February 10, 2023

Carole Johnson
Administrator
Health Resources & Services Administration
Department of Health and Human Services
5600 Fishers Lane
Rockville, MD 20857 USA

Re: Advisory Committee on Heritable Disorders in Newborns and Children February Meeting

Dear Administrator Johnson,

On behalf of the rare disease community, the EveryLife Foundation is pleased to offer the following comments regarding the February 9th conduction of the Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC) related to the evidence review of Krabbe disease for consideration to the Recommended Uniform Screening Panel (RUSP).

The EveryLife Foundation for Rare Diseases is a nonprofit, nonpartisan organization dedicated to empowering the rare disease patient community to advocate for impactful, science-driven legislation and policy that advances the equitable development of and access to lifesaving diagnoses, treatments, and cures.

Newborn screening is a unique public health program, with more than four million newborns utilizing the program every year. Approximately 1 in 300 newborns receive a diagnosis through newborn screening, providing them the opportunity to begin life-saving treatment at the earliest moment possible. As innovation in rare disease therapies progresses, so too does the expected rise in conditions seeking to utilize the newborn screening pathway as a diagnostic tool.

EveryLife and our rare disease community partners are grateful for the ACHDNC's many efforts to conduct thorough and thoughtful evidence reviews of nominated conditions. We further understand that – as described in Title XI § 1111 (42 U.S.C. § 300b-10) Section b item 3 Duties, the ACHDNC shall:

"(3) make systematic evidence-based and peer-reviewed recommendations that include the heritable disorders that have the potential to significantly impact public health for which all newborns should be screened, including secondary conditions that may be identified as a result of the laboratory methods used for screening"

The discussion during day one of February's meeting and vote yielded a vote of 7-7. That tie vote was interpreted at the conclusion of the Committee meeting as a vote NOT to move Krabbe disease forward for consideration to the RUSP by the Secretary. **The rare disease community urges HRSA and the ACHDNC to reconsider the interpretation of the tie vote. Indeed, the February 9th meeting did not yield a 'no'.** Instead, it yielded a need for further clarification of questions that were raised during the discussion that could not be addressed by participating members of the discussion.

Further, in this same ACHDNC Charter Title XI § 1111 (42 U.S.C. § 300b-10) Section C Membership Item 1 states that –

"(1) In general The Secretary shall appoint not to exceed 15 members to the Advisory Committee. In appointing such members, the Secretary shall ensure that the total membership of the Advisory Committee is an odd number."

While the Charter does not explicitly require that the purpose of the composition of membership being an odd number is to ensure that no vote ever end in a tie, we believe strongly that providing a path forward for further discussion and resolution of this tie is in keeping with the intention with which this Advisory Committee was established.

For these reasons, the EveryLife Foundation and the rare disease community urge the ACHDNC to revisit the conclusion of the vote and consider ways to ensure that the Krabbe disease nomination receives the full and complete consideration that it deserves.

Further, we appreciate the efforts to date to enhance the Evidence Review Matrix but last week's discussion illuminated critical gaps in the data being considered as central in the Committee's decision-making. Our current decision-making model that informs the benefit-risk tradeoffs are not yet comprehensively inclusive of critical data elements and considerations that reflect patient experience data, data that has been defined in statute and is not required as a part of decision-making in neighboring ecosystems such as our regulatory partners at the US Food and Drug Administration (FDA). In your ongoing assessments to ensure that the decisions of the ACHDNC are in the best interest of the public's health, we urge that the ACHDNC expand and formalize the data included in the evidence review matrix.

In addition, the EveryLife Foundation is aware that the February 9th evidence review was the second time that an evidence review was conducted by the ACHDNC for a nomination of Krabbe disease. Following the 2009 nomination of this same condition, the Krabbe disease community was provided with specific recommendations for strengthening the nomination. The February 9th discussion did not include any review or discussion of whether those key evidence requirements had been met. Such detail would have provided critical insight to the ACHDNC during the discussion and proceedings and informed the considerations of the voting members of the Committee.

Related to the composition of the members of the ACHDNC who participate in discussions during the review of a nominated condition and the presentation of evidence review, we have the following recommendations for the ACHDNC:

- Once again, we request the ACHDNC add a patient representative as a voting committee member. As defined by the National Health Council and adopted by FDA for use in the *PFDD Guidance 1: Collecting Comprehensive and Representative Input*, "'Representativeness' means a sufficient number of and types of people are included in the engagement activity to ensure that those engaged can speak on behalf of the target population." Discussions that articulate and project experiences and opinions onto a community that lacks formal representation reflect a significant imbalance in representation.

- We ask the ACHDNC formally include an expert member of the nominated disease community in every discussion of an evidence review to participate in the discussion to be available to address questions that arise and inform the discussion.
    - As examples, February's ACHDNC discussion included significant time devoted to concerns around the impact screening might have on families identified as false positives based on older literature and practices that have since been updated.
    - The discussion also included discussion of late onset phenotypes of the condition when the nomination was specific to infantile-onset Krabbe.
- The February meeting's discussion contained thorough discussion about the perceived negative impact of receiving a late-onset diagnosis for families. However, recent data from the Babyseq experiment showed that at three months following their participation, 86.8 percent of parents were very interested in receiving information on their baby's risk of developing a disease in childhood that can be prevented, treated, or cured. In addition, 84.6 percent were interested in receiving information regarding the on their baby's risk of developing a disease in adulthood that could be prevented, treated, or cured.
- We request that Organizational representatives be permitted to participate in the evidence review discussion. These individuals have been invited on to the Committee because of the fact that they represent stakeholder groups who are within the newborn screening ecosystem; silencing their perspectives at the time they arguably matter most negates the purpose of their membership.

Thank you for your dedication to our rare disease patient community. The EveryLife Foundation and members of our Community Congress Newborn Screening & Diagnostics Working Group look forward to our continued engagement over the coming months. If you have any questions, please be in touch with Annie Kennedy at akennedy@everylifefoundation.org.

Sincerely,

Dylan Simon

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CC: ACHDNC
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