August 1, 2023

Division of Dockets Management (HFA-305)
U.S. Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: FDA-2022-D-2870: Decentralized Clinical Trials for Drugs, Biological Products, and Devices; Draft Guidance for Industry, Investigators, and Other Stakeholders

Dear Sir or Madam,

In service of the neuromuscular disease (NMD) patient community, the Muscular Dystrophy Association (MDA) thanks the Food and Drug Administration (FDA or "Agency") for the opportunity to comment on the Agency's Draft Guidance entitled, "Decentralized Clinical Trials for Drugs, Biological Products, and Devices; Draft Guidance for Industry, Investigators, and Other Stakeholders". We are grateful for the Agency's efforts to guide the stakeholder community on how best to construct decentralized clinical trials (DCTs).

MDA is the #1 voluntary health organization in the United States for people living with muscular dystrophy, ALS, and related neuromuscular diseases. For over 70 years, MDA has led the way in accelerating research, advancing care, and advocating for the support of our families. MDA's mission is to empower the people we serve to live longer, more independent lives.

Neuromuscular diseases are a group of rare, serious, progressive, mostly irreversible conditions that, while each unique, are collectively defined by progressive muscle weakening and degeneration leading to physical disabilities and, for many, early mortality. Innovative treatments for NMDs are particularly difficult to test within traditionally structured clinical trials for several reasons. First, the mobility disabilities and fragile health that often accompany living with a neuromuscular disease make traveling to central clinical trial sites challenging. Second, each NMD is a rare disease, and most would be considered ultra-rare. Consequently, only a handful of clinical trial sites may exist in a traditionally structured clinical trial, potentially causing participants to have to travel hundreds of miles to the nearest site. Finally, like in many other disease areas, clinical trials in neuromuscular diseases have historically disproportionally excluded minority populations. Consequently, decentralized clinical trials hold the potential to alleviate or overcome these barriers to participation for the neuromuscular disease patient community.

The Draft Guidance states,

> "By enabling remote participation, DCTs may enhance convenience for trial participants, reduce the burden on caregivers, and facilitate research on rare diseases and diseases affecting populations with limited mobility or access to traditional trial sites. This may help improve trial participant engagement, recruitment, enrollment, and retention of a meaningfully diverse clinical population."

MDA could not agree more. First, many individuals with NMDs are children, so any participation in a clinical trial involves the whole family. Particularly for children with NMDs with active clinical development pipelines, such as Duchenne muscular dystrophy (DMD), participating in a clinical trial at any given time is common. Parents often need to forgo employment opportunities and dedicate themselves to the care and clinical trial participation of their child. DCTs would allow for kids with NMDs and their parents to stay home (more often, at least), thus facilitating life opportunities and greatly reducing the travel and participation burdens.

Second, as stated earlier, many individuals with NMDs choose not to participate in clinical trials altogether due to the inaccessibility of airplanes, local transportation, and hotels. In fact, a recent MDA survey found that 29 percent of individuals with NMDs who do not participate in clinical trials cite travel and distance as their reason for not participating.[1] Increasing the eligible and interested participant pool this substantially could allow trials to enroll and complete quicker, thus potentially accelerating life-changing treatments reaching our community.

Finally, clinical trials in NMDs are most available to those who can afford to travel, take time off from work, and potentially cover ancillary costs. DCTs make clinical trial participation more affordable, thus potentially opening opportunities for participation to those of lower socioeconomic means.

Overall, we are grateful for, and encouraged by, FDA's efforts to accelerate the use of DCTs by issuing this Draft Guidance. If finalized, we believe this proposal appropriately balances the promises and challenges of conducting DCTs. With the further additions and alterations proposed below, we hope this proposal will successfully accelerate the use of DCTs in neuromuscular disease clinical trials.

FDA Should Include the Development of Diversity Action Plans in the Roles and Responsibilities of Sponsors of DCTs

MDA, as a member of the Rare Disease Diversity Coalition (RDDC), endorses RDDC's recommendation within its comment letter to require sponsors that use DCTs to incorporate a diversity action plan into their efforts. Already FDA has put forward a draft guidance on the use of diversity action plans in clinical trials more generally, but given the promise DCTs hold to make clinical trials more diverse, we encourage FDA to more specifically recommend (if not require) the use of diversity action plans in DCTs. We encourage the Agency to add this stipulation prior to finalizing the Draft Guidance.

[1] ONEVoice: Insights and Observations from a National Survey of Adults and Families Living with Neuromuscular Disease (2018, December 9). Retrieved August 1, 2023, from https://www.mda.org/sites/default/files/2018/12/MDA_OneVoice_Whitepaper.pdf

Encouraging Patient-Level Considerations for the Site of Trial Participation

Within the Draft Guidance, FDA generally assumes that patients would choose remote clinical trial participation options over in-person participation, and that it should be left up to the sponsor or investigators to choose participation locations if more than one is available. For example, FDA states, "In general, investigators can consider telehealth visits instead of in-person visits with trial participants if no in-person interaction is needed. The protocol should specify when a telehealth visit with a trial participant is appropriate and when a participant should be seen in person."

The NMD community has had extensive experience with telehealth due to the pandemic and MDA has found that the NMD community does not have a monolithic preference for telehealth over in-person visits. Many in the community may prefer in-person visits for certain care, and telehealth for others.

Consequently, MDA encourages FDA to recommend to sponsors that telehealth can be used rather than in-person visits, but if both options are available, to consult with trial participants on which they would prefer. While many participants are likely to prefer telehealth, some others may prefer in-person participation, and hybrid DCTs should allow for this flexibility.

Greater Clarity on Investigator and Healthcare Provider (HCP) Care and Participation

MDA encourages the Agency to clarify several points throughout the guidance on the participation and qualification of other HCPs as non-trial investigators. First, FDA states that, "The trial-related services that (non-trial HCPs) provide should not differ from those that they are qualified to perform in clinical practice (e.g., performing physical examinations, reading radiographs, obtaining vital signs). Determining who is truly "qualified" to provide potentially specialized and complex services to those with rare diseases is complicated and perhaps shouldn't be solely left to the sponsor to determine. Instead, we encourage FDA to add a recommendation for sponsors to coordinate with expert patients and patient organizations on which non-trial HCPs are qualified to provide services as part of the trial.

Second, we recommend that FDA better define what care is provided as part of the trial, and what care is provided outside of the trial. Often the line between each can become quite blurry as care offered to patients participating in neuromuscular disease clinical trials could be defined either way. We ask FDA to better differentiate between the two.

Finally, the FDA states that "Investigators should take steps to help ensure that participants have access to an appropriate level of local care". We again ask for greater clarity on what constitutes "an appropriate level of local care". We are hopeful sponsors will utilize this guidance to employ DCT designs, but if the Agency is ambiguous on certain expectations, this could disincentivize sponsors from crafting DCTs.

Greater Efforts to Include Individuals from Lower Socioeconomic Classes

We appreciate FDA's emphasis on the salience of DCTs on greater inclusion of individuals from lower socioeconomic classes in clinical research. We believe there are several parts of the Draft Guidance that can be strengthened further to facilitate greater inclusion. First, the FDA states, "Sponsors should ensure that [digital health technologies] used in a DCT are available and suitable for use by all trial participants." While we certainly agree with the sentiment, often its not the DHT that could exclude certain trial participants, but the physical location in which the DHT would be used. For example, the ability to climb stairs is often used as an endpoint in neuromuscular diseases, and certain DHTs could capture such abilities at home. But many individuals, particularly those of lower socioeconomic classes, may not live in a location with stairs, thus potentially excluding them from the trial. We recommend that FDA add a stipulation that not only should the DHT itself be suitable for all trial participants, but also the DHT must be able to be used in a location available to all trial participants.

Second, an impediment for many individuals in lower socioeconomic classes from participating in clinical trials is the lack of reimbursement for their time spent participating. Many traditional clinical trials do indeed reimburse for time spent participating in the clinical trial and it is imperative that DCTs do the same. We ask that FDA add a recommendation that DCTs reimburse participants for their time just as traditional clinical trials may do.

Finally, FDA discusses within this draft guidance the importance of video assessments for DCTs. We again ask the FDA to emphasize that sponsors of DCTs are responsible for ensuring the proper broadband, wifi, and equipment (such as a laptop or tablet) will be provided to participants free-of-charge to facilitate their participation and not provide an advantage to those of greater socioeconomic means.

In conclusion, we are grateful for the opportunity to comment on FDA's efforts to facilitate the use of decentralized clinical trials. For questions regarding MDA or the above comments, please contact me at 202-253-2980 or pmelmeyer@mdausa.org.

Sincerely,

Paul Melmeyer, MPP
Vice President, Public Policy and Advocacy
Muscular Dystrophy Association