Beyond Counting Documents — Evolving Risk-Based Review Under ICH E6(R3)

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Meet the Speaker

Donna Dorozinsky

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As the Founder and CEO of Just in Time GCP, Donna leads a highly respected organization dedicated to supporting life sciences companies in maintaining Good Clinical Practice (GCP) compliance and optimizing clinical trial operations. Her expertise in inspection readiness has helped numerous organizations successfully navigate regulatory inspections and implement remediation strategies for eClinical systems, quality management systems, and TMF services. She serves as a member of the TMF Reference Model Steering Committee and is currently leading the implementation of the TMF Standard Model.

Disclaimer and Disclosures

- *The views and opinions expressed in this presentation are those of the author(s) and do not necessarily reflect the official policy or position of CDISC.*

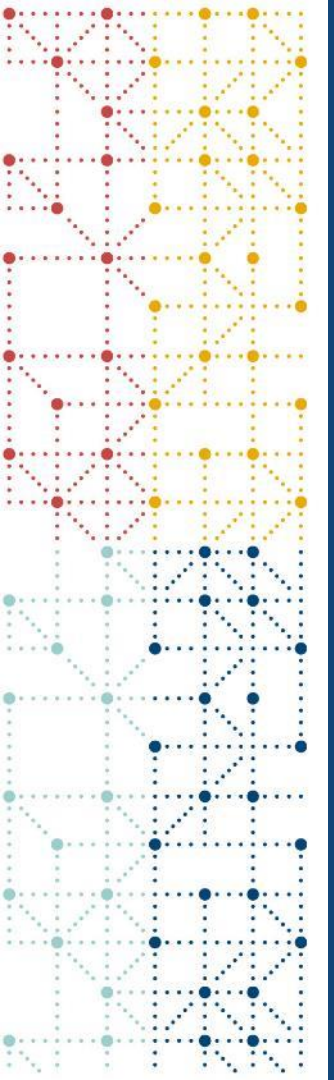
Agenda

1. Why are we having this conversation?
2. Beyond Counting Documents
3. Rethinking Risk: A Dynamic, Data-Informed Model
4. Translating this into Practice

Why Risk Based Oversight of the TMF Matters Now

- Clinical trials are more complex than ever — biologics, biomarkers, decentralization, data volume
- Regulators now expect evidence of oversight, not just completed documents
- ICH E6(R3) shifts from process compliance → risk-based quality management
- Missing documents don’t cause inspection failures — unmanaged risks do
- TMF must tell the story of control: who acted, when, and why

Compliance is no longer about checking boxes — it’s about proving you were in control.



Beyond Counting Documents

Evolving Risk-Based Review Under ICH E6(R3)

Redefining Risk: From Document Review to Data-Driven Oversight

- Risk-based TMF review isn't about counting, it's about connecting data to risk
  - Risk isn't defined by what's missing—it's revealed by what the data is telling you.
  - Oversight today demands connection between documents, decisions, and data flow.

- ICH E6(R3) is reshaping expectations: oversight must be dynamic, data-informed, and quality-focused
  - Quality signals don't live in silos. Neither should your TMF review.
  - The question is no longer "Is it complete?" but "Does it show control?"

Traditional Approaches Are Falling Short

Old Approach:
Completeness %, Milestones, Document Checklists

New Approach:
CTQs, Accountability, Quality Signals

- Legacy models = static checklists, document counts, completeness metrics
- Miss true compliance vulnerabilities (ownership gaps, process failures)
- Overemphasis on “missing docs” vs. “quality drivers that matter”

What are CTQs and How does that Relate to My TMF?

- CTQs identify what matters most to trial quality and subject safety
- TMF provides the documented evidence that those critical factors were managed
  - Oversight activities show how we managed it
- Every CTQ should map to traceable oversight within the TMF
- Together, CTQs + TMF tell the full “story of control”

CTQs tell us what's critical - the TMF tells us if we controlled it.

ICH E6(R3) Changes the Oversight Game

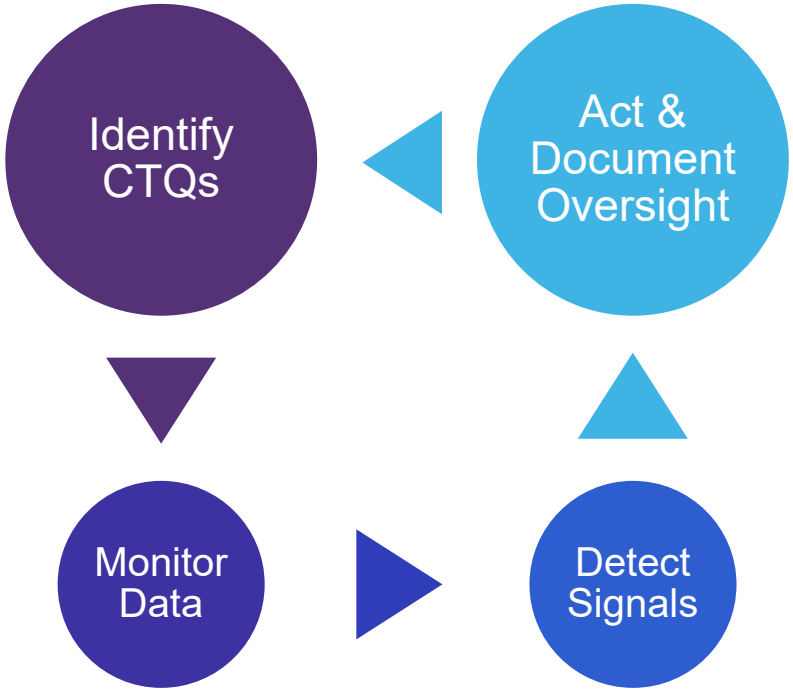
Oversight must shift from activity tracking → evidence of control

Quality by Design and CTQs redefine what's "critical"

Compliance isn't one-size-fits-all—it's contextual and data-driven

Inspectors now want to see how you think, not just what you file

The Continuous Risk Loop



Rethinking Risk: A Dynamic, Data-Informed Model

Risk Isn’t Predefined — It’s Discovered

- Strictly using pre-set “risk lists” can blind teams to emerging issues
  - Risk isn’t predefined — it’s discovered through data and context
- Real risk emerges when you analyze CTQs + operational data

Early Detection → Proactive Action → Fewer Inspection Surprises

Connecting CTQs to the TMF: From Critical Process to Critical Evidence

CTQs identify *what matters most* to trial quality and subject safety

TMF provides the *documented evidence* that those critical factors were managed

Every CTQ should map to traceable oversight within the TMF

Together, CTQs + TMF tell the full “story of control”

Translating this into Practice

Slides Using Images

Where Do We Start?

CDISC Risk Management Tool

Records that consistently drive quality

- Study Plans
- Protocols & Amendments
- Key oversight activities
- CSV

Where Do We Start?

Understand study risks

- Study Plans and specific study requirements
- Risk Management & KPI
- Protocol Deviations

Apply learnings from historical reviews

- Internal processes
- Vendors
- Trends in findings

Example: Oncology Pivotal Trial

CTQ Example	Why It's Critical	TMF Evidence That Demonstrates Control
Safety Oversight	Impacts subject safety & regulatory compliance	Safety review meeting minutes, safety communications, issue resolution timelines
Vendor Oversight	Unmonitored risk in critical functions	Vendor oversight reports, meeting minutes beyond the CRO, KPIs, governance
Data Accuracy & Integrity	Supports endpoint reliability	Data review meeting minutes, query resolution reports, monitoring reports
Protocol Deviations	Uncontrolled datt	Deviation logs, CAPA, escalation reports

Turn Findings int Action

Go beyond “fix the missing doc” → resolve root cause

Use dashboards/heat maps to visualize risk areas

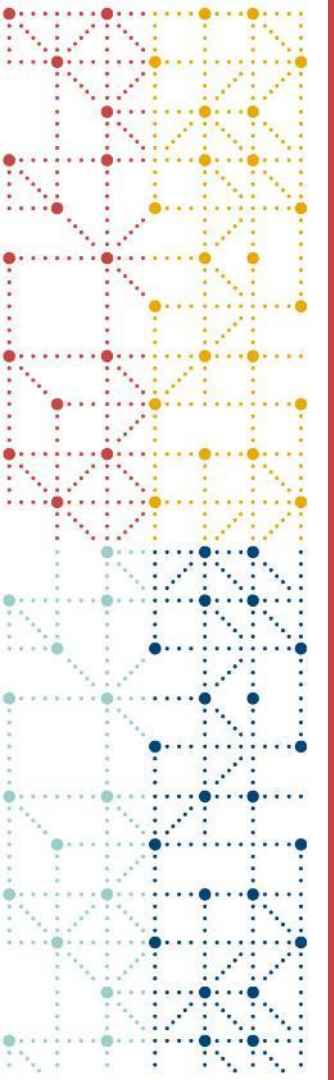
Document decision-making to show regulators your process

Elevate your Mindset

Move beyond document counts — focus on quality and risk impact

Build a defensible compliance story, backed by data

Prepare not just your TMF, but your thinking, for ICH E6(R3)



Risk-based thinking replaces routine with responsibility. That’s where real quality lives.

Thank You!

Let’s continue the conversation!

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