Request for Proposal

Supplemental Funding to Expedite Public Health Implementation of Newborn Bloodspot Screening (NBS) to Detect Spinal Muscular Atrophy (SMA)

Date Issued: November 7, 2018

Date Due: Applications will be accepted on a rolling basis until December 7, 2018

CDC FOUNDATION CONTACT

Jalisa Hinkle
Program Officer
jhinkle@cdcfoundation.org

SUMMARY OF REQUEST

Spinal Muscular Atrophy (SMA) is the most common genetic cause of death in infants, and it results in severe lifelong disability for most children who survive. In December 2016, the U.S. Food and Drug Administration (FDA) approved an oligonucleotide therapeutic that prevents death and disability. In July 2018, the secretary of the US Department of Health and Human Services (DHHS) accepted the recommendation of the Advisory Committee on Heritable Disorders in Newborns and Children that SMA be added to the Recommended Uniform Screening Panel (RUSP). SMA is the most recent of the 35 core conditions to be included on the DHHS RUSP. The causative SMA mutation specified in the recommendation can be detected by Newborn Bloodspot Screening (NBS) using validated laboratory methods to analyze dried blood spot specimens obtained from newborn heelsticks.

The CDC Foundation was awarded limited funding in 2018 to provide one-time supplemental support to selected public health programs that are committed to implementing population-wide Newborn Bloodspot Screening for SMA (NBS-SMA). Three to six awards ranging from $50,000 to $200,000 each are anticipated. The overall purpose of these funds is to expedite the implementation process. Applicants may propose any use of the requested funds that will augment existing resources, accelerate work in progress, and shorten the time required for NBS-SMA to become a routine part of their NBS program. The preferred timeline would anticipate completion of a population-based pilot study within 18 months and transition to routine NBS-SMA within 20 months of receiving supplemental funds.

PROPOSAL AND BUDGET REQUIREMENTS

Project Budget: The range for requesting supplemental funds is $50,000 to $200,000 per program. Indirect costs must be limited to no more than eight percent of the total request to maximize funds available for direct program costs. Travel funds should not be included. Please note that the CDC Foundation is an independent 501(c)(3) organization and is not subject to federally negotiated indirect rates.

Contract and Budget: The Statement of Work (SOW) comprises five tasks relevant to implementing NBS-SMA. The proposal should specify the amount and purpose of supplemental funds requested for each of the five tasks. It should also include a timeline and pathway for completing all five tasks, including those that would not make use of supplemental funds awarded by the CDC Foundation.

Proposal Requirements: Proposals should be submitted by email to the CDC Foundation. Proposals should be no more than 10 pages, single spaced, 11-point font, not including appendices, and should address the following:

- The program's proposed approach to each of the five tasks outlined in the scope of work;
- Current status of each task at time of application;
- Proposed use of supplemental funds in each task for which such funds are requested; and
- Projected time of completion for each task (presuming supplemental funds are received).

Proposals should be submitted by email and will be accepted beginning November 7, 2018. Please email the entire proposal to Jalisa Hinkle at the CDC Foundation at jhinkle@cdcfoundation.org. Proposals will be evaluated as they are received. Funds will be awarded to programs with applications that meet the requirements stated herein and demonstrate a high probability of achieving routine population-based NBS-SMA within 20 months of receiving supplemental funds. This funding opportunity will be closed no later than December 7, or earlier if all available funds have been awarded.

Key Contact: Jalisa Hinkle, Program Officer at the CDC Foundation. Send email inquiries to jhinkle@cdcfoundation.org.

SCOPE OF WORK (BY TASK)

Task 1: Acquire, install, and operationalize the essential laboratory equipment necessary for the proposed NBS-SMA assay.

The assay of choice uses real-time quantitative PCR (qPCR) instrumentation, because of its existing widespread use in NBS laboratories to detect T-cell immunodeficiencies. Applicant programs currently running such assays may request additional real-time qPCR instruments for SMA assay development and implementation. Funds for other equipment may also be requested. All requests must be justified in the context of expediting NBS-SMA implementation.

> NOTE 1: Equipment purchased with this funding may be retained by the applicant program.
>
> NOTE 2: This task must include provisions for the integration of such equipment into the program's electronic data processing, result generating, and reporting systems (i.e., the laboratory information management system or analogous data management system).

Task 2: Select, develop, and validate the analytical method to be used for NBS-SMA.

The analytical method may be a commercially-available FDA-approved in vitro diagnostic device or an in-house laboratory-developed test (LDT) method. In either case, the relevant FDA and Centers for Medicare and Medicaid Services (CMS) requirements must be observed and documented. Validation must include recurrent analysis of external Quality Control (QC) materials and participation in periodic inter-laboratory evaluations from the Newborn Screening and Molecular Branch (NSMBB) at the Centers for Disease Control and Prevention (CDC). Validation should also include analysis of residual newborn dried blood spot specimens received by the program. The validation should establish provisional criteria for identifying presumptive screen-positive results (which may require adjustment as experience with the assay increases). All validation methods and parameters should be consistent with the program's policies and with the relevant FDA and CMS requirements.

> NOTE: If the NBS-SMA method is multiplexed with the measurement of one or more additional analytes to screen for other conditions (such as quantifying TREC to detect immunodeficiencies), the multiplexed assay must be validated for all measurands.

Task 3: Establish protocols that will be used to follow up newborns with screen-positive results.

Documentation for this task should begin with the immediate within-laboratory actions such as repeating the test on additional punches from the original bloodspot collection card. For specimens confirmed as screen-positive, the follow-up plan should delineate the pathway for prompt referral to a pediatric neurologist who can conduct the appropriate diagnostic work-up and begin treatment as indicated. Special considerations may be necessary for programs that encompass large, sparsely-populated areas with limited access to pediatric neurologists. All follow-up protocols should be consistent with the program's policies and relevant laws.

Task 4: Conduct a population-based pilot study using the validated assay to identify screen-positive newborns and engage the follow-up procedure.

The pilot study should emulate routine NBS as nearly as possible, with special attention to laboratory processes and follow-up activities. During the pilot, the same attention should be given to any tests for other conditions that are multiplexed with the SMA analyte, such as TREC measurements to detect immunodeficiencies. Results from the pilot study should be used to refine provisional criteria for screen-positive SMA results and any other conditions detected in the same multiplexed analysis. Because of the relatively high birth prevalence of SMA-affected newborns (about 1:10,000), programs should be fully prepared to engage their follow-up protocols as soon as the pilot study begins.

Task 5: Compile the results of the population-based pilot study and transition directly to routine NBS-SMA.

The proposal should describe how continuity in NSB-SMA will be maintained in the transition from the pilot study to routine practice.

EXPECTED TIMELINE FOR TASK COMPLETION

Within four months after receiving supplemental funds: Completion of Task 1 and method selection described in Task 2.

Within eight months after receiving supplemental funds: Completion of Task 2 and the majority of Task 3.

Within twelve months after receiving supplemental funds: Completion of Task 3 and initiation of Task 4.

Within eighteen months after receiving supplemental funds: Completion of Task 4 and transition to Task 5.

Within twenty months after receiving supplemental funds: NBS-SMA is part of routine practice in the public health NBS program.