Submitted electronically

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Dr. Arati Prabhakar
Director
Office of Science and Technology Policy
The White House
Washington, DC 20502

Re: Request for Information on Clinical Research Infrastructure and Emergency Clinical Trials - Federal Register Document Citation 87-FR-64821

Dear Dr. Prabhakar,

FasterCures is pleased to respond to your Request for Information on clinical research infrastructure and emergency clinical trials. FasterCures strongly believes that it is critical in this moment to make real change and transform the way that local institutions conduct clinical research so that it better represents the diverse communities that comprise the American population. Because of this, we are gratified that this concept is being seriously considered.

As you may know, FasterCures, a center of the Milken Institute, is driven by a singular goal: to save lives by speeding scientific advancements to all patients. With an independent voice, FasterCures is working to build a system that is effective, efficient, and driven by a clear vision: working with our partners to build a patient-centric system where science is accelerated, unnecessary barriers are overcome, and lifesaving and life-enhancing treatments get to those who need them as rapidly and as safely as possible.

Since 2020, FasterCures has engaged in activities to further understand changes to clinical research in response to the COVID-19 pandemic and the growing impetus to prioritize community needs and access to clinical research. As we are all acutely aware, the COVID-19 Public Health Emergency (PHE) revealed the heavy price of a lack of a comprehensive community-based research system. The pandemic also saw the development of many best practices from organizations, networks, and partnerships that are now leading the way in community-based clinical research. These advances offer many ideas that could contribute to a government-led, coordinated clinical trials system to respond to outbreaks and emergencies. Below we explore ways to expand upon those existing best practices as well as identify common infrastructure gaps and potential solutions to strengthen community-based research.

Governance for Emergency Clinical Trials Response

Descriptions of models that could be used to establish a U.S.-level governance structure for emergency clinical trials

An essential next step to establish a US-level governance structure for emergency clinical trials is to **coordinate government-funded networks and sites**. The federal government currently supports multiple trial networks and sites across many federal agencies that have reach into diverse communities and populations. The National Institutes of Health (NIH), the Department of Defense (DoD), the Veterans Health Administration, the Health Resources and Services Administration's (HRSA) Health Center Program, and the Centers for Medicare and Medicaid Services' (CMS) Minority Research Grant Program all fund networks.

A federated approach linking other private health-care systems and networks and establishing a better view across the existing infrastructure is needed. The NIH's Clinical Trial Capacity Inventory and geotracking tool—established during the pandemic—should be maintained and expanded to involve other government-funded health systems, such as the Department of Veterans Affairs (VA), the DoD, and the Federally Qualified Health Centers. Additionally, data definitions and data collection tools need to be aligned to create one common approach among the NIH, Food and Drug Administration (FDA), CMS, HRSA, and other relevant agencies. This alignment will help address the current landscape of differing expectations, difficult reporting, and challenging data aggregation.

Priority setting is another essential aspect of a US-level governance structure for emergency clinical trials. A national authority should be tasked with identifying useful networks, policies, and resources utilized during the COVID-19 PHE and enable their use against varying public health priorities without the need to declare a formal emergency.

A cross-agency working group guided by representatives of diverse communities and researchers should be convened to establish a plan to train and keep community-based research sites engaged. Researchers and companies supporting commercial clinical trial sites should be included in this group to maximize the potential reach into communities and support of community-based research sites. This prioritization must also be informed by increasing and improving data monitoring and advancing analytics to identify patterns of disease in communities. This may lead to other threats, such as cancer, opioids, or suicide, being deemed a PHE and deploying existing infrastructure and resources to address those problems similarly to the COVID-19 pandemic. Finally, Congress should ensure that agencies are directing funding toward such research priorities.

Procedures whereby the U.S. Government, together with external stakeholders, could oversee the development of clinical trial protocols and, where appropriate, the selection of investigational agents

The COVID-19 pandemic saw an unprecedented scale and speed of collaboration between public and private entities to tackle challenges presented by the PHE. The federal government partnered with companies and research institutions to identify products in the pipeline that could address the new threat. A prime example is the US National Institute of Allergy and Infectious Diseases partnering with Moderna to develop a vaccine, a longtime collaboration that bore fruit in a critical moment.

Another key example is the Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) public-private partnership. This partnership brought together US federal health agencies, the European Medicines Agency, and several biopharma companies, academic institutions, and philanthropies to develop a research strategy that would prioritize and quicken the development of treatments and vaccines. By bringing together all these stakeholders, ACTIV has improved the sharing of preclinical resources, set up master protocol trials to test candidates, and maximized existing trial infrastructure. The US government should document, characterize, and quantify the benefits of these partnerships as well as continue to explore and deepen its collaborations with external stakeholders. Existing partnerships such as ACTIV should be directed toward other high-priority, unmet health needs, and Congress should invest in the important platforms and tools created through pandemic-era public-private partnerships.

Best practices, including "quality by design" principles, for designing trials so that they capture the data needed without unnecessary complexity that can complicate execution
Many administrative and regulatory protocols burden clinical trial sites and investigators, creating unnecessary complexity and slowing the research and discovery process. These include contracting, the Institutional Review Board process, consent requirements, and more. Small and less experienced research entities are not the only groups bogged down by these complexities; more experienced government research agencies, such as the VA, face slow execution of interagency agreements, even in the face of a PHE.

Other complicating factors include differing state and institutional requirements for research conduct and administration. The COVID-19 Evidence Accelerator, an initiative launched by the Reagan-Udall Foundation for the FDA in partnership with Friends of Cancer Research, provides an opportunity for organizations to work through challenges such as real-world data (RWD) standardization, interoperability, and methods. This initiative should remain active as a way for stakeholders to advance RWD/real-world evidence (RWE) and address data collection issues.

Although randomized controlled trials have long been considered the "gold standard" in product evaluation and approval, recent years have exposed their limitations. Those limitations include accurately capturing the likely performance of treatment approaches in actual practice, and the associated complexities and requirements have led to a wall between the systems of clinical research and clinical care when it comes to data, personnel, and processes, contributing to higher costs and longer timeframes. To solve some of these pressing challenges, the federal government must support, expand, and link clinical trial networks and move toward pragmatic trials to quickly generate RWD/RWE. This includes improved methods for collecting data that are "lightweight" for clinicians and take place where patients are regularly receiving their care.

This support also includes running larger, simpler trials and maintaining and building upon COVID-19 trial infrastructure, such as platform trials and networks, to incentivize research on topics of high unmet need. These trials must be interoperable and readily able to link in networks of networks or pivot rapidly to areas in urgent need of greater capacity. These pragmatic trials may not collect all possible data, but, especially when operating complementary to more detailed, costly studies, will provide important, and otherwise unknown, findings.

Best practices for designing trials that can enroll vulnerable populations, such as the pediatric population, as needed in particular circumstances

Best practices for trial design specifically to include vulnerable populations can be pulled from the NIH's Community Engagement Alliance (CEAL) and COVID-19 Prevention Network (CoVPN). During the pandemic, CEAL leveraged relationships formed and lessons learned from the All of Us Research Program to engage communities that were most impacted. The initiative successfully reduced vaccine hesitancy, improved vaccine uptake, and increased participation of racial and ethnic minority populations in COVID-19 clinical trials**.**

CoVPN was created on the foundation of the HIV trials networks that have a strong history of engaging local communities. The program helped enroll in clinical trials for COVID-19 medical countermeasures people with underlying medical conditions, people with greater chances of exposure at their jobs, and people from racial and ethnic groups disproportionately impacted by the pandemic. CoVPN also successfully improved the process of designing, implementing, and analyzing vaccine trials; streamlining the development of protocols maintaining input from diverse stakeholders; and setting new statistical standards for the field. These two initiatives demonstrated the importance of continuous engagement with vulnerable communities to foster trust during the clinical trial process.

Additional best practices include bringing patient advocates and underrepresented community members into the trial design process as co-designers to ensure the research outcomes align with a broader impact and benefit. By developing relationships with community leaders and local health centers, academic institutions and principal investigators can address the barriers that limit patients' participation in trials. Finally, developing inclusive patient and research navigation programs created by community health workers, lay health workers, and health educators can help support capacity building, outreach, cultural competency, and health literacy in clinical trials.

Identifying and Incentivizing Research Institutions and Networks; Building Diversity and Equity

Community outreach

Patients bring unique expertise and knowledge to the R&D process due to lived experience, and engaging them into the decision-making processes in the earliest stages would prove beneficial. Community-based participatory research is a growing discipline, and utilizing community

outreach to engage diverse populations in research is essential to developing treatments and cures of value to all communities. It is essential to focus on community engagement in the early stages of the R&D process to obtain feedback on protocol design, subject eligibility/ineligibility criteria, and outcome measures. As opposed to viewing patients as subjects in research, this approach holds deep respect and value for their contributions and treats patients as participants in the research process.

Community outreach opportunities are numerous in historically underrepresented communities, especially among community-based organizations such as the National Black Church Initiative, Historically Black Colleges and Universities, and Minority Serving Institutions, and policy organizations, such as the National Minority Quality Forum. The first and most important step to community outreach, however, is building trust with communities. This process is long overdue and will take time and prioritization. As was the case during the COVID-19 pandemic, successful recruitment in minority communities includes direct engagement and physical outreach to target populations. A successful community outreach campaign must also address hesitancies, mistrust, and fear at all levels in the clinical trial process in a sincere and authentic manner.

Non-traditional workers, such as community health workers or health educators, have a significant role in supporting these community outreach programs. This broadening of the workforce can ensure communities are consistently and meaningfully represented in a clinical trials network and improve its overall reach and preparedness. Such a critical workforce needs predictable funding, and sustainable payment and reimbursement models for this type of workforce are needed.

Use of decentralized clinical trial (DCT) design elements and technological innovations that allow remote participation

A central way to involve diverse populations in clinical trials is through the use of large and simple trial designs. Decentralized clinical trials became a standard during the pandemic and will likely become a mainstay as it allows researchers to meet patients where they are. An estimated 70 percent of potential trial participants live more than two hours away from a trial site.[1] Decentralization creates opportunities for trials to have a much broader reach. Remote and digital tools are essential to decentralizing trials and engaging underserved populations. During the pandemic, the FDA allowed many clinical trials to utilize decentralized and remote approaches such as remote check-in with participants (by phone or video), shipment of study products to patients' homes, and the use of mobile devices.

The use of decentralized trials and remote tools during the pandemic relied heavily on flexibilities put in place during the PHE. Actions need to be taken to preserve that progress and the use of those tools to continue their valuable contribution to clinical trials. Hindrances to their continued use include policy barriers such as cross-state licensing restrictions on

[1] Milken Institute, 2022. Building Community-Based Infrastructure for Inclusive Research: Lessons from the Pandemic for Federal Action.

physicians, as well as inertia and risk aversion by sponsors. However, researchers must be careful not to disenfranchise underserved communities through decentralized trials and remote tools, despite their usefulness. Although these methods aim to engage more communities, they may contribute to further barriers for patients who lack the technology required to participate.

Building on existing programs that target diversity in clinical research, including initiatives within research institutions and public-private collaborations

Despite an NIH mandate in 1993 to increase the inclusion of more racial and minority participants in federally funded research, little progress has been made. Early in the pandemic, most states did not have mechanisms for reporting data on race/ethnicity with regard to COVID-19 cases or deaths. Now the majority of states are reporting these data, but they remain incomplete.

Research institutions and public-private collaborations have made strides in addressing diversity in clinical research and can serve as examples to build upon. Many organizations have invested in new positions to address diversity, equity, and inclusion. Some are announcing specific investment plans, such as one that is making a $300 million investment to improve diversity across their own programs, including a five-year plan focused on hiring practices, clinical trial recruitment, raising disease awareness, and access to care. Others have partnered directly with minority-serving medical schools to better understand and address health inequities in minority communities using fit-for-purpose data resources. The NIH has initiated a program working with community partners in its network to share public health information and encourage participation in COVID-19 therapeutic and vaccine trials.

Several elements came together during the first stages of response to COVID-19 that increased engagement of diverse sites and patients, including:

- Identification of existing government-funded research infrastructure and community-engaged researchers to participate in initiatives such as CEAL and CoVPN;
- Federal action by agencies, including the FDA and CMS, to enable and encourage the use of more decentralized and remote methods and tools to conduct trials during the pandemic (many of which will explicitly be terminated at the end of the PHE);
- Federal leadership in directing sponsors of COVID-19 vaccine trials to achieve greater diversity in the study population; and
- Leveraging an arm of the RADx program to accelerate innovation in COVID-19 diagnostics to focus specifically on understanding and addressing the needs of underserved populations.

Despite individual organization plans to institute change and facilitate more diverse clinical trials, there is a need for more cohesive plans and leadership to set priorities and hold people and groups accountable and encourage systems change. Government and philanthropy can spur commitments, collect data, and issue report cards on areas of success or in need of improvement.

Leveraging the networks and community access of retail chains, including retail pharmacy chains

Supporting community research requires the development of new pathways and ways to engage people at all stages of the research pipeline. Examples include involving pharmacists, PhDs, and research coordinators. The longstanding MD-centric clinical trial investigator model needs to be rethought, and more "boots on the ground" actors, such as pharmacists and clinical hospitalists, need to be incorporated into clinical trial functions. Additionally, there is a need for greater infrastructure and support for pharmacy, specifically for inpatient clinical trials. Investigational pharmacy is a unique field, and many trial sites do not have support of this kind. To engage partners such as retail pharmacies, local imaging and diagnostics labs, and mobile nurses, it is imperative to clarify and modernize regulations.

Some progress has been made in this area, with large pharmacy chains and independent community pharmacies alike serving as instrumental components in providing access and engaging historically underrepresented groups in our country's pandemic response.[2] Large pharmacy chains and retailers are also now entering the clinical research space.[3] These examples are promising indicators of the potential for pharmacies to improve access to care and research for all populations.

"Warm Base" Research

Disease areas that should be targeted in protocols for "warm base" clinical research

"Warm base" clinical research should address conditions that are disproportionately experienced by underserved and underrepresented populations. Black, Latinx, and Native Americans are more likely than White Americans to suffer from chronic conditions such as diabetes, heart disease, and asthma. Rural populations face many challenges accessing clinical trials and have long been underrepresented in research due to the lack of nearby locations conducting research and the limited involvement of community providers. Setting up clinical research infrastructure in community-based settings presents a unique opportunity to engage more diverse populations in research.

Decisions about what disease areas and research to prioritize for such a "warm base" network are complex and have far-reaching implications for many people and communities. A cross-stakeholder **Grand Challenges Working Group—**made up of representatives from across the Department of Health and Human Services and other federal-supported biomedical research agencies as well as non-federal representatives of patients, industry, public health experts, and others as needed—could prioritize research challenges to support via this infrastructure. The working group could consider high public health needs, high health-care costs, and low innovation activity as criteria for prioritizing disease categories.

[2] One example of this analysis can be found https://www.sciencedirect.com/science/article/pii/S1544319122002795

[3] See, for example: https://www.reuters.com/business/healthcare-pharmaceuticals/walmart-compete-with-walgreens-cvs-recruiting-clinical-trial-subjects-2022-10-11/

How "warm base" research could best be implemented to provide training to sites that are inexperienced with clinical trial research, and to create a basic level of surge capacity at the staff level for emergency clinical trial research and "warm base" research supported as a public-private partnership

An essential component for "warm base" research is consistent funding to develop new research infrastructure, as well as maintain existing infrastructure and personnel. Additionally, preexisting relationships may provide the greatest path to establish stronger research opportunities in community-based settings and move forward quickly during a PHE. This may include involvement from academic or commercial centers to mentor and support community health care facilities that are frequently overburdened or have limited resources for research. Successful networks and partnerships that largely led the pandemic response, including ACTIV and CoVPN, had strong foundations of existing clinical trial infrastructure and stressed the importance of clinical trial networks that can rapidly engage to support the coordination of research during a PHE.

In addition to mentorship and partnership, there are opportunities to creatively support community sites such that they are prepared and enthusiastic to participate in research. A growing commercial sector is working to address gaps felt by community-based sites, a layer between traditional contract-research organizations and the sites themselves. Companies in these sectors are rolling out platforms that help community hospitals anticipate upcoming research and stabilize their research pipelines or working to embed clinical research personnel in community hospitals as a type of core service akin to onsite clinical labs managed by external companies. These possibilities suggest a path to enable consistent and seamless integration of community sites into a larger research network.

Thank you again for the opportunity to offer our input. We are happy to discuss these ideas further and help OSTP advance any ideas shared in this response.

Sincerely,

Esther Krofah
Executive Vice President of Health
Executive Director, FasterCures and Center for Public Health
Milken Institute