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Clinical Whitepaper

From Reactive to Predictive: How Clinical Quality Intelligence Can Redefine Inspection Readiness in Clinical Trials

ClinQC Studio: Deployed Through Agilisium's FDX (Forward Deployment Experience)

> ICH E6(R3) represents a paradigm shift - a comprehensive risk-based quality management framework that demands not just compliance, but continuous, data-driven quality oversight across the full trial lifecycle.
>
> — International Council for Harmonization, GCP E6(R3) Final Guideline, January 2025

Executive Summary

> ICH E6(R3) represents a paradigm shift: a comprehensive risk-based quality management framework that demands not just compliance, but continuous, data-driven quality oversight across the full trial lifecycle.

Clinical trial quality teams now need continuous, risk-based oversight rather than late-stage remediation. With ICH E6(R3) in effect as the new global GCP standard, sponsors and CROs are expected to monitor Critical to Quality factors prospectively across the trial lifecycle instead of relying on point-in-time inspection preparation.

Most organizations are not yet operating that way. TMF gaps are often discovered close to inspection, EDC anomalies are escalated late, and protocol deviations are recorded without consistent trial-level trending or CAPA linkage, leaving quality teams to respond under time pressure rather than manage risk continuously.

ClinQC Studio is positioned as a practical response to that gap. It gives quality leaders earlier visibility into emerging risk, helps teams prioritize the issues most likely to affect inspection outcomes, and connects signal detection to documented follow-through across eTMF, EDC, deviation management, and readiness monitoring. It is deployed through Agilisium's FDX framework, described in full later in this paper.

This white paper explains why the regulatory shift matters now, where current quality operations break down, and how ClinQC Studio helps organizations move from reactive compliance activity to proactive quality intelligence across the trial lifecycle.

1 The Regulatory Landscape: Why the Moment Is Now

1.1 ICH E6(R3) — A Paradigm Shift in Quality Expectations

The immediate implication of ICH E6(R3) is clear: quality oversight must become continuous, risk-based, and demonstrable throughout trial conduct. Finalized in January 2025, the guideline shifts global GCP expectations away from retrospective, documentation-led quality management and toward a quality-by-design model in which risks are identified, monitored, and mitigated prospectively from protocol inception through study close.

The practical implication for quality teams is significant: E6(R3) does not permit passive quality management. Sponsors, CROs, and investigator sites must demonstrate continuous and documented evidence of quality oversight - and that evidence must be traceable, proportionate, and risk-informed.

Key provisions with direct implications for quality operations include:

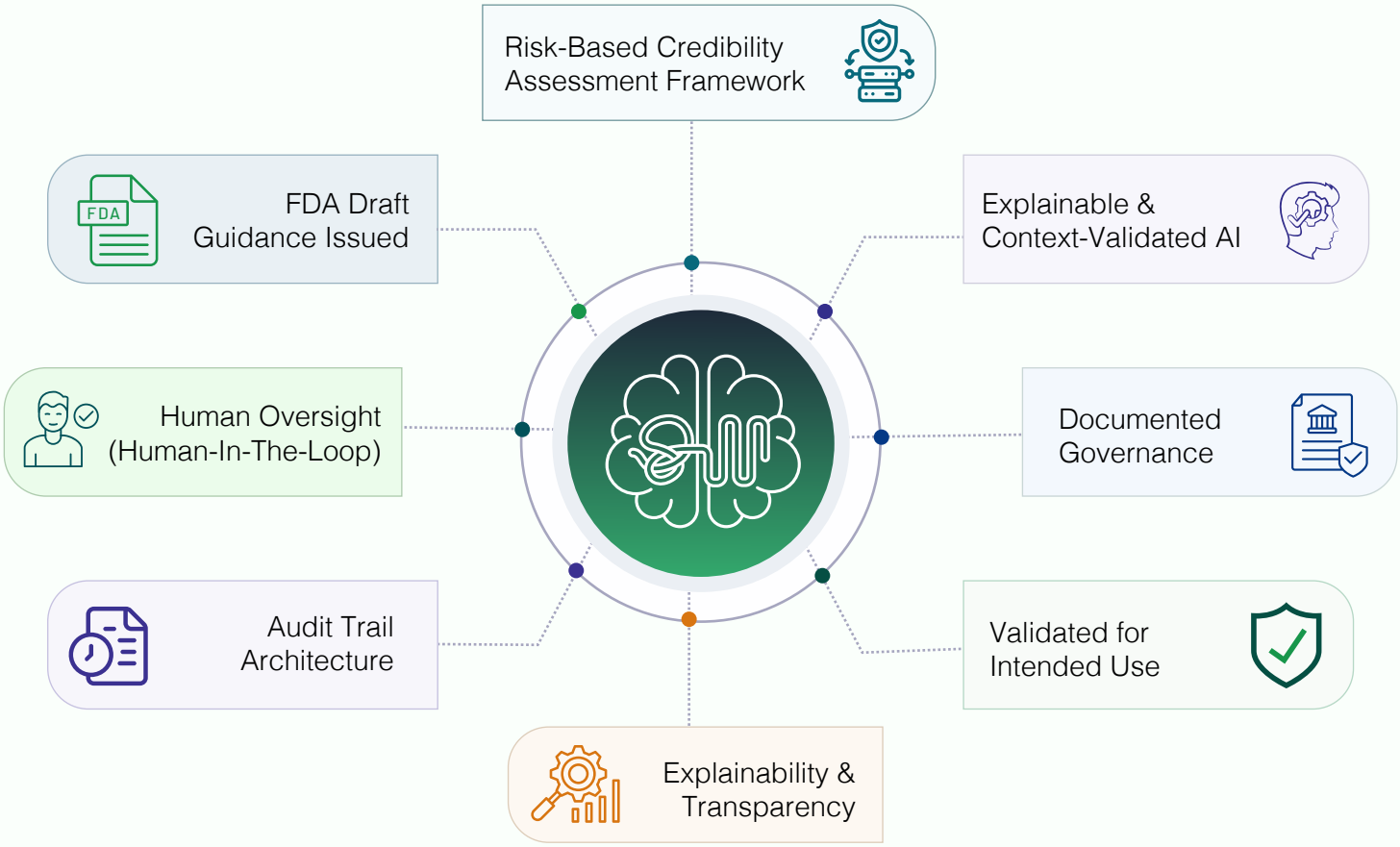
- Proportionality and risk-based oversight: Sponsors are required to define Critical to Quality (CtQ) factors at study design and maintain oversight of those factors throughout the trial lifecycle, not only during audits.
- Sponsor oversight of investigator sites: Protocol deviation management must include systematic trending and CAPA linkage at the trial level - not just site-level logging. Sponsors are accountable for identifying systemic deviation patterns across investigator networks.
- Technology and data integrity: eTMF completeness, ALCOA+ compliance, and audit trail integrity are explicit expectations, with regulators empowered to assess these directly during inspection.
- Centralized and remote monitoring: Centralized monitoring, including statistical and data-driven approaches, is now a standard oversight mechanism - reinforcing the regulatory legitimacy of AI-assisted anomaly detection across EDC domains.

1.2 FDA Guidance on AI in Regulatory Decision-Making

In January 2025, the FDA issued draft guidance on the use of artificial intelligence to support regulatory decision-making for drug and biological products. The guidance proposes a risk-based credibility assessment framework for AI models used in regulated contexts. Critically, it signals that AI-generated insights used to support regulatory decision-making should be explainable, validated for their context of use,

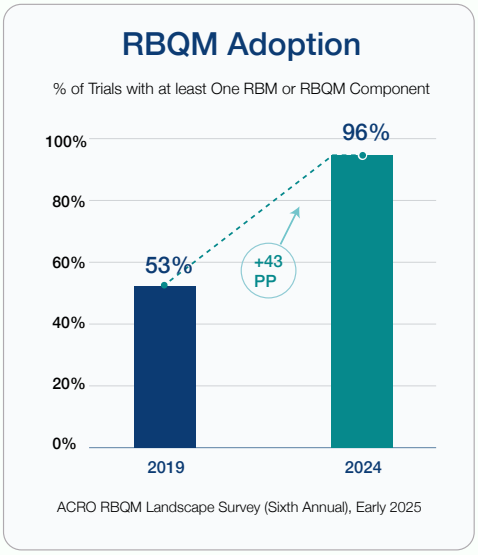
and governed by documented human oversight.

This positions AI-augmented quality tools not as experimental technology but as a credible component of the regulatory-quality infrastructure - provided they are built with appropriate validation, audit trail architecture, and human-in-the-loop review workflows.



1.3 RBQM Adoption: Progress and Persistent Gaps

ACRO's sixth annual RBQM landscape survey, conducted in early 2025, reported that 96% of clinical trials in its 2024 dataset included at least one RBM or RBQM component, up from 53% in 2019. Despite this progress, persistent execution challenges remain - organizations continue to face fragmented data, limited real-time oversight, and uneven adoption of centralized, cross-functional quality workflows.



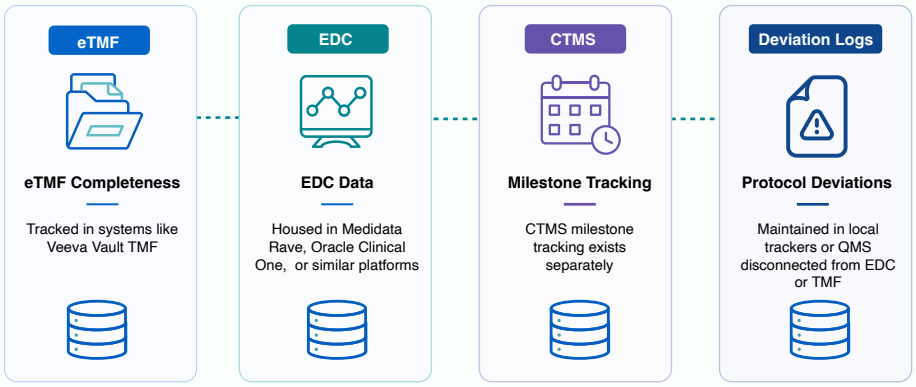
Despite this progress, persistent execution challenges management-flagged by Everest Group as a defining trend - underscores the direction of the industry: quality management that operates at the data layer, in real time, across the full spectrum of trial signals from eTMF to EDC to deviation logs. This is precisely the operational gap ClinQC Studio is designed to close.

2 The Structural Problem: Where Clinical Quality Management Fails

2.1 Fragmentation Across eClinical Systems

> ***Regulatory anchor:*** *ICH E6(R3) requires proportionate, risk-based oversight supported by integrated quality signals across the trial lifecycle.*

In clinical practice, quality management is distributed across platforms that were not designed to share a unified quality signal. eTMF completeness is tracked in systems such as Veeva Vault TMF.



EDC data is housed in Medidata Rave, Oracle Clinical One, or similar platforms. CTMS milestone tracking exists separately. Deviation logs are frequently maintained in local trackers or quality management systems disconnected from the EDC or TMF environments.

The result is a quality oversight model that requires significant manual reconciliation effort to generate a unified view of trial health - and that view is, by definition, retrospective. By the time quality teams have assembled signals from multiple systems, the inspection window is already approaching.

2.2 Manual TMF Classification and Completeness Management

> ***Regulatory anchor:*** *DIA TMF Reference Model v3.0 and ICH E6(R3) reinforce contemporaneous, complete, and inspection-ready trial master file maintenance.*

Trial Master File management remains one of the most labor-intensive quality activities in clinical operations. Under the DIA TMF Reference Model v3.0, documents must be classified, filed, and reviewed to artifact-level completeness standards, and this work is still largely manual in many studies.

Misclassification and missing artifacts often surface during pre-inspection reviews rather than during the study, forcing last-minute remediation under pressure. At that stage, teams may need reconstruction, re-execution, or explanatory documentation that increases scrutiny instead of reducing it.

2.3 Reactive EDC Anomaly Detection

> ***Regulatory anchor:*** *ICH E6(R3) recognizes centralized, data-driven monitoring as a standard mechanism for sponsor oversight.*

Across EDC platforms, anomaly detection still relies heavily on study-build range checks and manual query generation. These controls can catch individual field discrepancies, but they often miss cross-domain patterns such as implausible timing between an adverse event and study drug dispensing or laboratory values that are inconsistent with the enrolled population.

Query drafting in this environment varies substantially across reviewers. Without standardized clinical context, queries issued to investigator sites are inconsistent in specificity and tone - creating variable quality signals across a multi-site study and increasing the likelihood of incomplete responses that require follow-up cycles.

2.4 Protocol Deviations Without Systemic Insight

> ***Regulatory anchor:*** *ICH E6(R3) requires systematic deviation analysis, root-cause understanding, and CAPA linkage beyond site-level event logging.*

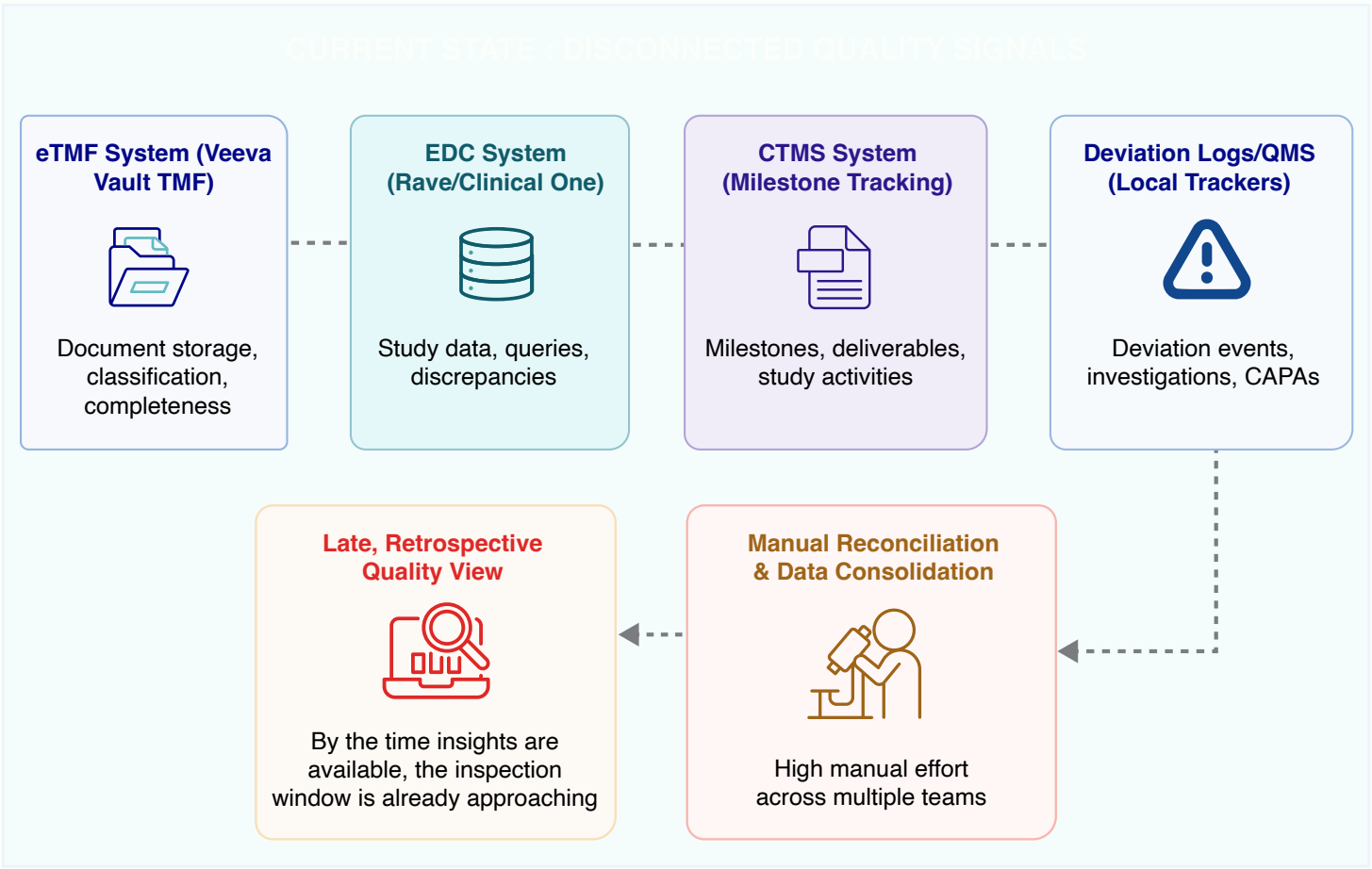
Protocol deviations are among the most consequential quality signals in clinical trial conduct. Under ICH E6(R3), sponsors are required not only to log deviations but to analyze them for systemic patterns - and to implement CAPAs that address root causes at the trial level, not solely at the site where the deviation was recorded.

In practice, deviation management frequently operates as individual event logging without clustering by underlying cause. A consent process failure at Site A and an identical failure at Site B may be recorded as separate events, investigated independently, and closed with site-specific CAPAs - when the root cause is a protocol-level deficiency in the informed consent procedure that requires a trial-wide corrective action. This pattern persists across investigator site networks and compounds regulatory risk with each deviation cycle.

2.5 Inspection Readiness as a Point-in-Time Activity

> ***Regulatory anchor:*** *FDA, EMA, MHRA, and PMDA inspection frameworks evaluate ongoing control effectiveness, not only pre-inspection remediation snapshots.*

Pre-inspection preparation - often referred to as a mock inspection or pre-inspection readiness review - is the point at which most quality teams first obtain a consolidated view of their trial compliance posture. TMF completeness reports are generated, outstanding queries are escalated, and deviation logs are reviewed for completeness. This activity typically occurs within a compressed 4–8-week window prior to an announced inspection or audit.



The limitation is structural. Quality risks that have accumulated over months of trial conduct are reviewed in weeks. Remediation prioritization relies on reviewer judgment rather than a risk-scored, data-driven assessment of which findings are most likely to generate inspection observations. The outcome is significant effort expended under pressure, with no guarantee of coverage across all high-risk signals.

WHY CLINICAL OPERATIONS NEED INTELLIGENT AUTOMATION

FRAGMENTATION ACROSS eCLINICAL SYSTEMS

Regulatory anchor: ICH E6(R3)

MANUAL TMF CLASSIFICATION & COMPLETENESS MANAGEMENT

Regulatory anchor: DIA TMF Reference Model v3.0 & ICH E6(R3)

REACTIVE EDC ANOMALY DETECTION

Regulatory anchor: ICH E6(R3)

PROTOCOL DEVIATIONS WITHOUT SYSTEMIC INSIGHT

Regulatory anchor: ICH E6(R3)

INSPECTION READINESS AS A POINT-IN-TIME ACTIVITY

Regulatory anchor: FDA, EMA, MHRA, PMDA Inspection Frameworks

3 ClinQC Studio: Architecture and Approach

3.1 Design Approach

ClinQC Studio was shaped through direct engagement with sponsor and CRO quality workflows, with the design grounded in recurring operational failures, data review bottlenecks, and inspection-readiness pain points observed in practice. That grounding makes the platform more relevant to day-to-day quality operations because it reflects how teams actually work, where oversight breaks down, and what evidence leaders need in order to act earlier and with more confidence.

The resulting AI agent design is specific to the clinical environment in which it operates, governed by the regulatory frameworks applicable to that environment, and validated against representative trial data before deployment. ClinQC Studio is delivered through Agilisium's FDX framework - see the About FDX section later in this white paper for how that deployment model works end to end.

3.2 Regulatory and Standards Alignment

ClinQC Studio is built against the following standards and regulatory frameworks:

FRAMEWORK	APPLICATION WITHIN CLINQC
ICH E6(R3) GCP	RBQM principles, CtQ monitoring, deviation management per §5.20, audit trail requirements
DIA TMF Reference Model v3.0	Zone 1–8 completeness taxonomy, artifact classification, gap prediction
CDISC CDASH / SDTM	Domain-specific anomaly detection across AE, LB, VS, CM, DS, EX
21 CFR Part 11	Electronic records, audit trail, electronic signatures, system validation
ICH E8(R1)	Quality by design, CtQ factor identification in trial planning
EMA Annex 11	Computerized systems validation, access control, data integrity
EMA Annex 22 (draft, 2025)	Draft expectations for AI transparency, model validation, and ongoing performance monitoring
FDA AI Guidance (Draft, January 2025)	Risk-based credibility assessment framework, human oversight, and explainability expectations

3.3 Platform Architecture: Five Integrated AI Modules

Module 1: eTMF Document Intelligence & Auto-Classification

AI automatically classifies Trial Master File (TMF) documents using the DIA TMF Reference Model, identifying missing artifacts, misfiled documents, and ALCOA+ compliance issues in real time. Human reviewers validate AI recommendations through a single interface, ensuring complete oversight. Continuous TMF completeness scoring highlights quality gaps early, while predictive models identify documents at risk of being missing before trial close.

Module 2: CDISC-Aware EDC Data Anomaly Detection

AI analyzes EDC data across key CDISC domains (AE, LB, VS, CM, DS, and EX) to detect protocol deviations and clinically relevant anomalies with reduced false positives. The platform generates context-aware query drafts, enabling data managers to review, refine, and issue high-quality queries more efficiently while improving response tracking and resolution.

Module 3: Protocol Deviation Clustering & Root Cause Analysis

AI groups protocol deviations by underlying root causes, helping quality teams identify systemic issues across investigator sites rather than isolated events. The solution recommends CAPA actions, flags reportable deviations aligned with ICH E6(R3), and maintains a complete human-reviewed audit trail.

Module 4: Predictive Inspection Readiness Simulator

Continuously assesses study readiness against global regulatory standards, including FDA, EMA, MHRA, and PMDA. The platform evaluates TMF completeness, data integrity, protocol compliance, and monitoring quality while providing prioritized remediation plans to address inspection risks proactively.

Module 5: Unified Quality Dashboard

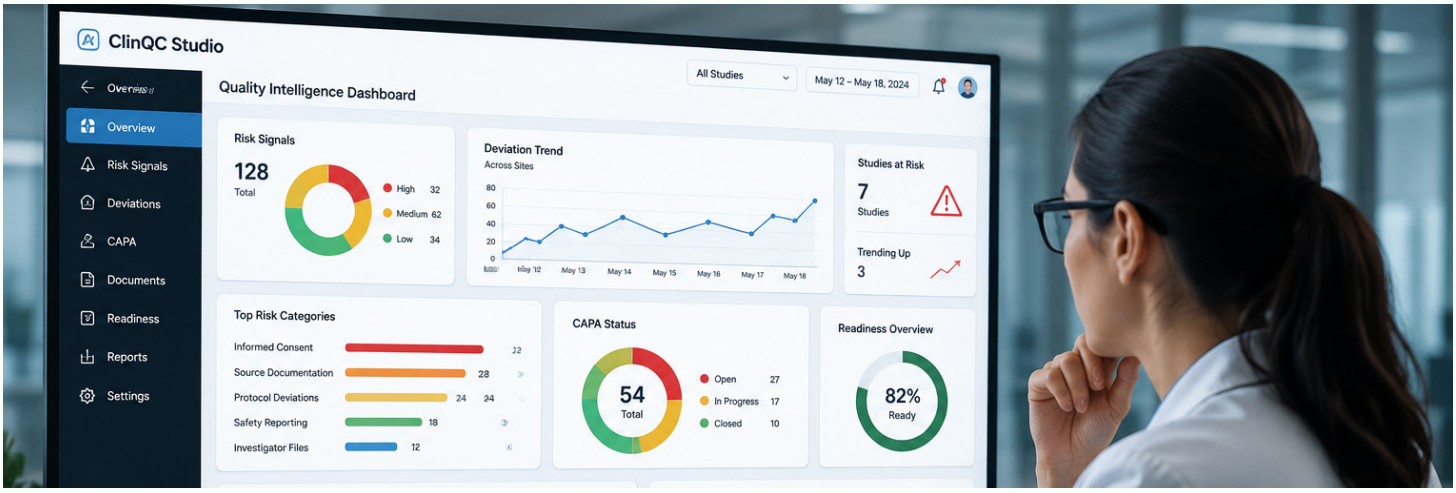
A centralized dashboard consolidates TMF quality, EDC anomalies, protocol deviations, and inspection readiness into a single view. Role-based insights and cross-study analytics help teams identify recurring quality trends, monitor portfolio performance, and drive continuous improvement across clinical trials.

4 Clinical Value: From Quality Activities to Quality Intelligence

4.1 Shifting from Retrospective Reporting to Proactive Oversight

The operational distinction between traditional quality management and ClinQC's AI-augmented model is not one of tool sophistication - it is one of temporal position. Traditional quality management reports on what has occurred. ClinQC Studio identifies potential findings before they emerge.

This shift from reporting to prediction is central to ClinQC's value. CtQ factors are monitored continuously, risk signals are prioritized earlier, and remediation happens during the trial rather than in the final weeks before an audit. For example, instead of discovering a cluster of consent-related deviations during a pre-inspection review, a quality lead could see the pattern emerge across sites in real time, confirm the shared root cause, and launch a trial-wide CAPA before the issue escalates into an inspection finding.



4.2 Reducing Manual QC Effort Without Reducing Oversight

A persistent concern in AI-augmented quality management is over-automation without sufficient human review. ClinQC Studio's human-in-the-loop architecture is designed to reduce manual effort while preserving the documented oversight regulators expect.

Every AI-generated recommendation - document classification, anomaly query, deviation or CAPA, readiness action - is presented to a qualified human reviewer before action. The reviewer approves, modifies, or rejects the recommendation, and that decision is captured in a full audit trail per 21 CFR Part 11 requirements. AI assists the quality professional; it does not replace the clinical judgment that regulatory agencies expect to find documented in inspection-ready trial records. The practical outcome is a significant reduction in repetitive, low-value manual effort - TMF document sorting, range check query drafting, individual deviation log review - while preserving and documenting the human oversight that RBQM-compliant quality management requires.

4.3 Inspection Readiness as a Continuous State

Under the ClinQC model, inspection readiness is built into day-to-day trial oversight. The simulator scores readiness across FDA, EMA, MHRA, and PMDA expectations throughout the study, providing teams with a current, prioritized view of compliance posture whenever an inspection window opens.

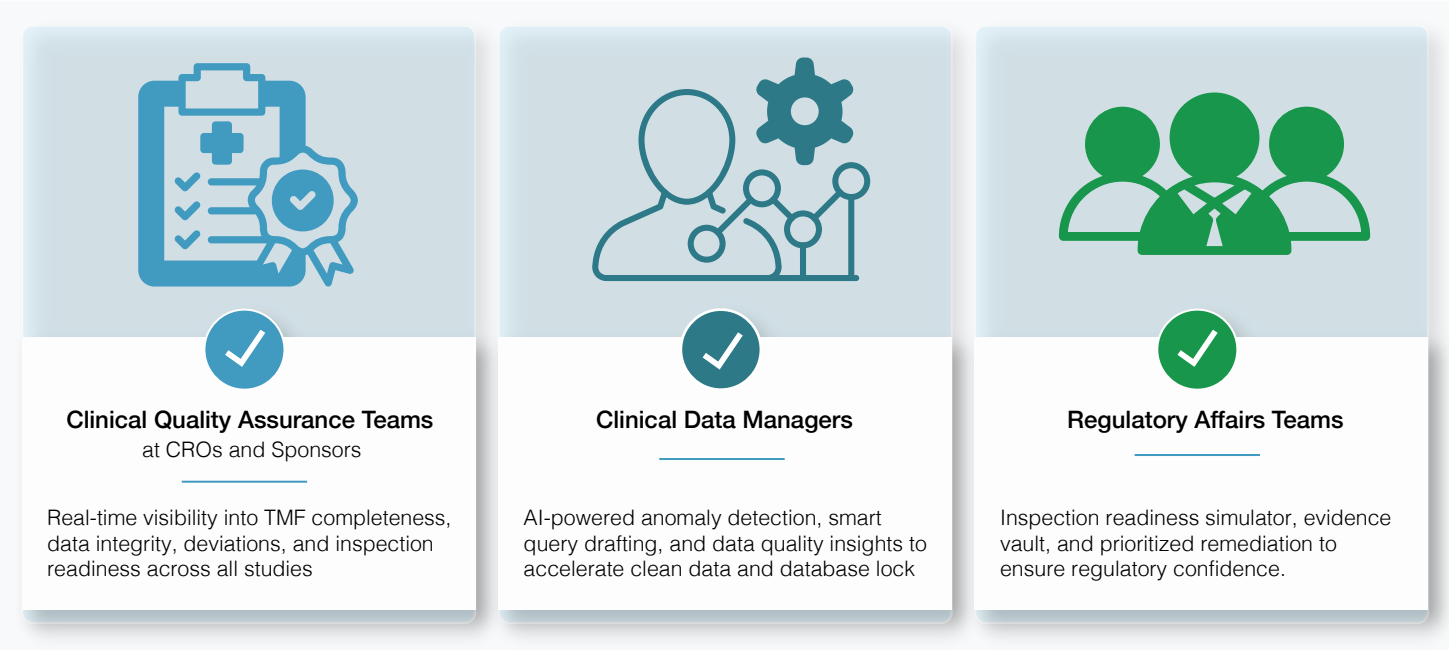
This capability is particularly consequential in the context of EMA and MHRA unannounced inspection programmes, where preparation windows may be absent entirely. Sponsors operating with continuous readiness scoring are structurally better positioned for unannounced oversight activities than those relying on periodic manual preparation.

5 Deployment Context and Target Environment

5.1 Organizations and Roles Served

ClinQC Studio is designed for clinical trial environments where quality management complexity scales with trial volume, investigator site diversity, and multi-regional regulatory scrutiny.

Three core operational groups are served:



5.2 Trial Types and Therapeutic Areas

ClinQC Studio supports Phase I–IV, adaptive, platform, decentralized (DCT), and multi-regional clinical trials. Its CDISC-aligned anomaly detection engine is tailored by therapeutic area - including oncology, rare disease, CNS, immunology, and infectious disease - to deliver protocol-specific quality oversight.

6 Competitive Context: Where ClinQC Studio Differs

The clinical quality technology market already includes strong point solutions across eTMF, RBQM, and clinical data management. The case for ClinQC Studio is not that these systems are inadequate, but that quality teams still struggle to connect their outputs, prioritize risk consistently, and turn dispersed signals into timely action. ClinQC is differentiated by the way it brings those signals together and supports more consistent decision-making across the workflow.

Capability	Point Solutions (ETMF / RBQM / EDC)	ClinQC Studio
eTMF completeness tracking	● Within eTMF platform only	✓ Unified with EDC and deviation signals
CDISC-aware anomaly detection	● Limited / range checks only	✓ ML models across AE, LB, VS, CM, DS, EX
Deviation root cause clustering	X Not available	✓ AI clustering with trial-wide CAPA generation
Cross-system quality signal view	● Requires manual reconciliation	✓ Real-time, unified command center
Inspection readiness scoring	● Periodic / manual assessment	✓ Continuous, multi-regulator predictive scoring
Regulatory framework alignment	● Platform-specific	✓ ICH E6(R3), DIA TMF RM, CDISC, 21 CFR Part 11, EMA Annex 11/22
Human-in-the-loop architecture	● Varies	✓ Built-in across all AI recommendation workflows

A further differentiator is the degree to which ClinQC can be shaped around existing quality operations rather than forcing teams to adapt to a rigid product model. That matters because the usefulness of any quality platform depends less on feature breadth alone and more on whether it fits the actual review, escalation, and CAPA practices already in place - and that fit is precisely what the FDX engagement is designed to produce.

7 The ICH E6(R3) Implementation Imperative

The January 2025 adoption of ICH E6(R3) creates an implementation timeline that is already active. Regulatory agencies across ICH regions - FDA, EMA, MHRA, PMDA, Health Canada - are aligning inspection expectations to E6(R3)'s RBQM requirements. Sponsors and CROs initiating new studies in 2026 are expected to demonstrate quality by design principles, continuous CtQ monitoring, and documented CAPA linkage as standard elements of their quality management systems.

For quality teams operating with fragmented eClinical platforms and manual quality processes, E6(R3) compliance is not achievable at scale without technology augmentation. The documentation burden alone - continuous CtQ monitoring evidence, systematic deviation trending records, CAPA effectiveness assessments - exceeds the capacity of manual quality workflows in complex multi-site programmes.

ClinQC Studio's design is explicitly aligned to E6(R3)'s operational requirements: continuous monitoring of CtQ factors, systematic deviation analysis and CAPA linkage, TMF completeness and ALCOA+ validation, and proportionate, risk-based site oversight. The platform generates the documentation artefacts that E6(R3) requires - not as a reporting exercise, but as a byproduct of continuous quality intelligence operation.

RAJ BABU

Founder & CEO, AGILISIUM

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The biggest constraint in AI adoption in Life Sciences is no longer technology - it is talent. The organizations that will lead the next decade will not simply adopt AI; they will build AI capability into the fabric of their business. That is the vision behind Agilisium's FDX (Forward Deployment Experience) initiative. By combining deep Life Sciences expertise with AI-first skills, domain-led innovation, and continuous learning, we are creating a workforce that can responsibly design, deploy, and scale AI solutions. Our competitive advantage comes not just from the AI technologies we use, but from the compounding institutional knowledge, scientific expertise, and AI capabilities we continue to build across our organization.

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About FDX

ClinQC Studio is not delivered as standalone software. It is deployed through Agilisium's FDX - Forward Deployment Experience - an enterprise execution framework purpose-built to operationalize AI across Life Sciences and Healthcare. FDX exists because deploying an AI model is not the same as operationalizing it: most enterprises can stand up a pilot, but far fewer get that pilot into production, adopted, and generating measurable outcomes.

Agilisium's own research puts that gap at 67% of enterprise AI projects failing to reach production. FDX is the response to that specific failure mode, and ClinQC Studio is one of the Forward Deployment Agents delivered through it.

Three Pillars, One Framework

FORWARD DEPLOYMENT AGENTS

Intelligent AI systems - like ClinQC Studio - that automate complex enterprise workflows.

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FORWARD DEPLOYMENT SERVICES

Transformation services that operationalize the agent inside the client's existing environment.

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FORWARD DEPLOYMENT EXPERTS

Domain specialists who embed with the client's team to drive adoption and change management.

How an FDX Engagement Runs

Every FDX engagement, including a ClinQC Studio deployment, follows the same five-phase flow:

IDENTIFY

Discovery and workflow mapping to find operational bottlenecks.

DEPLOY AGENTS

ClinQC Studio (or the relevant FDX agent) is deployed for targeted automation.

ENABLE SERVICES

Managed services handle configuration and integration with eTMF, EDC, CTMS.

EMBED EXPERTS

Domain specialists drive adoption and change management.

SCALE

Continuous optimization and expansion enterprise-wide.

This sequence is why ClinQC Studio's five modules, described in Section 3, map directly to the five failure points identified in Section 2 - the FDX process is what connects the operational problem to the deployed product, and what keeps the product in active use afterward rather than becoming another shelved pilot.

What FDX Delivers in Practice

67%
of enterprise AI projects fail to reach production - the gap FDX is built to close

70%
reduction in manual processing time with FDX agents

90%
inspection readiness improvement

2x
commercial rep productivity

Figures reflect outcomes reported across the FDX framework; the inspection readiness improvement is directly relevant to ClinQC Studio deployments.

8 Conclusion: The Quality Intelligence Imperative

Clinical trial quality management has long been shaped by reactive workflows: documents are reviewed after filing, data anomalies are queried after entry, deviations are logged after occurrence, and readiness is assessed late in the process.

ICH E6(R3), FDA's AI guidance, and the progressive convergence of RBQM with clinical data management collectively signal that this model is no longer sufficient. Regulators expect continuous, documented, proportionate quality oversight - and they have the inspection frameworks to assess whether it exists.

ClinQC Studio represents a practical response to that expectation. By bringing together quality signals from eTMF, EDC, and deviation management into a more usable operating view, it gives teams a stronger basis for earlier intervention, clearer prioritization, and better documented quality oversight across the trial lifecycle.

The result is not just a faster QC. It is a quality programme aligned to regulatory expectations and able to show, at any point in the trial lifecycle, which risks have been identified, which actions are underway, and how inspection of readiness stands. That is the standard ICH E6(R3) set, and the operating model for ClinQC Studio is built to support.

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Balaji Thiyagarajan is a clinical technology professional at Agilisium with expertise in AI-enabled solutions for Life Sciences. With a background in health informatics, clinical research, and an MBA from IIT Madras, he specializes in clinical quality, RBQM, eTMF, EDC, CTMS, and AI-driven workflow modernization. His focus is on helping sponsors and CROs enhance clinical quality, regulatory readiness, and operational efficiency through practical, scalable AI solutions.

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