ARTICLE

The primary constraint on AI in clinical trials is organizational uncertainty, not regulatory objections

A KEY QUESTION

What are the real barriers to AI adoption in clinical trials?

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Industries everywhere have been rapidly adopting and innovating with artificial intelligence (AI) in the relentless search for efficiency. So, what's holding the drug development industry back?

Apart from the not-inconsiderable technical challenges of integrating AI into well-established workflows, one of the most common misconceptions in this industry has been that of perceived regulator resistance. Yet this narrative is increasingly out of step with reality. Signals from regulators, particularly the Food and Drug Administration (FDA), tell a different story. In this article, we explore whether the real inertia sits elsewhere: In fragmented interpretation, organizational anxiety and a tendency to self-restrict well beyond regulatory intent.

Regulators are signaling openness, not resistance

FDA commentary around real-time clinical trials (RTCT),[1] risk-based approaches and the use of advanced analytics, consistently emphasizes intent rather than prohibition. As digital health techniques became more commonplace, the agency encouraged adaptive designs, continuous data review and earlier integration of digital technologies.

We're now seeing a similar position on AI. In January 2025, the FDA issued draft guidance for *Considerations for the use of artificial intelligence to support regulatory decision-marketing,*[2] it's first formal guidance on the use of AI in drug development.

In early 2026, the FDA and its European cousin, the European Medicines Agency (EMA), jointly articulated high-level principles for AI use[3] in which it published ten guiding principles that correspond with an overall ethos of fit for purpose, transparency, auditability and human accountability.

This framing is critical. Neither the FDA or the EMA are prescribing specific technologies nor mandating adoption pathways. Instead, they are defining outcomes: Reliability, traceability, context of use and patient protection.[4,5]

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The real constraint? Interpretation, not regulation

Despite this, many CROs and sponsors remain in a somewhat defensive posture. Organizations appear paralyzed less by regulatory text than by how they imagine it might be interpreted in an audit.

This manifests in several familiar ways:

- **Inconsistent internal interpretations** of the same guidance across QA, clinical operations, IT and statistics
- **Fear of retrospective scrutiny,** driving an over-rotation toward "tried and true" manual controls and duplicated processes
- **Excessive pilot validation cycles** even where human-in-the-loop controls already exist
- **Avoidance of decision adjacent AI** despite regulators explicitly distinguishing decision support from autonomous decision-making

The result is a self-inflicted throttling effect, with programs constrained not by what regulators have said, but by what teams fear regulators might say later.

Self-limiting beyond regulatory intent

What we are seeing is that sponsors and CROs often seem to apply stricter internal constraints than regulators actually require. Risk based quality management (RBQM) offers a useful parallel. While regulators advocate proportionality, many organizations continue to operate as if full verification remains mandatory, simply because that was once the norm and/or because the costly risk (or is that also "fear") of getting it wrong prevents them from innovating.

The same dynamic is now playing out with AI. Instead of leveraging AI to support monitoring, feasibility, protocol optimization or trial management, organizations limit use to low-impact tasks (e.g., summarization, drafting or operational reporting), stifling innovation upstream of meaningful value.

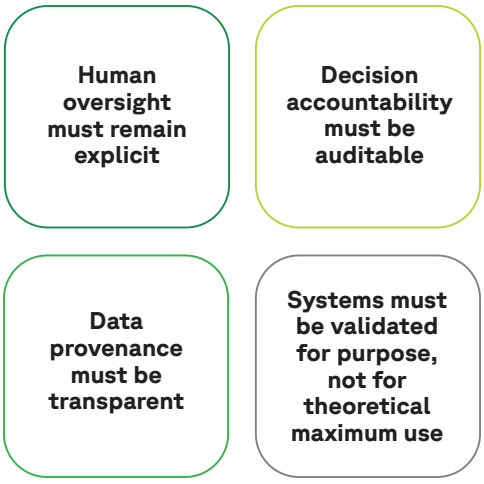
This seems to be less about regulatory conservatism and more about organizational risk aversion masquerading as compliance.

Real-time trials expose the gap

FDA interest in real-time clinical trials makes this tension unavoidable. Continuous data review, adaptive decision making and earlier signal detection cannot coexist with rigid, sequential governance structures designed for retrospective validation. The transition to real time models forces organizations to confront a hard truth:

Speed and control are not opposites, but poorly designed governance makes them seem that way.

Crucially, FDA commentary consistently reinforces that:



Nowhere does the agency require perfection, determinism or zero change over time.[1]

An industry-wide clarion call: What needs to change

If regulation is not the primary blocker, the path forward becomes clearer, more palatable and more urgent.

First, earlier regulatory engagement must become standard practice, not a last-resort defensive tactic. Proactive dialogue clarifies context, reduces ambiguity and prevents teams from inventing constraints that regulators themselves do not enforce.

Second, shared industry playbooks are essential. Many organizations are solving the same governance questions in parallel—AI validation, auditability, human-in-the-loop controls, etc. Yet few are codifying lessons learned and sharing those widely. Pre-competitive collaboration could dramatically reduce duplicated effort while raising baseline confidence.

Third, leaders must separate risk from fear. Risk can be managed through evidence, controls and transparency. Fear produces inertia. When organizations default to fear, the consequence is not safety; it is opportunity cost borne by patients and programs alike.

Real-time clinical trials: What the FDA has actually said, and what it means

The FDA has formally signaled a shift toward what it terms "real-time clinical trials (RTCT)", marking an evolution in how regulators may oversee early-phase drug development. In April 2026, the Agency announced the successful initiation of two proof-of-concept trials designed to transmit pre-specified safety signals and clinical endpoints to FDA reviewers during trial conduct, rather than after phase completion.[1]

According to the FDA, this initiative is intended to address structural inefficiencies in early-stage clinical development, where data is traditionally collected at sites, cleaned and analyzed by sponsors and only then submitted for regulatory review—often introducing long periods of administrative latency.[6] The Agency has explicitly framed RTCTs as a means of enabling earlier safety signal detection and more dynamic regulatory oversight, particularly in small, high-uncertainty early-phase populations.[1]

What the FDA is (and is not) implementing

Importantly, the FDA has been careful to describe RTCTs as proof-of-concept implementations, not a wholesale replacement of established regulatory or Good Clinical Practice (GCP) requirements. In its April 28, 2026 press announcement, the Agency emphasized that FDA scientists would receive pre-agreed, sponsor-defined signals rather than full underlying patient-level datasets, thereby maintaining existing boundaries around sponsor responsibility, data governance and trial conduct.[1]

The FDA has further clarified that RTCTs do not imply real-time regulatory decision-making or continuous approvals. Instead, the objective is to enable regulators to observe emerging safety and efficacy indicators as a trial progresses, allowing for more informed dialogue and earlier intervention when necessary, without compromising patient protections or evidentiary standards.[1,7]

Alignment with existing FDA risk-based oversight frameworks

From a regulatory perspective, RTCTs are best understood as a logical extension of long-standing FDA policy on risk-based quality management and monitoring. The Agency has, for more than a decade, encouraged sponsors to focus oversight on data and processes most critical to participant safety and trial integrity, rather than relying on exhaustive retrospective review.[8]

FDA guidance on risk-based monitoring explicitly supports centralized and near-real-time data review as a mechanism to identify emerging risks, protocol development or safety concerns during trial conduct.[6] The RTCT model described by the Agency aligns with these principles by prioritizing early visibility of predefined safety and efficacy signals, while leaving responsibility for trial execution and decision-making firmly with the sponsor.[1,6]

The role of AI: Support, not substitution

The FDA has also explicitly situated RTCTs within its broader framework for the responsible use of AI in drug development. In its January 2025 draft guidance, *Considerations for the use of artificial intelligence to support regulatory decision-making for drug and biological products,* the Agency made clear that AI tools may be used to support regulatory decision-making, provided their outputs are credible, transparent and fit for a defined context of use.[2]

Crucially, the guidance emphasizes a risk-based credibility framework, under which AI-generated outputs must not replace human judgement or obscure the evidentiary basis for decisions.[7] In the context of RTCTs, this reinforces the FDA's stated intent: Automation may accelerate data flow and signal detection, but decisions remain human-led and evidence-anchored.[1,7]

What comes next: Pilot expansion, not mandate

Alongside the proof-of-concept trials, the FDA has issued a Request for Information (RFI) to inform the design of a broader RTCT pilot program expected to launch in summer 2026.[1] The Agency has explicitly invited stakeholder input on pilot structure, implementation criteria and success metrics, signaling that this remains an iterative and consultative process, not a regulatory mandate.[1]

At present, the FDA has not issued guidance requiring or endorsing RTCTs as a standard development pathway. Instead, the Agency continues to position real-time data approaches as optional, context-dependent innovations, particularly relevant to early-phase programs where uncertainty is high and timelines are most constrained.[1,5]

Regulatory takeaway

The FDA's RTCT initiative does not represent deregulation, nor a departure from established evidentiary standards. Rather, it reflects a consistent regulatory trajectory: Using technology to reduce administrative delay, improve situational awareness and strengthen risk-based oversight—while preserving sponsor accountability and human regulatory judgement.

For sponsors and CROs, the implication is not that trials must become "real-time," but that regulatory expectations around timely, high-quality signal visibility are continuing to rise, especially as data infrastructures and analytic tools mature.

From permission to intent

The regulatory signal is already there. The FDA is not asking whether AI may be used in clinical trials, it's asking whether sponsors can demonstrate that it is used responsibly.

The gap between intent and execution is no longer external—it's internal. Until organizations address ambiguity, misalignment and cultural fear, the promise of real-time clinical trials will remain constrained, not by regulators, but by those involved in conducting clinical trials.

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