ACHDNC
Advisory Committee on Heritable Disorders in Newborns and Children

Nomination Form

Nomination of a Condition for Inclusion in the Recommended Uniform Screening Panel: Full Package

Introduction

The ACHDNC Nomination and Prioritization Workgroup reviewed the preliminary nomination form and supportive references for each section and verified that the nominated condition met the four basic requirements needed for a condition to be considered for review. The next step requires the completion and submission of the full nomination package for the condition.

Little information might be available for some of the questions in this package. The ACHDNC does not expect nominators to provide comprehensive answers for every question. The information you provide will be used to decide whether there is likely sufficient evidence related to the benefit of screening for the targeted condition to proceed with an evidence-based review. The ACHDNC will use the information provided to address the criteria in Appendix 1.

Please provide a citation to the most relevant peer-reviewed publication for responses in Table 1: References Table. In many cases, that will just be one citation and for some there might be no citation. These peer-reviewed publications can range from single- to multi-site studies and can be from the United States or outside of the United States.

Most newborn screening will lead to identification other than the targeted condition. When answering these questions, please focus on the nominated targeted condition. The optional worksheet in Appendix 2 may be helpful in completing these questions by separating the different conditions that could be identified.

The Corresponding Nominator is encouraged to contact HRSA staff (achdnc@hrsa.gov) with any questions or concerns at any time about this process. Newborn screening is complex and the process to submit the full package can be challenging. Please do not hesitate to reach out for help in completing this form.

Name of the Targeted Condition:

Corresponding Nominator Contact Information:
Name:
Professional Affiliation:
Telephone Number:
Email Address:

ACHDNC
Advisory Committee on Heritable Disorders in Newborns and Children

Nomination Form

Other Nominator information:

Name	Professional Affiliation (if any)

ACHDNC
Advisory Committee on Heritable Disorders in Newborns and Children

Nomination Form

Succinctly answer each question below.

The Condition

1. What is the clinical case definition for the condition being proposed for newborn screening (i.e., the targeted condition)? Be specific about whether screening is for a particular phenotype and for a specific biochemical profile or genotype.
2. What is the estimated prevalence of the condition? This could be in the United States or outside of the United States. If information is not available about the prevalence in newborns, describe the prevalence at other ages.
3. Without newborn screening, what is the typical age of diagnosis?
4. Without newborn screening, what is the process for establishing the condition after the development of clinical symptoms?
5. What treatment guidelines are available for individuals with the targeted condition diagnosed clinically ?
6. Briefly describe the current outcomes and ages associated with clinical diagnosis (e.g., premature death, need for mechanical ventilation, neurologic impairment).
7. Please describe any patient registries.

Screening

8. What approach is recommended for newborn screening? Please be specific regarding the type of sample and screening algorithm leading to diagnostic referral.
9. What information is available from studies of screening for the targeted condition? Outcomes could be one or more screening test characteristics (e.g., sensitivity, specificity, positive predictive value, negative predictive value), birth prevalence of the targeted condition, or rates of detection of non-targeted phenotypes or conditions. If possible, focus on prospective studies of screening. Do not include studies of only anonymized dried blood spots without follow-up of human subjects.
10. What other conditions could be identified by screening for the targeted condition as nominated? This includes phenotypes of the condition that are not nominated for newborn screening (e.g., late-onset disease, mild variants). Will screening for the targeted condition identify carriers? What is the recommended or expected follow-up for these non-targeted conditions?
11. What is the process for confirming the condition after newborn screening? Please also describe if there are non-targeted phenotypes or non-targeted conditions including later-onset conditions that would be identified during the diagnostic evaluation.
12. What treatment guidelines are available for individuals who are diagnosed through newborn screening or who are known to have the condition for other reasons (e.g., prenatal diagnosis, affected sibling) but are presymptomatic?

Impact of Screening

13. What is the expected benefit to infants from detection through newborn screening compared with clinical identification?
14. What is the expected benefit to families from detection through newborn screening compared with clinical identification?
15. Are there known harms to infants or to families from detection through newborn screening compared with clinical identification?

The following table provides a framework for considering harms related to newborn screening.

Table 1 Potential harms associated with newborn screening

Aspect of newborn screening	Type of potential harm	
	Newborns	Parents/families
Screening (bloodspot or point-of-care)	Pain or other adverse impacts from screening False positives or false negatives of screening	Psychosocial harms associated with false positive laboratory results for unaffected infants
Diagnosis evaluation	Pain or other adverse impacts from diagnostic testing Missed or incorrect diagnosis Disparities in access to diagnostic testing[a]	Psychosocial harm from diagnostic or prognostic uncertainty in diagnosis, or degree or age of onset of disease manifestations
Treatment and long term follow-up	Pain or other adverse impacts of treatment Treatment with an uncertain impact of disease severity and/or the timing of manifestations Disparities in access to treatment[a]	Psychosocial harm from uncertainty of outcomes Psychosocial, financial or other harms associated with long-term treatment Psychosocial harm from treatment decisions

[a] Such disparities could be considered a harm if disparities associated with screening were more pronounced than those encountered with clinical presentation

Goldenberg, A. J., Comeau, A. M., Grosse, S. D., Tanksley, S., Prosser, L. A., Ojodu, J., Botkin, J. R., Kemper, A. R., & Green, N. S. (2016). Evaluating Harms in the Assessment of Net Benefit: A Framework for Newborn Screening Condition Review. *Maternal and child health journal*, *20*(3), 693–700. https://doi.org/10.1007/s10995-015-1869-9

Other Considerations

16. Please share any information that is not captured above but important for the ACHDNC to understand. This may be left blank.

References

Please include citations to published peer-reviewed articles to support the responses listed above. In the first column, list the questions that are addressed by the article. Some questions might not have a supporting reference.

Table 1: References

Relevant Question Numbers	Reference

*A PDF of each reference should be submitted with this completed document.

Appendix 1: ACHDNC Criteria to consider whether to proceed with a full evidence-based review

Informational purposes only. The ACHDNC will use the information provided in your answers to address the following criteria.

1. The nominated condition is medically serious.
2. The case definition and the spectrum of the condition is well-described to help predict the phenotypic range of those children who will be identified based on population-based screening.
3. Prospective pilot data from population-based assessments are available for the condition.
4. The screening test has established analytic validity.
5. The characteristics of the screening test is reasonable for the newborn screening system (e.g., a low rate of false positives).
6. There is a widely available confirmatory test or diagnostic process, with CLIA- and/or FDA-approval as appropriate.
7. There are defined treatment protocols for the condition when identified presymptomatically and treatment is general available.
8. The results have clinical utility, balancing benefits and harms.
9. Screening will identify those most likely to benefit from treatment.

Appendix 2. Worksheet

This optional worksheet can help focus the responses on the targeted nominated condition.

Name of Condition or Phenotype	Nominated Targeted Condition (Yes/No)	Case Definition Available (Yes/No)	Medically Serious (Yes/No)	Prospective Population-Based Screening Project (Yes/No)	Diagnostic Confirmation Process Available (Yes/No)	Early Identification Associated with Net Benefit for the Infant (Yes/No)

The following is a hypothetical example based on a condition referred to as “Condition”:

Name of Condition or Phenotype	Nominated Targeted Condition (Yes/No)	Case Definition Available (Yes/No)	Medically Serious (Yes/No)	Prospective Population-Based Screening Project (Yes/No)	Diagnostic Confirmation Process Available (Yes/No)	Early Identification Associated with Net Benefit for the Infant (Yes/No/Uncertain)
Condition, Severe	Yes	Yes	Yes	Yes	Yes	Yes
Condition, Mild	Yes	Yes	No	Yes	Yes	No
Condition, Late Onset	No	Yes	No	No	No	Uncertain