Dear Chairwoman Powell and members of the Advisory Committee for Heritable Disorders in Newborns and Children,

On behalf of the over 30 million Americans living with rare diseases, the EveryLife Foundation is pleased to offer the following comments to inform the Advisory Committee's ongoing conversations about the review process for new RUSP nomination packages. 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.

To inform our policy work, we convene the Community Congress, a forum for collaboration across stakeholders, representing over 200 individual rare disease patient advocacy organizations in addition to over 90 other healthcare and biotechnology organizations. Our Newborn Screening and Diagnostics Working Group is dedicated to ensuring that patients receive the earliest possible access to lifesaving diagnostic opportunities through newborn screening and other diagnostic tools. Newborn screening serves as the first step in reaching a diagnosis, preventing the years associated with the diagnostic odyssey that impacts too many with rare diseases. Importantly, newborn screening eliminates disparities in accessing a diagnosis, ensuring equitable, timely access to earlier clinically appropriate intervention and treatment. Newborn screening provides individuals with the right to a healthy life, continually proving the fact that newborn screening is one of the most successful public health programs in the country.

As the Advisory Committee is aware, over the next decade we anticipate a steady increase in the number of patient advocacy organizations submitting RUSP nomination packages for their conditions. The pace of medical and technological innovation is swift and is at odds with the ability to bring forward a successful RUSP nomination package. Since the creation of the RUSP, patient advocacy organizations have led the nomination effort for multiple conditions, often spending years to drive the evidence generation necessary to submit a successful RUSP nomination package. Patient organizations will continue to commit to these extensive efforts, but the current requirements make it impossible for patient advocacy groups to bring forth RUSP approvals fast enough to keep pace with the opportunities innovation is bringing to our communities, particularly those that represent very rare diseases.

We are aware that the Advisory Committee is working to evaluate how you review conditions for the RUSP. As you consider recommendations for the improvement of decision making, we urge you to consider the significant challenges associated with gathering evidence and conducting pilot studies for rare diseases.

- Successful RUSP nominations require prospective, population-based pilots that may cost millions of dollars and take several years to complete. It may not be feasible for many patient organizations to shoulder the burden of building a framework for and funding a newborn screening pilot. Other diseases are so rare that conducting a state pilot that satisfies decision making criteria may not be feasible.
- Delayed diagnosis due to a lack of newborn screening results in the inability to study a treatment or intervention in infants and young children. In the absence of early detection,

it is challenging to demonstrate the benefit of earlier diagnosis to satisfy decision making criteria.

- The same challenges associated with developing a treatment for a rare disease will exist when assessing the benefit of newborn screening. Disease rarity, heterogeneity, and other disease-specific considerations may impact the ability to assess the benefit of newborn screening within a population.
- Not all rare diseases will follow the same trajectory. Some diseases, when left untreated, may result in death within the first years of life. Many other rare diseases are progressive and equally devastating, with irreversible decline beginning early in life. In such cases, clinical outcomes may take years to measure.

Recognizing the significant workload of the Advisory Committee, and the pipeline of conditions that may be nominated to the Committee in the near term, we urge you to consider the following recommendations for streamlining and accelerating the review of new disorders to the RUSP.

- The assessment of the benefit of screening for new conditions should recognize the challenges above, accepting a degree of uncertainty regarding the amount of data available following the approval of a treatment or the availability of an intervention, and include all sources of information, such patient community insights. Parallels can be drawn from the review and regulation of treatments, where FDA weighs such factors in order to speed the availability of new treatments for serious or life-threatening diseases to address unmet medical needs.
- In determining the population for which a drug is deemed safe and effective, FDA when scientifically justified may approve an indication broader than the population studied in clinical trials. This is especially important for rare conditions that may be heterogeneous and lack well-established endpoint. The Advisory Committee should consider opportunities to streamline its review by leveraging FDA decision making regarding the benefit of treatment in infants and young children.
- The use of long-term data plays a vital role in understanding the potential impact of conditions being considered for RUSP nomination. The use of long-term newborn screening data can help to close health equity gaps, improve health outcomes, inform earlier clinical care guidelines, and provide important data to guide health policy. The creation of a central database for review of long-term data would provide the Advisory Committee the ability to track incoming data for conditions planning to submit a RUSP package as well as provide the ability to better evaluate longer term outcomes for conditions on the RUSP.

We appreciate that the COVID-19 pandemic has placed even greater demands on the precious commodities of time and resources on our newborn screening leaders, and we are especially grateful for your unwavering dedication to our rare disease patient communities. The EveryLife Foundation and the membership of our Community Congress Newborn Screening and Diagnostics Working Group stand ready to support your work and we look forward to engaging with you over the coming months.

Sincerely,

The EveryLife Foundation for Rare Diseases