

A background graphic featuring a network of interconnected nodes and lines in shades of blue and grey, overlaid on a wavy, light blue pattern. The nodes vary in size, and the lines represent connections between them, creating a complex, web-like structure.

# **Preparing for Virtual Inspections and Ongoing Regulatory Changes**

March 10, 2022

# Introduction



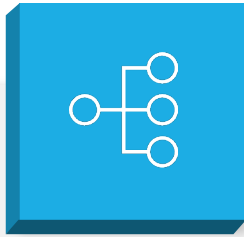
**Fran Ross**

TMF Reference Model Steering Committee  
Managing Partner, Lucid GxP Consulting

# Table of contents



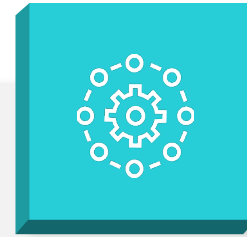
**Latest on  
Remote  
Inspections**



**New and  
Upcoming  
Regulations**



**Implications  
for TMF**

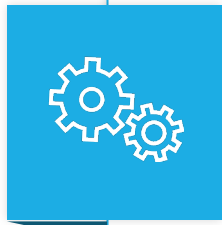


**Risk-Based  
TMF  
Management**

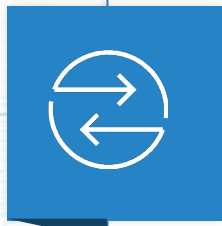
# Latest on remote inspections: ICMRA



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

