Decentralized Trials & Research Alliance

Response to Advancing Clinical and Translational Science through Accelerating the Decentralization of Clinical Trials (Notice #NOT-TR-23-006)
Submitted to National Institutes of Health (NIH)
Submitted on behalf of the Decentralized Trials & Research Alliance (DTRA)
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Background

The NIH RFI invites stakeholders throughout the scientific research, advocacy, clinical practice, industry, patient and lay communities, including the general public, to comment on how DCTs may be designed to be more effective, efficient, and equitable to bring more interventions to all people, faster. DTRA is pleased to provide our feedback and constructive suggestions to the RFI below.

The Decentralized Trials and Research Alliance (DTRA) is a non-profit collaboration with over 100 member organizations working together to ease the global adoption of decentralized research methods. DTRA members represent bio-pharmaceutical companies, technology and service providers, site networks and research centers, advocacy groups, and government agencies.

DTRA workstreams have produced a number of valuable resources in this space which we encourage the NIH and other stakeholders to leverage as they consider the implementations of DCTs. Such examples include a glossary of DCT terms, best practices handbook, patient journey maps, and evidence of DCT impact. DTRA also remains actively engaged with interested parties who are seeking more information about decentralized clinical trials. For example, on January 23, 2023, DTRA hosted a Listening Session for the White House Office of Science and Technology Policy (OSTP) RFI on Clinical Research Infrastructure and Emergency Clinical Trials. This session included members of the DTRA community along with invited guests from OSTP, the Office of Science and Technology Policy, ONC, the Office of the National Coordinator for Health Information Technology, and other federal agencies participating in this RFI.

A recording of this listening session may be found at: https://bit.ly/DTRA-ONC-RFI

The listening session included three themes with insights from DTRA members including:

- How might decentralized research be used to enhance equitable participation in emergency clinical trials?
- How might regulatory flexibility help accelerate emergency clinical trials using decentralized methods?
- How might we develop a pilot or demonstration project to use decentralized research for emergency clinical trials in a 6-12 month timeframe?

A link to the letter submitted to OSTP may be found here. More broadly, DTRA welcomes the opportunity to share our membership's unique perspective and suggestions regarding federal initiatives to improve the decentralized trial research infrastructure.

As we modernize our clinical research enterprise to make it more patient-friendly, it will require reducing the exclusive reliance on hospitals and medical centers, and enabling broader access, including participants from underserved communities, to trials using decentralized approaches. Likewise, utilizing decentralized trials and research methodologies offers significant potential to improve access and diversity in clinical research. Our nation's hospitals and health systems will remain a cornerstone of our clinical research enterprise, but these institutions don't necessarily provide access to traditionally underserved populations. A national plan for a modern clinical trial ecosystem meant to also support diversity and inclusion must include the thoughtful use of decentralized research methods.

Clinical trial participation can be a burden and may disproportionately create access barriers which may be mitigated through decentralized methods. DTRA believes that NIH will serve as an invaluable partner in advancing the decentralized trial ecosystem in the United States. Specifically, through a combination of workforce development programs, community engagement, and partnering, we outline suggested research areas and next steps for the NIH to consider in response to this RFI.

Information Provided

Accordingly, we suggest the NIH consider the following actions to promote the development of a research-workforce adequately suited to conduct DCTs and engage with the relevant stakeholders as trusted partners in the process of advancing accessible research through decentralized trials.

Workforce development

- The future of clinical trials in the US is poised to leverage new tools such as cloud computing, AI, digital devices, etc. A workforce that is fluent in the use of these tools is therefore essential to enable smooth adoption of decentralization methods. Given the NIH's crucial role in training and upskilling our national research workforce, including the next generation of clinical investigators and the workforces that support clinical research, we believe this poses an opportunity for future focus and programming.[1]
- There are several nuances of decentralized clinical trial conduct that can differ for investigators compared to conventional clinical research. For example, central to the conduct of DCTs is the use of telemedicine and digital health technologies to assess patient outcomes.[2] The intersection of technology with clinical research may pose an adjustment or challenge for investigators who have not previously leveraged such platforms.[3] NIH should consider mechanisms to expand existing fellowship opportunities to provide training on decentralized clinical methods within the context of clinical trials. One example is through the Medical Research Scholars Program. NIH may also consider establishing new fellowship programs that would enable physician-scientists to gain familiarity and experience with DCT approaches.
- In addition to the creation of a NIH-sponsored fellowship on DCTs, we suggest the NIH partner with existing organizations and aligned initiatives in this space. For example, recently the National Minority Quality Forum (NMQF) announced the launch of the Alliance for Representative Clinical Trials (ARC) and its PI Institute, which trains community clinicians to be clinical trial principal investigators (PIs).[4] This, or other similar initiatives, provides a venue for the NIH to not only support the development of a diverse group of community clinicians in becoming principal investigators, but could also impart the skills needed to adequately conduct decentralized and technology-enabled clinical research.
- In conceiving and implementing new training opportunities, we encourage NIH to consider organizations that could serve as partners, like DTRA, in development of curriculum or facilitating informal training of this cohort.

[1] https://clinicalcenter.nih.gov/training/mrsp
[2] Framework for the Use of Digital Health Technologies in Drug and Biological Product Development https://www.fda.gov/media/166396/download
[3] https://researchtraining.nih.gov/infographics/physician-scientist
[4] https://foryourhealth.news/wp-content/uploads/2022/10/ARC-Press-Release-2022.pdf

Improving diversity of the workforce and clinical trial participants

- It is important to identify and develop a clinical research workforce with knowledge, skills, and abilities to engender diversity. Some considerations include:

    - Supporting scholarships, fellowships and traineeships to build a diverse clinical trial workforce.
    - Supporting sponsors partnering with institutions whose staff are diverse. For example, the NIH could encourage the use of diversity supplements specifically for studies leveraging decentralized approaches.[5]
    - Encouraging adoption of a diverse investigator and clinical trial navigator pool. More diverse investigators and navigators may result in a shared understanding between clinical trial participant and investigator, which allows for more open and honest communication and trust. A fully trained and informed investigator and navigator should be able to understand the social and/or cultural nuances of diverse communities and the patients within them.
    - Supporting the professional development, mentorship, and exposure programs for underrepresented populations of clinical researchers which are critical to fostering a diverse clinical research workforce.
    - A diverse workforce is a best-practice in addressing the broader issue of trust in the healthcare system, ultimately leading to better outcomes for all patients that are treated.[6]

Community engagement to expand our national clinical trial infrastructure

The NIH should play a central role in serving as a means to foster organic community engagement and input to the decentralized trial ecosystem. Some potential means to achieve this engagement include**:**

- Identifying the needs of participants, and paying particular attention to those who traditionally experience health disparities or are part of an underserved population, to participate in DCTs
    - Assess the needs of diverse patient communities up-front and seek input from them to align/change the study protocol accordingly.

[5] https://grants.nih.gov/grants/guide/pa-files/pa-20-222.html
[6]https://buildingtrust.org/wp-content/uploads/2021/06/20210602_NORC_ABIM_Foundation_Trust-in-Healthcare_Part-23.pdf

- Establishing knowledge and procedures to co-design studies with communities
    - NIH should convene workshops and roundtables with underrepresented and underserved communities to understand challenges faced by these communities for clinical trial participation.
    - These conversations should in turn lead to a set of actionable solutions, e.g. meaningful trial designs, which seek to investigate the outcomes that matter most to a diverse range of patients, [7] and should be shared with the wider clinical trial community.
- Create a standing advisory board to advise both the clinical research and patient community on these topics and suggested initiatives.
- NIH should leverage its clinical trial network to pilot decentralized approaches and evaluate their success in promoting diversity in clinical trials.
    - For example, the NIH could develop Key Performance Indicators (KPIs) for diversity in CTs and share with the broader community. We urge the NIH to work in collaboration with FDA and develop these KPIs that could be used by sponsors as means to assess how they are progressing in designing trials that promote diverse participation. Consider leveraging the draft KPIs developed by the DTRA Initiative to quantify impact, especially regarding participant diversity, geographic range, and patient experience.
    - More broadly, the NIH should encourage development of studies that investigate the linkage between trial decentralization, the reduction of clinical study barriers, and ultimately how these methods can promote/increase participant diversity.
- Encourage NIH sponsored/funded studies to adopt DCT approaches and other meaningful steps to increase a diverse trial participant population.
    - Within these studies, collect robust data that analyzes the impact of trial decentralization on participant diversity and share with broader stakeholders, including the FDA
- Leverage other workforce development initiatives (see above) to create deep community ties which can enable community-based participation in DCTs.
- Facilitate authentic, meaningful, and community-driven engagement (e.g., embedding clinical trials into community health care settings)
    - Gaining trust within communities of interest is vitally important to the success of clinical trials and it is important to take the time to understand the reputation of the sponsor and trial site within the community. Those involved in clinical trials should be mindful of building community

[7] https://www.rtihs.org/publications/advancing-equity-diversity-inclusion-and-belonging-patient-centered-drug-development

engagement into budgets and timelines, and engage the community throughout the trial process, not just during recruitment. Those responsible for clinical research should communicate success, improvement opportunities, and continue partnerships even in times when applicable trials are not being pursued.

- Community outreach activities can succeed by: providing mobile screening, leveraging trusted intermediaries/community connectors, education campaigns, leveraging census and disease prevalence information to understand location of potential participants as well as clinicians/investigators, ensuring patient facing vendors are diverse and/or have a strategy to reach diverse populations, and developing specific recruitment strategies for diverse populations within specific geographies/communities.
- NIH should leverage its extensive national clinical trial network to partner with reputable community-based organizations and make inroads into local, difficult to reach areas. By investing in community clinics, health centers etc., and improving their infrastructural capacity, NIH can help expand our national clinical trial network. In addition to core infrastructure investment, e.g. equipment, labs etc., encouraging improvements in workforce and technical capabilities of local health workers will enable these community centers to develop critical health care and clinical trial provider status. Allowing community-based health centers to participate in DCTs via pilot studies sponsored by NIH, will build confidence in the ability of these centers to become able partners in larger clinical trials and eventually partner with industry sponsors in registrational studies. NIH has a crucial role in supporting, encouraging, and developing this national need to meet our future clinical trial aspirations.

Partnerships and Collaborations

In a similar theme as the community engagement section above, we encourage the NIH to consider partnering with existing organizations in this space to promote NIH-led initiatives. Given the complexity of the topic, the wide range of interested stakeholders, and the variation of healthcare delivery across the United States, strong collaborations will be critical to any successful initiative. Potential areas for exploration include:

- Identifying partnerships and/or collaborations essential for DCTs to be successful (inclusive of government agencies, industry, non-profit organizations, academia, etc.)
- Developing partnerships and/or collaborations to enhance engagement with diverse and/or underserved participants for DCTs
    - Community engagement is crucial for successfully recruiting and working with diverse or underserved participants of clinical trials. When a trusted foundation is formed, an investigator can have a member of the community be the advocate and information provider. They can speak to the participants from a personal relationship perspective and serve as that crucial connection for the clinical trial participants and the sponsor. Therefore, building and nurturing these relationships is crucial for the long-term goal of improving clinical trial capacity.
    - NIH should expand its support of training community engagement specialists and look to recruiting members from underrepresented and underserved populations.
- Establishing meaningful and efficient integration of community health hospitals, pharmacies, and community providers for DCTs
    - QHCs, Rural Health Clinics, and Urban Indian Health Programs are located where the most diverse patient populations live and receive care. Additionally, the clinicians have long-standing relationships and trust with community members. Bringing research into the community removes a barrier to more diverse clinical trial participation.[8] Similar to the dynamic between Community-based Organizations (CBOs) and the communities they serve, strong trust can lead to better recruitment and retention rate when paired with greater ease of access to participation and return of results information. [9]
    - It is important that the research being done within a community's population benefits that community, beyond just the timeframe of the clinical trial.
    - Thus, long-term partnerships that have been well-established should continue to be supported, and in-fact, enriched, such that the strong foundation established can be built upon and extended to implement DCTs. As mentioned above, establishing pilot studies, improving

[8] Brandt HM, Young VM, Campbell DA, Choi SK, Seel JS, Friedman DB. Federally Qualified Health Centers' Capacity and Readiness for Research Collaborations: Implications for Clinical-Academic-Community Partnerships. Clin Transl Sci. 2015 Aug;8(4):391-3. doi: 10.1111/cts.12272. Epub 2015 May 11. PMID: 25962873; PMCID: PMC4553115.

[9] Shaibi, G.Q., Kullo, I.J., Singh, D.P. *et al.* Returning genomic results in a Federally Qualified Health Center: the intersection of precision medicine and social determinants of health. *Genet Med* **22**, 1552–1559 (2020). https://doi.org/10.1038/s41436-020-0806-5

workforce training, and listening to community partners to develop strong, sustainable clinical trial practices, will be essential to the success of DCTs.

Developing, Sharing and Implementing DCT Learnings and Best Practices

- As the largest public funder of clinical trials, NIH can provide a standing forum for creating a knowledge-sharing network. As DCTs embed themselves into the clinical research enterprise, we will learn more about their advantages and disadvantages. Each DCT study will provide new information and learnings about what tools, approaches and practices enable rather than disable these methods. Sharing these viewpoints, especially from the vantage point of the diverse spectrum of stakeholders in this space i.e. patients, caregivers, PIs, CT navigators, sponsors, vendors and others will be an invaluable resource for the community and one that NIH is uniquely positioned to provide.
- Building on these learnings, NIH can create a national repository of best practices that can be updated as the ecosystem evolves and adapts to DCT approaches. The best practices can and should be updated as a new cohort of PIs and other CT personnel is trained and enters the workforce. It should also reflect developments in technology and other tools e.g. teleconsults, remote monitoring digital tools; and how they can best be integrated in a fit-for-purpose manner to maximize ease of patient participation in clinical studies.

Next Steps

As stated in DTRA's mission, we seek to be a preeminent, cross-functional organization that unites organizations in promoting the global adoption of decentralized research methods. Given our diverse member base (ranging from CROs, patient groups, pharma and biotechnology sponsors, technology and service providers, etc) and existing resources, we encourage the NIH to reach out for assistance in any future initiatives where we may be of service or a trusted partner.

DTRA kindly requests that the NIH reach out to us at the contact information provided below if they would like to discuss any of the suggested topics or research areas suggested in this letter in greater detail with us.

Kind regards,

DTRA Leadership and Regulatory Affairs Council

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