms in E6(R3)

- Quality by Design (QbD)
  - Embedding quality into trial design, not just post-hoc checks
  - Identification and management of Critical-to-Quality (CtQ) factors
- Critical-to-Quality (CtQ) Factors
  - Elements directly affecting participant safety and data reliability
  - Example: accuracy of primary endpoint measurement, safety monitoring
- Proportionate / Risk-Based Approach
  - Oversight and monitoring scaled to the level of trial risk
  - Simplification possible for low-risk studies

# New & Emphasized Terms in E6(R3)

- Real-World Data (RWD)
  - Data from routine healthcare (EHRs, registries, insurance claims)
  - Requires suitability assessment and quality validation before integration
- Decentralized Clinical Trials (DCTs)
  - Trial designs with remote elements
  - eConsent, tele-visits, direct-to-patient IMP delivery, ePRO
- ALCOA+
  - Data integrity principles: Attributable, Legible, Contemporaneous, Original, Accurate
  - Complete, Consistent, Enduring, Available

# Scope of RWD

- 1. Healthcare System Data
  - Electronic Health Records (EHR) / Electronic Medical Records (EMR)
  - Hospital/clinic databases
  - Health insurance claims and billing data
  - Prescription/dispensing records
- 2. Patient-Generated Data
  - Patient-reported outcomes (PROs / ePROs)
  - Diaries, symptom trackers
  - Mobile health applications (mHealth)
  - Data from patient communities or registries

# Scope of RWD

- 3. Registries & Cohort Data
  - Disease registries (e.g., cancer, rare diseases)
  - Treatment registries (post-marketing safety registries)
  - Prospective/retrospective observational cohorts
- 4. Digital Health & Device Data
  - Wearables (e.g., smartwatches, fitness trackers)
  - Implantable sensors (e.g., glucose monitors, cardiac monitors)
  - Remote monitoring devices (blood pressure, spirometry, ECG patches)

# Scope of RWD

- 5. Laboratory & Imaging Data (External)
  - Routine clinical lab results
  - Central lab databases
  - Imaging archives (e.g., PACS) used in routine care
- 6. Administrative & Societal Data
  - Public health surveillance data
  - Mortality, birth, disease incidence registries
  - Socio-demographic databases (e.g., census-linked health data)

# Scope of RWD

- 7. Post-Market & Pharmacovigilance Data
  - Spontaneous adverse event reports
  - Post-marketing safety surveillance systems
  - Expanded access/compassionate use program data

# Scope of RWD

| RWD Type | Design Phase Use | Conduct Phase Use |
|---|---|---|
| **Healthcare System Data** | EHR/EMR, claims, prescribing data<br>→ Define populations, estimate disease prevalence/incidence, asse ss recruitment feasibility | EHR updates, hospital records<br>→ Interim safety evaluation, integrate external care information |
| **Registries & Cohorts** | Disease registries, observational cohorts<br>→ Synthetic control arms, endpoint definition | – |
| **Administrative & Societal Data** | Public health surveillance, mortality registries, census-linked datasets<br>→ Demographics, estimate eligible population size | – |
| **Post-Market & Pharmacovigilance Data** | Safety surveillance databases, expanded access data<br>→ Early safety signals, inform risk mitigation in design | Spontaneous AE reports, real-world safety monitoring<br>→ Long-term safety follow-up, outcome validation |
| **Patient-Generated Data** | – | PROs/ePROs, diaries, mobile apps<br>→ Capture patient-reported symptoms, monitor adherence |
| **Digital Health & Device Data** | – | Wearables, implantables, remote monitoring devices<br>→ Remote monitoring, DCT data capture |
| **Laboratory & Imaging Data** | – | Routine labs, central lab databases, imaging archives<br>→ Safety/efficacy assessments, integrated with trial data |

# Key Shifts Reflected by New / Emphasized Terms

| Trial Design Philosophy | Data Availability and Utilization | Operational Models | Ethics & Oversight |
|---|---|---|---|
| • from compliance to design | • Not limited to trial-only data | • Decentralized / Patient centricity | • Proportionate separation by "risk" |

## Operationalizing ICH E6(R3): Practical Site Strategies for IRBs, RWD, etc.

# Implications

# ICH E6(R3) Principles × Key Changes Matrix

| ICH GCP Principle | Trial Design Philosophy (from compliance to design) | Data Availability & Utilization (beyond trial-only data) | Operational Models (Decentralized / Patient centricity) | Ethics & Oversight (Proportionate by risk) |
|---|---|---|---|---|
| 1. Ethics (Helsinki, participant rights) | – | – | – | Risk-based review, proportionate protection of rights & safety |
| 2. Informed Consent | – | eConsent, multimedia materials, RWD-informed explanations | Remote consent, improved accessibility for participants | – |
| 3. Independent Review (IRB/IEC) | – | – | – | Risk-based continuing review, data-driven oversight |
| 4. Scientific Soundness | Shift from compliance to design, embed scientific rationale | Use of RWD, external data, updated scientific evidence | – | – |

# ICH E6(R3) Principles × Key Changes Matrix

| ICH GCP Principle | Trial Design Philosophy (from compliance to design) | Data Availability & Utilization (beyond trial-only data) | Operational Models (Decentralized / Patient centricity) | Ethics & Oversight (Proportionate by risk) |
|---|---|---|---|---|
| 5. Qualified Individuals | – | – | Need for digital experts, DCT-ready skillsets | – |
| 6. Quality by Design | Quality built into design, avoid unnecessary complexity | – | – | – |
| 7. Risk-Proportionate Approach | Risk and quality factors integrated into trial design | – | – | Oversight scaled to risk level |
| 8. Clear Protocol | Operational feasibility emphasized | – | Incorporation of decentralized and patient-centric elements | – |

# ICH E6(R3) Principles × Key Changes Matrix

| ICH GCP Principle | Trial Design Philosophy (from compliance to design) | Data Availability & Utilization (beyond trial-only data) | Operational Models (Decentralized / Patient centricity) | Ethics & Oversight (Proportionate by risk) |
|---|---|---|---|---|
| 9. Reliable Results | – | Broader data sources (e.g., RWD, digital health), greater reliability | – | – |
| 10. Roles & Responsibilities | – | – | Clear allocation across multiple providers/sites | Documented oversight and accountability |
| 11. Investigational Product Management (GMP) | – | – | Direct-to-patient delivery, home use, strengthened logistics & quality controls | – |

# Reflections – IRB vs Investigator

| ICH GCP Principle | IRB/IEC focus | Investigator focus |
|---|---|---|
| **1. Ethics** | • Apply **risk-proportionate ethical review**;<br>• assess **privacy/data protection adequacy** in decentralized/remote procedures | • Continuously reassess risk–benefit as new data emerge;<br>• implement **additional safeguards for vulnerable groups** in decentralized models |
| **2. Informed Consent** | • Review **eConsent and multimedia methods**, remote identity verification, re-consent triggers;<br>• verify use of tech-enabled consent | • Operationalize **remote/eConsent**, ensure usability for diverse populations;<br>• document **re-consent when new data** become available |
| **3. Independent Review** | • Conduct **risk-based continuing review**, not just fixed cycles;<br>• integrate ongoing external safety signals | • Rapidly notify IRB of significant **data-driven changes** impacting risk or conduct |
| **4. Scientific Soundness** | • Review use of **RWD/external data** as part of protocol justification;<br>• check bias-mitigation methods | • Incorporate **RWD-linked eligibility/safety checks** during execution |

# Reflections – IRB vs Investigator

| ICH GCP Principle | IRB/IEC focus | Investigator focus |
|---|---|---|
| **5. Qualified Individuals** | • Confirm investigator team has **digital health / DCT / data governance competencies** | • Train staff on **wearables, remote platforms, cybersecurity, RWD integrity** |
| **6. Quality by Design** | • Ensure **CTQ (critical-to-quality) factors** explicitly identified in protocol;<br>• assess burden minimization | • Build **QbD into SOPs/checklists**, concentrate on CTQ processes/data |
| **7. Risk-Proportionate Approach** | • Approve **risk-based monitoring (RBM)**, escalation triggers<br>• verify proportionate mitigation plans | • Execute **RBM and central monitoring**, adjust plans dynamically when new risks emerge |
| **8. Clear Protocol** | • Require protocol clarity on **remote visits, data flows, decentralized elements** | • Prepare operational playbooks for **hybrid/DCT processes** |

# Reflections – IRB vs Investigator

| ICH GCP Principle | IRB/IEC focus | Investigator focus |
|---|---|---|
| **9. Reliable Results** | • Review **plans for integrating external/RWD sources**, validation of digital data capture, long-term data governance | • Maintain **ALCOA+** for hybrid datasets;<br>• validate and log **RWD integration** |
| **10. Roles & Responsibilities** | • Ensure **clear allocation across sponsor, CRO, vendors, data holders**, especially in decentralized models | • Maintain **vendor oversight records**, confirm third-party compliance, escalate digital/data issues |
| **11. Investigational Product Management** | • Assess **direct-to-patient (DTP) shipment, home storage, blinding risks** | • Implement **home-use IP tracking**, educate participants, enforce chain-of-custody |

# Operationalizing ICH E6(R3): Practical Site Strategies for IRBs, RWD, etc.

# Implementation

# IRB/IEC: Risk-Proportionate Ethical Review

- Framework & SOP Revision
  - Establish risk categories (high / moderate / low)
  - Risk Criteria example
    - High-risk: First-in-human, DCT with home IP use, vulnerable populations
    - Moderate-risk: Phase II/III with established product, mixed digital elements
    - Low-risk: Minimal-risk interventions, bioequivalence, registry-based trials
  - Adapt review depth and scope proportionate to risk

- Risk Assessment at Submission
  - Require sponsors/investigators to submit risk assessment and mitigation strategies
  - Ensure vulnerable populations receive additional protection

# IRB/IEC: Risk-Proportionate Ethical Review

- Documentation & Transparency
  - Record rationale for risk classification
  - Maintain clear audit trail of proportionality decisions
- Capacity & Expertise (considering risk-based continuing review)
  - Strengthen IRB expertise in digital health, RWD, DCT contexts
  - Provide training on risk evaluation methodologies
- Balance Protection vs Burden
  - Ensure strong protection for participants
  - Avoid creating unnecessary regulatory burden on investigators

# IRB/IEC: Risk-Based Continuing Review

- Adaptive Scheduling (action by category may not be changed)
  - High-risk: frequent review (e.g., quarterly)
  - Moderate-risk: semiannual review
  - Low-risk/minimal-risk: annual or as-needed

- Establish Review Triggers
  - Major safety updates or SUSARs
  - Significant protocol amendments
  - Use of RWD integration or new digital tools (eConsent, wearables, DCT)
  - Early warning from RBM (risk-based monitoring) signals

# IRB/IEC: External Data Integration

- Review points
  - Review of Data Flow & Integration
    - Require clear mapping of how external data enter the trial database
    - Verify data transfer security (encryption, authentication, audit trails)
  - Governance & Accountability
    - Ensure sponsor/investigator defines who owns, accesses, and controls external data
    - Confirm third-party vendors/registries are covered by proper oversight & contracts
  - Bias & Integrity Safeguards
    - Review plans for validating external data before integration
    - Confirm methods to mitigate bias, missing data, and duplication
  - Privacy Risk Management
    - Evaluate risks of re-identification when linking datasets (EMR + PRO + registry)
    - Check compliance with local/global privacy regulations (GDPR, HIPAA, etc.)

# IRB/IEC: eConsent & Multimedia Materials

- Update Submission Requirements:
  Require sponsors/investigators to submit:
  - eConsent platform details (system validation, audit trail)
  - Multimedia content (videos, graphics, interactive modules)
  - Usability testing results (comprehension checks, readability)

- Develop Review Criteria
  - Assess whether multimedia aids improve understanding without coercion
  - Ensure consistency of content across languages/formats
  - Verify identity authentication for remote consent

# IRB/IEC: eConsent & Multimedia Materials

- Privacy & Data Security
  - Confirm storage and transmission of eConsent data comply with privacy regulations
  - Ensure audit trail logs of who, when, and how consent was obtained
- Training & Expertise
  - Train IRB members on digital usability evaluation and human factors
  - Engage external experts when reviewing complex multimedia/eConsent systems
- Participant-Centered Focus
  - Require inclusion of comprehension assessments (e.g., quizzes, feedback loops)
  - Pay special attention to accessibility for vulnerable populations (elderly, minors, low literacy)

# IRB/IEC: RWD Integration & Digital Competence

- Integration of RWD & External Data
  - Update review templates to require:
    - Justification for RWD use in trial design or endpoints
    - Bias-mitigation strategies (data validation, handling missing/duplicate data)
    - Data privacy & governance plans for external datasets
  - Verify methods for secure transfer, storage, and audit trails

- Digital Competence Assessment
  - Ensure IRB membership includes or has access to digital health & data governance expertise
  - Establish training modules for IRB members on:
    - Wearables, eConsent, remote monitoring systems
    - Cybersecurity & data protection principles
    - Evaluation of DCT operational risks

# IRB/IEC: CTQ (Critical to Quality) Review

- Update Submission Requirements
  - Require investigators/sponsors to highlight CTQ factors in protocol submissions
  - Ensure QbD rationale (why certain procedures are critical) is documented
- Develop Review Criteria
  - Evaluate whether CTQ factors are aligned with trial objectives
  - Check if non-critical or redundant procedures have been minimized
- Burden vs Benefit Assessment
  - Assess whether participant visits, procedures, or data collection are proportionate to their scientific value
  - Pay special attention to vulnerable groups where burden can outweigh potential benefit

# IRB/IEC: CTQ (Critical to Quality) Review

- Documentation & Transparency
  - Record IRB/IEC's reasoning when accepting high-burden procedures
  - Maintain audit trails of CTQ-related deliberations

- Capacity Building
  - Train IRB members to differentiate critical vs non-critical elements
  - Encourage dialogue with investigators to refine protocols around CTQ considerations

# IRB/IEC: Risk-Based Monitoring (RBM)

- Update Submission Requirements: Request sponsors/investigators to submit-
  - RBM strategy overview (central vs on-site monitoring mix, justification)
  - CTQ linkage: how monitoring focuses on critical-to-quality factors
  - Thresholds & triggers (QTLs, KRIs, escalation paths)

- Develop Review Criteria
  - Assess whether monitoring intensity is proportionate to participant risk
  - Verify if monitoring plans avoid both under-monitoring and unnecessary burden
  - Confirm mechanisms for data integrity validation when using remote/central monitoring

# IRB/IEC: Risk-Based Monitoring (RBM)

- Clarify Oversight & Reporting
  - Ensure roles of sponsor, CRO, and vendors in monitoring are clearly documented
  - Define what types of monitoring findings must be reported to the IRB (e.g., systemic protocol deviations, major safety impacts)
  - Confirm timelines for urgent vs routine reporting

- Capacity & Training
  - Train IRB members to interpret RBM strategies and monitoring triggers
  - Build ability to evaluate external data sources and digital monitoring tools used in DCT settings

# IRB/IEC: Protocol Clarity & Role Oversight

- Protocol Clarity on DCT
  - Require protocols to specify:
    - Decentralized elements (home visits, telehealth, local labs, wearables, apps)
    - Data origin and flow from source → integration → analysis
    - Participant burden (frequency, logistics, accessibility)
  - Review feasibility and equity of access (e.g., for rural/elderly participants)
  - Ensure vulnerable participants are not disadvantaged by DCT procedures

- Role & Responsibility Oversight
  - Ensure documentation of who is responsible for what across all parties:
    - Sponsor, CRO, site, technology vendor, lab, data holder
  - Verify delegation of responsibilities is formalized in contracts or agreements
  - Confirm existence of supervision mechanisms for third-party vendors
  - Require clear escalation pathways for safety, data integrity, or protocol deviations

# IRB/IEC: Data Reliability & Governance

- Update Submission Requirements
  - Request data validation and traceability plans from sponsors/investigators
  - Require documentation of data origin, flow, and transformation

- Review Criteria for Reliability
  - Assess whether systems maintain ALCOA+ principles (Attributable, Legible, Contemporaneous, Original, Accurate, + Complete, Consistent, Enduring, Available)
  - Check that external/RWD integration includes methods for handling bias, missing data, duplication

- Governance & Retention
  - Confirm data retention policies are proportionate to trial risk and regulatory requirements
  - Ensure that audit trails allow regulators and IRBs to verify data integrity

# IRB/IEC: Data Reliability & Governance

- Vendor & System Oversight
  - Verify third-party systems (EHR, registries, ePRO, wearables) undergo proper validation
  - Require clear agreements/contracts on data ownership, access rights, and security responsibilities

- Capacity & Expertise
  - Strengthen IRB/IEC competence in data governance frameworks and digital tool validation
  - Provide training on data integrity risks in decentralized and hybrid trials

# Institution/Research Staffs Readiness

| Investigator Preparation | SOP Needed | Training Needed | Protocol Compliance |
|---|---|---|---|
| **Ethics & Participant Protection** | – | risk–benefit reassessment, (vulnerable groups) | apply safeguards as per protocol |
| **Informed Consent Execution eConsent, multimedia, re-consent** | consent documentation, re-consent SOP | digital platform, comprehension check | consent method per protocol |
| **Data Integration & RWD Handling** | capture, validation, audit trail, bias mitigation | RWD interpretation, bias awareness | integration method per protocol |
| **Digital Competence & DCT Readiness** | – | use of wearables, apps, cybersecurity | DCT elements specified in protocol |
| **Quality by Design - CTQ Implementation** | identify CTQ, minimize non-critical steps | – | implement CTQ-related requirements |

# Institution/Research Staffs Readiness

| Investigator Preparation | SOP Needed | Training Needed | Protocol Compliance |
|---|---|---|---|
| **Risk-Based Monitoring Compliance** | CAPA process, delegation log SOP | understanding RBM signals, QTL/KRI | follow monitoring plan in protocol |
| **Protocol Clarity & DCT Operations** | – | – | telehealth, home visits, local labs execution |
| **Roles & Responsibilities : Delegation, Vendor Oversight** | delegation log mgmt, vendor oversight SOP | – | execute as defined in protocol/agreements |
| **Data Reliability & Governance** | ALCOA+ application, data retention SOPs | training in data integrity & digital tools | data mgmt methods per protocol |
| **Investigational Product Management in DCT** | storage/accountability procedures, chain of custody | site staff & participant training | DTP delivery, return/disposal per protocol |

# Recommended SOP lists

| SOP titles | Action from R2 version | Key Delta (Revision/New Elements) |
|---|---|---|
| **Informed Consent** | **Revise** | Add eConsent, remote ID verification, multimedia tools, comprehension checks, re-consent triggers, audit trails, accessibility/vulnerable populations |
| **Data Integration & RWD Handling** | **New** | Procedures for capturing, validating, and integrating external data (EHR, registries, wearables); manage bias, missing/duplicate data; ensure data lineage, governance, and security |
| **Quality by Design (CTQ)** | **Revise** | Explicit identification of CTQ factors, prioritization, minimization of non-critical procedures, site-level QbD checklists/metrics |
| **RBM & CAPA** | **Revise** | Expand to include central monitoring analytics, QTLs/KRIs, escalation paths, digital/DCT signal handling, rapid CAPA workflow |
| **Roles & Responsibilities / Delegation** | **Revise** | Expand to include vendors/data holders, DCT operations (home visits, local labs, platforms), clear reporting/escalation pathways |
| **Data Reliability & Governance** | **Revise** | Apply ALCOA+ to eSource/RWD, external data validation/traceability, vendor/system validation, retention/access, cross-border data transfer |
| **Investigational Product (IP) Management** | **Revise** | Add DTP shipment, home storage/returns, temperature excursions, chain-of-custody, participant education, remote accountability, blinding protection |

# Recommended training lists

| Training topics | Key Focus | Purpose |
|---|---|---|
| **Digital Competence for DCT** | Use of ePRO, wearables, mobile apps, remote monitoring tools | Ensure staff can operate digital platforms and support participants |
| **Cybersecurity & Data Privacy** | Secure handling of digital/RWD data, authentication, breach prevention | Protect participant confidentiality and meet regulatory standards |
| **Informed Consent (incl. eConsent)** | Conducting eConsent, multimedia tools, comprehension assessments, re-consent triggers | Guarantee that participants provide valid, informed, and documented consent |
| **RWD/External Data Handling** | Understanding bias, missing data, validation of EHR, registries, device data | Enable investigators to integrate external data reliably and responsibly |
| **Risk-Based Monitoring (RBM) Familiarization** | Interpreting QTLs, KRIs, central monitoring signals, CAPA processes | Ensure site staff respond appropriately to monitoring findings and escalations |
| **QbD & CTQ Awareness** | Identifying critical-to-quality factors, minimizing unnecessary procedures | Focus resources on trial elements most important for safety and data integrity |
| **Participant Protection in DCT** | Safeguards for vulnerable groups, remote safety monitoring, balancing burden vs benefit | Maintain participant well-being in decentralized/remote settings |
| **Investigational Product Handling in DCT** | DTP shipment, home storage, accountability logs, participant education | Guarantee investigational product integrity and participant safety in home use |

# Reference example

ACRO

Initiatives | Advocacy | Membership | About ACRO | Sign Up for Updates

ACRO's DCT Toolkit includes five resources: (1) a detailed QbD Manual for DCTs; (2) an accessible, quick-reference QbD Manual; (3) a Risk Assessment Considerations template; (4) DCT Data Flow Maps; and (5) a Change Management Question-and-Answer resource. In addition to the DCT Toolkit, ACRO's White Paper provides an overview of key issues in the decentralization of clinical trials.

## ACRO Expands DCT Toolkit with a Fifth Resource

Stakeholders are experiencing a paradigm shift in the clinical trial enterprise from conventional trials to studies where at least one or more DCT components are utilized (e.g., direct-to-patient shipment and home health visits). The use of DCT components is here to stay, and stakeholders need the tools to successfully embrace this change. While the Quality-by-Design (QbD) Manual, Risk Considerations Tool, and Data Flow Maps focus on providing educational resources to build confidence and trust in DCTs, this new ACRO resource focuses on the final hurdle to greater DCT adoption – which is the change management needed to address risk aversion and the difficulty in adopting brand new ways of working. **Access the latest toolkit resource here.**

## The Complete ACRO DCT Toolkit – Additional Resources

- Navigating Change During Rapid Transformation: A Q&A Resource for Decentralized Clinical Trials
- ACRO DCT White Paper: A New Quality-by-Design, Risk-Based Framework
- Bringing the Trial to the Patient: A Quality-by-Design Manual for Decentralized Clinical Trials
- QbD Manual for Decentralized Clinical Trials: The Quick Reference Guide
- Decentralized Clinical Trials Risk Assessment Considerations
- Decentralized Clinical Trials Data Flow Maps

## Advancing DCTs

ACRO members are dedicated to helping bring quality-based principles, risk-assessment tools, and patient-centricity to the decentralized trials process.

Explore some of ACRO's additional DCT resources:

- Press Release
- ACRO Op Ed in Pharma Letter: Realizing the promise of decentralized trials
- White Paper feature in DIA Global Forum October 2020

https://www.acrohealth.org/dct/

# Take Home Message

- Risk-Proportionate Oversight is Essential
  IRBs/IECs and investigators must shift from static, checklist-driven reviews to risk-adaptive oversight, ensuring participant protection without unnecessary burden.

- RWD Integration Requires Governance
  Use of EHRs, registries, wearables, and other external data must come with validation, traceability, and privacy safeguards to ensure reliability and compliance.

- Digital & DCT Readiness is Non-Negotiable
  eConsent, remote monitoring, and direct-to-patient IP delivery are now mainstream; sites must build digital competence and operational workflows to implement them.

- Quality by Design & Clear Accountability
  Protocols should identify Critical-to-Quality factors and allocate roles and responsibilities transparently across sponsor, CRO, vendors, and investigators to prevent oversight gaps.

Hosted by GHC Global Harmonization Center
National Institute of Food and Drug Safety Evaluation Republic of Korea
Operated by KONECT Korea National Enterprise for Clinical Trials

## 2025 Global Harmonization Center Clinical Trials Webinar
## Implementing ICH E6(R3)

# Operationalizing ICH E6(R3): Practical Site Strategies for IRBs, RWD, etc.

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