May 29, 2026

Grace R. Graham,
Deputy Commissioner for Policy, Legislation, and International Affairs.
US Food and Drug Administration
Silver Spring, MD 20993

Re: Notice of Request for Information; AI-Enabled Optimization of Early-Phase Clinical Trials Pilot Program; Docket No. FDA-2026-N-4390

Dear Ms. Graham,

FasterCures, part of the nonprofit and nonpartisan Milken Institute think tank, focuses on biomedical innovation as a critical driver for improving lives and health in the US. Through our many years of research on the clinical trials ecosystem and establishment of the ENRICH-CT[i] (Enabling Networks of Research Infrastructure for Community Health through Clinical Trials), a precompetitive coalition, which is working toward enabling more community-based research, we have engaged with industry, government (including the FDA), academia, health systems, technology companies, patients, and community-serving organizations to identify opportunities to modernize trial infrastructure and strengthen the broader research enterprise through policy and practice change. We offer here our insights derived from that diverse group.

We commend the FDA for initiating the real-time clinical trials (RTCT) program and for inviting broad stakeholder input on pilot design. The proof-of-concept work with AstraZeneca and Amgen seeks to demonstrate that real-time signal sharing is technically achievable; the design questions the FDA is now asking will determine whether this program drives systemic change or remains a capability limited to the top tier of well-resourced sponsors. A core concern shapes our perspective on those design questions: the clinical trial system's persistent failure to enroll enough participants from real-world populations is not primarily a technology problem—it is an infrastructure, incentive, and access problem. AI-enabled real-time trials hold genuine promise, but that promise will be realized only if the pilot is designed from the outset to include, and generate learnings from, the full range of sites and sponsors that must eventually adopt these approaches.

We respond selectively to the Request for Information (RFI) questions where we have the most substantive experience and perspective through the ENRICH-CT coalition's work: participant selection (A.2), collaboration models (A.3), operational structure (A.4), knowledge sharing (A.6), trial efficiency metrics (B.1), data integrity (B.3), and qualitative outcomes (B.7). We close with brief observations on enabling conditions outside the pilot's immediate scope that will determine whether it scales.

Section A: Pilot Program Design and Implementation

A.2: Participant Selection

Criteria must deliberately include community and lower-resource sites.
The RFI asks what criteria FDA should use to select sponsors and trials, and how the pilot can ensure representation across organization size, capability, and therapeutic area. We urge the FDA to treat these as design requirements, not aspirational goals.

More than 80 percent[ii] of clinical trials are delayed or fail to launch due to enrollment challenges. Most research remains concentrated[iii] in a narrow set of academic medical centers that are well-resourced and geographically inaccessible to most

Americans. AI-enabled infrastructure built primarily for and piloted exclusively with large academic sponsors and global pharmaceutical companies will replicate this concentration at higher speed, not solve it.

FasterCures recommends that the FDA apply the following participant selection criteria:

- Mandatory inclusion of at least one community-based or non-academic-medical-center site in the pilot cohort;
- Tiered selection by organizational AI maturity, not a single capability threshold;
- Explicit therapeutic area diversification beyond oncology and rare diseases;
- Inclusion of investigator-initiated trials—often the testing ground for pragmatic and community-embedded designs—alongside industry-sponsored studies.

A.3: Collaboration Models

Patient and community engagement in AI governance must be structured and required, not aspirational.
The RFI specifically asks what role patient groups and investigators should play in AI governance. In our view, it should be the same structured, documented, required role they should play in trial design generally, which is to say, a far more substantive one than they typically play today.

Clinical trial AI governance is not merely a technical matter. Decisions about which safety signals trigger alerts, what constitutes a meaningful endpoint, how recruitment algorithms prioritize patient outreach, and what information is surfaced to investigators in real time are decisions with direct consequences for access and participant welfare. These decisions should not be made by technical teams alone.

We recommend FDA require the following as conditions of participation in the pilot:

- a documented patient and community engagement plan for participating trials' AI governance structure;
- use of FDA's Patient-Focused Drug Development (PFDD) guidance as the methodological baseline for how patient input is gathered and documented;
- community investigator and patient advocate representation in pilot governance bodies; and
- precompetitive knowledge sharing on AI governance practices through existing entities such as FasterCures' ENRICH-CT, TransCelerate BioPharma, Clinical Trials Transformation Initiative, and the Duke Margolis Institute for Health Policy.

A.4: Operational Structure

Infrastructure support must account for sites at varying AI maturity levels.
The RFI asks what infrastructure is needed and how the pilot can accommodate varying levels of AI maturity across participants. ENRICH-CT has observed that community-based and lower-resourced sites—precisely the settings most critical to broadening research participation—face the steepest infrastructure gaps. These sites often manage more than a dozen unconnected systems[iv] with scores of logins[v] per study, lack standardized electronic consent platforms, and cannot readily use their electronic health records (EHRs) to screen patients for eligibility or contribute structured data to a research network. Real-time data flow to the FDA presupposes a data infrastructure that many sites do not have.

FasterCures recommends that the FDA take the following steps in the pilot's operational design:

- Make FDA's Center for Clinical Trial Innovation a formal coordinating body for the pilot;
- Provide tiered technical assistance, not a uniform infrastructure requirement, to enable inclusion of community sites;
- Address the EHR interoperability prerequisite explicitly;
- Develop and publish a clear open data format and specifications for real-time signal submission to the FDA, to lower the barrier to entry and promote broader ecosystem adoption;
- Engage OHRP and the Association for Accreditation of Human Research Protection Programs (AAHRPP) to prepare IRBs for AI-enabled trial review (see "Enabling Conditions Beyond the Pilot's Immediate Scope" below).

A.6: Knowledge Sharing

Use established precompetitive consortia as the primary channel.
The RFI asks how lessons learned should be captured and disseminated, and what mechanisms can promote transparency while protecting proprietary information. ENRICH-CT is itself a knowledge-sharing mechanism of this kind, and we offer the following recommendations based on direct experience:

- Designate precompetitive consortia such as ENRICH-CT, TransCelerate, CTTI, and/or the Duke Margolis Institute for Health Policy as primary channels for nonproprietary learnings.
- Require public, structured lessons-learned reporting as a condition of pilot participation.
- Publish lessons-learned syntheses before finalizing any expansion phase or drafting any guidances as outgrowths of the pilot.

Section B: Evaluation Metrics and Success Criteria

B.1: Trial Efficiency and Speed

Enrollment metrics must capture representativeness, not just speed.
The RFI asks how improvements in trial efficiency should be measured, including time to initiation, enrollment, and completion, as well as reductions in time from Phase 1 to Phase 2 initiation. These are important metrics. But faster enrollment at sites that were already fast is not a success story for the broader clinical trial ecosystem.

Traditional eligibility criteria exclude as many as 70 to 90 percent[vi] of real patients with the condition being studied, limiting enrollment and undermining the generalizability of trial results to the populations that will eventually use approved products. An AI pilot that accelerates enrollment of the narrow patient populations currently included in early-phase trials without broadening eligibility or diversifying site types might improve speed and efficiency at highly selective academic sites but will not improve the quality or generalizability of the evidence. Accelerating the pipeline from Phase 1 to Phase 2 without addressing population representativeness may lead to late-stage trial failures, post-approval safety surprises, and/or disappointing results in real-world patient populations.

FasterCures recommends the following efficiency metrics:

- Enrollment rate and speed by site type (academic medical center, community health system, FQHC-affiliated network, independent site, etc.;
- Participant demographic representativeness (recruitment and retention) relative to the epidemiology of the disease or condition under study;
- Whether Phase 2 eligibility criteria were broadened relative to Phase 1 using real-world data, as the FDA's own RWE guidance already supports.

B.3: Participant Safety and Data Integrity

Automating over-collection is not an improvement.
The RFI asks what measures can be used to assess improvements in data completeness, accuracy, and consistency. These are important quality dimensions. But a prior question is whether the data being collected in real time is the right data.

ENRICH-CT's members have illuminated a well-established problem: Clinical trials routinely collect far more data than are necessary to answer primary and key secondary questions, with Tufts and TransCelerate research showing approximately 30 percent of procedures are non-core[vii] or non-essential. This over-collection is not necessarily driven by regulatory requirements; existing FDA guidance, including ICH E6(R3)[viii] Good Clinical Practice and the Selective Safety Data Collection framework[ix], explicitly supports leaner, quality-by-design approaches. Over-collection is driven by cultural defaults: "collect everything just in case."

An AI pilot that automates real-time transmission of a maximally large dataset to the FDA will not solve the data over-collection problem; it will accelerate it. The pilot should be designed to test AI-enabled data rationalization—the use of AI

tools to define, enforce, and optimize the minimum necessary dataset—alongside real-time transmission of that rationalized dataset.

FasterCures recommends the following data integrity metrics:

- proportion of collected data elements with a documented decision-use justification;
- protocol deviation rates by site type; and
- data completeness by site type, to help identify whether community-based sites are generating incomplete datasets due to infrastructure gaps or operational burdens.

B.7: Qualitative Outcomes

Trust, usability, and scalability must be measured from the community site perspective.
The RFI asks how stakeholder trust in AI-enabled trial approaches can be assessed, how usability and integration into clinical workflows can be evaluated, and how scalability and operational feasibility should be measured. Trust in AI-enabled approaches is not uniform across the ecosystem. Among investigators at well-resourced academic centers, sponsors, and regulatory bodies, trust in AI tools is relatively high (though tempered by appropriate concerns); these are the settings where AI tools are being developed and validated. The trust gap that matters for scaling is at community-based sites, among community investigators and participants from underrepresented populations who have had little role in designing or validating these tools.

FasterCures recommends the following qualitative outcome metrics:

- investigator trust and usability ratings, disaggregated by site type;
- participant trust assessments, with particular attention to historically underrepresented populations;
- site activation timeline by site type;
- staff burden assessment of technology tools; and
- sites' post-pilot capability to continue, without ongoing technical assistance.

Enabling Conditions Beyond the Pilot's Immediate Scope

FasterCures wishes to flag three structural conditions that are prerequisites for RTCT to scale beyond the current proof-of-concept tier, and that require parallel action by the FDA and partner agencies. These are not pilot design questions, but the pilot's ultimate value will be limited if they are not addressed concurrently.

1. EHR interoperability and research-capable certification
Real-time data flow to the FDA is downstream of a data infrastructure that many community sites do not have. The Office of the National Coordinator for Health Information Technology (ONC) should incorporate research requirements into EHR certification criteria and should add research as a permitted Exchange Purpose under TEFCA[x]. Without these changes, RTCT at community sites will require bespoke, expensive integrations that most sites cannot afford. FDA and ONC should treat these as parallel workstreams, not sequential ones.

2. Informed consent modernization at community sites
AI-enabled real-time trials continuously generate data on participants and may surface results faster than traditional consent frameworks contemplate. This creates informed consent questions that are unresolved. As of 2025, only about 40 percent of studies use eConsent platforms, despite up to 80 percent of cancer centers[xi] having the capability to do so. The barrier is not regulatory permission—FDA and OHRP guidance[xii] already support eConsent—it is the absence of standardized specifications, resources for under-resourced settings, and a clear signal that eConsent is the expected approach. RTCT pilot participants should be required to use eConsent platforms and to document consent processes in ways that address the real-time monitoring dimension, and FDA and OHRP should issue updated guidance framing eConsent as the expected default for FDA-registered research.

3. IRB preparedness for AI-enabled trial review
IRBs are responsible for reviewing and approving AI-enabled trial protocols, but few have developed systematic expertise in evaluating AI governance structures, algorithmic decision-support, or real-time safety monitoring frameworks. OHRP

and AAHRPP should be engaged as partners in developing training resources and updated accreditation standards in parallel with the pilot. Without concurrent IRB readiness work, the pilot may produce approved protocols at well-resourced sites with established IRBs while creating bottlenecks at community sites reliant on less-resourced boards.

Conclusion

FasterCures supports the FDA's RTCT initiative and sees genuine potential in AI-enabled real-time data flow to accelerate regulatory decision-making. Our recommendations are designed to ensure that the pilot tests not only technical feasibility but the conditions under which real-time trials can scale broadly and equitably.

The design choices the FDA makes now will determine whether real-time clinical trials become a transformative tool for the full clinical research ecosystem or a high-speed lane available only to sponsors and sites that were already advantaged. **A pilot cohort that includes community sites from the start, structured patient and community engagement in AI governance, tiered technical assistance, and equity-sensitive metrics will yield learnings that the full ecosystem can act on.** A pilot cohort limited to large industry sponsors and academic institutions may produce impressive proof-of-concept data that does not transfer.

FasterCures and ENRICH-CT welcome the opportunity to engage further with the FDA on pilot design and implementation. We are happy to facilitate connections between FDA and ENRICH-CT member organizations—including community health systems, patient advocacy organizations, and precompetitive consortia—that could contribute meaningfully to the pilot.

Sincerely,

Esther Krofah
Executive Vice President, Health
Milken Institute

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