Preparing for Virtual Inspections and Ongoing Regulatory Changes

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Introduction

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Latest on remote inspections: ICMRA

International regulatory authorities adapted inspection approaches due to pandemic

Remote inspections are challenging (and impossible for some scenarios)

Remote inspections will continue but not supplant in-person

What is ICMRA?

- International Coalition of Medicines Regulatory Authorities
- COVID-19 working group with representatives from around the world
- Developed remote inspection reflection paper

ICMRA remote inspection insights

No universal remote best practices yet

Remote inspections take more time

No notable differences in inspection results

TAKEAWAY: Prepare for remote, hybrid, and face-to-face inspections, ensuring rigor of systems and process

> The more things change, the more they stay the same.
> - Jean-Baptiste Alphonse Karr

Regulations to know and watch

ICH E8 – Revision 1

- Released Oct. 2021; first update since 1998
- Mandates quality by design (QbD) and assessment of study factors critical to quality (CtQ)
- **TMF impact:** Trialists need to record risk management, QbD, and CtQ actions

EU CTR (536)

- Start-up impact: single CTA submission for multiple EU countries
- CTIS platform for EU CTAs
- Live Jan. 2022; mandate over three years
- **TMF impact:** Slot sub-artifacts in Reference Model

Other HA Activity

- MHRA seeking feedback on UK CT legislation update
  - Closes March 14, 2022
- GCP conference March 8-10
  - Virtual conference with MHRA, FDA, and Health Canada
  - Topics – GCP implications of pandemic, DCT, AI, biosim trials
- **Takeaway:** Interaction, queries, and dialogue *welcome*

TMF Core – Reference Model and ICH E6

Reference Model

- TMF Reference Model likely joins CDISC before EOY
- **TMF impact:**
  - Remains freely available
  - More rigor as data standard (e.g., SDTM)
  - Formal seat at the table with HA & life science consortia

ICH E6 – Revision 2

- Global GCP standard (2017)
- Mandates risk-based trial management
- **TMF impact:**
  - Risk management documentation
  - Essential documents, not all
  - Controls for TMFs
  - Controls for eTMF systems
  - PI controls PI's records

ICH E6 – Revision 3

- Draft expected Q322
- **Likely TMF impact:**
  - More demand for risk-based trial management and focus on Quality by Design
  - Demand to include all stakeholders
  - Additional risk management artifacts

IMPLICATIONS FOR TMF

KEEP CALM, FORGE ON

IMPLICATION 1: Prepare and dry run

Prep for live, hybrid, and remote inspections:

- Consult HAs and inspection rulebooks; seek the counsel of experts and industry colleagues
- During mock inspections, include test of remote access and craft sufficient tech support and fail-safe plans
- Remember that each inspector has personal preferences and practices

> Immature poets imitate; mature poets steal.
>
> - TS Eliot

IMPLICATION 2: Focus on TMF fundamentals

Regardless of inspection type, each TMF must be:

- **Timely** with audit trials; more critical than ever to post TMF records with immediacy
- **Accurate** by checking and correcting records to be consistent with ALCOAC
- **Complete** via trial's TMF Index confirmation and with trialists' attention

> It's a small world, but I wouldn't want to have to paint it.
>
> - Stephen Wright

IMPLICATION 3: Forge a risk-based TMF approach

Improve TMF management without sacrifice:

- Remember that it's GCP (good), not PCP (perfect)
- Leverage the magic of metadata — eTMF systems provide a wealth of information
- Take a risk-based approach to TMF GCP compliance

> Without data, you're just another person with an opinion.
>
> - W. Edwards Deming

Components of Risk-Based TMF Management

TMF RISK-BASED MANAGEMENT COMPONENTS:

ASSESS	Find and stratify high-risk records and processes; plan measurements
TEST	Activate the TMF risk management plan
LEARN	Measure the impact
CELEBRATE	Publicize results; celebrate wins and lessons

TAKEAWAY:

As the clinical trial landscape evolves and trial complexity increases, adopt risk-based TMF management to wisely achieve TMF compliance

Final perspective – do it wisely, do it once

1

TMF is not ancillary - it is the definitive results of trial expense and effort

2

“Only pay for TMF once” takes iterative actions in plan and execution from trial start through finish

3

Regulators demand GCP risk-based approaches, which should be applied to TMF

Q&A