January 19, 2023

Dr. Arati Prabhakar
Director
Office of Science and Technology Policy
1650 Pennsylvania Avenue NW, Washington, DC 20502

RE: 87 FR 64821 | Request for Information; Clinical Research Infrastructure and Emergency Clinical Trials

Dear Dr. Prabhakar:

The Digital Medicine Society (DiMe) appreciates the opportunity to provide input in response to the joint request for information made by the Office of Science and Technology Policy (OSTP) and the Office of the National Coordinator for Health Information Technology (ONC) on the development of a scaled and coordinated clinical research infrastructure that better supports the nation's capacity to address future public health emergencies. The input provided in this document pertains to the unique opportunity for digital innovation to support the development of a more nimble and distributed emergency trials infrastructure and to increase the volume and diversity of trial sites, providers, and patients able to participate in research to address acute data needs.

DiMe is a global non-profit that partners with experts from across the technology, health care, and public sectors to conduct field-leading research and develop pre-competitive resources that accelerate the ethical, effective, equitable, and safe use of digital medical products. DiMe's portfolio spans efforts in digital measures, regulatory science, and healthcare and public health, including programming aimed at enhancing the evidence generation capacity of the clinical trials enterprise with digital medical products and increasing diversity, equity, and inclusion in digital clinical trials. Through this programming, DiMe has identified the unique capacity of digital medical technologies for supporting emergency evidence generation across a set of several basic and advanced dimensions–this is the focus of the input provided in our response.

DiMe supports both the OSTP's establishment of a Pandemic Innovation Task Force and the White House's establishment of the Steering Committee for Pandemic Innovation to address gaps in innovation and pandemic preparedness and to identify priority areas for investment. Further, DiMe applauds the work of ONC on furthering the adoption of common standards for data interoperability and exchange in research

as well as its important work on the certification of health information technologies so that they meet appropriate technical, functional, and security specifications.

DiMe also applauds the emphasis on the role of digital medical products, such as wearables, connected sensing products, biometric monitoring technologies, and more for real-time monitoring of disease and other important pandemic preparedness and response measures in the National Biodefense Strategy. This work, alongside other public and private sector efforts, will contribute to the future ability of the federal government and clinical trials enterprise to address key issues in clinical trial design and conduct that prevented an effective national response to the COVID-19 public health emergency.

Key challenges in the nation's response to the COVID-19 pandemic included issues in:

1. Activating clinical trial sites quickly enough to keep pace with rolling surges in COVID-19 rates across the country
2. Recruiting and enrolling a sufficient volume and diversity of participants in COVID-19 research
3. Providing resources to equitably address the trial participation needs for underserved communities
4. Aiding health care providers in carving out time to collect data on investigational medical products during the provision of emergency care
5. Comparing the results of multiple ongoing trials because of discrepancies in clinical outcome measures and standards for data collection
6. Collecting and leveraging real world data to inform real time decision making and an efficient public health response

Such challenges can be disintermediated, in part, through the equitable and effective implementation of digital medical technologies to support patient screening, trial enrollment, clinical data collection, and real world monitoring for product safety and effectiveness. Effective implementation of evidence-based and trustworthy digital medical products can improve our ability to:

1. Reimagine trial sites, automate data collection, decrease costs, and integrate research with care to streamline workflows and increase efficiencies
2. Decentralize research, expand trial access, and increase representative enrollment
3. Ensure efficient trial matching and surge trial enrollment
4. Leverage data collected in real world care and life settings to inform decision making

1. **Reimagine trial sites, automate data collection, decrease costs, and integrate research with care to streamline workflows and increase efficiencies**

The ability to automate and integrate aspects of clinical research with routine and emergency care delivery will be critical to improving the evidence generation capacity and representative nature of the emergency clinical trials. Federal investment in data collection infrastructure (i.e. platforms and standards) and support for the adoption of turn-key clinical trial management software that allows for the automatic transfer of patient health record data to fields in an electronic data capture system will be especially supportive of research that fits in with routine and emergency care delivery. The implementation of such software can simplify trial participation, making it more feasible for health systems and providers who don't typically participate in clinical research to be included in an emergency clinical trials network. This emergency trials network, or "warm base" that is activated, or can more quickly activate through the expedited implementation of turn-key clinical trial management software, to address priority research questions with a targeted investment in data collection infrastructure can provide trial access to patients underrepresented in research. The enrollment of such patients in emergency clinical trials can improve trial generalizability and expedite trial completion, via a larger and more representative sample of patients enrolled, and can produce information about treatment efficacy across subpopulations of interest.

To enhance the emergency clinical trials infrastructure, federal programing should consider the development of appropriate incentives for research participation, provide health system level support for technology adoption, and plan for workforce preparedness with systematic and industry-aligned training, standards, and vetting to ensure consistent quality in data collection. This will allow for trials that are quickly and sufficiently powered to produce evidence about treatment efficacy across a generalizable sample of the US population. Federal efforts should also continue to promote common Health Level 7 (HL7) Fast Healthcare Interoperability Resources (FHIR), to ensure that data automatically captured by this software meets consensus-based standards for data integration (e.g. Sensor Data Integration), interoperability, and exchange, expediting the generation of high-quality evidence to meet emergency information needs.

2. **Decentralize research, expand trial access, and increase representative enrollment**

Digital research platforms that enable telehealth visits, simplified electronic consent, and remote data collection can extend clinical trial access to a larger and more diverse group of patients. This offers an expedited and accessible pathway to higher

quality, more generalizable insights into treatment effects across subgroups representative of the nation's population. Such platforms can also reduce the administrative burden of participation in research, precluding the need to navigate complex consent and data collection processes as well as the need to travel for research visits.

Executive branch sponsors of research should consider how to effectively leverage digital research platforms for remote data acquisition to make it easier to enroll harder to reach patients and supplement the capacity of site-based data collection during future public health emergencies. This approach may be especially helpful during public health emergencies where isolation is essential to reduce disease transmission and where health systems are too overwhelmed with the care of acutely ill patients to devote resources to data collection in the clinic.

3. Ensure efficient trial matching and increase trial enrollment

Artificial Intelligence (AI)/Machine Learning (ML)-enabled screening software can accelerate understanding of disease progression and support trial matching to assist in cohort selection and patient enrollment, critical and often time consuming dimensions of clinical trial conduct. AI/ML analysis of healthcare and federal real world data/real world evidence (RWD/RWE) sources can be an integral part of protocol development and used to identify additional patients for enrollment based on specific inclusion and exclusion criteria, disease epidemiology, and patient health history. AI/ML technologies have the potential to transform the volume and speed with which we put patients on protocol, but there are gaps in the research base related to the ethics and effectiveness of algorithm driven trial matching technologies. Federal stakeholders should consider launching systematic research efforts to assess the performance of the software, including sponsoring the development of criteria for the ethical, effective, equitable, and safe use of AI/ML – and the data sets they mine –in clinical trial enrollment processes.

Other tools that simplify and expedite trial enrollment include eConsent platforms, which have tremendous potential for transforming the way patients navigate and consent to participation in an emergency clinical trial where efficiency of enrollment and decreased patient burden to support retention matters a great deal. These platforms have the capacity to reduce the administrative burden of enrollment as well as enrollment-related protocol deviations, supporting increased trial participation and speeding time to results. These tools also promote health equity, as eConsent allows for approaches that ameliorate disparities in health literacy (i.e. through the use of videos etc.) that impact trial access and enrollment. Finally, these tools can ensure more seamless design of consent processes so patients can consent to the

use and reuse of their data, as well as to participation in trials with innovative designs, important for enhancing the evidence generation capacity of the clinical trials enterprise as a whole.

4. **Leverage data collected in real world care and life settings to inform decision making**

Connected sensor technologies that support patient monitoring and remote data collection can allow us to extract insights from the wealth of continuously collected health data generated during the course of routine care delivery. These tools can also help us to efficiently gather the most essential data about medical product safety and effectiveness in real world settings outside of health systems to inform ongoing treatment decisions. Real world data generated via sensor-based technologies are especially useful in novel pandemic situations where the evidence base for what works best is limited but patients still need to receive treatment for acute conditions. To enhance our ability to leverage real time learnings from real world data generated using sensor-based technologies, federal stakeholders should consider supporting the development of guidelines, standards, and recommendations to address real and perceived deficits in the quality of real world data and to increase trust in sensor-based technologies that support real world data collection. This work would address important issues that can help unlock the promise of flows of real world data from sensor-based technologies to support emergency evidence generation that drives faster and better decisions across the healthcare continuum in real time.

DiMe firmly believes that there is value in the demonstration program suggested by OSTP. Pilots would enhance our ability to identify and resolve key issues preventing quick trial activation at scale to address gaps in the clinical evidence base. These pilots could be completed in therapeutic areas where there is an acute unmet medical need and a large and diverse patient population, such as cardiovascular disease, to ensure that their results are more broadly applicable to emergency trials. DiMe, and others, are already undertaking work to identify and scale approaches that support site readiness and expedited decision making by developing standards to guide and incentivize the adoption of digital health tools which can expedite and democratize data collection across the evidence generation life cycle.This work can be extended by federal stakeholders by harmonizing data requirements, investing in digital trial infrastructure, de-risking novel trial methods, and making the best use of the wealth of digital health data already generated by the healthcare system.

Additionally, DiMe believes there is a need for multi-stakeholder education and training to build the skills, capabilities, and trust that support successful implementation of the digital technologies mentioned above in clinical trial conduct.

To fully realize the benefits of digital tooling to support emergency evidence generation, and evidence generation more broadly, the need for change management and workforce training is as important as efforts to develop technologies and infrastructure that have the potential to transform trial conduct. To ensure successful implementation – and to enable the clinical trial enterprise to address acute data needs – we have to define the value of digital technologies within R&D, communicate this value across stakeholders, and equip them with the necessary knowledge, tools, and experience to better execute their roles with the help of digital tools.

Finally, DiMe emphasizes that many of these recommendations to enhance emergency clinical trials offer the positive externality of a more modern, robust, sustainable, and equitable trials infrastructure outside of the public health emergency context. Appropriately leveraging digital tools to better integrate medical product development and biomedical research into routine clinical care will improve our collective ability to respond to viral public health emergencies, but also to the public health crises of health inequity, healthcare costs, and declining life expectancy.

DiMe commends OSTP for taking this important step to improve the readiness of the clinical trials enterprise to address emergency data collection needs and welcomes further questions about the input we have provided. DiMe also welcomes the opportunity to collaborate with OSTP and ONC on the development and implementation of validated standards and frameworks for digital innovation to further support the evidence generation capacity of an improved emergency trials infrastructure.

Please direct any follow-up to this letter and other related topics to sarah.sheehan@dimesociety.org

Sincerely,
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on behalf of:
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