August 23, 2026

Kyle Diamantas, Acting Commissioner
Grace R. Graham, Deputy Commissioner for Policy, Legislation, and International Affairs
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

Re: Docket No. FDA–2026–N– 4699 for "Expedited Investigational New Drug Pilot Program; Request for Information."
Submitted electronically via Regulations.gov

Dear Commissioner Diamantas and Deputy Commissioner Graham,

The Multi-Regional Clinical Trials Center of Brigham and Women's Hospital and Harvard (MRCT Center) appreciates the opportunity to comment on the request for information published by FDA on June 24, 2026, entitled "Expedited Investigational New Drug Pilot Program."

The MRCT Center is a research and policy center that is dedicated to improving the ethics, conduct, oversight, and regulatory environment of international, multi-site clinical trials. Founded in 2009, it functions as an independent convener to engage diverse stakeholders from industry, academia, patients and patient advocacy groups, non-profit organizations, and global regulatory agencies, including the U.S. Food and Drug Administration. The MRCT Center seeks to identify challenges relating to the global clinical trial enterprise and deliver ethical, actionable, and practical solutions to make clinical trials more efficient, ethical, and productive of reliable evidence, leading to novel therapies that improve health. The responsibility for the content of this document rests with the leadership of the MRCT Center, not with its collaborators nor with the institutions with which its authors are affiliated.[1]

We strongly endorse a renewed focus on early clinical product development, pre-IND and IND processes, and acceleration of first-in-human (FIH) trials. Current practices are inefficient, and the stated goal of the pilot, "to address overall time to the first in human trials," is welcome. We support the Agency's objective of shortening the interval between drug identification and first-in-human (FIH) study initiation, and we commend FDA for pursuing this goal through a voluntary pilot that preserves the Agency's full regulatory authority over clinical holds, investigator qualifications, inspections, and all other IND decisions.

As FDA highlights, a reduction in time cannot compromise participant safety, data integrity, ethical standards, scientific rigor, or the evidentiary standard. We first address the questions posed in the Request for Information and then offer additional suggestions for consideration.

General comments

The central hypothesis of the pilot, that structured, expert third-party input earlier in development can improve submission quality and thereby shorten time to FIH without weakening participant protections —

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is worth testing. At the same time, the value of the pilot will ultimately turn on operational details that the notice leaves open, including the precise scope of Qualified Research Institution (QRI) review, the mechanics of the rolling-submission platform, and the sequencing of QRI, sponsor, and FDA interactions.

We encourage the Agency to publish a draft of key operational specifications for public comment before implementation, including expectations regarding the QRI review scope, sponsor engagement, rolling review processes, documentation standards, performance metrics, and technology platform functionality. Early stakeholder review would improve transparency, consistency, feasibility, and adoption.

We stress the need to treat the initial cohort explicitly as a means of stress-testing the model rather than as a fully settled process. We further recommend that FDA measure the pilot's impact on an end-to-end basis — from initial sponsor engagement through first participant enrolled and dosed — so that any front-loaded burden introduced by QRI engagement is captured rather than obscured by measuring only the post-QRI portion of the timeline.

QRI Qualification and Capabilities

The RFI description of QRI qualifications and capabilities suggests that FDA is envisioning any QRI to demonstrate each of the four eligibility criteria: multidisciplinary expertise across nonclinical, clinical, and CMC disciplines; Phase 1 clinical trial infrastructure, including IRB and trial site capabilities; leadership with expertise in drug development and IND execution; and a track record of success in IND submissions to regulatory authorities across therapeutic areas and product modalities. These functions may be embodied in a single institution, but it is equally likely that a consortium of relevant institutions and organizations would provide the desired expertise; differentiation of functions may even be preferable in certain circumstances.

We recommend that the Agency avoid requiring every capability to reside within a single corporate or organizational structure. Academic medical centers, health networks, contract research organizations, and hybrid research organizations should each be eligible if they can demonstrate, directly or through documented, well-governed partnerships, the ability to bring nonclinical, clinical, CMC, regulatory, and operational expertise to bear on an integrated development strategy. A rigid, one-size-fits-all ownership requirement risks excluding organizations — including smaller research networks and community-based institutions — that could otherwise support the pilot effectively through subcontracted or affiliated expertise, provided that roles, responsibilities, and oversight are clearly documented.

FDA should distinguish between the expertise required to evaluate IND components and the infrastructure required to generate the underlying data. The QRI role is fundamentally advisory and integrative. Accordingly, qualification should depend principally on the ability to critically evaluate pharmacology/toxicology, clinical, and CMC information and to integrate that assessment into a coherent development strategy, rather than on ownership of laboratories, manufacturing facilities, clinical infrastructure, or other study-execution resources.

We encourage FDA to weigh an applicant's demonstrated program-level integration capability: its ability to integrate and synthesize clinical, nonclinical, CMC, regulatory, statistical, quality, and operational

considerations into a unified and coherent assessment and development strategy. This integrative capability is distinct from disciplinary expertise alone.

Many early-stage sponsors address these workstreams sequentially rather than concurrently, which can result in either over- or under-developed supporting packages relative to the proposed FIH protocol. A QRI's ability to align these disciplines from the outset — and to calibrate the nonclinical and CMC packages to what a Phase 1 study actually requires — is likely to be a stronger predictor of pilot success than the breadth of services housed in any individual entity.

In addition to applications for comprehensive QRIs as described, we suggest that FDA define requirements and consider applications for specialized, domain-specific QRIs. QRIs should be permitted to define areas of specialized expertise in product development and Phase 1 FIH IND submissions inherent to certain populations (e.g., neonates, children), therapeutic areas (e.g., neurodevelopment and neurodegeneration, oncology), and modalities (e.g., cell and gene therapy) to aid sponsor-QRI matching, without establishing formal specialization tiers that could unnecessarily constrain participation by well-qualified generalist institutions. Requiring all four eligibility criteria to qualify as a QRI ignores critical domain expertise that should be readily available when needed. Specialized QRIs should be qualified by FDA to participate in the pilot program, and FDA should consider matching sponsors with QRIs whose approved therapeutic area or modality expertise aligns with the characteristics of the development program under review.

We encourage FDA to consider additional areas of specialized expertise: translational and clinical pharmacology pharmacokinetic/pharmacodynamic modeling, biomarker strategy, bioanalytical method development and qualification, AI-enabled development support tools and optimization platforms, and experience navigating FDA meeting pathways such as pre-IND meetings, among others.

IRB and Clinical-Site Ownership Should Not Be a Threshold Requirement

We do not believe QRIs should be required to own and operate their own institutional review board (IRB) or clinical trial site as a condition of qualification. Requiring self-owned IRB infrastructure could disadvantage otherwise capable health networks and smaller research organizations, and existing timelines for obtaining ethics review already vary considerably across institutions, regardless of ownership structure. A documented reliance arrangement[2] with a qualified external IRB or a formal partnership with an established Phase 1 clinical trial site network should be sufficient, provided the arrangement includes clearly defined roles, escalation pathways, and quality oversight.

FDA should define the characteristics of an acceptable partnership arrangement, including written agreements, documented quality oversight, clearly assigned responsibilities, escalation pathways, performance expectations, and mechanisms for demonstrating ongoing capability and accountability.

[2] See, for example, SMART IRB https://smartirb.org

Where a QRI does serve simultaneously as regulatory advisor and as IRB of record, FDA should require structural and documented safeguards to preserve the ethics review's independence. These should include separation of personnel who provide sponsor-facing advisory input from those who participate in IRB deliberation and voting, disclosure and recusal for any financial or institutional conflict, a prohibition on compensation tied to approval or study-initiation milestones, and audit-ready documentation demonstrating how any actual or perceived conflicts were identified and resolved. These expectations are consistent with the independence principles that already govern IRB review under existing human subjects protection regulations and formalizing them within the pilot would help build confidence in the integrity of dual-role QRIs without imposing a new regulatory framework.

Pre-IND and IND Review Process

QRI Output Should Be Standardized, Advisory, Voluntary, and Clearly Bounded

We support FDA's framing of the QRI's role as advisory, with the sponsor retaining ownership of, and accountability for, the IND submission, and FDA retaining sole authority over all regulatory determinations.

Sponsor engagement of a QRI should be voluntary and undertaken only if the sponsor concludes that the QRI's advisory role improves development efficiency, submission quality, and decreases the risk of a clinical hold.

To make that advisory role useful rather than duplicative, we recommend that FDA require a standardized written output from each QRI review — for example, a concise readiness assessment identifying completed sections, unresolved risks, cross-disciplinary dependencies, and any issues the QRI believes warrant FDA attention before the review clock begins. Standardization across QRIs would allow FDA to compare recommendations, identify recurring issues across development programs, and evaluate whether the QRI mechanism is, in fact, improving submission quality — while keeping the documentation burden proportionate rather than duplicative of the IND itself.

FDA should consider standardized templates for QRI recommendation reports, sponsor response summaries, change summaries, and final reconciliation documents to facilitate consistency across QRIs and efficient FDA review.

Material recommendations should clearly identify the scope of review, materials reviewed, assumptions, limitations, unresolved issues, and the rationale underlying the recommendation.

Material disagreements among sponsors, QRIs, and FDA should remain visible within the review record rather than being obscured during reconciliation activities.

FDA should also clarify precisely what QRI review displaces, if anything, in FDA's own process. Absent that clarity, there is a meaningful risk that QRI review becomes an additional step layered on top of full FDA review rather than a substitute for part of it, which would lengthen rather than shorten the path to FIH.

FDA should clarify whether and how favorable QRI readiness assessments will influence the scope, timing, or intensity of FDA review activities, information requests, or clinical hold considerations during the formal 30-day review.

Readiness for QRI Review and Rolling Review

FDA should distinguish between readiness for substantive QRI review and readiness for rolling FDA review. A development program should be sufficiently mature to permit meaningful multidisciplinary assessment before extensive QRI review begins. At the same time, IND components submitted through a rolling-review process should be sufficiently complete and stable to support substantive FDA evaluation rather than preliminary drafting.

FDA should establish expectations regarding version control, change management, documentation of revisions, preservation of superseded versions, linkage of recommendations to specific document versions, and reconciliation of reviewed components before final IND submission.

Preserving Objectivity

Because QRIs will be compensated by the sponsors whose programs they review, FDA should require documented safeguards to preserve independence: separation between personnel who assist a sponsor's development strategy and personnel who conduct the QRI's readiness assessment, disclosure of financial relationships with the sponsor, prohibition on compensation contingent on a favorable IND outcome or accelerated timeline, and standardized review procedures that leave a clear evidentiary trail for FDA. These expectations should apply regardless of whether a given QRI also serves in an IRB capacity, though the risk is most acute in that dual-role scenario.

Expedited INDs Should Not Reflect a Lower Evidentiary Standard

We recommend that FDA state explicitly that participation in the pilot does not alter the substantive requirements governing whether a clinical investigation may proceed. The statutory and regulatory framework governing IND content, investigator qualifications, informed consent, safety reporting, and IRB review should apply identically inside and outside the pilot. The appropriate distinction between an expedited and a standard IND should lie in process and sequencing — namely, the ability to submit and receive feedback on discrete, completed IND components on a rolling basis, allowing issues in CMC, nonclinical, or clinical protocol sections to surface and be resolved earlier — rather than substantive (i.e., any reduction of the underlying data expected to support a safe FIH study. We would also encourage FDA to confirm that sponsors may continue to rely on phase-appropriate CMC and nonclinical packages calibrated to the scope of the proposed Phase 1 study, consistent with FDA's existing risk-based approach to early-phase development.

We further recommend that FDA clarify how QRI engagement will interact with existing FDA meeting pathways, including pre-IND and Type B meetings, so that sponsors and QRIs understand whether QRI review is intended to precede, supplement, or substitute for those existing touchpoints.

The pilot should not blur regulatory accountability. Sponsors must remain responsible for development strategy, submission content, maintenance of the authoritative IND record, and fulfillment of sponsor obligations, while QRIs should remain responsible for multidisciplinary assessment, expert recommendations, and documentation of their review activities.

Drug Eligibility and Pilot Scope

We suggest that FDA initially prioritize product classes and disease areas where scientific and regulatory expectations are relatively well established — for example, small molecules and well-characterized biologics — so that the pilot can evaluate the QRI review process itself without the confounding factor of introducing highly novel scientific questions at the same time. As the model matures and demonstrates value, eligibility could reasonably expand to include more complex modalities, such as cell and gene therapies, radiopharmaceuticals, and other products for which guidance exists but development experience is comparatively limited. We would also encourage FDA to ensure the initial cohort represents a range of sponsor sizes and resource levels, rather than concentrating participation among the most established, well-funded organizations, so that the pilot's lessons are broadly generalizable.

With respect to scale, we recommend that FDA include a meaningful number of participating QRIs — reflecting the different institutional types described in the notice — and that each be expected to complete a sufficient volume of projects (on the order of several completed programs per QRI) before FDA draws conclusions about the model's effectiveness. A pilot phase of at least one to two years is likely necessary to generate a cohort large and mature enough to support meaningful evaluation.

Implementation and Feasibility

Leverage Existing Infrastructure Rather Than Requiring New Systems

Many organizations likely to serve as QRIs — CROs, academic medical centers, and health networks — already maintain quality management systems, standard operating procedures, and document-control infrastructure appropriate to their existing regulatory work. FDA should avoid requiring QRIs to stand up entirely new, pilot-specific systems where existing, appropriately scoped infrastructure already meets the underlying objective. Compensation models should be transparent, public, and service-based rather than tied to outcomes or milestones such as IND clearance, IRB approval, or enrollment, in order to avoid creating pressure that could compromise objectivity.

A Shared Technology Platform Would Strengthen the Pilot

We recommend that FDA give serious consideration to establishing a single, centralized, auditable technology platform to support the rolling submission process, rather than allowing each QRI to develop a bespoke system. A common platform would support standardized data collection across QRIs, enable meaningful cross-QRI comparisons of outcomes, and provide the audit trails and data security controls necessary to protect confidential sponsor information and patient data throughout the review process. The

platform should support version control, audit trails, issue tracking, review-status designations, unique component identifiers, linkage of recommendations and FDA feedback to specific versions reviewed, preservation of superseded versions, role-based access controls, and final reconciliation of IND components. Permitting a fragmented, QRI-by-QRI approach to technology would add unnecessary complexity and would make it more difficult for FDA to evaluate whether the pilot, in aggregate, is achieving its stated purpose.

Precedents Worth Considering

Several existing models may usefully inform implementation, including reliance-based single-IRB review frameworks that avoid requiring every participating institution to operate its own ethics board, NIH-supported clinical trial networks that have sustained multidisciplinary infrastructure across many studies, and international frameworks — such as reliance-based ethics review models and coordinated multi-authority review pilots — that illustrate how predictable timelines and clearly defined roles can shorten study start-up without lowering scientific or ethical standards. FDA's own experience with coordinated, multi-party review in other contexts may offer a useful template for defining roles, timelines, and decision rights among FDA, sponsors, and QRIs here.

Risks and Safeguards

Risk of QRI Review Becoming an Additional Layer

The most significant structural risk is that QRI engagement could become an additional procedural step that sponsors must complete before undergoing full FDA review, rather than a substitute for part of that review — lengthening, rather than shortening, the path to FIH. We recommend that FDA design the pilot so that QRI involvement is understood to displace specific elements of FDA's review effort, and that the Agency measure total time-to-FIH end-to-end so that this risk is visible in the pilot's own data rather than masked by measuring only the post-engagement interval.

Consistency Across QRIs

Variability in expertise, review rigor, and risk tolerance among participating QRIs could lead to inconsistent recommendations for similarly situated sponsors. Standardized review templates, clearly defined performance objectives, and periodic FDA feedback to QRIs on how their recommendations align with the Agency's own risk-based thinking would help mitigate this risk and would allow lessons to be shared across the QRI cohort.

Equitable Access

Because the pilot contemplates that sponsors will ultimately pay QRIs directly, there is a meaningful risk that the model becomes more accessible to well-resourced sponsors than to smaller biotechnology companies or academic innovators, particularly in fields such as rare disease development that rely heavily on grant funding. We encourage FDA, potentially in coordination with other components of the

Department of Health and Human Services, to consider funding mechanisms, subsidies, or vouchers that would allow smaller and academically based sponsors to access QRI support, and to monitor participation data, both during the pilot and thereafter, for evidence that access is skewing toward larger, better-resourced organizations.

Additional Risk Considerations

We also note that increasingly complex FIH protocols — including combined Phase 1b/2 designs intended to accelerate overall development — already drive much of the time and cost associated with initial IND preparation. FDA may wish to consider limiting the pilot's early scope to more traditional, single-objective FIH designs so that the pilot evaluates the QRI mechanism itself rather than the separate trend toward more complex early-phase protocols. We further recommend that the Agency establish a mechanism for sharing relevant deficiency trends or review themes with participating QRIs on an ongoing basis, so that QRI recommendations remain calibrated to FDA's current expectations.

Oversight and Accountability

Resolving Disagreements

FDA should remain the final decision-maker in any disagreement among FDA, a QRI, and a sponsor. We recommend a defined, time-bound process for escalating unresolved issues. For example, a concise written issue summary followed, where necessary, by a brief structured discussion involving FDA review staff, the sponsor, and relevant QRI subject-matter experts — with the outcome documented in the pilot record. Wherever possible, disagreements should be surfaced and resolved during rolling review, before the formal 30-day clock begins, to reduce the likelihood that they will later result in a clinical hold.

Performance Oversight of QRIs

We support a graduated, risk-based approach to QRI oversight rather than a fixed numerical threshold for intervention. Ordinary or correctable performance concerns should first be addressed through direct feedback and an opportunity to remediate; recurring or unresolved issues could warrant enhanced monitoring or temporary suspension from accepting new pilot projects; and removal should be reserved for serious, repeated, or uncorrected failures that compromise participant protections, submission quality, or objectivity. FDA should rely primarily on its existing inspection and compliance authorities over sponsors, investigators, IRBs, and clinical sites rather than constructing a wholly new, QRI-specific compliance regime. We also recommend that FDA distinguish, when evaluating performance, between shortcomings attributable to the QRI and outcomes driven by sponsor decisions, funding constraints, or the inherent complexity of a given product.

Transparency and Confidentiality

The pilot should support transparency at the aggregate program level — for example, by publishing de-identified information on the therapeutic areas represented, the general categories of issues identified, and overall timeline outcomes — while protecting sponsor-specific confidential commercial information,

trade secrets, and proprietary development data, consistent with existing statutory and regulatory protections. We do not believe new, pilot-specific confidentiality authorities are necessary; existing frameworks governing FDA's handling of confidential submissions should be sufficient if clearly applied to the QRI context.

The same confidence does not exist for QRIs. In the setting of one QRI engaging with multiple sponsors, however, there is concern over both confidentiality and independence. A QRI will have access to commercially confidential information and, in any therapeutic area, potentially have access to competing investigational medicines. While a contract between sponsor and QRI may specify the terms of confidentiality, there is a natural risk that QRIs will apply the knowledge learned from one sponsor to advice provided to a competitor; unlike FDA, QRIs do not have the experience in establishing appropriate and robust firewalls nor statutory requirements that direct their performance. FDA should issue guidance on how to mitigate this risk.

Success Metrics and Evaluation

We recommend that FDA collect a balanced set of metrics spanning timeliness, quality, and safety, rather than emphasizing speed alone. Relevant measures include time from first sponsor engagement with a QRI (or even completion of a given protocol) to first participant dosed, the number and nature of FDA information requests, the frequency and basis of clinical holds, deficiencies identified and resolved before formal submission, and any safety outcomes in pilot studies relative to comparable non-pilot FIH studies. Sponsor and QRI feedback should be collected and analyzed, to capture feasibility, utility, salient resolved or ongoing issues, and process improvements. Equity-related measures — such as the range of sponsor sizes, funding levels, and therapeutic areas represented in the pilot cohort — should also be tracked, given the access concerns noted above.

We further suggest that FDA consider incorporating structured forecasting tools, potentially including machine-learning-assisted analysis, to help QRIs anticipate likely sources of clinical holds, common deficiencies, and safety concerns implied by a given submission package. Such tools could meaningfully support the pilot's speed objectives if integrated as a QRI-facing aid rather than as a substitute for FDA's own review.

Rather than declaring success based on a single IND submission, we recommend that FDA evaluate the pilot after a sufficiently large and representative cohort has completed the process — reflecting a range of sponsor types, product modalities, and QRIs — with the option of interim reviews to refine the model before broader expansion. If the pilot demonstrates measurable improvement in submission quality and time-to-FIH without any degradation in participant safety, FDA should consider scaling the specific practices shown to add value (for example, standardized review templates or the rolling-submission platform) rather than simply increasing the number of participating QRIs.

Additional Considerations

Complementary Approaches

The QRI model need not be viewed as the only mechanism for accelerating FIH study initiation. FDA may also wish to consider expanding access to pre-IND engagement opportunities, issuing streamlined guidance on the minimum information needed to support a Phase 1 FIH study specifically (as distinct from guidance oriented toward later-stage or marketing-application content), and investing in digital tools that support more efficient review. These approaches are complementary to, rather than a substitute for, the QRI model, and several of the capabilities described above — such as early integration of clinical pharmacology and bioanalytical planning — could usefully be embedded within QRI practice regardless of which broader mechanism FDA ultimately prioritizes.

Comparative Advantages and Disadvantages

Compared with guidance-only or infrastructure-only alternatives, the proposed QRI model has the advantage of pairing multidisciplinary expertise with a specific development program, thereby surfacing program-specific risks that generic guidance cannot address. Its principal disadvantages are the resource intensity of building and sustaining QRI capacity, the risk of inconsistent practice across institutions absent standardization, and the potential for unequal access if participation ultimately depends on a sponsor's ability to pay. We encourage FDA to treat these as risks to be actively managed rather than reasons to narrow the pilot's ambition.

Risk-Based Treatment of Submitted Information

We support a risk-based framework in which the depth and timing of information FDA expects varies with the investigational product's novelty, available prior knowledge, and the proposed patient population, while the underlying safety standard for permitting a study to proceed remains constant across all products. Products with substantial prior human or platform experience may reasonably warrant more streamlined nonclinical or CMC packages at the FIH stage, whereas novel modalities, first-in-class mechanisms, or studies involving vulnerable populations should continue to receive more detailed product-specific review.

Closing Considerations

Finally, we encourage FDA to preserve sponsor accountability for the content and accuracy of the IND throughout the pilot, to avoid layering new documentation requirements on top of the IND itself, and to ensure that whatever governance structure emerges remains workable for both large, well-resourced sponsors and smaller or academically affiliated sponsors. We appreciate FDA's willingness to test new approaches to accelerating early clinical development and welcome the opportunity to discuss these comments further.

The MRCT Center is grateful for the opportunity to review and comment on this proposed pilot program. We stand ready to assist FDA in refining this proposal and collaborating as a component of a QRI pilot.

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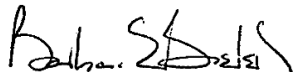
Please feel free to contact me (bbierer@bwh.harvard.edu) if we can be helpful or if you wish to discuss. We welcome continued dialogue as the pilot evolves.

Respectfully submitted,
On behalf of the MRCT Center



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