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HARVARD MEDICAL SCHOOL

MULTI-REGIONAL CLINICAL TRIALS
THE MRCT CENTER of BRIGHAM AND WOMEN'S HOSPITAL and HARVARD

Institute for Clinical and Economic Review (ICER)
Submitted: *publiccomments@icer.org*

Re**:** 2023 Value Assessment Framework- Proposed Changes

June 30, 2023

To whom it may concern:

The Multi-Regional Clinical Trials Center of Brigham and Women's Hospital and Harvard (MRCT Center) appreciates the opportunity to comment on the Institute for Clinical and Economic Review (ICER)'s request for input and comments on the proposed changes regarded the 2023 Value Assessment Framework. It is timely and we appreciate the recognition of the importance of considering diversity in the assessments of any healthcare product. We also appreciate the openness of the organization to public comment.

The MRCT Center is a research and policy center that addresses the ethics, conduct, oversight, and regulatory environment of international, multi-site clinical trials. Founded in 2009, it functions as an independent convener to engage diverse stakeholders from industry, academia, patients and patient advocacy groups, non-profit organizations, and global regulatory agencies. The MRCT Center focuses on pre-competitive issues, to identify challenges and to deliver ethical, actionable, and practical solutions for the global clinical trial enterprise. While the MRCT Center often collaborates and interacts with FDA, we have not discussed the comments provided herein with anyone at FDA. The responsibility for the content of this document rests with the leadership of the MRCT Center, not with its collaborators nor with the institutions with which its authors are affiliated.[*]

The proposed modifications to the Value Assessment Framework ("the Framework") does not replace but updates the Framework to ensure currency. The MRCT Center particularly appreciates the detail and instruction of the proposed changes; we commend ICER and endorse many of recommendations and proposals. Specifically, we value the attention paid to:

- Transparency not only of the changes proposed but also to the logic and reasoning behind those changes
- The importance and criticality of clinical trial diversity, representativeness, and other dimensions of health equity
- The challenge of developing value assessments when data on disease-specific prevalence estimates by demographic are not available
- The challenge of value assessments for the US population that are based on data derived from global clinical trials

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- The tension between ICER's Framework that analyzes evidence relevant to the population versus decision-making for individual patients
- The appreciation that ICER's focus on and attention to clinical trial diversity will animate further progress toward representation.
- The creation of an ICER Patient Council
- The inclusion of caregiver time, burden, and quality of life in value calculation.

In the context of enthusiastic support for the proposed changes, the MRCT Center has a number of considerations and further thoughts for ICER to consider:

- It would be helpful to understand which non-health impacts are being considered, and how those non-health impacts affect different populations. Are the non-health impacts free from bias? What are the measures being used? Are the measures themselves free from bias?
- In the utilization of a "human capital approach," is value assessed or attributed if a person is not in the "formal" or "informal" labor force? How is productivity measured and valued for those not in the labor force?
- We remain critical of the use of QALYs as they devalue the lives of people with disabilities. Should QALYs themselves be replaced? Are there more appropriate alternatives that value lives equivalently? QALYs are also inadequate for pediatric assessments.
- The focus appears principally to be race and ethnicity, but only 4 categories are rated (Table 2.2). The limited categories of race and ethnicity currently endorsed by OMB are problematic; we trust that if OMB restates the categories, ICER will reassess. But we also believe that ICER could bring an independent lens to these problematic groupings rather than concretize categories that we know are inaccurate and insufficient, expand the rating categories, and broaden the representation score. Specifically:
    - Awarding additional value if sponsors focus on and achieve representative participation of relevant subpopulations for the condition (e.g., pediatric populations, LGBTQI+ populations, etc.)
    - Attention to social determinants of health (SDoH) and the value of inclusive populations that represent different SDoH populations
    - Inclusion of pediatric populations
    - Inclusion of people with disabilities
- Are race/ethnicity valued equivalently to sex (and age)? Table 2.2 appears to value race/ethnicity as having greater significance and weight than other parameters.
- We encourage ICER—and pharmaceutical companies—not only to justify (and value) inclusion of some subgroups but also justify exclusion of others.

Three overarching considerations that we wish ICER to consider:

- It is well known that **pediatric populations** are understudied and underserved. People under that age of 18 are often not included in clinical trials even when the potential treatment is directly relevant to them. Evidence of safety and efficacy—no less of value—of therapeutic interventions for pediatric indications is lacking. We strongly

advocate that ICER include pediatric representation in their revision and in their value assessment. In addition, please consider:

- Mention pediatric populations in the definition of clinical trial diversity: *"ICER will provide an overall diversity rating for the following demographic characteristics: race/ethnicity, sex, and age, specifically, adults aged 65 and older…."* Here and throughout the document, there is an opportunity to strengthen the inclusion of pediatrics
- Call out pediatric subpopulations as an underserved population of interest
- The Medicare-eligible population is specifically identified for dynamic pricing for small molecule and biological products. Mention of and applicability to pediatric populations would be beneficial.
- The patient engagement program presents multiple opportunities for the inclusion of adolescents and young adults and for parents/guardians of children too young or otherwise able to represent themselves.
- The rating categories in Table 2.2 specify and value age specified when age includes "Older Adults (≥ 65). Here there is an opportunity to include categories for pediatric populations.
- It would be helpful to include special pediatric considerations, including the valuation of productivity for both patient and carer in Table 3.1.
- Will ICER conduct a dynamic pricing scenario for small molecule and biological products that are predominantly targeted to pediatric populations as well?

- Similar to pediatric populations, **people with disabilities** are the most prevalent underserved population and, frankly, data on disabilities is rarely collected in clinical trial demographic information. It would be helpful for ICER to call out this population, to ensure that all materials and communications are accessible and that all meetings accommodate people with disabilities.
- The term shared **decision-making** recurs in the document. We feel that it is important to emphasize that the decision to participate in a trial, or to avail oneself later of an approved intervention is indeed the participant's or patient's decision. It would be helpful to reframe the concept of decision-making as one that belongs to the participant or patient, after discussion with the provider, and with the assistance of a supporter for supported decision-making when requested.

Thank you again for the opportunity to comment on the proposed changes to the ICER Framework. We believe that the ICER has taken an important step in calling further attention to the importance of clinical trial diversity. That participant demographic representativeness should align with disease-specific prevalence estimates is foundational to understanding the heterogeneity of treatment effect and thus of the value assessment. The proposed changes will bring attention to these important topics. The questions and considerations we mention are intended to enhance the process and bring attention to other underserved populations, including children, adolescents, young adults, people with disabilities, and others.

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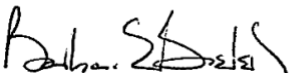
Please feel free to contact the MRCT Center (bbierer@bwh.harvard.edu, sawhite@bwh.harvard.edu, or mark.barnes@ropesgray.com) if we can be helpful or if you wish to discuss.

Respectfully submitted,



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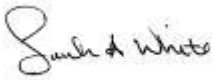

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