December 4, 2023

SUBMITTED ELECTRONICALLY

Dockets Management Staff (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Muscular Dystrophy Association Comments on "Medical Devices; Laboratory Developed Tests" - Docket No. FDA-2023-N-2177

To whom it may concern;

In service of the neuromuscular disease (NMD) patient community, the Muscular Dystrophy Association (MDA) thanks the Food and Drug Administration (FDA or "the Agency") for the opportunity to comment on the Agency's Proposed Rule (RFI) entitled "Medical Devices; Laboratory Developed Tests." Lab-developed Tests (LDTs) are often used to screen for or diagnose neuromuscular diseases, particularly within newborn screening and neuromuscular disease specialty clinics. Consequently, MDA takes an intense interest in the regulatory pathway under which these products may or may not reach our community.

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 community. MDA's mission is to empower the people we serve to live longer, more independent lives.

Generally speaking, we support the creation of a regulatory oversight structure for lab-developed tests. The medical decisions being made by our community in consultation with their clinicians are far too consequential to be based upon potentially inaccurate tests. This is why we supported efforts in Congress to enact the VALID Act and are heartened when such efforts gain momentum. We would prefer to see such a regulatory structure created via legislation, but with several failed attempts, we understand why the Agency is moving forward with this proposal.

MDA will not support nor oppose FDA's approach outlined within the Proposed Rule. Instead, we will provide the Agency with several important points we hope the FDA will consider as it moves to promulgate a final rule.

Availability of Diagnostics for Rare and Ultra-Rare Neuromuscular Diseases:

By and large, the greatest consideration we have when evaluating any new LDT regulatory scheme is whether it will still facilitate safe and effective, valid and reliable, screening tools and

diagnostics to reach the neuromuscular community. This is particularly salient when we consider the rare and often ultra-rare nature of NMDs in which only a few hundred at the most, and often only a handful, individuals are diagnosed every year with the condition.

Much like our concerns about ultra-rare therapeutic development in which we seek to ensure the marketability and financial atmosphere for developing orphan drugs is strong enough to warrant commercializing, similarly we would seek assurances from the FDA that this regulatory proposal would not result in laboratories or other entities that are developing a diagnostic for an ultra-rare neuromuscular disease dropping the effort altogether as the regulatory hurdles make further development financially unviable.

It appears that the FDA is taking a rather "one-size-fits-all" approach to the pre-market requirements of rare and ultra-rare LDTs compared to mass-market LDTs within this proposal. This departs from previous proposals, including the VALID Act and previous draft proposals from the Agency itself, that constructed regulatory flexibility for LDTs qualifying for a humanitarian device exemption (HDE). Some proposals excluded LDTs that qualify for an HDE altogether opting instead for the FDA to continue exercising enforcement discretion.

We would not oppose the FDA from similarly excluding LDTs with an HDE from this proposal. We would strongly encourage that the Agency, at the very least, consider constructing some amount of regulatory flexibility for LDTs with an HDE compared to mass-market screens or diagnostics. Otherwise, we risk the very troubling possibility of screens and diagnostics for NMDs being abandoned altogether due to the inappropriately and unnecessarily high pre-market regulatory requirements imposed by this proposal.

Newborn Screening:

We similarly ask that the FDA pay care and attention to the effects this proposal may have on newborn screening. Newborn screening is a public health program administered by each state or territory that screens for over thirty mostly genetic conditions that, if not diagnosed early and subsequent treatment is applied, can lead to irreversible morbidity and often mortality. Two NMDs are recommended by the Federal government for state newborn screening: spinal muscular atrophy (SMA) and Pompe disease, and a third, Duchenne muscular dystrophy, is under consideration.

The screening involved for these conditions involve a several step process in which the newborn is first screened for an indication that one of these disorders may be present, and then if screening is positive, a confirmatory test (often a genetic test) is used to confirm the diagnosis.

Each one of these screens and diagnostics may be FDA-approved or authorized, but many others may be LDTs and have not gone through FDA's review. Of particular concern are the confirmatory genetic testing that may only be conducted a few hundred times a year across all screening programs, but will need FDA pre-market approval before being applied not only at a population level within each state, but also in the pilot studies that test if or how newborn screening for these conditions can be administered by states. These pilot studies are required for the Federal government to consider recommending states screen for these conditions.

We ask that the FDA consider how this proposal will affect the development and availability of screening tests and confirmatory diagnostics used within newborn screening. We ask that the FDA ensure that their review process does not extend the already extensive timeline for implementing newborn screening across the country.

Companion Diagnostics:

For many of the gene and cell-based therapies under development for NMDs, companion diagnostics will be required to confirm that the prospective recipient 1) does not have antibodies against the AAV viral vector, and/or 2) has the specific genetic mutation amenable to the therapy. Consequently, the regulatory pathway for companion diagnostics is particularly salient for the NMD community.

We ask that as the FDA proceeds with promulgating this rule, that it considers the intersection between therapeutic approval (via a New Drug Application or Biologics Licensing Authorization) and the approval of the LDT companion diagnostic. These should occur concurrently, and the approval of the LDT companion diagnostic should not delay access to the promising therapy.

FDA Resources Necessary for Oversight:

We share concerns with other commenters that the Agency's current resources for pre-market review are inadequate to meet the demands of the proposed rule and consequently could result in extensive FDA review times and bottlenecks obtaining an FDA approval or authorization. We understand that LDTs are not adequately included within the current MDUFA framework, thus user fees from LDT applicants would not adequately cover the staffing necessary to avoid slow review timelines or bottlenecks.

We understand that the Center for Devices and Radiological Health (CDRH) will seek to include LDTs within the next MDUFA agreement, but seeing as that is several years away, we ask that FDA carefully consider what resources are available currently to implement this regulatory pathway adequately to avoid any bottlenecks or delays.

Academic Medical Centers:

We are grateful for the Agency's recognition that the laboratories within non-profit academic medical centers should potentially be treated differently under this proposal than commercial and/or for-profit laboratories. We agree that this distinction is warranted.

Many individuals with NMDs are diagnosed in specialty neuromuscular clinics located within AMCs, and the specialists and the labs within the AMC work collaboratively to obtain a genetic diagnosis of the individual. These tests are not marketed widely and only available in very specific, targeted circumstances.

Consequently, we would support FDA approaching LDTs developed by labs within AMCs in a more flexible manner.

Conclusion

We are grateful for the opportunity to comment on the FDA's proposal for regulating laboratory developed tests. For questions regarding MDA or the above comments, please contact Paul Melmeyer, Vice President, Public Policy and Advocacy, at 202-253-2980 or pmelmeyer@mdausa.org.

Sincerely,

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