



January 27, 2023

Dr. Arati Prabhakar
Director of the Office of Science and Technology Policy
Eisenhower Executive Office Building 725 17th Street NW
Washington, D.C., 20500

Submitted online via emergencyclinicaltrials@ostp.eop.gov

Dear Dr. Prabhakar,

The Infectious Diseases Society of America (IDSA) and the HIV Medicine Association (HIVMA) appreciate the opportunity to provide feedback to the Office of Science and Technology Policy (OSTP) on clinical research infrastructure and emergency clinical trials.

IDSA and HIVMA represent more than 12,000 infectious disease physicians, scientists, public health practitioners and other health care professionals specializing in infectious diseases. IDSA members focus on the investigation, diagnosis, prevention and treatment of infectious diseases, and are involved in both patient care and clinical research. We are pleased to offer recommendations to OSTP that we believe will help strengthen the clinical research infrastructure and increase participation in clinical trial research, including emergency clinical trials.

Governance for emergency clinical trials response

COVID-19 has demonstrated the importance of establishing strong protocols and infrastructure for emergency clinical trials well in advance of an emergency. Federal interagency collaboration is critical to facilitate clinical trials in emergency situations. **To achieve this, it's important to develop formal collaborations and partnerships between agencies, including OSTP, the Food and Drug Administration (FDA), the National Institutes of Health (NIH), the Centers for Disease Control and Prevention (CDC), the Agency for Healthcare Research and Quality (AHRQ), the clinical research community and the health care provider community to strengthen and improve the clinical trial infrastructure, expand funding mechanisms and develop better analytical and predictive tools.** Additional federal efforts should re-evaluate the US Food and Drug Administration's emergency use authorization process for therapeutics and the interplay between expanding access prior to drug approval with the need for sufficient clinical trial data from a diverse patient population to support approval. IDSA and HIVMA recommend adopting policies that align with those applied to the COVID-19 vaccine authorization and approval process, such as publicly communicating data for EUA and for

subsequent approval in addition to publicly releasing clinical data before authorization and prior to subsequent approval.

IDSAs and HIVMA recommend that the FDA:

- Establish and publicly communicate benchmarks for vaccines, diagnostics and therapeutics for pathogens causing an emergency to receive an EUA, as the agency did for COVID-19 vaccines, and requirements for receiving licensure after an EUA is granted
- Require the public release of clinical trial data both before a therapy receives an EUA and before it receives subsequent routine approval
- Require the sponsor to have a plan for completing and publishing data from definitive clinical trials post-EUA and to articulate a plan for pursuing approval or licensure once granted an EUA.
- Require the sponsor to include plans for recruiting children, individuals who are pregnant and breastfeeding, and individuals who are immunocompromised, including people with HIV, in addition to populations who are typically disproportionately impacted by infectious diseases and emergencies, including Black, Indigenous and other people of color, Latinx communities and other underserved populations.
- For products available through an EUA, collaborate with manufacturers, health care facilities, private and federal payers and other federal agencies to collect additional evidence to monitor safety and efficacy.

Federally supported infrastructure should provide an integrated framework to link individuals diagnosed with emerging infectious diseases to appropriate trials and encourage large-scale collaboration across many different types of facilities, including community hospitals and community health centers. Such an approach will increase the reach of trials of promising therapeutics to populations that are typically underrepresented in studies, including African American/Black, Latinx and Indigenous populations, children and adolescents, and adults aged 75 and older. This goal is best accomplished by performing studies on larger, more diverse populations, with a focus on settings outside the traditional urban tertiary care academic centers. Increasing access to clinical trials in rural areas should also be considered through this approach. These considerations increase access to treatments for patients and the ability to gather data across a broader range of participants more rapidly.

In addition to clear communication across federal agencies, communication with the clinical research community should remain a priority. When communicating the decision to begin emergency clinical research, institutions should receive clear, unified guidance from the federal government that outlines next steps in carrying out emergency clinical trial research.

Additionally, the federal government should support the expansion of pragmatic trials networks (e.g., FDA Reagan Udall COVID-19 Diagnostics Evidence Accelerator, Sentinel, PCORnet, NIH Collaboratory), including networks that enroll pediatric populations, to

rapidly generate real world data and inform the development of therapies and diagnostics in the case of a public health emergency (PHE). In the development of these trials, federal agencies should increase efforts to engage frontline physicians and community clinicians in clinical trial research and development, especially in ongoing clinical trial infrastructure. Specifically, the federal government should involve from trial inception clinicians, researchers and community members representing the population being studied or who have lived experience of the health issue. Frontline physicians and other community clinicians can offer insight to trial planning. As active members and trusted figures in trial site communities, these individuals help build transparency and public trust in addition to improving clinical trial design. Additionally, they help expand potential trial participant pools, which can improve trial diversity. [Studies](#) **have shown that involving clinical researchers can ease the translation of research results into clinical care.** We also can learn from the success of the United Kingdom and other countries in setting up rapid pragmatic trials during the COVID-19 pandemic.

Designating funding in federally funded clinical trials to support training and logistical support for community and frontline physicians can incentivize involvement from these groups. When developing emergency trials in response to emerging infectious diseases, it is also crucial to involve ID physicians working in healthcare settings when possible, as well as pediatric ID physicians to better engage pediatric populations.

A successful effort to build clinical trials infrastructure for public health emergencies must be coupled with an effort to strengthen the infectious diseases (ID) workforce, including ID physicians and ID physician-scientists, who are often called upon to lead clinical trials and enroll patients, as we saw during COVID-19 and mpox. Unfortunately, the ID workforce is struggling to recruit, as only 56% of ID fellowship training programs filled their slots in 2022. Persistent recruitment challenges and workforce shortages are due in part to financial issues. ID is one of the lowest paid medical specialties, and high medical student debt is a key factor that drives many to higher paid specialties. IDSA and HIVMA recommend:

- Improve reimbursement for non-procedural care.
- Establish a new mechanism to ensure that clinicians are able to be reimbursed for additional work performed during an emergency, including clinical trial enrollment.
- Fund and implement the new BIO Preparedness Workforce Pilot Program to provide loan repayment for ID clinicians working in underserved areas.
- Increase NIAID funding and strengthen NIAID policies to support early career investigators, mentorship and transitions from training to faculty, and opportunities for community-based physicians to participate in clinical research.
- Additional recommendations to strengthen the ID physician-scientist workforce are available [here](#).

Identifying and incentivizing research institutions and networks; building diversity and equity

Diversity, equity, inclusion and accessibility (DEIA) should be at the forefront of considerations in clinical trial design at the federal level. **Especially during a PHE, it is critical that medical**

countermeasures and clinical guidance are tailored to diverse populations, for example, considering differences in age, sex assigned at birth, gender identity, ability, racial and ethnic identity and sexual orientation. In funding and designing clinical trials, research should prioritize including diverse participants from a variety of ethnic, racial, gender identity, socioeconomic, geographic and age backgrounds to improve representation in clinical research. African American/Black, Latinx and Indigenous populations and adults aged 75 and older [often have markedly low participation in clinical trials](#), which contributes to health inequities and skewed data and limits applicability of research findings. This imbalance in clinical research inclusion also leads to limitations in applying clinical data to treatment options. Additionally, it is important to increase inclusion of key populations at higher risk for serious illness, such as pregnant and immunocompromised people in clinical research trials, especially in vaccine trials.

To address the lack of diversity and equity in clinical trials, it is important to fund research that looks for the root causes of the issue. **Federal agencies should prioritize and support studies focusing on critical areas in clinical trial research, including research on the effectiveness of recruitment strategies for clinical trial volunteers, factors and barriers that may prevent these strategies from reaching underrepresented populations and the effectiveness of incentives used in clinical trial recruitment, such as paying participants who sign up or reimbursing the time spent on clinical trial activities.** Research into these areas can strengthen and improve the overall effectiveness of clinical trial infrastructure and DEIA efforts.

To increase diversity and equity in clinical trials, it is also essential to develop, strengthen and sustain relationships with underrepresented communities through increased outreach. **This can be accomplished through research teams developing and sustaining partnerships with community-based organizations that have established trust in underrepresented communities.** These collaborations also are also critical to increase participation from underrepresented populations. Sustained work with community groups will require additional funding and long-term investments in research. Community partnerships are important to increase the visibility of research in underrepresented communities, support research literacy and aid in outreach and recruitment of clinical trial participants.

Faith based organizations and institutions in these communities can also be effective partners in disseminating and communicating information to diverse populations and facilitating outreach for clinical trials recruitment in underrepresented communities. When working with underrepresented communities in clinical trials, communication is critical to consider. A [recent study in Trials](#) identified that language and communication remain two of the largest barriers to clinical trial participation. Requiring clinical trial research leaders to draft strategies for investigators and researchers to communicate with community leaders to spread information about the trial can help increase participation. Communication strategies should be transparent, and focus on trial procedure, importance of trial participation and impacts and side effects when applicable. Transparency in these communications builds trust with the community and the populations researchers seek to work with. Any communication materials used in trials should be written at an appropriate reading level and available in multiple languages, particularly those commonly spoken in affected communities. All written materials used in the study, especially consent forms, should also be available in multiple languages to encourage

accessibility for participants. Additionally, ensuring translators are readily available for participants is important to increase inclusion and demonstrate a respect for participants and stronger cultural competency in clinical trial design.

Diversity in clinical trial staff is also critical. [Research](#) from Tufts found that clinical trial sites with higher racial and ethnic diversity among staff members saw higher enrollment of patients from minority groups. These sites were also more likely to report that they viewed diversity as a critical part of operating procedures and research success. This prioritization of diversity can support more favorable views of researchers and trials by the communities that researchers seek to work with and is critical in furthering DEIA in clinical trial research.

Trial design should address and mitigate barriers for patients from underrepresented groups to participate. For instance, distance to the clinical trial site and travel cost is often a limitation. To address this barrier, clinical trial design should prioritize carrying out trials and procedures at facilities in areas easily accessible to underrepresented populations. Providing transport or ensuring trial locations are near public transit locations can alleviate transport concerns.

Telehealth and mobile vans also should be fully leveraged to extend clinical trial participation to rural communities and to urban health care deserts with limited or no clinical or clinical trial sites.

Additionally, co-locating sites that can perform rapid diagnostic testing with treatment sites, especially in clinical trials occurring during public health emergencies, can facilitate enrollment into clinical trials. This solution reduces inequities related to access (such as transportation) that occur when testing and treatment are separated. Working within the community can also alleviate participant concerns about accessing trial sites. Identifying local clinics and medical centers that can partner with the government or with academic medical centers carrying out clinical trials can greatly increase the proportion of participants from underrepresented groups.

Beyond the incentives identified in the RFI, introducing referral bonuses to trial participants who recruit new participants would be beneficial in increasing overall participation. Other ways to increase participation could include connecting research sites with childcare options, providing opportunities to participate in clinical trials on weekends and/or evenings after 5 PM and compensating participants for travel expenses.

“Warm base” research

Maintaining a “warm base” for clinical trials can help strengthen overall efforts at participant engagement and provide infrastructure. The NIH supported AIDS Clinical Trials Group, HIV Vaccines Trials Network and ACTIV clinical trials demonstrated during the COVID-19 pandemic and the mpox outbreak the value and importance of maintaining clinical trial infrastructure, including researchers and scientists, that can quickly pivot as new infectious diseases threats emerge. Supporting well established clinical trial networks that can be mobilized quickly in the event of a PHE is critical to effective research. [Studies](#) show that the mobilization of these existing networks allowed cross-study comparisons that dramatically increased the

speed of review and approvals of COVID-19 vaccinations. However, these efforts should be in place well before emergency trials are necessary. **Warm base research partnerships with communities over long periods of time, as exemplified with HIV research mobilized for COVID-19 trials, builds on established trust with patient groups, and can increase overall inclusion of patients from diverse backgrounds in emergency clinical trials.**

Additionally, federal efforts can leverage private-public partnerships with relevant stakeholders to ensure sustained funding and resources to maintain “warm bases” for clinical trials. **These models should engage diverse, underrepresented populations and utilize community engagement strategies similar to those listed above. Engaging community and frontline clinicians in these efforts can help maintain these “warm bases” through active community outreach.**

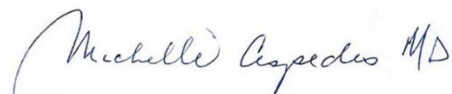
“Warm base” research can be incredibly useful in infectious diseases clinical trials. **Emerging infectious diseases threats require infrastructure and patient populations that can be rapidly leveraged to develop an understanding of a possible unknown pathogen and methods to prevent and treat it.** Funding “warm base” research on existing infectious diseases creates this infrastructure. For example, [studies](#) have outlined how the US National Institute of Allergy and Infectious Diseases (NIAID) supported collaborative government to government research in countries like Mexico and Indonesia that focused on different infectious diseases such as acute febrile illness and respiratory diseases. When COVID cases surged in 2020, these clinical trial studies were able to be rapidly repurposed to COVID testing and study. Similar efforts in the US can leverage research on endemic infectious diseases, and then be rapidly repurposed to study future emerging infectious diseases. Ongoing research and clinical trials on infectious diseases such as COVID-19 or influenza can then be utilized to rapidly study and conduct emergency clinical trials for emerging respiratory viruses.

IDSA appreciates the opportunity to comment on improving clinical trial infrastructure and emergency clinical trials. If you have questions about these comments or would like to connect, please contact Eli Briggs, Director of Public Policy, at ebriggs@idsociety.org or Andrea Weddle, Executive Director of the HIV Medicine Association, at aweddle@hivma.org.

Sincerely,



Carlos Del Rio, MD, FIDSA
President, IDSA



Michelle Cespedes, MD, MS
Chair, HIV Medicine Association