FDA REAL-TIME CLINICAL TRIALS · UPDATED AFTER MASTERMIND SESSION 9

The Fundamentals Still *Decide the Trial*

The FDA's move toward real-time clinical trials raises the bar for what a site has to prove. It does not retire the basics of site selection. **It makes getting them right the first time non-negotiable.**

Apr 28, 2026	Jun 29, 2026	Aug 2026	One trial
RTCT ANNOUNCED	RFI COMMENTS CLOSED	PILOT SELECTIONS	DEFAULT FOR APPROVAL

WHAT CHANGED SINCE THE JUNE BRIEFING

Signals reach the FDA through a platform RTCT

Two proof-of-concept trials are live: AstraZeneca's **TRAVERSE** (Phase II, treatment-naive mantle cell lymphoma, sites including MD Anderson and the University of Pennsylvania) and Amgen's **STREAM-SCLC** (Phase Ib, limited-stage small cell lung carcinoma). Both report pre-agreed safety and efficacy signals as data emerges. The data does not move from the site straight to the agency. It passes through an intermediate platform, Paradigm Health in the current pilots, which validates the signal first.

One pivotal trial, one shot SINGLE-TRIAL

In February 2026 the FDA made a **single pivotal trial** with confirmatory evidence the default for approval, ending the two-trial standard set in the 1960s. A sponsor now gets one chance to get the study right. A misjudged site no longer costs a few months of enrollment. It can cost the approval, and under RTCT the agency sees the damage while it is happening.

THE PILOT TIMELINE IS MOVING FAST

Apr 28	May 27	Jun 29	Jul 2026	Aug 2026
RTCT announced	**Comments extended**	**Comments closed**	**Criteria published**	**Selections complete**
Two proof-of-concept trials unveiled, RFI released	FDA pushes the RFI deadline to June 29	Final window for sponsor and site input on pilot design	FDA expected to release final pilot selection criteria	Broader pilot participants, sponsors and platforms, finalized

On the leadership question. Two of the initiative's most visible champions, Commissioner Makary and Jeremy Walsh, have both left the agency, and no successor has taken up the file publicly. The pilot timeline has not moved. Once an agency sees how much faster it can review a submission, that capability tends not to get handed back, which makes early and well-documented site readiness worth more, not less.

OPERATIONAL REALITY

Real-time data demands real-time sites.

Capture at the point of care

Signals recorded and transmitted as they occur, not batched for a monthly export.

Interoperable systems

EHR, EDC, and safety tools that talk to each other without manual reconciliation.

Faster query turnaround

A delayed response now has a visible cost to the sponsor and the agency in near real time.

Continuous safety vigilance

Adverse event review and escalation can no longer wait for a scheduled monitoring visit.

Staff bandwidth for oversight

Coordinators need dedicated time for continuous review, not just visit-day documentation.

Data integrity under speed

Faster reporting cannot come at the cost of accuracy, source verification, or patient privacy.

WHERE THE MODEL ACTUALLY BREAKS

Every step survives. The clock underneath them does not.

RTCT does not remove steps, it compresses them and runs several of them continuously. The steps in bold change character, not just speed.

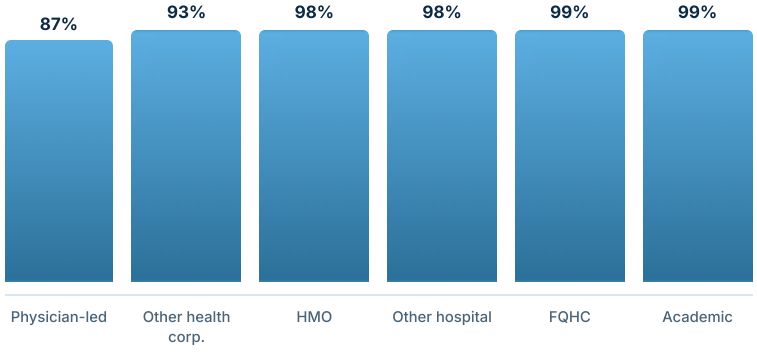
THE STANDARD Traditional model	THE SHIFT RTCT model
Site identified	Site identified
Feasibility	**Feasibility, in depth.** Data framework and EHR capability assessed, not just clinical fit
Selected	Selected
Activated	**Activated** with the data framework and IT routing already standing up
Patient enrolled	Patient enrolled
Data collected on the CRF	**Data collected on the CRF, or signals streamed.** The clinician documents in the EHR at the visit and pre-agreed safety and efficacy fields flow into an intermediate platform
Source data verification	Source data verification, **in real time**
Entered in the EDC	Entered in the EDC, modified, **or an intermediate database**
Monitor reviews, queries	Monitor reviews and queries, **real time and remote**
Database lock	**Ongoing.** What it takes to change data already streamed to the agency is still an open question
Statistical analysis	Statistical analysis **as data becomes available**
Clinical study report	Clinical study report becomes a **supporting document**
NDA submitted to the FDA	NDA becomes a **supporting document**

THE TECHNOLOGY QUESTION HAS CHANGED

The question is no longer whether a site has an EHR.

Certified EHR adoption is close to universal, so the presence of a system tells a sponsor almost nothing. **Which system, whether it exposes an API, and how much manual work sits between the visit and the data** are what separate a site that can stream from a site that cannot.

Certified EHR use among office-based physicians, by practice ownership



MOST COMMON EHR

Epic

27.7% of office-based physicians report Epic as their primary system.

Meditech	11.1%
eClinicalWorks	7.5%
athenahealth	7.3%
Cerner / Oracle Health	5.5%

Epic's lead widens in hospitals: 43.7% of acute-care hospitals and 56.9% of inpatient beds.

Solo and physician-owned practices lag furthest behind, and academic centers lead. But size cuts both ways. A large institution where the investigator sees the patient and the clinic note reaches the EHR two or three days later is not real-time ready either, whatever the system on the label says.

SELECTING THE RIGHT SITES IS NOW RISK MANAGEMENT

Feasibility stops being a checklist and becomes an assessment.

The fundamentals did not move. What sits beside them did. A site now has to clear both columns, and it has to clear them before the first patient is enrolled rather than during the study.

STILL REQUIRED

The fundamentals

Expertise
Verified depth in the indication, not a claim of it.

Experience
A real track record of running trials to enrollment and clean data.

Documented patient access
A **current, verifiable** referral pipeline, and evidence the site converts those patients into participants.

Operational discipline
Process workflows mapped clearly enough to show how data and decisions move at the point of care.

Dedicated staff capacity
Coordinators and investigators with bandwidth to monitor continuously, not when other work allows.

Reputation is not evidence
A site's brand, or a long relationship, does not guarantee it can meet RTCT reporting speed today.

NOW ALSO REQUIRED

RTCT readiness

Interoperable EHR
A modern system supporting **FHIR and HL7** exchange. Paper or closed systems are a go / no-go risk.

Real-time capture at the point of care
Data recorded during the visit, not dictated and entered weeks later.

Connected EDC and safety reporting
A defined source-verification and query model for streamed data, and a routing path to the intermediate platform.

Hours, not weeks
Query turnaround and adverse-event escalation the site can sustain continuously, not in bursts.

Capacity and budget
Dedicated staff for ongoing review, and contract language that **pays the site** for the added technology work.

Willingness to be trained
Real-time workflow is new to nearly every site. The ones that will succeed say yes to training up front.

PUT THESE IN YOUR NEXT FEASIBILITY

Six questions that belong in every questionnaire now.

None of these are clinical questions, and the investigator often cannot answer them alone. Expect the site to pull in IT or its EHR administrator, and build that time into the feasibility window.

01 **Are assessments done at the point of care ready for sharing, or do they require internal review first?**
The single best predictor of whether a site can stream at all.

02 **Which certified EHR does your site, practice, or institution currently use?**
The sponsor needs the system's capabilities to judge compatibility with the study's EDC.

03 **Can your site or research team commit to responding to queries within 48 hours?**
Ask for the commitment in writing and put the number in the contract.

04 **Can your site report adverse events directly to the FDA as they occur, if pre-agreed?**
Surfaces both the technical path and the site's comfort with using it.

05 **What is the study coordinator's role in real-time assessment and data documentation?**
Names the person who owns the cadence, before activation rather than after.

06 **Is your site willing to be trained to manage RTCT?**
Almost no site has done this before. Willingness matters more than experience right now.

Why question 03 is the one to hold the line on. Query volume is the pressure point. A single trial can accumulate tens of thousands of queries over its duration, and under RTCT that backlog is visible to the agency while the study is still running. Site performance stops being measured on enrollment alone and starts being measured on responsiveness, which means the median query cycle time already sitting in your EDC becomes a site selection input rather than a closeout statistic.

RAISED IN SESSION, STILL UNANSWERED BY THE AGENCY

What nobody can tell you yet.

Does every site have to participate?

Partial participation would skew an analysis that runs continuously. **Our reading, shared by several public comments, is that it has to be every site in a study.** The FDA has not said so.

What counts as clean enough to stream?

Whether a CRA and the sponsor verify and freeze a field before the interface pushes it to the agency is undefined. Nobody wants conclusions drawn from unreviewed data.

How does this fold into risk-based monitoring?

RBM already targets specific fields for near-real-time review. Whether RTCT absorbs it, runs alongside it, or replaces it is not settled.

How do you correct data already streamed?

There is no published mechanism for retracting or amending a signal the agency has already received. This is the question sponsors raise first.

Who trains the sites, and when?

Whether the site initiation visit still carries this, and who funds the added effort, is open. The training burden is real and it lands on the site.

What does the consent say?

Participants may need to be told that data about their response reaches the agency before the study ends. Expect consent language to catch up.

One more point from the room: **not every protocol suits RTCT.** In rare disease, where a site can go months between eligible patients, continuous signal reporting may distort more than it reveals. Expect sponsors to designate which protocols take the real-time route.

WHEN A SITE UNDERPERFORMS MID-STUDY

Set the trigger before activation

Define the screening or enrollment threshold, and the date it gets checked, in the contract. Not in the first steering committee after it is already late.

Make closing out normal

A site or network that can say "we thought we had these patients and we do not" early is worth more than one that waits. Transparency has to be safe, or it does not happen.

Identify the backup first

If a region has to contribute a set number of patients, the replacement site should be known before the original one stalls, not sourced afterward.

Widen the funnel before you close

Geofenced referral outreach in a 10 to 50 mile radius around an otherwise strong site can restore supply without losing the investigator and the activation spend.

THREE QUESTIONS THAT SEPARATE A READY SITE FROM A RISK

01 Can this site reach the right patients **today**, not eventually?

02 Can it report data at the **speed** the protocol demands?

03 What is the plan when it **underperforms** mid-study?

The fundamentals of site selection have not changed. **What has changed is the cost of getting them wrong.** A weak site is no longer a delay you absorb. It is a risk to the program, visible to the agency while the study is still running.

Sources: FDA, "FDA Announces Major Steps to Implement Real-Time Clinical Trials" (Apr 28, 2026); FDA RFI comment-period extension, Federal Register (May 27, 2026); Makary and Prasad, New England Journal of Medicine, single-pivotal-trial default (Feb 2026); Commissioner Makary resignation reported May 12, 2026 (NBC, Washington Post, CBS, Time); FDA Chief AI Officer estimate of a 20 to 40% timeline reduction; ONC / HealthIT.gov, 2024 National Electronic Health Records Survey (N=1,725); KLAS 2026 EHR Market Share Report. Open questions and site-level practice reflect the discussion at LINEA Mastermind Session 9, July 23, 2026.