

NIH Office of Science Policy (OSP)

RE: NOT-OD-26-113, "**Request for Information: Draft NIH Policy on Sharing Summary Level Study Results with Clinical Research Participants**"

Submitted electronically via <https://osp.od.nih.gov/comment-form-draft-sharing-summary-results-policy/>

October 26, 2026

To the NIH Office of Science Policy,

The Multi-Regional Clinical Trials Center of Brigham and Women's Hospital and Harvard ("MRCT Center") appreciates the opportunity to comment on NOT-OD-26-113, "Request for Information: Draft NIH Policy on Sharing Summary Level Study Results with Clinical Research Participants." The MRCT Center is a research and policy center dedicated to improving the ethics, conduct, oversight, and regulatory environment of international, multi-site clinical trials. 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. The MRCT Center seeks to identify challenges in the global clinical trial enterprise and deliver ethical, actionable, and practical solutions to make clinical trials more efficient without compromise to quality or reliability. 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

For more than 15 years, the MRCT Center has worked with its stakeholders to define not only whether aggregate results should be returned, but how they can be returned responsibly, sustainably, and in a manner that participants can understand and use.

We strongly support NIH's objective of ensuring that participants in NIH-supported clinical research have access to summary-level study results. Sharing summary-level study results is an element of the research relationship with participants that begins at consent. Additionally, the commitment to sharing summary-level study results made at enrollment and honored at completion supports recruitment, retention, and trust. The ethical rationale is clear: participants contribute time, effort, data, specimens, and trust to research, and the research enterprise should make reasonable efforts to tell them what was learned.

In 2017, the MRCT Center's multi-stakeholder Return of Aggregate Results workgroup, comprising 53 members from industry, academia, patient advocacy, and nonprofit organizations, published principles, a guidance document, and a toolkit for sponsors of all types.² Those materials begin with the premise that participants should be offered plain-

¹ Brigham and Women's Hospital, Mass General Brigham, Harvard Medical School, and Harvard University.

² Version 3.1 of *MRCT Center Return of Aggregate Results to Participants Guidance Document* (<https://mrctcenter.org/wp-content/uploads/2023/04/2017-12-07-MRCT-Return-of-Aggregate-Results-Guidance-Document-3.1.pdf>), *MRCT Center Return of Aggregate Results to Participants Toolkit*

language summaries of study results across clinical studies. While our work focused on the return of clinical trial results, we fully endorse the NIH draft policy and its scope, which extends to all clinical research involving human participants. Our comments, therefore, focus on the policies, processes, and considerations necessary to make the policy feasible, durable, and harmonized with existing domestic and international requirements. They are meant to strengthen the policy and supplemental guidance as we fully endorse the foundations upon which the policy is built.

SECTION 1: General Comments on the Draft Policy

General comments follow on the draft policy; we appreciate that some of the detail is better addressed in supplemental guidance. We note, however, that questions raised regarding the policy's framing, scope, and definitions will create challenges for implementation. We therefore advocate that selected information be included in the policy, not only in the supplemental guidance.

I. Purpose:

The section is clear as written. (Note: We address the definition and clarity of “summary research results” below.)

II. Scope

While we appreciate the limits of NIH jurisdiction, we strongly encourage NIH to work with FDA to issue a joint policy with respect to clinical trials. The MRCT Center has previously drafted a proposed FDA guidance applicable to FDA-regulated trials that includes many of the suggestions here, and to which we refer (see <https://www.regulations.gov/document/FDA-2017-D-5478-0001>).

Divergent definitions, content, and expectations create burdens, and the possibility that two participants in one study will receive different summaries of the same research. We strongly encourage NIH to align definitions, timelines, content elements, recipient definitions, and posting expectations with existing frameworks (e.g., Regulation (EU) No 536/2014 and the United Kingdom (UK)'s Medicines for Human Use (Clinical Trials) Regulations) and with FDA. A single well-prepared summary, appropriately translated and adapted, can satisfy multiple obligations, decrease cost, increase clarity, and align with the goals of Operation TrialBlazer.

The current policy applies to applications received on or after six months following publication of a final policy, and to intramural projects conducted on or after that date, including “ongoing” studies. We understand and agree that the policy will apply prospectively to new competing awards, but we also recognize that certain exceptions to ongoing studies may be necessary in the transition period. For example, biobanks that have distributed data and/or biospecimens prior to this policy's effective date may not have the

(<https://mrctcenter.org/wp-content/uploads/2023/04/2017-12-07-MRCT-Return-of-Aggregate-Results-Toolkit-3.1-1.pdf>), *Return of Aggregate Results to Participants Principles* (<https://mrctcenter.org/wp-content/uploads/2023/04/2017-11-27-Return-of-Aggregate-Results-Principles.pdf>) Version Nov 2017 released

ability to amend data use agreements to discharge the responsibility for or directly accommodate the return of summary results. Other exceptions should be entertained (e.g., the communication of secondary endpoints when the primary endpoints have not been communicated; in the absence of a prespecified plan for communicating results at study initiation, investigators may not retain participants' contact information). We also recommend enforcement discretion during this transition period.

The MRCT Center strongly encourages NIH to require public dissemination of summary research results to complement the communications to participants. The general public also can benefit from learning about research funded or supported by public funds, and patient communities have an interest in (and are often eager to understand) research related to their health. In general, participant privacy and confidentiality do not pose challenges to sharing summary results publicly, provided that only aggregate results are reported, no personal identifying information of research participants is included, and care is taken to anonymize rare events. In special situations (e.g., very small studies such as ultra-rare diseases or N of 1 studies) or for rare adverse events that may be challenging to anonymize, additional consideration may be needed to protect individuals from the risks of re-identification. In all other instances, we recommend publicly posting a plain-language, aggregate summary of the research results to ensure transparency and respect for the contributions of participants.

III. Compliance and Enforcement

The compliance provisions would benefit from further clarification. One policy objective is meaningful participant communication. Investigators and institutions need clear guidance regarding what constitutes compliance, what documentation must be retained, what evidence demonstrates successful dissemination, and how reasonable but unsuccessful efforts to contact participants will be evaluated.

NIH should clarify (in policy or supplemental guidance):

- The definition of “meaningful” that they would like researchers to use.
- What documentation is sufficient to demonstrate compliance.
- Whether documentation requirements differ depending on the communication method used.
- How compliance will be evaluated in multicenter studies.
- Whether failure to reach a participant despite reasonable efforts constitutes noncompliance.
- Whether and how institutions should document participant preferences.
- Whether audits or monitoring activities will occur.
- How deficiencies can be corrected.
- Whether corrective action processes will precede formal enforcement actions.

Importantly, NIH should recognize that participant-facing dissemination differs from many other regulatory obligations, in that successful implementation depends on participant preferences, participant mobility, changing contact information, deaths, and other factors

that investigators cannot fully control. Enforcement should therefore focus on whether investigators implemented reasonable, well-documented dissemination plans.

We encourage NIH to balance the expectation of retaining identifiable participant information with the goal of protecting confidentiality and participant privacy. The simple documentation and tracking of participant preferences, in the absence of a highly secure technical environment, increase the risk of reidentification.

The policy applies to research supported "in whole or in part" by NIH. As currently drafted, the NIH will hold the recipient (grantee) institution of NIH funds responsible for ensuring that aggregate study results are returned. Many studies are co-funded by NIH, industry, foundations, and international funders. Additionally, in many circumstances, the relevant research is conducted at another site or institution or is multi-site or multi-national. Multi-site research, cooperative groups, public-private partnerships, adaptive platform trials, and consortium-based research may involve complex governance arrangements. Guidance should clarify how responsibilities should be allocated and coordinated among participating organizations. The policy should allow for a single accountable entity, identified at the time of award or designated as a part of the initiation of the research, to hold (or be responsible for discharging) the obligation. The NIH policy should allow a co-funder, sponsor, or other designated entity, documented by contract or agreement (e.g., data use, material transfer, clinical trial, or other), to satisfy the NIH requirement, provided participants have access to the summary. In those documented arrangements, NIH should hold the accountable entity directly responsible and not require the grantee institution to monitor the subrecipient.

NIH-supported research conducted outside the United States raises translation, channel, and legal questions that should be addressed in the policy. Where a study also falls under the EU or UK frameworks, the policy should defer to the harmonization provisions we propose below.

We support including the requirement in the terms and conditions of award. We recommend NIH state explicitly that the first response to non-compliance is notification and an opportunity to address the non-compliance, and that funding consequences are reserved for repeated or willful failure.

IV. General Definitions

The definitions in the policy are complex and would benefit from further clarification. Is the intention to include the return of summary results from biobanks and biorepositories? This has been a best practice in certain settings (e.g., posting aggregate results on the biorepository website whenever available), but the definition appears to require that "an investigator (or colleague) [who] directly interacts" with the participant. The investigator of a specific research study may not be the same person as the individual who collects the biospecimen and associated data and may be a clinician (e.g., surgeon, technician) and not an investigator at all. Whether biospecimens and data that are collected or deposited for future research purposes are included in the definition, and therefore in the policy, should be clarified.

With our genuine hope that policy alignment between NIH and FDA can be achieved, the definition of clinical trial (NIH) and clinical investigation (FDA) should also be aligned, if not now in a future iteration of a harmonized policy.

The definition of plain language lacks clarity; further supplemental guidance is recommended. We also believe that the policy should specify that any communication includes accommodations for people with disabilities, whether or not those individuals are majority or incidental participants of the research.

Many clinical research and clinical trial programs have poorly defined "primary outcomes," rendering the definition of primary completion data problematic. Examples include adaptive and/or platform clinical trials, natural history studies, registries, and health services research. We propose a more nuanced definition of primary completion data, arrayed by the type of clinical research program. For example, there are many "primary outcomes" in adaptive and platform trials; waiting until the study is 'closed' would not be consistent with the policy's intent. We suggest that NIH establish reporting triggers (e.g., when an arm is terminated, a major amendment alters the direction of the study, interim results are available, or a publication includes results). Investigators need clarity in order to comply. Similarly, if a natural history study is published, a plain-language summary should be made available to registrants concurrently. As a guiding principle, whenever research is published or the results made available to scientific audiences, participant notification should occur.

The definition of "summary level study results" appropriately identifies key content elements, including study objectives, methodology, findings, limitations, and implications. However, NIH should further clarify what results are expected to be included. For clinical trials, we believe that primary results and key safety information must be reported (and this expectation should be included in the policy), but the question of which secondary outcomes to include is less clear. To avoid "cherry-picking" after results are known, we argue that key secondary outcomes – including those important to participants – should be prespecified and consistently reported across similar studies. With some exceptions, reporting of exploratory findings should not be required. Investigators would benefit from guidance on how to present risk and statistical analyses in plain language; negative, inconclusive, or underpowered findings; why trials are terminated for scientific (e.g., benefit, safety, futility) and non-scientific reasons (business priorities, low accrual) and what can or cannot be learned; and how to approach study endpoints in studies that continue to mature with further data collection.

The MRCT Center suggests adding a '*relevant person*' definition to better define the intended recipient within the policy. The "relevant person" definition found in the UK regulations resolves the questions the community has raised about legally authorized representatives, critically ill participants, participants who lose capacity during the study, and participants who die before results are available. We recommend NIH adopt it substantially as written.

V. Requirements

The broad scope of the proposed policy appropriately reflects the principle that respect for participants should not depend on study type. Nevertheless, additional clarification regarding specific research contexts would be beneficial. These include longitudinal cohort

studies, registries, natural history studies, adaptive designs, platform trials, biobanks, studies involving secondary use of identifiable data or biospecimens, studies conducted under waiver of consent, and international studies conducted under different regulatory frameworks. Clarification is also needed regarding responsibility and accountability in multicenter studies involving multiple awardees, coordinating centers, and/or collaborative networks.

Particularly important is clarification regarding timing. While the proposed policy establishes deadlines for dissemination, many studies continue generating meaningful findings long after the initial analysis is complete. NIH should clarify whether dissemination obligations are satisfied through a single summary of results or whether important subsequent analyses, long-term follow-up findings, pooled analyses, secondary analyses, or materially changed interpretations create additional obligations. Longitudinal and natural history studies may yield findings for many years after participant enrollment, and investigators would benefit from guidance on when ongoing communication is warranted and when obligations should be considered complete. One specific comment regarding the direction of timing for clinical trials: while we agree that the return of summary research results requirement should align with existing reporting requirements, we believe that the timing should align with the earliest of reporting requirements, not whichever is later.

NIH should clarify, in the policy or supplemental guidance, what constitutes an adequate offer to receive study results; whether participants should be given opportunities to opt in, opt out, or modify preferences over time; whether participant communication preferences should be documented; the degree to which translation and accessibility accommodations are expected; and the minimum information that should be provided in all summaries. Clarification would also be helpful regarding participant support obligations, including expectations for responding to questions, addressing requests for clarification, and providing resources for participants who seek additional information.

The relationship between participant dissemination, publication, ClinicalTrials.gov reporting, and other dissemination requirements would also benefit from clarification. Investigators may encounter circumstances in which participant summaries are prepared before publication, after publication, or simultaneously with publication. Clear guidance regarding preferred sequencing and associated considerations would promote greater consistency and reduce uncertainty.

→ Relatedly, we believe that NIH should engage with the International Committee of Medical Journal Editors (ICMJE) to establish that the return of summary research results to participants—and the public—does not constitute prior publication.³

The proposed exception process would benefit from further elaboration. While the draft policy appropriately recognizes that dissemination may sometimes be "justifiably not appropriate," investigators and institutions would benefit from additional guidance on the circumstances that may warrant exceptions. Examples may include substantial privacy concerns, inability to identify or contact individual participants despite reasonable efforts, certain studies conducted under waivers of consent, highly sensitive research contexts, or

³ The MRCT Center previously communicated with ICMJE on this issue, and the (most unsatisfying) response was, "It depends."

circumstances in which dissemination may create significant risks that cannot reasonably be mitigated. NIH should clarify the criteria for review, documentation requirements, timing of requests, and standards by which exceptions will be evaluated.

The draft appropriately encourages consultation with IRBs and institutional officials, but significant uncertainty remains regarding oversight responsibilities. NIH should clarify whether participant-facing summaries are subject to IRB review; whether review expectations differ before and after study completion; whether dissemination plans should be reviewed prospectively; and what roles institutional communication offices, participant engagement offices, and human research protection programs play. Some clinical trials are ongoing at the time summary results are shared: Is IRB review recommended, expected, or required? Clear delineation of responsibilities will promote efficient implementation and avoid unnecessary duplication of review. In our assessment, and consistent with the position of the UK Health Research Authority, a review of the specific participant-facing communication is not required when the overall plan for returning results is consistent with what the IRB approved at the outset.⁴ We further recommend against including operational details about the return of results in the protocol, as doing so may prompt a protocol amendment if the delivery method changes. The option to receive and the intent-to-return results belong in the informed consent document, where the participant will see them. IRBs could approve, or HRPPs could create, a template or shell in advance, with results populated later. NIH stating these positions plainly would resolve uncertainty.

Additional clarification regarding governance and responsibility is also needed. In large collaborative studies, platform trials, public-private partnerships, international collaborations, and research consortia, responsibility for creating summaries, translating materials, maintaining contact information, responding to participant inquiries, and documenting dissemination activities may need to be distributed across multiple entities. As stated earlier, we believe that the NIH should allow NIH awardees to assign the responsibility of returning summary results to appropriate individuals (e.g., investigators) and/or other entities through clinical trial, data use, material transfer, or other agreements, and if the responsibility is appropriately discharged and documented, the primary awardee should not be held responsible for compliance. NIH should also address situations in which investigators change institutions, studies transfer to another organization, funding ends, or sponsoring organizations cease operations.

SECTION 2: Proposed Supplemental Guidance

The MRCT Center endorses the NIH proposal to provide supplemental guidance. Guidance should be practical, example-driven, and designed to reduce duplication across institutions, minimize burden, and address implementation challenges.

I. Participant Preferences and Experiences

⁴ Of course, IRBs always retain the authority to require review, either specifically or generally as their own policy, but it should not be federally required.

Participant needs and expectations vary substantially across populations, study types, cultures, languages, and life circumstances. A single communication strategy is unlikely to meet the needs of all participants. NIH guidance should therefore underscore the flexibility that participant-centered communications require while identifying and promoting best practices that can be broadly adopted.

Guidance should first address how to obtain and what information participants consider valuable. Participants often seek more than the principal findings of a study. They may want to understand why the study was conducted, what was learned, which uncertainties remain, how the findings compare with expectations, what the limitations were, and how the results may affect future research or clinical care. Guidance should therefore address both the method (soliciting input from the population and/or community) and the content of study summaries, as well as the broader context needed to help participants understand the significance of the findings.

A principal tenet of returning aggregate research results is that the summary is fair, balanced, transparent, and understandable to the recipients of the communication. Therefore, we suggest:

- As discussed above, the primary aims and/or endpoints of a study should always be communicated, and secondary aims, whenever possible, should be selected in advance of the study. Broad representation from the study's intended population should be consulted in preparing the plan for return, including soliciting differences in participants' perspectives.
- The NIH should provide detailed guidance regarding the communication of scientific uncertainty. Participants deserve clear and balanced explanations of negative findings, inconclusive findings, exploratory analyses, conflicting evidence, and findings that may evolve as additional research becomes available. Investigators frequently struggle to explain uncertainty in understandable ways while avoiding oversimplification. Examples of participant-centered language addressing uncertainty would be particularly valuable.
- Timing is another area where supplemental guidance would be helpful. Participants should understand from the beginning of a study whether and when they are likely to receive summary-level study results. Guidance should address whether participants should receive periodic updates during long studies, how delays should be communicated, and whether status updates should continue while analyses remain ongoing. In many studies, multiple years may pass between participation and the dissemination of results. Guidance regarding maintenance of participant engagement throughout this period would be valuable.
- Participant choice deserves particular attention. NIH should consider providing guidance regarding whether participants should be allowed to opt in, opt out, or modify communication preferences over time. Guidance should also address how preferences should be documented, whether preferences should be periodically reconfirmed, and how participant preferences should be handled following death, loss of decisional capacity, or requests from family members and legally authorized

representatives. Participant preferences are not static and may evolve over the course of a study and after study completion.

- NIH guidance should evaluate the strengths, limitations, and appropriate uses of different communication methods, including participant portals, email, mailed communications, telephone discussions, in-person meetings, video communications, community forums, and other dissemination approaches. Guidance should help investigators select methods that align with participant preferences, accessibility needs, literacy levels, language needs, technological resources, and study characteristics.
- Health literacy, numeracy, accessibility, disability accommodations, language access, and cultural adaptation deserve dedicated attention within supplemental guidance. NIH should specifically address how to make information understandable and meaningful for participants with varying educational backgrounds, disabilities, language proficiency levels, and experience with scientific information. Without careful attention to these issues, dissemination efforts may inadvertently exclude populations that are already underrepresented in research.
- Participant and family concerns should also be addressed. Participants may have concerns about the interpretation of findings, implications for health, disappointment with study results, the receipt of unexpected information, or persistent unanswered questions. Guidance should address approaches for managing expectations, responding to participant concerns, providing contact information for questions, and supporting participants who seek additional information after dissemination.
- Finally, guidance should address community expectations and community-level dissemination. Many studies are conducted in partnership with patient advocacy groups, disease communities, Tribal communities, community-based organizations, and other stakeholder groups. In some contexts, dissemination may appropriately extend beyond individual participants to broader communities that helped make the research possible. Guidance should address when and how community-level dissemination can appropriately complement individual participant communications.

II. Best Practices for Researchers

Researchers broadly support sharing study results with participants, but many lack experience, templates, staffing, processes, or institutional support for doing so effectively. NIH has an opportunity to substantially reduce burden and improve quality through comprehensive guidance and practical implementation tools.

Guidance should provide detailed recommendations regarding the development of plain-language summaries. Investigators would benefit from recommendations regarding reading levels, plain-language terminology, communication of risk and uncertainty, use of graphics and visuals, translation practices, numeracy principles, and culturally appropriate communication. NIH should consider providing examples of effective participant-facing summaries drawn from various research study types and participant populations.

We recommend NIH supplement the definition of plain language with a non-binding target – a sixth to eighth grade reading level – and an organized list of health literacy best practices including:

- Lead with the conclusion,
- Use familiar vocabulary, short sentences, and descriptive headings,
- Use bullets rather than paragraphs when appropriate,
- Ensure accessible formatting like including adequate white space, and
- Include definitions for any medical terms that must be used.

We caution against adopting a single readability score as a requirement. Readability formulas measure sentence and word length, not comprehension, and optimizing to them can produce text that scores well but communicates poorly to the audience.

In addition to what is noted above, the MRCT Center 2017 Guidance set out a workable core to use:

- One idea per paragraph.
- Absolute rather than relative risk.
- Natural frequencies with consistent denominators, and consistent time frames.
- Whole numbers.
- Simple visuals with one message each.
- Language that avoids claims and promotional language

MRCT Center's Toolkit's neutral language guidance offers paired examples of language to avoid and language to consider, developed specifically to address the promotional language concern.

Finally, people with lived experience should be involved in the writing and review of the summaries. We recommend that the supplemental material recommend that summaries should be reviewed before release by at least one person who does not have the condition under study and at least one who does. Furthermore, piloting with a small group, including through the use of "teach-back," is a reliable check on comprehension.

Participants consistently want three things that a technical results summary does not provide: who was studied, what the results do and do not mean for them personally, and what happens next. Participants cannot interpret a result without knowing its context. Summaries should clearly state that the results apply to the population studied and not to others, that individual participants may have had different outcomes, and where the study fits within a larger development or evidence pathway.

Guidance should identify recommended content elements that promote consistency while preserving flexibility. Such elements may include study purpose, study design, participant population, interventions evaluated, principal findings, important safety information, limitations, significance of findings, future research directions, ongoing uncertainties, and contact information for questions. Establishing common expectations will facilitate the

development of participant-facing materials and improve consistency across studies. With respect to clinical trials, the EU and the UK have already specified common elements to be included. As we have suggested previously, for the limited case of plain-language clinical trial summaries, the following should be considered as necessary elements, although the order of inclusion is flexible:

- o A statement of recognition and appreciation of the participants' contributions
- o Study title
 - A short study title in plain, non-scientific language
 - The full title (official title) of the study
 - US NCT number (and other identifying information, e.g., the protocol number)
- o Study purpose
 - Why the study was conducted
- o Study information
 - The product(s) under study and any comparators (the names for each being the name used in the study registration)
 - Start and end dates of the study
 - Countries where the study took place
 - The number of participants enrolled
 - The type and phase of the study
 - The date the summary was produced
- o Study overview
 - A high-level description of the study design, treatment(s), and other pertinent information that may be helpful to understand the results
 - A picture or diagram, as appropriate
- o Study population
 - Demographics (e.g., age, sex/gender, race, and other important descriptors of the intended population)
 - Key inclusion/exclusion criteria
- o Primary outcome(s)
 - Describe the results for the primary endpoint(s) for each study arm
 - Describe the outcome measures in plain, non-technical language
 - Present data in simple tables or images (e.g., pie charts) or visual representations using, if appropriate, both absolute numbers and percentages
 - Differences that are not statistically significant should be indicated
- o Safety:
 - The plain language term "side-effects" may be used in this context to indicate "adverse events"
 - Provide the incidence of investigator-determined "serious adverse events" to indicate a potential causal relationship between the products or interventions under study and an adverse event. Serious "side effects," including participant deaths, should be listed
 - Include adverse events (e.g., non-serious "side effects") if the incidence or severity is greater than anticipated, using a reasonable and disclosed cut-off for those that are common
 - Include a link to the reported scientific results for a listing of additional safety information

- Additional safety data important to the overall results of the study may be included so long as inclusion is balanced and there is reasonable justification
- o Comments on outcome of the study
 - High-level statement(s) regarding the study results, applicability to participants, and generalizability to others?
- o Additional information
 - A statement that patients should consult their physicians and/or study doctors with further questions about their individual care, and should not make changes in the treatments based on the results of this study
 - A statement that the summary includes the results of a single study and that multiple studies are used together to assess the risks and benefits of any product or intervention
 - Where additional information may be found (including a link to the scientific summary posted on www.ClinicalTrials.gov or another website, as appropriate)
 - Whether further research is anticipated, as needed, and as available in the public domain
 - Contact information for the study sponsor, investigator, or call center, if applicable.

Communication of uncertainty warrants special attention. Researchers frequently encounter challenges when explaining negative findings, exploratory analyses, subgroup analyses, conflicting results, early study termination, protocol modifications, and evolving scientific evidence. Guidance that provides examples and model language would improve consistency and support accurate, transparent communication while minimizing the risk of misunderstanding.

NIH guidance should also address which results should be shared and under what circumstances. Investigators would benefit from recommendations regarding primary outcomes, secondary outcomes, exploratory findings, subgroup analyses, safety findings, interim analyses, and long-term follow-up results. Guidance should help investigators determine how much information is necessary to create an informative and meaningful participant summary without unnecessarily increasing complexity.

Additional guidance is needed regarding studies involving multiple stakeholders. Multi-site trials, cooperative groups, public-private partnerships, adaptive platform trials, international collaborations, and consortium-based research may involve complex governance arrangements. Guidance should clarify how responsibilities should be allocated and coordinated across participating organizations.

NIH should provide recommendations regarding scientific accuracy review, readability review, translation review, quality-control procedures, participant review where appropriate, and institutional or IRB review processes. Clear guidance would help ensure that participant summaries are both accurate and understandable.

Guidance should further address dissemination beyond individual participants. Researchers would benefit from recommendations regarding communications with parents, guardians, legally authorized representatives, caregivers, designated family members, and community stakeholders. These issues often involve complex questions regarding participant preferences, privacy, consent, and autonomy. The 2017 MRCT Guidance enumerates many of these special considerations.

Finally, NIH should consider providing operational resources, including model consent language, model dissemination plans, sample participant summaries, frequently asked questions, translation resources, readability tools, and implementation checklists. For many investigators, access to such resources may be the single most effective strategy for reducing burden while improving quality and consistency.

III. Implementation Needs

Effective dissemination requires expertise in plain-language communication, health literacy, cultural adaptation, community engagement, translation, disability accommodations, and participant support. NIH should consider identifying expected competencies and developing educational resources that can be shared across institutions.

NIH should address participant portals, electronic communication platforms, accessibility requirements, privacy protections, cybersecurity considerations, authentication approaches, and mechanisms that permit participants to update communication preferences over time. NIH should work with the National Library of Medicine website, ClinicalTrials.gov (see <https://clinicaltrials.gov>), to include an option to post a link to the plain-language summary of aggregate results or post the summary itself. NIH should establish a common platform for all studies not registered on ClinicalTrials.gov and work with journal editors to develop a means to post plain-language summaries of published papers alongside the technical abstract. NIH should develop “best” practices for communication, including how to ensure that the plain-language summary for all research involving human participants is findable, accessible, and understandable.

Guidance should address maintenance of participant contact information, long-term participant tracking, dissemination documentation systems, secure communication methods, electronic portals, translation support, accessibility resources, and long-term archiving of study summaries. These needs are particularly important for multi-site studies and studies extending over many years. As mentioned elsewhere, attention should be paid to the risks of documentation and tracking that compromise participant privacy and confidentiality.

One of the more important issues requiring clarification is funding. Many studies complete enrollment and final analyses after grant funding has ended. In some cases, dissemination obligations may arise years after the end of the award period. NIH should therefore provide explicit guidance regarding how dissemination activities will be funded when active grant support is no longer available. Investigators and institutions cannot reasonably be expected to absorb these activities indefinitely without dedicated resources.

Potential approaches worthy of consideration include:

- Allowing planned closeout and dissemination costs within award budgets.
- Creating administrative supplements for dissemination activities.
- Permitting no-cost extensions specifically related to participant communication obligations.
- Supporting a centralized institutional infrastructure that can serve multiple studies.
- Developing NIH-supported dissemination platforms and shared resources.

Clarification regarding these issues will be essential for successful implementation.

NIH should also provide guidance regarding allowable costs. Dissemination activities may require personnel effort, participant-tracking systems, summary preparation, health-literacy review, translation services, accessibility review, technology platforms, communication systems, participant support services, and documentation. Guidance should clearly identify allowable direct and indirect costs and should encourage prospective budgeting during study planning.

IV. Additional Suggestions

We recommend supplemental guidance that directly addresses certain circumstances.

Special considerations re: guardians, LARs, caregivers:

For children, our guidance recommends that where a child is of an age when assent is possible, the child should be involved in the decision; that for young children the parent or legal guardian should be asked first and the child approached for assent thereafter; that for a teenager both parent and child should be asked; and that where no resolution can be reached, the teenager should be informed that they have an independent right to the information at age eighteen.

Participants often wish to discuss their participation in clinical research with another person (e.g., a family member, friend, third party). Participants should have the option to share the study results with a designated third party. Any concerns about protections and liability are arguably less significant because personally identifiable information will not be shared.

When vulnerable populations are included in research, special IRB oversight and additional safeguards are often included to ensure the research is conducted in an ethical and considerate manner. Similar attention is needed to ensure these individuals or their legally authorized representatives receive the general results of the study. The sponsor, investigator, and IRB, if involved, should consider whether the return of results presents any specific or additional risks (e.g., psychological, behavioral, social, or legal) to the individual. The research participant should be involved to the extent that they are able, with assent as appropriate.

Laws and practices vary with respect to the definition of legally authorized individuals (LARs) and guardians. US state law establishes hierarchies for appointing an LAR for healthcare decisions. Legally appointed LARs are permitted to make decisions for clinical research participation. If an individual has an LAR, the LAR may serve as the proxy for receiving communications about summary research results. LARs, however, are often unfamiliar with clinical research generally or with participants' wishes specifically, and are often not legally appointed. In these circumstances, guardians or next of kin, or the individual appointed as a healthcare proxy, may serve in the capacity to receive summary research result communications. Again, the sponsor investigator and IRB (if involved) should consider whether the summary communication presents any special or additional risks (e.g., psychological, behavioral, social, or legal) to the individual if delivered to the LAR or other designated parties.

The death of a participant presents particular challenges in planning for the return of summary results. General recommendations are difficult to make, as this situation is often

informed by the specific facts of the death. Death can be anticipated (e.g., as an endpoint of the trial) or likely (e.g., salvage chemotherapy for cancer); death can be a consequence if known and anticipated (e.g., infection and sepsis secondary to chemotherapy-induced neutropenia, stem cell transplant) or unanticipated (e.g., adverse events). Each of these situations will demand different responses as to whether and when the next of kin or designated third parties should receive general research summaries. If possible, similar to a healthcare proxy, this eventuality should be anticipated and discussed with the participant as early as possible. It may be helpful and useful to consider asking the study participant if they would like to have a family member receive the summary communication in the event that they are unavailable, die, or are incapacitated. Care should be taken to be respectful and sensitive in discussing their possible death.

National Infrastructure and Shared Resources

NIH should supply or endorse shared resources: templates, examples of well-drafted summaries, a durable posting location, plain-language and numeracy guidance, accessibility expectations, and worked examples for common study types. Central resources would reduce duplicative effort, improve consistency, and help smaller and/or less-resourced study teams meet the same ethical expectations as larger research programs.

NIH should consider establishing a shared national infrastructure to support implementation. Such infrastructure could include a centralized repository of templates, model participant summaries, model consent language, translation resources, health-literacy tools, implementation guides, frequently asked questions, dissemination planning resources, and examples of successful approaches from diverse studies. Where successful approaches are unknown or uncertain, NIH should fund research to obtain the empirical data needed to refine implementation and recommendations. Necessary infrastructure and implementation pathways are likely to differ depending on the study question, research type, the population studied, the intervention, and other variables.

A shared resource model(s) would reduce burden, improve consistency, support smaller institutions that may lack dedicated communications expertise, and promote more equitable implementation across the research enterprise. It would also facilitate continuous improvement by enabling dissemination of emerging best practices.

Measurement and Evaluation

Supplemental guidance should address how effectiveness can be assessed. Questions that merit consideration include:

- Did participants receive the information?
- Was the information understandable?
- Was it viewed as useful and meaningful?
- Were certain dissemination approaches more effective than others?
- Did dissemination efforts reach participants equitably across populations?
- What barriers were encountered?
- What unintended consequences emerged?

Establishing mechanisms for evaluation and continuous improvement will help ensure that dissemination remains participant-centered and achieves the goals of the policy.

We suggest that collecting certain metrics will help align the goals of this policy. We suggest the following metrics be considered for routine collection:

- Proportion of studies providing a summary or status update on time
- Proportion using a central versus bespoke channel
- Participant-reported comprehension where available, and cost per study based on study type.

Little is known empirically about how participants respond to receiving aggregate results. The new NIH policy creates an opportunity to collect valuable data.

When sharing summary-level study results may not be possible or desirable

Our 2017 guidance identified categories in which results are likely to be indeterminate, unavailable, or of limited value to participants, or in which return creates risk. Returning results to participants in these situations might not be appropriate, although communication to the community and the public (and to which participants have access) may be possible. We recommend NIH adopt a list along these lines, subject to documentation and Institutional Review Board concurrence rather than prospective Institute, Center, or Office approval:

- Research conducted under a waiver of consent, and pragmatic or cluster randomized studies in which participants are not aware that they were participants
- Biospecimen contributions to a repository where the consent has stated that no results will be returned
- Exploratory or pilot studies are not powered to produce interpretable results
- Studies in which the participant population is small enough that returning creates a meaningful risk of re-identification, as in some ultra-rare disease research
- Studies of illegal or stigmatized behavior in which return could breach confidentiality or conflict with a Certificate of Confidentiality

For the de-identification example in particular, we note that requiring investigators to retain identifiers solely to enable a future return of results would increase privacy risk. The alternative, that is, a communication that could be accomplished through a public posting, should be considered. Public posting should also be considered in instances in which return to individual participants is infeasible (e.g., NHSR studies, exempt studies, studies conducted under a waiver of consent, pragmatic studies, studies in which identifiers are destroyed by design at data or biospecimen collection, etc.)

Resources

The *MRCT Center Return of Aggregate Results to Participants Guidance Document* and accompanying *MRCT Center Return of Aggregate Results to Participants Toolkit* are publicly available and free to use.² The Toolkit includes templates for Phase 1 and randomized Phase 2 and 3 trials, a template for trials that close early, a checklist for plain-language summary reviewers, a plain-language endpoint table, neutral-language guidance, and an ethics

committee checklist. The UK Health Research Authority already directs study teams to these materials. We would welcome the opportunity to work with NIH to adapt them for this policy.

In addition, the MRCT Center has several relevant resources that support this initiative, including the Clinical Research Glossary, the Health Literacy in Clinical Research website, and the Accessibility by Design Toolkit.

Beyond our own resources, the European Commission's Good Lay Summary Practice, the UK Health Research Authority's guidance on writing a plain language summary of research findings, TransCelerate's implementation guide and non-promotional language recommendations, and institutional templates such as those developed at Vanderbilt's Clinical and Translational Science Award program all exist and are in use.

Anything NIH itself hosts should meet Section 508 and Web Content Accessibility Guidelines AA standards, and guidance should address participants without reliable internet access.

In summary

We strongly support NIH's effort to establish participant-facing dissemination of summary-level study results as a standard component of NIH-supported clinical research. The proposed policy reflects the important principle that participants are partners in research and should be offered meaningful opportunities to learn about the outcomes of studies to which they contributed.

As NIH finalizes the policy, we encourage the agency to preserve flexibility while promoting consistency. Clinical research encompasses a broad spectrum of study designs, participant populations, institutional settings, and regulatory environments. A flexible framework that establishes clear expectations while allowing adaptation to local circumstances is likely to be more effective than highly prescriptive requirements.

We also encourage NIH to make findability and accessibility a central implementation objective. Meaningful dissemination requires attention to language access, disability access, digital access, health literacy, cultural appropriateness, and community engagement. Without deliberate attention to these factors, dissemination efforts may inadvertently exacerbate existing disparities in access to research information.

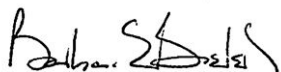
Harmonization should be another goal of implementation. Researchers currently face varying expectations across sponsors, institutions, research networks, and jurisdictions. NIH is uniquely positioned to promote consistency through shared templates, model language, implementation resources, and guidance developed with broad stakeholder input. Such harmonization would reduce burden while improving the participant experience.

Finally, we encourage NIH to frame dissemination of summary-level study results not primarily as a compliance activity but as a participant engagement activity. The ultimate measure of success should not be whether a summary was transmitted, but whether meaningful communication occurred. Effective dissemination requires attention to

participants' preferences, understanding, trust, and experience. A participant-centered approach to implementation, evaluation, and continuous improvement will best advance the policy's stated goals and strengthen the partnership between researchers and the individuals who make clinical research possible.

We would welcome the opportunity to discuss these comments, to contribute the MRCT Center's expertise to any supplemental materials NIH develops, and to convene further multi-stakeholder discussions as the policy is finalized and implemented. Please direct inquiries to me at bbierer@bwh.harvard.edu.

Respectfully submitted,
On behalf of the MRCT Center,



Barbara E Bierer, MD
Faculty Director, MRCT Center



Sylvia Baedorf Kassis, MPH
Program Director, MRCT Center