2026 Europe Interchange

THE FUTURE IS CONNECTED: STANDARDS AND AI POWERING DIGITAL TRANSFORMATION

MILAN, ITALY | MAIN CONFERENCE: 20-21 MAY | TRAININGS & WORKSHOPS: 18, 19, & 22 MAY

Leveraging AI to Enhance TMF Risk Assessment: A Practical Framework

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Agenda

1. The problem with traditional TMF risk assessment
2. What ICH E6(R3) changes and why it matters for AI
3.Information domains
4.AI as an anomaly detector
5. The updated framework
6.Triggers for oversight initiation
7. The output: risk profile, narrative, and recommendationn

Speaker

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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 embedding clinical AI capabilities. Her work emphasizes the intersection of TMF, structured clinical data, and emerging AI-enabled technologies to improve operational efficiency and data quality across the clinical trial lifecycle. Christina is also co-host of The State of TMF podcast and a returning CDISC presenter, having previously spoken at the 2023 TMF Interchange on data integrity in eTMF systems.

Why Traditional TMF Risk Needs to Change

- **Risk assessments are inconsistent across sponsors, CROs, and eTMF platforms**
  - Driven by subjective discussions rather than structured criteria
  - Retrospective metrics applied after issues emerge, not proactively
- **FDA 483 and EMA GCP inspection findings confirm the same recurring gaps:**
  - Inadequate oversight of key trial processes is a recurring theme
  - Missing, incomplete, or untimely essential records dominate inspection findings
- **ICH E6(R3) mandates a proportionate, risk-based approach but does not really prescribe how**

Traditional TMF risk assessment lacks consistency, relies on subjective judgment, and is often driven by retrospective data. No two organisations do it the same way.

What ICH E6(R3) changes and why it matters for AI

“Records” replaces “documents” and “artifacts”

Reflects modern data environments where records may not be discrete files

Essentiality is a functional test, not a checklist (Appendix C, section C.3.1)

A record is essential if produced AND it meets the criteria, determined per trial

C.3.3: some listed records “may not be produced” depending on trial design

Sponsors must identify risks across key trial processes (section 3.10)

Process risk is the primary lens — record risk is inherited from process risk.

This process-first structure is precisely what gives AI a coherent framework to operate within by telling AI where to look, what rules apply and what deviation means.

Two Complementary Lenses for TMF Risk Assessment

- **Option A (R3-first): Process-led assessment**
  - Start with critical-to-quality trial processes (ICH E6(R3) 3.10).
  - Records inherit risk from the process that produces them (clear, auditable logic).
  - Maps naturally to inspection themes where findings link to process breakdowns.
- **Option B (common today): Record-type assessment**
  - Assess risk per record type using the study risk assessment as context.
  - Apply essentiality criteria (Appendix C, C.3.1) at the record level for the trial.

Both lenses start from the same foundation: the study risk assessment (CTQ + proportionality).

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The study risk assessment

What it is

- Structured risk evaluation at study initiation to identify critical-to-quality processes and configures domain-level risk weights
- Output is the study risk assessment — a living record

What E6(R3) demands

- Section 3.10: identify critical-to-quality factors impacting safety, data integrity, or trial results
- Oversight and record requirements (C.3.3) must be proportionate to identified risks
- Aligns with ICH E8(R1) — critical-to-quality factors identified at protocol design stage

How AI can help

- Mines historical inspection and query data to provide evidence-based risk starting points
- Analyzes protocol design and calibrates risk weights against FDA 483 and EMA GCP findings
- The team still makes the judgment calls while AI ensures they're informed by the best available evidence

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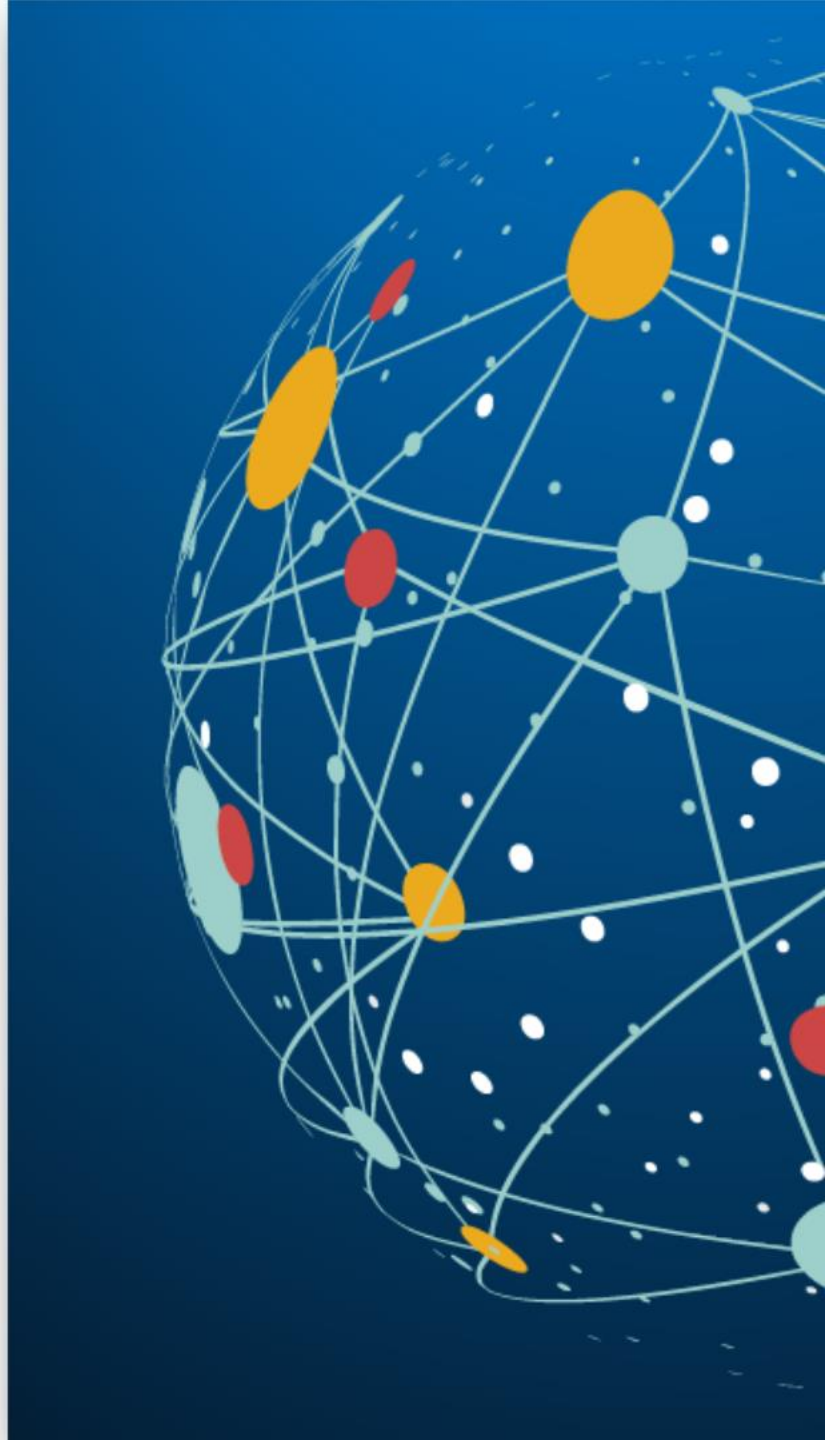
Introducing information domains

- An information domain is a **discrete area of trial activity** defined by its own:
  - Processes
  - Record types and relationships
  - Quality and timeliness rules and expectations
- The domain defines what normal looks like and AI detects deviations from it
- Important! While the most powerful risk signals come from **cross-system consistency** checks, true interoperability across eTMF, ISF, CTMS, and EDC is not yet standard.

Cross-system consistency checks are the future via digital data flow



7 core domains for *most* trials

- **ICF version governance and enrolment oversight**
- **Investigational product accountability**
- **Regulatory and ethics submissions and approvals**
- **Safety reporting and oversight**
- **Delegation and site staff**
- **Site and centralized monitoring**
- **Data governance and management documentation**

Protocol and Investigator's Brochure serve as the shared consistency baseline across all domains — every domain checks record content and version alignment against these foundational documents.

The domain structure is not fixed i.e. trial design determines which domains apply and how the rules are configured within each.

AI as an anomaly detector

Define the rules for a domain → **AI monitors continuously** → **Outputs a prioritized deviation list**

Example: ICF version governance rules

1. ICF version in use at a site must match the IRB/IEC approved version in effect at that date
2. IRB/IEC approval must be on file before the version enters use
3. Amendment-triggered ICF updates must be distributed to sites and documented within agreed timeframes
4. Version history must be complete with no gaps between successive approved versions

eTMF Risk Monitor — ICF Version Governance

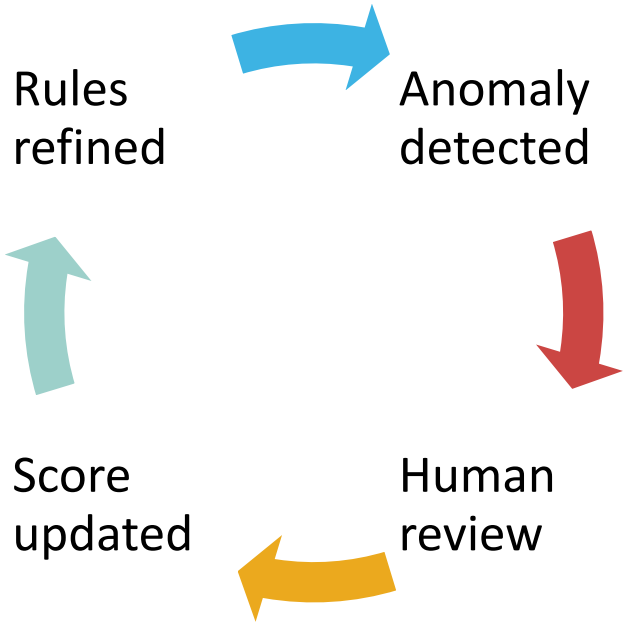
Generated: 27 Apr 2026 | 14:32 UTC
Scan scope: 47 sites · 4 ICF versions · 312 records checked

3 Deviations flagged | 1 Critical | 2 Major | 0 Minor | 44 Sites clear

#	SEVERITY	RULE BREACHED	DETAIL	SITE	TRIGGERED	STATUS
01	CRITICAL	Version in use precedes IRB/IEC approval	ICF v3.0 filed in use from 14 Jan 2026 IRB approval for v3.0 dated 21 Jan 2026 → Consent obtained 7 days before approval	US-004	Auto · 26 Apr 2026	Open
02	MAJOR	Amendment-triggered ICF update overdue	Protocol amendment 02 issued: 03 Feb 2026 ICF update distribution record: not on file → 52 days elapsed against 30-day SLA	DE-002	Auto · 25 Apr 2026	Open
03	MAJOR	Version history gap — chain incomplete	ICF v1.0 and v2.1 on file — v2.0 absent Approval chain for v2.1 cannot be fully reconstructed from records held	US-004	Auto · 27 Apr 2026	Open

*AI-generated sample output

How AI makes risk scoring dynamic




Completeness threshold breached


Milestone proximity


Query rate escalation


Quality event

When to perform oversight?

Oversight is not a one-time or regularly scheduled event. As the trial progresses, risk changes and the framework must respond.

What AI integration in TMF risk management looks like

AI operates within defined rules

The domain structure determines what AI monitors

Risk scoring must be dynamic, not point-in-time

Scope must be explicit and understood

Human accountability is non-negotiable

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The Output: Risk Profile, Narrative, and Recommendations

- A standardised framework produces three consistent outputs
- **1. Risk profile**
  - Overall average risk score by record, dimension, and trial
  - Dynamic — updated after each oversight cycle, confirmed anomaly or quality event
- **2. Narrative rationale**
  - Explains what is driving risk and why — defensible at inspection
  - AI-supported: consistent language across studies and sponsors
- **3. Actionable recommendations**
  - Targeted QC activities, oversight strategy adjustments, and escalation paths
  - Aligned with ICH E6(R3) proportionality principle — no unnecessary burden
- **Result: inspection-ready at any point in the trial lifecycle**

Questions?