U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

Print Date: 5/15/20

Title:	Pilot PT Program for Spinal Muscular Atrophy (SMA)
Project Id:	0900f3eb81b383d2
Accession #:	NCEH-DLS-4/30/20-383d2
Project Contact:	Ding_Yan (Shirley) (yad6)
Organization:	NCEH/ATSDR/DLS
Status:	**Pending Clearance**
Intended Use:	**Project Determination**
Estimated Start Date:	04/13/2020
Estimated Completion Date:	04/03/2021
CDC/ATSDR HRPO/IRB Protocol #:	
OMB Control #:	
Source System #:	2020-0076

Determinations

Determination	Justification	Completed	Entered By & Role
HSC: **Does NOT Require HRPO Review**	Not Research	5/15/20	Davis_Stephanie I. (sgd8) CIO HSC
PRA: **PRA Applies**		5/15/20	Davis_Stephanie I. (sgd8) CIO OMB / PRA

Description & Funding

Description

Priority:	Standard
Date Needed:	05/30/2020
Determination Start Date:	04/30/20
Description:	The goal of this project is to pilot test an SMA proficiency testing program with partner domestic newborn screening programs. The MQIP team has developed a protocol to make dried blood spot materials that are needed by newborn screening labs in support of SMA testing including: 1) SMA-like specimens that are homozygous for the SMN1 exon 7 deletion 2) SMA- carrier specimens that have one normal SMN1 exon 7 and one deletion of SMN1 exon 7 3) "Negative" or normal specimens that will amplify the SMN1 exon 7 4) UNSAT samples that have no amplification These materials will be sent to partner newborn screening labs that have agreed to assist MQIP in testing the logistics of the PT program. This pilot will evaluate the shipping logistics and processes related to the send out of PT materials, the data collection tool, data receipt, analysis and report generation process by CDC as well as the data reporting and results receipt within domestic newborn screening programs prior to full PT implementation. The MQIP team will work closely with NSQAP's data management team with the above processes.
IMS/CIO/Epi-Aid/Chemical Exposure Submission:	No
IMS Activation Name:	Not selected
CIO Emergency Response Name:	Not selected
Epi-Aid Name:	Not selected
Assessment of Chemical Exposure Name:	Not selected
Goals/Purpose	MQIP is dedicated to supporting state screening programs in their effort to identify newborns with Spinal Muscular Atrophy (SMA). An integral component of this support is the development, preparation and distribution of quality assurance materials that can be used by newborn screening labs to meet their quality and regulatory needs. The MQIP team has been developing and testing a protocol to make dried blood spot materials that are needed by newborn screening labs in support of SMA testing. MQIP has validated these materials as fit for purpose for newborn screening of SMA. We now propose the establishment of a pilot of an SMA PT program in domestic newborn screening programs.
Objective:	In 2018, SMA was added by the HHS Secretary to the recommended uniform screening panel (RUSP) for newborn screening and currently 22 domestic public health programs have begun routine screening. It is expected that all U.S. newborn screening laboratories will adopt SMA screening in the next few years. Infants born with infantile or type 1 SMA become incapacitated and typically die within 2 to 4 years of life. However, if SMA is diagnosed and treated prior to onset of symptoms with an FDA approved drug, children with Type 1 SMA can avoid severe, deleterious effects of the disease and may retain the ability to live relatively normal lives. Newborn screening for SMA allows for early detection of affected infants that may appear normal at birth and early treatment can halt irreversible neuronal damage. Newborn screening programs count on CDC's quality assurance program for dried blood spot materials to help them assure that their assays are accurately detecting babies affected with SMA. If a child is missed, the baby would die unnecessarily. In addition, public health programs rely on CDC for PT challenges to comply with their clinical testing regulatory requirements.
Activities or Tasks:	Purchase, Use, or Transfer of Information, Data, Biospecimens or Materials
Target Populations to be Included/Represented:	Other
Tags/Keywords:	DLS 2020-0076, SMA, pilot, real time PCR, , Laboratory Proficiency Testing
CDC's Role:	CDC is provider of materials/services TO an institution, CDC is recipient of private data/specimens FROM an institution

Method Categories:	QA/QI
Methods:	Quality assurance materials that will be used for the pilot PT were created from samples received from two sources including: de-identified patient samples collected by the Sequoia Foundation in collaboration with the California Department of Public Health that represent an SMA patient sample (ie homozygous SMN1 exon 7 deletion), an SMA carrier sample (ie heterozygous SMN1 exon 7 deletion) and an SMA unaffected sample (ie intact SMN1 exon 7 region); and leukodepleted blood from Tennessee Blood Services. These quality assurance materials will be fully validated by the following criteria with the MQIP quality representative: 1) Transduced cell confirmation relative to initial blood received - microsatellite analysis a. Results must match those obtained from initial patient donor blood sample and master bank cells 2) Homogeneity testing - real-time PCR assay that detects the RPPH1 gene a. DNA concentrations are used to evaluate homogeneity and must return a "Yes" result when using the SAS program described in NSMB-B/C-LABOP.014 3) Fit for purpose testing - real-time PCR triplex assay that detects SMN1 (exon 7)/TREC/RPP30 a. Assay run on different instruments using different DNA extraction methods and be within expected ranges MQIP will develop forms, templates, Excel macros and SAS programs as needed for 1) PHL data collection and instructions; 2) CDC data receipt from PHL and aggregation programs; 3) data analysis programs and SOPs; 4) report templates and lab verification pages (along with needed SAS programs). NSQAP will incorporate SMA into the CRM system including: 1) all information and documentation associated with a new PT program; 2) develop shipping materials and logistics plans; 3) develop system to receive data via Excel data collection forms and 3) develop system to vet final reports, assure 508 compliance and report dissemination to PHLs.
Collection of Info, Data or Biospecimen:	Materials will be shipped via FedEx along with instructions (pdf) and an Excel data collection form to participating state public health laboratories (PHLs) for evaluation. PHLs will run their routine SMN1 detection assay(s) to assess if any of the five pilot PT specimens give a result that suggests the sample is at risk for SMA. The PHLs will input the following information on to the data collection form: 1) Lab code number; 2) Type of screening method; 3) Method of DNA extraction; 4) SMN1 assay primer and probe information; 5) Reference gene assay primer and probe information; and 6) Clinical assessment based on presence or absence of SMN1 exon 7. Once complete, the PHLs will return their evaluations to NSQAP DMT for assessment. The MQIP team will perform the evaluation on the submitted data and generate an SMA program newsletter with individual laboratory assessments, which will be returned to the participants by email.
Expected Use of Findings/Results:	In 2018, SMA was added by the HHS Secretary to the recommended uniform screening panel (RUSP) for newborn screening and currently 22 domestic public health programs have begun routine screening. It is expected that all U.S. newborn screening laboratories will adopt SMA screening in the next few years. Infants born with infantile or type 1 SMA become incapacitated and typically die within 2 to 4 years of life. However, if SMA is diagnosed and treated prior to onset of symptoms with an FDA approved drug, children with Type 1 SMA can avoid severe, deleterious effects of the disease and may retain the ability to live relatively normal lives. Newborn screening for SMA allows for early detection of affected infants that may appear normal at birth and early treatment can halt irreversible neuronal damage. Newborn screening programs count on CDC's quality assurance program for dried blood spot materials to help them assure that their assays are accurately detecting babies affected with SMA. If a child is missed, the baby would die unnecessarily. In addition, public health programs rely on CDC for PT challenges to comply with their clinical testing regulatory requirements. The results of this Pilot SMA PT event will not be disseminated to the public; although, respondent labs will be notified of their own performance results as part of the pilot of methods and procedures. CDC will use these results to finalize the SMA PT methods.
Could Individuals potentially be identified based on Information Collected?	No

Funding

Funding Type	Funding Title	Funding #	Original Budget Yr	# Years Award
CDC Funding Intramural	Project Funding and Partners			

Review Attributes

Quality Assurance / Improvement

Regulation and Policy

Do you anticipate this project will be submitted to the IRB office	No
Estimated number of study participants	
Population - Children	
Population - Minors	
Population - Prisoners	
Population - Pregnant Women	
Population - Emancipated Minors	

Suggested level of risk to subjects Do you anticipate this project will be exempt research or non-exempt research

Requested consent process waviers

Informed consent for adults	No Selection
Children capable of providing assent	No Selection
Parental permission	No Selection
Alteration of authorization under HIPPA Privacy Rule	No Selection

Requested documents of informed consent

Informed consent for adults	No Selection
Children capable of providing assent	No Selection
Parental permission	No Selection

Consent process shown in an understandable language

Reading level has been estimated	No Selection
Comprehension tool is provided	No Selection
Short form is provided	No Selection
Translation planned or performed	No Selection
Certified translation / translator	No Selection
Translation and back-translation to/from target language(s)	No Selection
Other method	No Selection

Clinical Trial

Involves human participants	No Selection
Assigned to an intervention	No Selection
Evaluate the effect of the intervention	No Selection
Evaluation of a health related biomedical or behavioral outcome	No Selection
Registerable clinical trial	No Selection

Other Considerations

Exception is requested to PHS informing those bested about HIV serostatus	No Selection
Human genetic testing is planned now or in the future	No Selection
Involves long-term storage of identfiable biological specimens	No Selection
Involves a drug, biologic, or device	No Selection
Conducted under an Investigational New Drug exemption or Investigational Device Exemption	No Selection

Institutions & Staff

Institutions

Name	FWA #	FWA Exp Date	IRB Title	IRB Exp Date	Funding #
Centers for Disease Control & Prevention	FWA00001413	10/31/24			

Staff

Staff Member	SIQT Exp. Date	CITI Biomedical Exp. Date	CITI Social & Behavioral Exp. Date	CITI Good Clinical Practice Exp. Date	Staff Role	Email	Phone	Organization
John Bernstein	09/26/2021				Project Officer		770-488-0973	NEWBORN SCREENING BRANCH
Kristina Mercer	09/17/2021	11/02/2021			Project Officer		404-498-0866	NEWBORN SCREENING TEAM 3

Data

DMP

Proposed Data Collection Start Date:	4/13/20
Proposed Data Collection End Date:	4/3/21
Proposed Public Access Level:	Non-Public

Non-Public Details:

Reason For Not Releasing Data:	Other - QA/QC
Public Access Justification:	QA/QC
How Access Will Be Provided for Data:	Project data is not public health data
Plans for Archival and Long Term Preservation:	

Spatiality

Spatiality (Geographic Locations) yet to be added .....

Dataset

Dataset Title	Data Publisher/Owner	Public Access Level	Public Access Justification	External Access URL	Download URL	Type of Data Released	Collection Start Date	Collection End Date
Dataset yet to be added...								


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