2026 CDISC US INTERCHANGE

The Connected TMF Mindset

Embedding Risk-Based Thinking and Engagement at Scale

Christina Mantzioros
Director, Product & Clinical Intelligence, Montrium

Denver, Colorado | Main Conference: 5–6 October



Speaker



Christina Mantzioros
Director, Product & Clinical Intelligence, Montrium

Christina is a clinical technology and product strategy leader with over 10 years of experience across clinical operations, TMF management, and digital clinical systems. As Director, Product & Clinical Intelligence at Montrium, she leads strategic product definition for next-generation eTMF capabilities focused on inspection readiness, process-driven workflows, and connected clinical intelligence. Her work sits at the intersection of TMF, structured clinical data, and emerging technologies that improve operational efficiency and data quality across the trial lifecycle. Christina co-hosts The State of TMF podcast and is a returning CDISC presenter.

Committed, but not yet complete

Most organisations have started on ICH E6(R3). Very few have finished.

85%

underway on ICH E6(R3)

11%

fully implemented

Where execution lags intent

50% still rely on the Core / Recommended column instead of a trial-specific framework

71% work from an oversight model that is not both defined and consistently applied

34% name risk-proportionate TMF management as their single biggest challenge

43% have audit trails that exist but are not routinely reviewed

Source: State of TMF – ICH E6(R3) survey, Montrium, n = 168

The landscape we're operating in

Systems of record stay authoritative. What needs to connect is their meaning.



ICH E6(R3), consolidated

Principles, Annex 1 and Annex 2 now form one guideline. Annex 2 adds GCP considerations for decentralised and pragmatic elements and real-world data, so more evidence is created outside the eTMF.



TMF Standard Model V1

Moving from a reference model to a standard: record groups and record types, stable unique identifiers, and richer metadata, making TMF content machine-readable by design.



Operational visibility

Regulators are signalling interest in more timely visibility into trial conduct (e.g., FDA's Real-Time Clinical Trials pilot), and data flow diagrams are increasingly expected.

The connected TMF mindset

From proving documents exist to proving the trial was controlled

FROM	TO
Documents and artifacts	**Records, wherever they live**
Checklist of essential documents	**Essentiality as a functional, per-trial test**
Completeness metrics	**Reconstructability and defensible decisions**
Filed = done	**Distinct conclusions: filed ≠ reviewed ≠ effective**
Scheduled QC sweeps	**Oversight triggered by risk signals**
Custodian of the file	**Information manager across systems**
Evidence scattered in inboxes	**Oversight captured at the moment of decision**

Start with what's critical to quality

Identified at study design (ICH E8(R1)), carried into risk-based quality management (ICH E6(R3) 3.10)

1 Planned processes

Which processes will this trial actually run?

e.g., informed consent, IP handling, safety reporting

2 Critical-to-quality factors

Of those, what must go right to protect participants and the reliability of results?

e.g., every participant consents on the approved version before any procedure

3 Risks to control

What could undermine those factors?

e.g., a version mismatch after a protocol amendment

What people bring

- Experience of similar studies and populations
- Judgement on what really matters here
- Context no dataset holds

What wider evidence could add

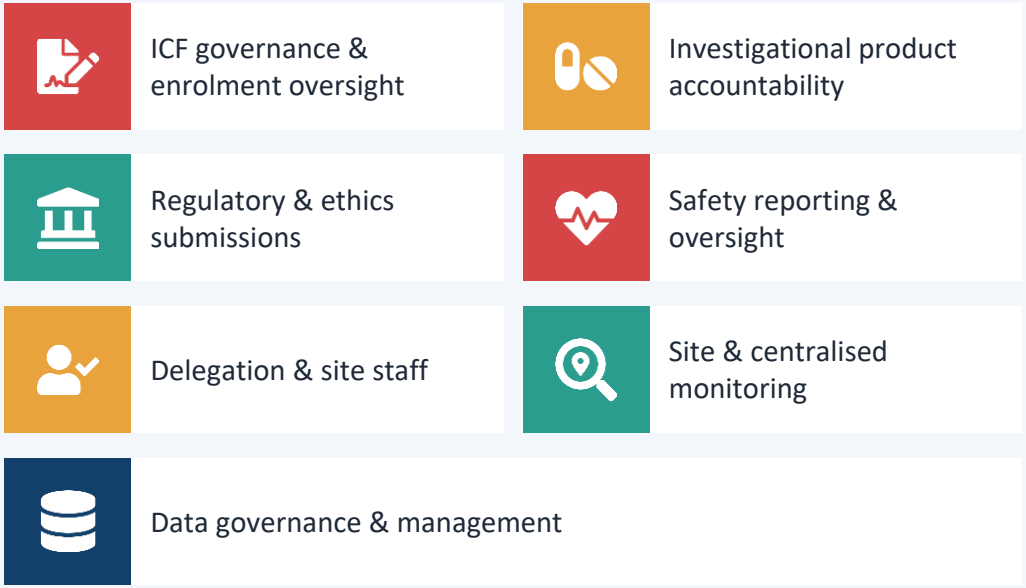
- Findings from previous regulatory inspections
- How trials with a similar design actually ran
- Risk signals in the protocol design itself

Information domains define “normal”

A discrete area of trial activity with its own:

- Processes
- Record types and relationships
- Quality and timeliness rules

When what should be produced is written down, absence becomes visible.



AT SCALE *Not just whether a record exists, but whether it says what it should, and what should now exist when the protocol changes.*

QUESTION 3 OF 5 · WHO NEEDS TO KNOW, AND WHEN?

Engagement at scale

The TMF is everyone's evidence, so risk has to reach everyone who owns it

Every domain has an owner

Clin ops, regulatory, safety, pharmacy, data management, and the CROs and sites acting for them.

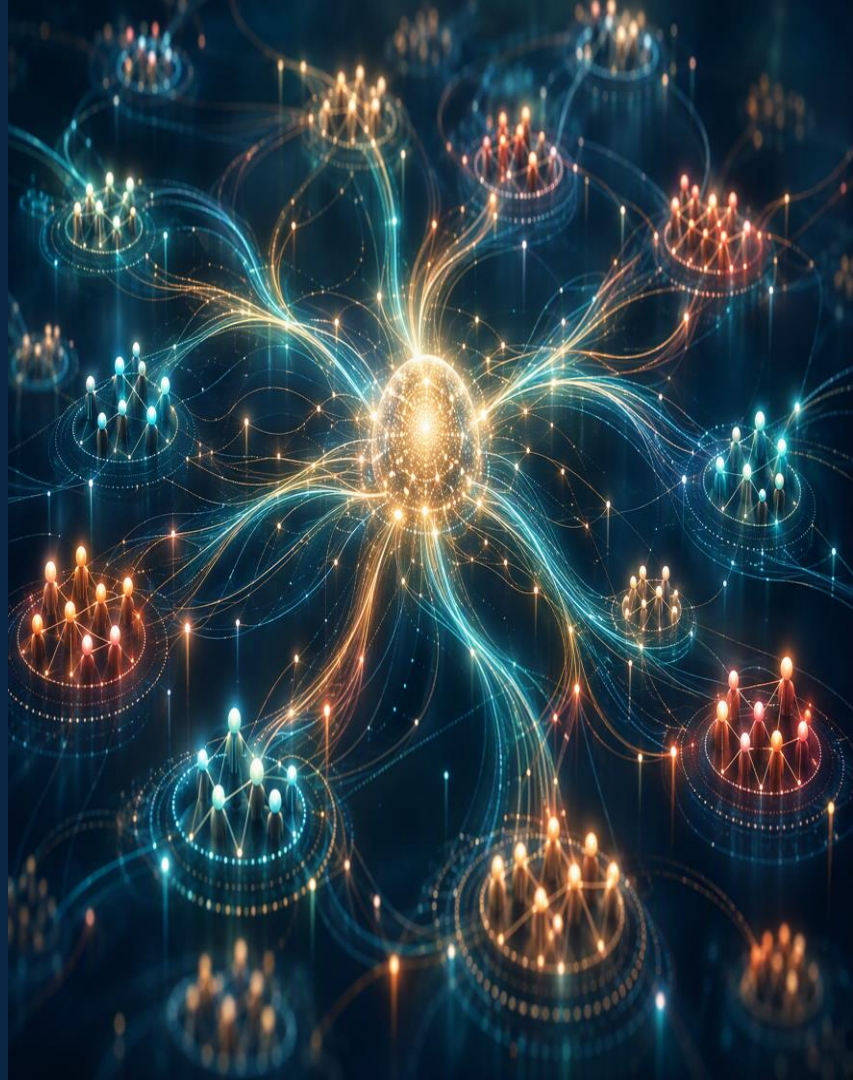
Signals reach the owner

Not only the TMF team. The person who can act sees the issue while it can still be fixed.

Boundaries don't break the chain

CRO and vendor evidence is evidence the sponsor relies on. The work can be delegated; accountability can't.

AT SCALE *Connecting signals no single owner would see, and letting anyone ask the evidence a question.*



Continuous, rules-based oversight

Illustrative example: the consent CTQ factor from Question 1, turned into rules

Define the rules for a domain → **Monitor continuously** → **Prioritised deviation list**

Rules

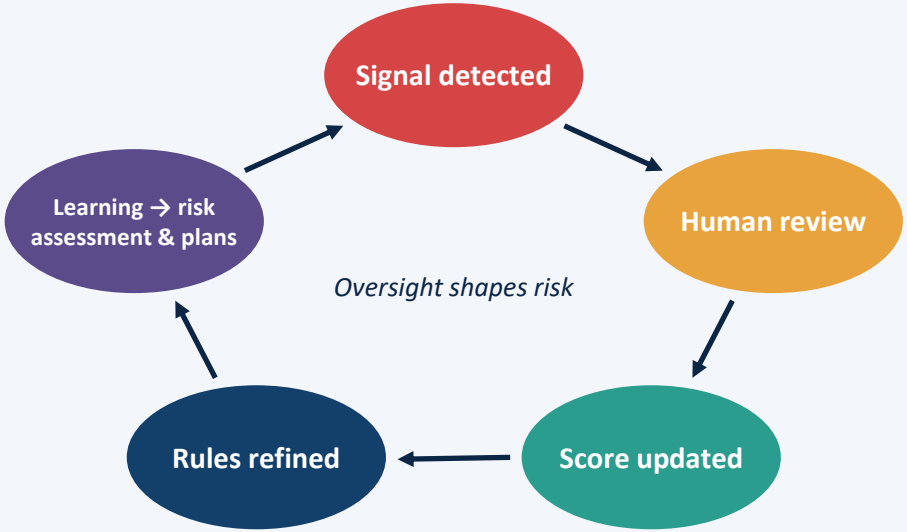
- ICF version in use matches the IRB/IEC-approved version in effect on that date
- Approval on file before the version enters use
- Amendment-triggered updates distributed within agreed timeframes
- Version history complete, with no gaps

CRITICAL	v3.0 in use from 14 Jan; IRB approval dated 21 Jan: consent obtained before approval
MAJOR	Amendment 02 issued 3 Feb; no distribution record after 52 days (30-day SLA)
MAJOR	v1.0 and v2.1 on file, v2.0 absent: approval chain can't be reconstructed

AT SCALE *Every rule checked across every site and record, continuously. Something does the looking, a person does the deciding.*

Oversight is triggered, not scheduled

A loop, not a line: what's learned feeds back into the process



Possible triggers

- Completeness threshold breached in a domain
- Milestone proximity: thresholds tighten before lock or inspection
- Query rate escalation across any dimension
- Quality event: audit finding or protocol deviation

AT SCALE *Patterns spotted across studies and partners, so what one study learns informs the next study's risk assessment.*

BACK TO THE QUESTION

“How did you decide where to focus your oversight?”

What the five questions could produce across studies, sponsors, and CROs



Risk profile

- Score per domain, dimension, and trial
- Updated after each oversight cycle, confirmed deviation, or quality event
- A live view, not a document



Narrative rationale

- Explains where oversight was focused, and why
- Drafted from the evidence; reviewed and confirmed by people
- Same logic + same data = same explanation



Recommendations

- Targeted QC, oversight adjustments, escalation paths
- Specific to domain, dimension, and record type
- Proportionate: effort where it matters

People bring the judgement. Scale brings the reach. The connected mindset puts them together.

Questions worth asking

Every organisation will answer them differently

1. What matters most in this trial?
2. If things go as planned, what should exist?
3. Who needs to know, and when?
4. How would you know something needs attention?
5. What changes next time?

Thank you

Christina Mantzioros
Director, Product & Clinical Intelligence, Montrium
cmantzioros@montrium.com

