ACMG
American College of Medical Genetics and Genomics

NBSTRN
Newborn Screening Translational Research Network

Request for Proposal

NBSTRN Website and NBS Research Repository

Issued February 6, 2019
Brief Statement Indicating Intent to Apply Requested by February 14, 2019
Responses Due by March 16, 2019
Award Date Estimated April 1, 2019

American College of Medical Genetics and Genomics
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General Information

Background

Each year the 4 million babies born in the US undergo laboratory and hospital-based screening for 60 genetic conditions. The laboratory portion of screening is conducted in state-based public health departments, and birthing hospitals screen newborns for hearing and congenital heart disorders. Screening is just the beginning and newborn screening (NBS) is considered a "system" involving prenatal education, neonatal screening, diagnosis, clinical referral, and treatment. The majority of NBS conditions are rare, and while NBS prevents morbidity and mortality, most of the conditions require lifelong clinical care and management. NBS began over 50 years ago and treatments have evolved from dietary interventions to medically complex and invasive procedures like stem cell transplant, gene therapy, intrathecal enzyme replacement using lumbar puncture, and genotype-directed therapies. Throughout the years, a better understanding of each of the 60 conditions has been possible because screening on a population basis enables unbiased ascertainment and the ability to longitudinally collect health information on each diagnosed newborn. These longitudinal natural history studies have profoundly improved knowledge of the diseases' etiology, pathophysiology, phenotypic heterogeneity, and comorbidities.

Federal Efforts

The *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) has played a role in NBS since the beginning but their leadership and role in NBS research were formalized in the NBS Saves Lives Act of 2008, and reaffirmed in the NBS Saves Lives Reauthorization Act of 2014. This legislation established and authorized the Hunter Kelly NBS Research Program within NICHD to carry out, coordinate, and expand research in NBS. The legislation also established and funded related efforts at the Centers for Disease Control and Prevention (CDC) and the Health Resources and Service Administration (HRSA), including continued support for the HHS Secretary Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC). ACHDNC included representation for genomics and industry in 2005, and ACHDNC is the body that reviews evidence and makes recommendations for which conditions should be part of nationwide screening. The current process is for any candidate condition, including genomics, to be submitted to ACHDNC for a formal evidence review. It is important to note that NBS is state based, so although HHS recommends a uniform panel, each state determines which conditions to include in screening.

ACMG

Founded in 1991, the American College of Medical Genetics and Genomics (ACMG) is the only nationally recognized medical society dedicated to improving health through the clinical practice of medical genetics and genomics. ACMG provides education, resources, and a voice

for more than 2,200 biochemical, clinical, cytogenetic, medical and molecular geneticists, genetic counselors and other healthcare professionals, nearly 80% of whom are board certified in the medical genetics specialties. The College's mission is to develop and sustain genetic initiatives in clinical and laboratory practice, education and advocacy. To obtain more information about ACMG please visit https://www.acmg.net.

NBSTRN

Through two consecutive five-year contracts, the ACMG has led the development and implementation of a key component of the Hunter Kelly NBS Research Program, the NBS Translational Research Network (NBSTRN). The NBSTRN began as an effort to engage a variety of stakeholders across the NBS system and has matured into a dynamic and committed network comprised of researchers, public health professionals and clinicians with expertise in:

- The discovery and validation of novel technologies to screen and diagnose disease;
- The clinical care of newborns including execution of clinical trials and application of cutting-edge treatments and management strategies;
- Pilots of new technologies and treatments;
- The collection, analysis and dissemination of longitudinal health and genomic data; and
- The ethical, legal and social implications of NBS research.

In September 2018 ACMG was awarded a one-year contract as a base plus four option years to continue the NBSTRN. The NBSTRN contract outlines a series of resources, information technology tools, and expert workgroups to be maintained and enhanced by ACMG. To learn more about NBSTRN, please visit https://www.nbstrn.org.

RFP for NBSTRN Website and NBS Research Repository

This RFP is intended to solicit proposals to subcontract the enhancement and maintenance of the NBSTRN Website, and development and maintenance of the NBS Research Repository.

1. The NBSTRN Website serves as a centralized online presence for NBSTRN that highlights the tools and resources available to NBS researchers and related stakeholders. Ideally an enhanced website will include a virtual meeting and collaboration space for researchers, NBSTRN Workgroups and partners, and state NBS programs to post thoughts and share documents using discussion and message boards. In addition, the current website includes ELSI Advantage which is a series of focused tabbed web pages, a form

generator and a restricted search box that has an avatar overlay. An updated website should include and enhance the current functionality of ELSI Advantage. A detailed list of requirements is included below and a technical call will be scheduled to address any questions.

2. The NBS Research Repository is envisioned to combine functionality of two of the current NBSTRN tools: (1) Virtual Repository of Dried Blood Spots (VRDBS, https://vrdbs.nbstrn.org) and (2) Region 4 Stork (R4S, https://nbstrn.org/research-tools/lab-performance-database).

Additional Background on Current Tools

The consolidation and update of VRDBS and R4S is based on: (1) changes to human subjects regulations related to research with dried blood spots (DBS); (2) feedback from users who requested additional functionality and increased access to analytical tools, cumulative pilot data, and de-identified data; and (3) NBSTRN staff review of how the VRDBS and R4S were being used to advance NBS research.

VRDBS - The VRDBS review showed that although researchers found de-identified case level data useful to understand the type of DBS available, the state NBS programs did not use this information when fulfilling and tracking orders. VRDBS has great name recognition and users report that the state profiles are useful.

R4S - NBSTRN leveraged R4S, a laboratory performance tool, to track data in a pilot of NBS for Severe Combined Immune Deficiency (SCID). R4S was developed by Mayo Clinic and focused postanalytical interpretation of tandem mass spectrometry results. Mayo expanded the functionality of R4S into a new tools called Clinical Laboratory Integrated Reports (CLIR). Access to CLIR is limited to data contributors, and while the NBS pilot sites utilize CLIR to interpret screening results for Pompe, MPS I and X-ALD, NBSTRN does not have access to the data. NBSTRN's goal is to track serial data to inform the results of NBS pilots, and this includes screening tests that are not interpreted by CLIR (e.g. molecular, genomics). R4S has been taken offline and our plan is to create new tool called the Clinical Laboratory Performance Resource (CLPR) for pilot sites and states to enter data to track results of NBS pilots.

Contact for RFP

Responses to the RFP should be submitted to both Dr. Michael Watson (mwatson@acmg.net) and Dr. Amy Brower (abrower@acmg.net).

Timeline for RFP

Issued February 6, 2019
Brief Statement Indicating Intent to Apply Requested by February 14, 2019
Responses Due by March 16, 2019
Estimated Award Date April 1, 2019

Suggested Project Phase	Timeline
Development- Phase I	Complete a prototype of the interactive website, the NBS research data repository and a training plan by August 1, 2019
*Development- Phase II	A final product including training of users to be completed by January 1, 2020
*Additional Enhancements	January 2019- September 2020
*Maintenance	October 2020- September 2021
*Maintenance	October 2021- September 2022
*Maintenance	October 2022- September 2023

**Note: Development-Phase II and following phases will be awarded based on option years.*

Preparing and submitting a response

Contractor Information Required to be Included with Response

The proposal must contain the full legal name and signature of the authorized representative of the contractor. Telephone, fax, email and business address of the point of contact person needs to be included.

Response Submittal

A very brief statement indicating intent to apply is requested by 5:00 pm EST on February 14, 2019. Complete responses must be submitted **by 5:00 pm EST**, **on March 16, 2019**. Responses can be sent via email to Michael Watson mwatson@acmg.net and Amy Brower abrower@acmg.net. It is the responsibility of the applicant to ensure that the response is received by this deadline.

Responses should be limited to 20 pages of text. References, charts and graphics are not included as part of the page limit.

Submitters will receive a confirmation of receipt of their response by ACMG. ACMG may terminate or modify the RFP process at any time during the response period. All changes to the RFP will be posted to the NBSTRN Website. No changes will be made to the RFP within one

week of due date. Responses that are not received by the stated deadline shall be determined to be non-responsive and, at ACMG's discretion, may not be considered in the review of respondents.

Applications are due by 5:00 pm EST on March 16, 2019 and will be evaluated for a two week period following submission. ACMG may request meetings or a teleconference with the respondents prior to announcement of final contract recipients.

General information, assumptions and references

This section on general issues, assumptions and preferences, while not requirements, provide an overview of the non-functional requirements and preferences that are important issues for consideration by respondents since they describe key aspects of the NBSTRN website and NBS Research Repository that would be most appropriate.

- Develop the technical requirements of an enhanced, interactive NBSTRN website and new NBS research repository system in collaboration with the NBSTRN team.
- Both the interactive website and the web interface to the NBS research repository must meet modern web standards and be browser-independent; must not require any plug-ins so it will work on every platform; must be HTML5 and 508 compliant; and must operate within a FISMA Moderate IT environment.
- Complete first phases of both the interactive website and the NBS research repository by August 1, 2019. A final product will be completed by January 1, 2020.
- The respondent can subcontract out any portion of the website or repository creation with prior approval from ACMG and NICHD, but is accountable for all project deadlines.
- Ability for the NBSTRN team, including their web developer, to provide incremental adjustments and feedback as well as perform content changes within the site(s).
- Participation in the NBSTRN Steering Committee by regularly attending committee calls.

General requirements of proposal

Instructions: Respondents must provide a point-by-point response to each of the General Requirements specified in this RFP. For each requirement, respondents should provide documentation as requested. The documentation demonstrates they understand the

requirement and agree to the requirement. Responses to general requirements must be in sequence and numbered as they appear in the RFP.

Executive summary

Provide a narrative summary of the proposal being submitted. The summary should identify the services that are being offered in the proposal including their design and development .

Organization/management capabilities

Respondents should describe their company's organizational structure and provide a brief history of their business.

References

Respondents should include a list of clients, organizations or institutions that can be used as references. At least one reference should be from an organizational client where a similar project was developed. Selected references may be contacted to determine the quality of work performed, competency of personnel assigned to the project, etc. The results of the reference checks will be provided to the evaluation and may be used in scoring the written proposal.

These references should be capable of verifying information supplied by the respondent in their proposal. The data required for each reference should include:

Company Name
Address
Contact person name, email, phone number and address
Description of the type of work performed and the results

Examples of successful efforts

Respondents should include a description of their relevant experience developing and implementing web-based resource systems. Please provide information about specific platforms used, dates implemented, and customer satisfaction. Testimonials are encouraged.

Staff qualifications

The respondent must provide a project team organizational chart, followed by resumes of key personnel that will be assigned to the system development and implementation. Each key personnel must be an employee of the respondent or be identified as a subcontractor. Include roles, responsibilities and estimated time allocated for each key personnel.

Budget

A budget should be presented for all phases of this project including development and maintenance. The budget must encompass all design, production, and software acquisitions necessary for the development and maintenance of the website and data repository. Please include any costs associated with additional maintenance, support, upgrades and long-term annual maintenance. This budget is not binding but will provide information to ACMG for project development.

Technical Requirements

The respondent must discuss the scope of the project with regards to developing an interactive website, ELSI Advantage, data repository and visualization for NBS pilot and state-based analytical and clinical validation and related data.

The applications must meet the following criteria.

1. *NBSTRN Website Structure Specifications -* The applicant for the enhanced NBSTRN website must describe how his/her organization will meet the following specifications:

    a. 508-compliant online environment for NBSTRN workgroup members and NBS researchers that includes discussion and message boards with file upload and download capability.

    b. NBSTRN staff-facilitated approval system for registration of researchers, clinicians, parents and patients for all NBSTRN tools.

    c. Functionality to enable NBSTRN staff to disseminate research findings communicated via print, presentation, and web-based reporting.

    d. Identifiable sections (below) for key stakeholders such as potential and current investigators, clinicians, public health partners, newborn screening laboratories, follow-up programs, and federal partners in newborn screening.

        i. NBSTRN expert workgroup-generated information including meeting minutes, meeting recordings, discussion forum, and copies of white papers generated from in-person meetings.

        ii. Hosting and archiving all webinars (e.g. NBSTRN Workgroups, National Pilot Calls).

        iii. Section for training information and manuals for the online NBS Research Repository and other NBSTRN Tools (e.g. Longitudinal Pediatric Data

Resource and Genomics Warehouse). Note that the LPDR may be developed by another party and your response should outline an approach to include information from the LPDR.

iv. Section for ELSI Advantage including information about regulatory requirements associated with state informed consent, Institutional Review Boards (IRBs), the "Common Rule," and state and local research policies associated with newborn screening.

v. NBS Research calendar of events (e.g., meetings, symposia, training workshops, etc.) and listing of funding opportunities related to NBS research.

vi. Data Dashboard for communicating key metrics (e.g. type and amount of data available for use by researchers who were not the primary source of the data).

vii. Links to external websites (e.g., state NBS programs, NICHD Hunter Kelly Newborn Screening Research Program, NICHD Data and Specimen Hub (DASH), NIH NLM Code Repository, NIH NCBI dbGaP, APHL NewSTEPs Repository, ACMG Clinical Decision Support Tools, HRSA ACHDNC, HRSA funded Regional Collaboratives, National Coordinating Center for the Regional Collaboratives, American Academy of Pediatrics, Centers for Disease Control and Prevention, NBS Clearinghouse, etc.).

viii. Patient, family and advocate focused pages that include information on research in newborn screening and links to related websites.

e. Enable State NBS Programs to deposit information that populates expanded profiles that include a virtual repository of specimens and subjects using a relational database that can be updated on demand from the State NBS Programs. A list of current data fields is provided for your reference below.

i. NBS Program Contacts

ii. Annual Births

iii. Ethnic Distribution

iv. Estimated incidence for each screened condition

v. Informed Consent for Research

vi. Multi-State Research Policies

vii. Dried blood spot (DBS) retention time

viii. DBS storage conditions

ix. Process for adding NBS conditions to the screening panel

x. National Coordinating Center (NCC) Region

xi. NBS Card Picture

xii. State Comments

xiii. Last updated

xiv. Material Transfer Agreement (MTA)

xv. Institutional Review Board (IRB) Information and Links

xvi. Frequency of Updates to VRDBS for Participating States

xvii. Recovery Costs for DBS

f. National, Regional and State-level data dashboards including active and completed NBS research projects, location of NBSTRN investigators.

g. Area to disseminate a listing of key NBS research and literature provided by NBSTRN staff.

h. Web application interface to the NBS Research Repository.

i. User friendly, modern, and easy to navigate.

j. Compatible with other NIH and NICHD websites (e.g. https://dash.nichd.nih.gov/; https://cde.nlm.nih.gov/; https://www.ncbi.nlm.nih.gov/clinvar/).

k. Migrate current nbstrn.org content in collaboration with ACMG. The current website was created in Drupal and content updates require direct editing of the page. You are encouraged to include a strategy for deploying a web platform and content management system of your choice which supports updating web pages using automated approaches with raw data stored in relational databases.

l. Maintenance of an online documented code repository.

m. Delivery to ACMG, upon the expiration date of the contract, all source code and object code developed, modified, and/or enhanced under this contract.

n. Provision of all documentation to properly compile the source code and related data on ACMG's internal infrastructure with hardware requirements.

o. Please provide mock-ups and visuals to support the project details listed above.

2. *NBS Research Repository System Specifications* - The applicant for the NBS Research Repository must describe how his/her organization will meet the following specifications.

a. 508-compliant online repository with controlled role-based access for researchers, pilot sites, state NBS programs and staff.

b. Maintenance and organization of serial, case level and aggregate data submitted online and compiled prospectively from NBS pilots of candidate and recommended conditions (e.g. number screened, true positives, false positives, variants of unknown significance, carriers).

c. Display of aggregate data related to laboratory performance assessments generated by state NBS programs and pilot sites and stored in Mayo Collaborative Integrated Laboratory Reports (CLIR) (https://clir.mayo.edu/). Note that this will require the state NBS programs and pilot sites to share data reports generated by CLIR.

d. Summaries of data related to candidate conditions (e.g. incidence, research, treatment). The data will be generated and provided by the NBSTRN team.

e. Summaries of data related to conditions recently added to nationwide screening (e.g. incidence, variant data). The data will be generated and provided by the NBSTRN team.

f. NBS Pilot reports for each condition including screening algorithm, diagnostic algorithm, clinical decision support tool(s), key considerations provided by the pilot sites.

g. Ability to generate standardized reporting at both the individual state level and pilot site level. This ad-hoc reporting system will include the incorporation of a user-friendly reporting tool, allowing raw data export for state programs and fixed reports that may be used by multiple groups. Dynamic reporting system

will allow each researcher and/or pilot site to explore their own data to meet research goals.]

h. Enable the uploading of data to 3rd party platforms as requested by NBSTRN (e.g. DASH, dbGaP).

i. Maintenance of an online documented code repository.

j. Delivery to ACMG, upon the expiration date of the contract, all source code and object code developed, modified, and/or enhanced under this contract.

k. Provision of all documentation to properly compile the source code and related data on ACMG's internal infrastructure with hardware requirements.

l. Please provide mock-ups and visuals to support the project details listed above.

3. Security Requirements

a. The Contractor shall provide appropriate artifacts from development, testing, and implementation in accordance with NIST Risk Management Framework (NIST SP 800-53) for FISMA Moderate systems. Provide all artifacts required to conduct secure software development activities.

b. Comply with the Privacy Act Requirements.

4. Operational Specifications: - The applicant for the NBS Research Repository must describe how his/her organization will meet the following specifications.

a. The ability to restrict access to different sections of the system using role-based access. Ability to restrict access to the data based on user's profile. Ability to monitor access logs including cumulative and serial totals of how many clinicians, patients, NBS state programs and other users accessed and/or downloaded data.

b. Options for Data Entry and Transfer - to allow data to be entered manually for each individual infant and by electronic transfer. For manual entry, beta testing of entry screens for logical/data processing concerns, aesthetics and usability.

c. Ability to use medical terminology including Logical Observation Identifiers, Names and Codes (LOINC) and Systematized Nomenclature of Medicine – Clinical Terms (SNOMED-CT) within the data upload file.

d. Ability to upload data to a test repository during interface development and testing.

e. Please provide mock-ups and visuals to support the project details listed above.

5. *Other Specifications*

a. The respondent must include requirements for security and discuss processes that will be developed to ensure compliance with HHS Enterprise Performance Life Cycle (EPLC) requirements.

b. Hosting location and storage/backup details should be discussed.

c. Respondent must include a training plan, to include administrator/configuration training as well as user training, and should address training at initial implementation and any training necessary as a result of new development or ACMG staffing changes.

d. Respondent must discuss their plan for making a test environment available for user testing and validation.

Evaluation Criteria and Subcontracting Reports

Applications will be evaluated based on budget, demonstration of technical understanding of the application, and creativity in the response. ACMG will evaluate each application based on the description of the General, Technical and Budget requirements listed in the RFP. The evaluation team will review each applicant and provide recommendations to the NBSTRN Director.

Subcontracting Reports - The subcontractor should provide the following deliverables to the NBSTRN team using the format specified below:

a. Cover page

i. All reports shall include a cover page prepared in accordance with the following format:

1. Contract Number and Project Title

2. Period of performance being reported

3. Contractor's name and address, telephone and fax numbers

4. Author(s)

5. Date of submission

6. Delivery Address

b. Monthly reports

This report shall include: An analysis of web traffic and tool use, budget update, a very brief overview of the work completed for the reporting period and/or justification for intended work not completed

c. Quarterly progress report

This report shall include: A statement of intended work for the reporting period, a brief overview of the work completed for the reporting period and/or justification for intended work not completed, and a brief overview of any problems (technical or financial) that occurred during the current reporting period and proposed solutions.

d. Annual Progress Report

This report includes a summation of the results of the entire contract work for the period covered. An Annual Progress Report will not be required for the period when the Final Report is due. A Quarterly Progress Report shall not be submitted when an Annual Progress Report is due. This report should include:

- Summary of work completed
- Maintenance and proposed upgrades
- Brief overview of any problems (technical or financial)
- Summary of access and use analytics
- Proposed future efforts
- Summary of changes in staffing

e. Final Report

This report includes a summation of work performed and the results obtained for the entire contract period of performance. This report shall be in sufficient detail to describe comprehensively the results achieved. An annual report will not be required for the period when the Final Report is due.

Disclaimer

This RFP is neither an agreement nor an offer to enter into an agreement with any respondent. Once evaluation is complete, ACMG may choose to enter into a definitive contract with the selected RFP applicant.

Each respondent shall bear its own costs associated with or relating to the preparation and submission of its application. All such costs and expenses will remain with such respondent and

ACMG will not be liable for these or for any other costs or other expenses incurred by a respondent in preparation or submission of its application, regardless of the conduct or outcome of the response period or the selection process.

Note

Subcontractors may respond to more than one RFP issued as part of the NBSTRN. If responding to more than one RFP, please explain the combined approach and any cost reduction.