October 18, 2019

Institute for Clinical and Economic Review
Two Liberty Square
Ninth Floor
Boston, MA 02109

Re: 2020 Value Assessment Framework: Proposed Changes

Dear Dr. Pearson,

The Muscular Dystrophy Association (MDA) thanks the Institute for Clinical and Economic Review (ICER or the Institute) for the opportunity to comment on ICER's "2020 Value Assessment Framework: Proposed Changes."

MDA is the nation's leading nonprofit organization dedicated to transforming the lives of individuals living with muscular dystrophy, amyotrophic lateral sclerosis (ALS), spinal muscular atrophy (SMA) and other neuromuscular diseases (NMDs) through innovations in science and innovations in care. MDA fulfills its mission by funding biomedical research, providing access to expert clinical care and support through its national MDA Care Center Network which is comprised of expert medical clinics at more than 150 of the top health care institutions across the US, and by championing public policies and programs that benefit those it serves. Since inception, MDA has funded more than $1 billion in research grants to accelerate treatments and cures for neuromuscular disorders, making MDA the largest source of neuromuscular disease funding in the U.S. outside of the federal government.

As of October 2018, 275 clinical trials for over 190 potential therapies were ongoing for the neuromuscular community, including for many therapies that could be the first FDA-approved treatments for their populations. As a result, MDA expects that ICER will conduct multiple reviews for NMD therapies under the proposed updated framework in the year 2020 and beyond.

Consequently, MDA is pleased to provide comments on ICER's updated framework and the proposed revisions within. We appreciate several of ICER's proposed revisions pertaining to the use and collection of real-world evidence, alternatives to quality-adjusted life years (QALYs), discussion of additional benefits to families, caregivers, and employment, and more robust stakeholder and patient organization engagement. However, we remain concerned with the quantitative exclusion of many non-traditional elements of value of importance to the NMD community, as well as revisions to the cost effectiveness thresholds for ultra-rare therapies.

Real-World Evidence:

MDA supports ICER's intent to expand its efforts to integrate real-world evidence (RWE) into its assessments. We are particularly supportive of ICER's intention to proactively collect real-world evidence in partnership with stakeholder organizations if no such evidence has already been collected.

As ICER recognizes, real-world evidence supplements data collected through clinical trials to further capture the lived experiences of patients with the disease or therapy in question. Clinical trials often offer only a limited snapshot on the safety and effectiveness of a therapy as inclusion/exclusion criteria limit the patient population from which data is captured, and only certain endpoints are included. This naturally leaves many patient experiences unexplored and unempirically investigated.

Real-world evidence collected by stakeholder organizations can help fill this gap, particularly in rare neuromuscular diseases that are still often misunderstood. MDA is collecting this data for the NMD community through our neuroMuscular ObserVational Research (MOVR) Data Hub. MOVR, launched in 2018, captures clinician-reported real-world evidence at locations throughout our network of over 150 clinical care centers. Currently we are capturing data for patients diagnosed with several neuromuscular diseases, including SMA, ALS, and Duchenne and Becker muscular dystrophy and we plan to expand this list as MOVR is implemented in more locations across the country.

We are pleased that ICER is committed to not only more extensively include RWE within its assessments but also to partner with stakeholders to collect RWE when otherwise unavailable. This will be particularly important for rare disease assessments where data and disease understanding are limited, and resources to collect such data are limited. We strongly encourage ICER to proactively and deliberately partner with patient organizations to collect such data necessary to fully understand the potential impacts of a new therapy.

Finally, MDA asks that ICER pause or delay the start of any review if data is missing that could enhance understanding of the safety and effectiveness of a new therapy. For example, RWE could be highly instructive on the potential benefits of new therapies for Duchenne muscular dystrophy (as well as many other NMDs), but such data, as of now, is not commonly collected. Within DMD, the six-minute walk test has been the most widely used endpoint even many patient advocates contend it poorly captures function that is important to patients. Instead, other endpoints pertaining to arm movements, lung and heart strength, and compensatory movements hold much more promise, and could be collected as RWE. In such a circumstance, rather than moving forward and concluding a review of new therapies in Duchenne muscular dystrophy (DMD) without salient RWE in hand, we ask that ICER delay such a review and collect instructive RWE to better inform any conclusion ICER may reach.

Alternatives to Quality Adjusted Life Years (QALYs)

MDA supports ICER's efforts to consider alternative measures of health improvement other than the QALY. We acknowledge and understand that many believe the QALY discriminates against

those with disabilities, and we agree that alternative measures of health improvement should be considered to better inform coverage and reimbursement decision making.

Consequently, ICER's continued use of equal value of life years gained (evLYG) as an alternative to QALYs will hopefully better inform decision makers on the implications of using the QALY in evaluating health improvements for individuals with disabilities. We urge ICER to continue to think innovatively on how best to measure health improvement outside of entrenched health economic practices.

Removal of Expanded Cost-Effectiveness Threshold for Ultra-Rare Disorders

MDA is concerned with ICER's proposal to apply uniform cost-effectiveness thresholds of $50,000, $100,000, $150,000 and $200,000 per QALY rather than expanding threshold estimates to $500,000 per QALY for ultra-rare disorders as is currently practiced. Empirical evidence has shown that treatments for ultra-rare diseases receive higher societal value than those for common disorders, hence justifying the higher cost effectiveness threshold. As far as we are aware, this higher societal value or willingness-to-pay for rare disease therapies has not changed over the previous several years.

Additionally, ICER's reasoning for eliminating the higher cost-effectiveness threshold for ultra-rare disorders is troubling. Whether biopharmaceutical companies are misusing the higher levels in order to justify higher prices should be inconsequential to an empirical, quantitative evaluation supported by evidence.

We ask that ICER reconsider this proposed move towards uniformity as ultra-rare conditions, including many neuromuscular conditions, are anything but uniform in the therapeutic development challenges they bring and the unique benefits they offer to patients, families, and society more generally.

Controversies and Uncertainties Section

To reiterate comments submitted to ICER on its proposed framework for SSTs,

> "MDA supports the addition of a section to identify uncertainties as ignoring them would result in an incomplete evaluation. However, we caution against the use of the word "controversies" within the title of the section. There will be uncertainties in economic reviews, and within those uncertainties there may be diverging views and perspectives, but divergent thinking and analysis does not necessarily result in controversy.
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> Within this section, we support ICER's intention to discuss alternative model structures submitted by outside stakeholders and would urge that any considerations and/or modeling that is proposed by outside stakeholders be published and responded to in finalized recommendations by ICER. Knowing the source of outside counsel is essential in the community evaluation of the recommendation, and transparency will be essential in such valuation exercises. We encourage ICER to remain open to alternative ways of

measuring the value of SSTs. By allowing for outside submissions, ICER will create a more inclusive process."

Additional Contextual Benefits and Considerations

MDA supports the additional inclusion of contextual benefits and considerations for family members, caregivers, and the ability to find employment. Each new therapy for neuromuscular diseases has the potential to substantially benefit family members and caregivers. Patients may be able to be more independent, allowing family and caregivers to work or pursue other passions. Additionally, seeing a loved one maintain their health, or even regain health previously lost, can be incredibly rewarding to family. In addition to familial benefits of new therapies, any therapy that maintains or improves the ability of the individual to work can have substantial beneficial impacts on the patient and their family. Finding employment not only facilitates self-sustainability but increases access to needed benefits and provides psychological rewards to those who desire to find employment.

While we are pleased that these additional benefits will be considered qualitatively by the independent voting committees, the continued quantitative exclusion of these benefits remains concerning. The quantitative exclusion of elements of value important to patients, such as the value of hope, scientific spillover effects, and insurance value, allows such values to be easily ignored by decision makers. To reiterate sections of MDA's comments on ICER's SST framework:

> "**Value of Hope**: ICER appears to misunderstand the "value of hope" in a way that allows the Institute to exclude this important value from its evaluations. ICER defines the "value of hope" to be the "value of having the *choice* among treatments with a different balance and timing of risks and benefits." MDA disagrees with this alternative definition. The "value of hope" is about the potential for a more healthy and happy life in the future than was previously expected. SSTs offer patients the possibility of substantially healthier lives many years into the future, and with this brings the hope of attending college, getting married, and other important life experiences. ICER's alternative definition ignores the hope for experiencing these seminal moments entirely.
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> **Insurance Value**: The exclusion of insurance value is concerning to MDA. ICER acknowledges that insurance value has been empirically measured by Lakdawalla et al. and through "explicit mathematical models of consumer utility maximization."[1] However, ICER dismisses these empirical values of SSTs by stating that insurance value, "overlaps significantly with considerations given to severity or burden of illness." We disagree; there is not enough overlap between insurance value and burden of illness to justify excluding insurance value. Burden of illness studies pertain mostly to those directly affected by the disease while insurance value pertains to those not yet affected. Insurance

[1] Lakdawalla DN, Doshi JA, Garrison LP, Jr., Phelps CE, Basu A, Danzon PM. Defining Elements of Value in Health Care-A Health Economics Approach: An ISPOR Special Task Force Report [3]. Value in health: the journal of the International Society for Pharmacoeconomics and Outcomes Research. 2018;21(2):131-139.

value, as ICER acknowledges, is about peace of mind for individuals who do not have the disease, and therefore such values are not captured within burden of illness values.

Additionally, ICER's assertion that including insurance value within its assessments in an empirical manner would result in too substantial of an impact is discouraging. If one takes this argument to its conclusion, it can safely be assumed that all substantial values of new therapies would need to be discarded due to their financial impact, and only values that fit within ICER's vision for appropriate spending levels should be included. We view this as an incredibly subjective method for approaching value assessments.

Scientific Spillover Effects: ICER's exclusion of empirical values pertaining to scientific spillover effects is subjective and serves to skew its value assessments. ICER again acknowledges that scientific spillover effects have been empirically measured but disregards such values as duplicitous with the value the future therapies will derive, and problematic due to the opportunity costs they will create for other patients.

MDA is concerned by ICER's stance on behalf of unnamed patients that including alternative values of therapies will present opportunity costs for other patients in the healthcare system. This argument can be used for any value anywhere within our healthcare system, (or our society in general), but ICER is only applying this concern to these additional elements of value.

In general, MDA is disappointed that ICER appears to be subjectively picking and choosing which empirical values it includes within its assessments based upon opinion and insufficient reasoning. We request that ICER reconsider excluding these empirical values."

MDA requests once more that ICER continue to explore empirical methods to include nontraditional elements of value to patients not captured by the QALY or evLYG. Without these values, patients and their advocates will continue to view ICER evaluations as incomplete and an inaccurate capture of the value derived from these therapies.

Potential Exclusion from Future Therapies:

To once again reiterate MDA's comments to ICER's framework on SSTs,

"MDA is supportive of ICER's intention to include considerations of the implication of SSTs potentially excluding patients from being able to take future SSTs due to the mechanism of action or immune response. We are aware that certain disease modifying therapies, particularly gene therapies and gene editing technologies, provide irreversible effects. These therapies may also disqualify patients from future ability to take other SSTs or disease modifying therapy.

This is a very real issue that patients today must grapple with. Including this possibility in an empirical manner within ICER's assessments is appropriate. However, including this potential harm of an SST while excluding many potential unique benefits is troubling. If

ICER is to include the potential unique harms of SSTs, it must also include the potential unique benefits.

However, we again wish to reiterate that this should not be the only unique benefit, or in this case disadvantage, of SSTs considered by ICER. There are many additional unique benefits that SSTs can offer to patients that ICER has chosen to exclude. We encourage ICER to assess our comments on the proposed SST framework for our fully elucidated perspective.

Stakeholder Engagement

MDA is broadly supportive of the proposed changes to methods of stakeholder engagement with patient organizations included within the proposal. We are pleased that ICER is expanding its interaction with patient organizations by conducting earlier outreach with the patient organizations representing patients affected by an upcoming review. We support ICER holding debrief calls with patient organizations at the conclusion of a review, as well as expanding the opportunity to submit written comments to ICER in conjunction with independent review committee hearings.

We also support ICER's proposed changes to its reports to broaden and further emphasize patient viewpoints submitted and considered by ICER. This includes adding a "patient insights" chapter in each report and expanding the "stakeholder input" section of each report to include further discussion of what was received and considered by ICER.

We still request that ICER give additional considerations to the time and resource burdens ICER reviews place on patient organizations, particularly small, under-resourced rare disease patient organizations, as it asks for assistance and partnership with these organizations. Engaging in a meaningful way in ICER reviews can be incredibly labor and resource intensive for any organization regardless of its size, and anything ICER can do to extend participation timelines or assist patient organizations in participatory opportunities would be appreciated. ICER is already proposing to do so in a limited fashion by extending the draft report public comment period by one week, but we encourage ICER to look at other similar extensions as well.

We again thank ICER for the opportunity to comment and look forward to continuing to work with the Institute to ensure clinical and economic evaluations of transformative therapies are thorough, accurate, and beneficial and inclusive to the neuromuscular disease community. For questions regarding MDA or the above comments, please contact advocacy@mdausa.org.

Sincerely,

Paul Melmeyer, MPP
Director of Regulatory Affairs