BUILDING TMF RESILIENCE IN AN EVER-EVOLVING CLINICAL TRIAL LANDSCAPE

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TMF WEEK 2022

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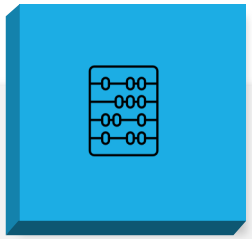
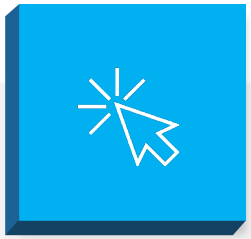
Latest on Remote Inspections



New and Upcoming Regulations



Risk-Based TMF

Keep Calm, TMF On

LATEST ON REMOTE INSPECTIONS: ICMRA

International regulatory authorities adapted inspection approaches due to pandemic

Inspectors have many challenges with remote inspections (impossible for some GxP scenarios)

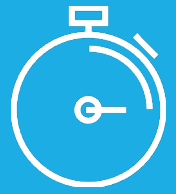
Remote inspections will continue but not supplant in-person

What is ICMRA?

- International Coalition of Medicines Regulatory Authorities
- Working group on COVID-19 with Health Authority reps from around the world
- Remote inspection reflection paper published late 2021

ICMRA REMOTE INSPECTION INSIGHTS

No universal remote best practices yet



Remote inspections take more time and offer less interaction

No notable differences in inspection results

Multimodal inspections are here to stay (remote, hybrid and face-to-face all possible - so ensure *flexibility* and *systems* rigor)

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 Mgmt, QbD and CtQ actions

EU CTR (536)

- Major 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 feedback on UK CT legislation update March 2022
- Joint GCP mtg March 8-10
  - Virtual conf with MHRA, FDA and Health Canada
  - Topics – GCP implications of pandemic, DCT, AI, biosim trials
- **Takeaway:** interaction, queries, dialog *welcome*

TMF CORE – REFERENCE MODEL AND ICH E6

Reference Model

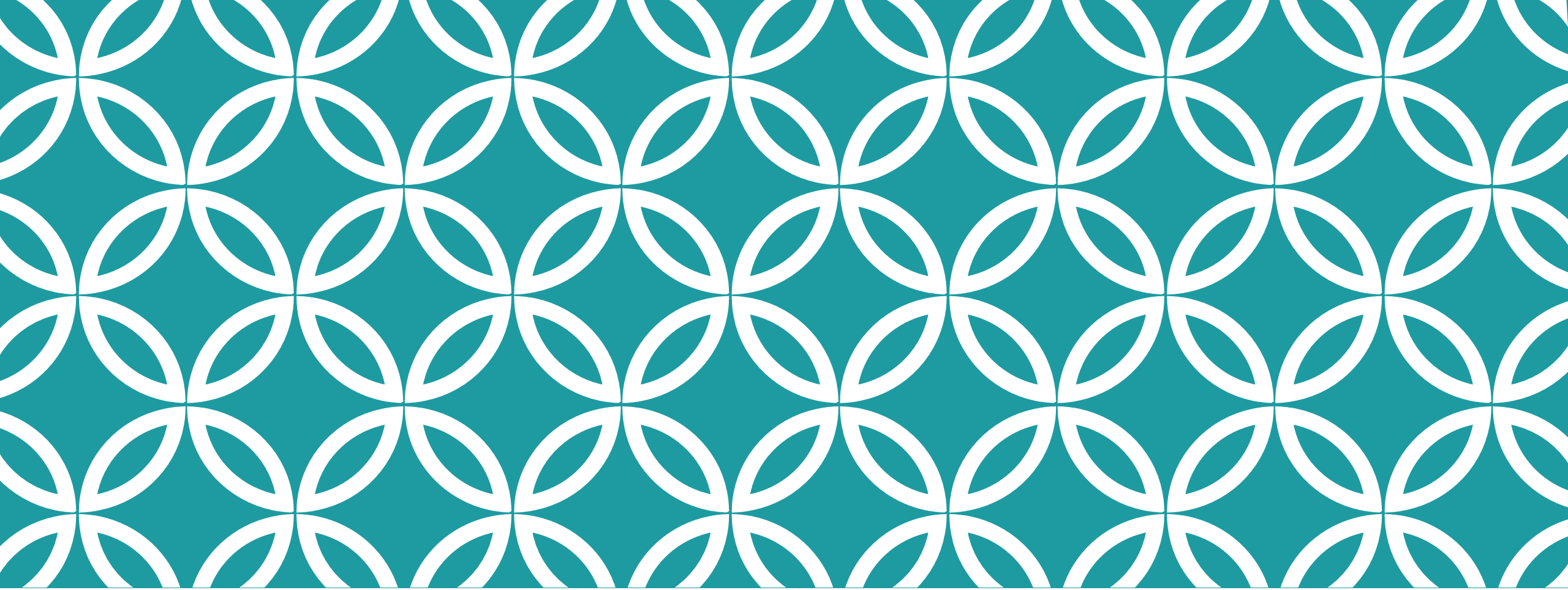
- TMF Reference Model affiliates with CDISC April 2022
- **TMF impacts:**
  - Remains freely available
  - More rigor as data standard (e.g., SDTM)
  - Formal seat at the table with HA & life science consortia

ICH E6 – Revision 2

- Global GCP standard (2017)
- Mandates risk-based trial management
- **TMF impacts:**
  - Risk mgmt 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



NO RISK = NO REWARD

Learning to love risk

COMPONENTS OF RISK-BASED TMF MANAGEMENT

TMF RBM COMPONENTS:

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

TAKEAWAY:

As CT landscape evolves and trial complexity increases, adopt risk-based TMF management to sanely achieve TMF compliance

IMPLICATIONS FOR TMF

KEEP CALM, FORGE ON

> Plus ça change, plus c'est la même chose
> - Jean-Baptiste Alphonse Karr

PREPARE AND DRY RUN

Prep for live, hybrid and remote inspections:

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

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

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

EMBRACE A RISK-BASED TMF APPROACH

Improve TMF management without sacrifice:

- Take a risk-based approach to TMF GCP compliance
- Iterative improvements – crawl, walk, run
- Data is possible with or without eTMF
- Celebrate the failures as much as the wins
- Do TMF right, do TMF once, be done with TMF

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

FINAL PERSPECTIVE – DO IT WISELY, DO IT ONCE

1

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

2

Only paying for TMF once takes iterative actions in plan and execution - from trial start through finish

3

Regulators demand GCP risk-based trial management, so lead the way with TMF

> It's GCP, not PCP
> - Frances L. Ross

Q&A