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Dear Dr. Kishnani:

The Secretary of Health and Human Services' Advisory Committee on Heritable Disorders in Newborns and Children (Committee) appreciates your nomination of Pompe disease for inclusion in the Committee's recommended uniform newborn screening panel for State newborn screening programs. The Committee requested a formal review of the evidence by its external evidence review group regarding screening, diagnosis, and follow-up care for Pompe disease, using both published and unpublished data. As you know, the decision to go forward with the review reflects positively on the importance of the condition and on the status of test development and treatment evaluation. The report from the comprehensive evidence review was presented to the Committee and thoroughly discussed at its October 2008 meeting. The Committee voted unanimously to recommend not adding Pompe disease to the Committee's recommended uniform newborn screening panel at this time. The Committee further recommended that additional studies should be done before the condition is to be renominated for consideration by the Committee. Specifically, the Committee identified the following issues:

1. **Screening test specificity should be improved.**
The initial test specificity for Pompe disease alone should be improved in comparison to the data shown by the Taiwan study (False Positive Rate 0.83%, Positive Predictive Value 0.4%), to minimize unnecessary follow up costs and potential harm due to false positive results. The Committee appreciated the challenge of improving specificity while maintaining high sensitivity, especially in a heterogeneous population that is representative of the U.S. The Committee also suggested further evaluation of alternative screenings methods that could be multiplexed to target additional conditions (for example, other Lysosomal Storage Disease conditions) in order to decrease the burden on public health laboratories.
2. **A standardized method of diagnosis after a positive newborn screen is required.**
The systematic review identified several different methods of case identification. The data presents no clear definition of a true Pompe disease case in the presymptomatic phase.
3. **More data are required about the benefit and harm of diagnosing late-onset Pompe disease during infancy.**

4. **No rigorous cost or cost-effectiveness data were identified in the systematic review.**

Although the Committee does not make decisions based on the cost-effectiveness of treatment, policy makers and state public health agencies need to know the cost to implement effectively the screening program.

The Committee understands that some data will be available soon that could address some of these knowledge gaps. However, the Committee encourages a U.S. population based pilot study to address many of these knowledge and technology gaps. One potential strategy to obtaining the requisite data would be to develop a research partnership with the National Institutes of Health's newly established Newborn Screening Translational Research Network.

The Committee will reconsider its recommendation after new evidence addressing the above issues is made available for evaluation.

Sincerely yours,

/s/

R. Rodney Howell, M.D.
Chairman