


Newborn Screening Translational Research Network Update

Heartlands Regional
Genetics and Newborn
Screening Collaborative


October 4, 2012



Overview


- **Introduction of New Members**
- **Review of NBSTRN-CC Work Group Activities**
 - **Legal and Bioethics**
 - **NBS Laboratories and Programs**
 - **Clinical Centers**
 - **Data Access, Sharing, and Use Limitations**
 - **IT and Informatics**
 - **Website**
 - **VRDBS**
 - **LTFU data sets**
 - **R4S**
- **NBSTRN Pilots**
 - **LSDs**
 - **SCID**

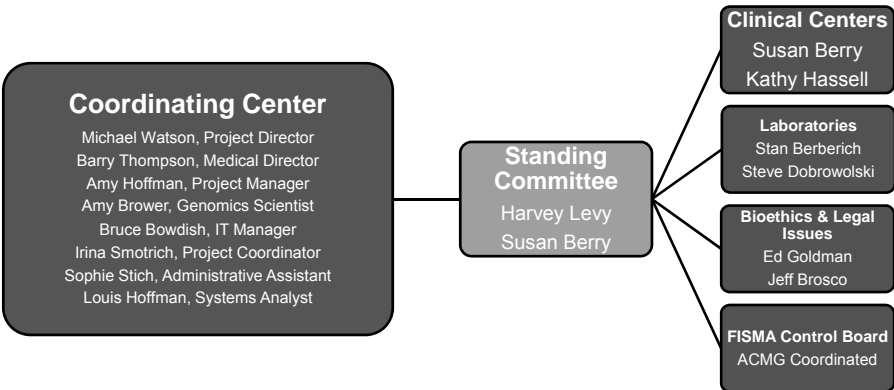
Newborn Screening Translational Research Network 2

 **Overview (continued)**

- **NBSTRN Program Grantees**
 - Spinal muscular atrophy: PI - Kathy Swoboda
 - Metabolic disease in NBS: PI Sue Berry and Cynthia Cameron
 - Newborn Screening for Lysosomal Storage Diseases: PI - Melissa Wasserstein
- **NBSTRN Program Contractees**
 - LSD comparative evaluation of NBS technologies: PI - Dieter Matern
 - SMA / SCID NBS technologies: PI - Steve Dobrowolski
- **NBSTRN-CC pilots to assess infrastructure and data systems**
 - SCID
 - LSDs

Newborn Screening Translational Research Network 3

 **Coordinating Center Organization**



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graph LR; CC[Coordinating Center] --- SC[Standing Committee]; SC --- CClinical[Clinical Centers]; SC --- CLab[Laboratories]; SC --- CBio[Bioethics & Legal Issues]; SC --- CFISMA[FISMA Control Board];
```

Coordinating Center
Michael Watson, Project Director
Barry Thompson, Medical Director
Amy Hoffman, Project Manager
Amy Brower, Genomics Scientist
Bruce Bowdish, IT Manager
Irina Smotrich, Project Coordinator
Sophie Stich, Administrative Assistant
Louis Hoffman, Systems Analyst

Standing Committee
Harvey Levy
Susan Berry


Clinical Centers
Susan Berry
Kathy Hassell

Laboratories
Stan Berberich
Steve Dobrowolski

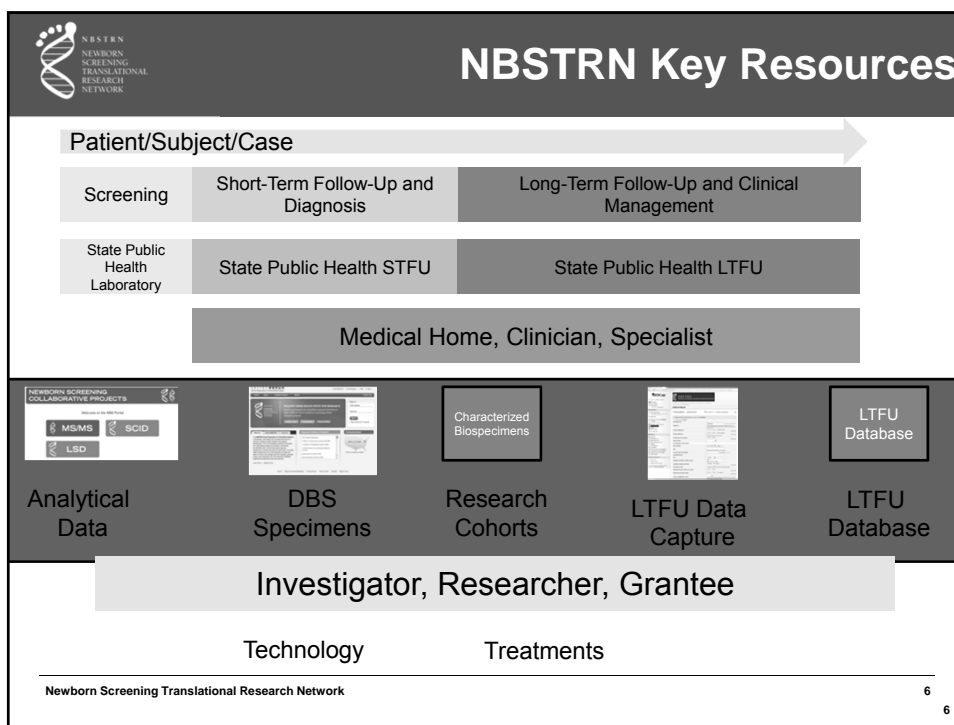
Bioethics & Legal Issues
Ed Goldman
Jeff Brosco

FISMA Control Board
ACMG Coordinated

Newborn Screening Translational Research Network 4

 Workgroups	
Workgroup	Focus
Clinical Centers	<ul style="list-style-type: none"> • Consensus data set • Disease specific data sets • Data capture tool • Data access and governance • Support grantees
Laboratory	<ul style="list-style-type: none"> • New technology development and validation • New test validation
Bioethics & Legal	<ul style="list-style-type: none"> • IRB 101 for investigators and IRBs • Model consent form modules • Describe patient protections
Information Technology	<ul style="list-style-type: none"> • Data capture tool • Data management system • Change control board • Data display tools for comparative research

Newborn Screening Translational Research Network 5





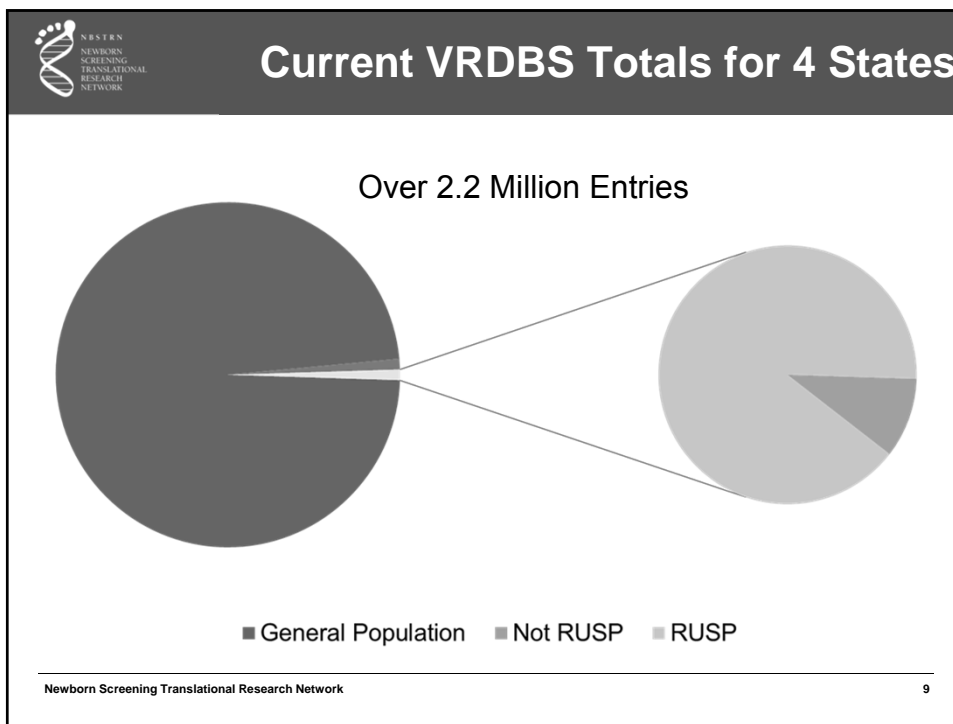
NBS Legal and Bioethics Work Group

- ◆ **Web site (NBSTRN and VRDBS) content recently revised**
- ◆ **Addressing new issues arising from grantees**
 - ◆ **SMA early lethality and need to identify patients as newborns to understand clinical history**
 - ◆ **Opt-in vs. opt-out consent**
- ◆ **Developing research agenda for NBS**
- ◆ **Considering a consultation function**



NBS Laboratories and Programs Work Group

- ◆ **Biospecimen Repositories**
 - ◆ **Virtual Repository of Dried Blood Spots (VRDBS)**
 - ◆ **Conditions in NBS**
 - ◆ **Unaffected**
 - ◆ **Cohorts from prior NBS research projects**
 - ◆ **Opened September 2012**
 - ◆ **Patient specimens**
 - ◆ **Consent to obtain dried blood spot punch**



Current Data

Search Results

You specified: No Criteria Specified

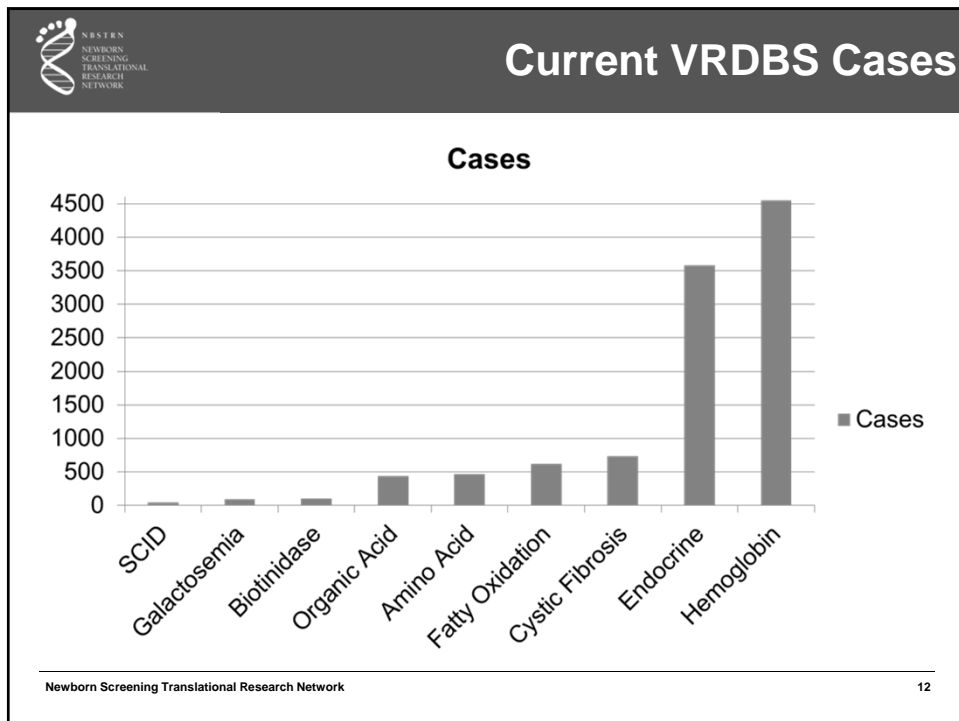
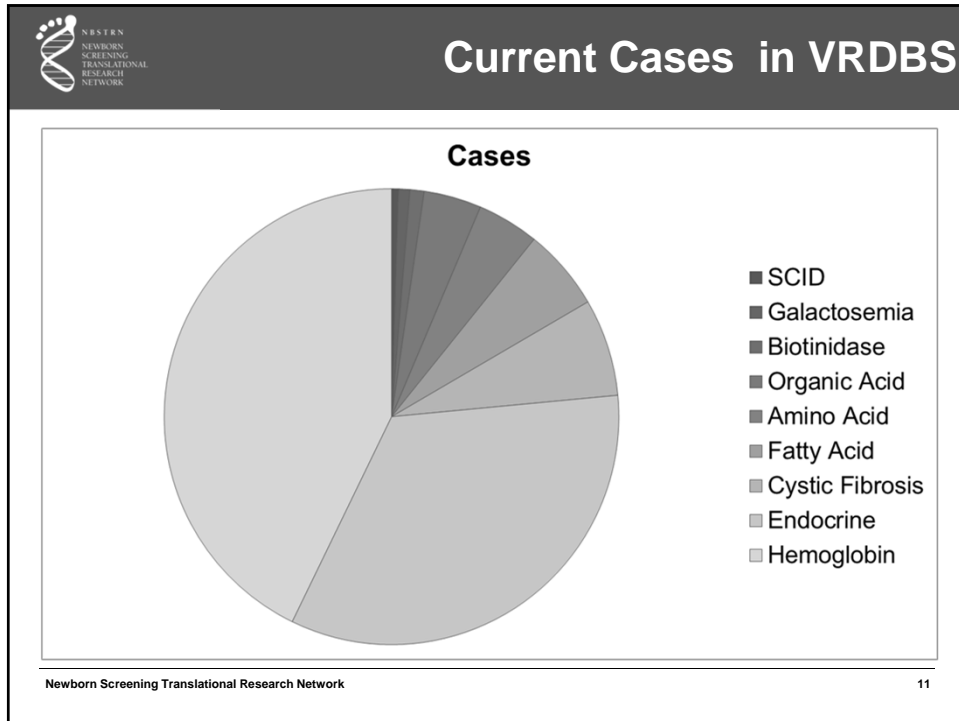
State	Stored Specimens	Qty Requested	Usage Restrictions
California	258,463	<input type="text"/>	DBS Specimen Use Restrictions
Iowa	127,611	<input type="text"/>	DBS Specimen Use Restrictions
Michigan	725,100	<input type="text"/>	DBS Specimen Use Restrictions
New York	1,188,937	<input type="text"/>	DBS Specimen Use Restrictions


1-4 of 4 Results 1 of 1 Page [<< First | << Prev 1 Next >> | Last >>] 20 Per Page

These numbers reflect only those cases in the virtual repository, not the incidence of the condition in the population.


Iowa: past five years excluding the most recent 12 months – updated monthly
 New York: 2007 – present – updated every 6 months
 Michigan: Oct 2003 – present – updated monthly
 California: cases 2006 – present (6 mo lag) negatives from last 6 months – updated every 6 months

Newborn Screening Translational Research Network 10




 VRDBS Conditions							
Condition	# DBS	Condition	#DBS	Condition	#DBS	Condition	#DBS
General Pop	2,289,327	3-MCC	214	CBL C	47	IBG	15
Hb S	3,073	CAH (SW)	211	CAH (NC)	43	ASA	15
CH	3,012	PKU	210	SCID	43	LCHAD	14
Other Hb w/out Hb S	937	SCAD	186	CAH (SV)	40	TYR-1	14
CF	733	BIO	106	CH2	37	CIT-I	12
Hb Barts/Alpha Thal	296	GALT	92	IVA	33	CAH (11B-OHD)	10
TBG	279	CUD	76	MSUD	25	FIGLU	7
MCAD	251	VLCAD	68	GA-2	18	CPT-II	7
Beta Thal w/out Hb S	248	MUT	62	PROP	16	HCY	5
H-PHE	214	GA-1	51	MET	15		

Newborn Screening Translational Research Network 13

 New Infrastructure and Resources	
<ul style="list-style-type: none"> ◆ Research cohorts in VRDBS <ul style="list-style-type: none"> • LSDs • MPS • Fra(X) • Cerebrotendinous xanthomatosis • SCID ◆ Clinical Centers and Standing Committee guidance on conditions to prioritize for research cohort development 	


Newborn Screening Translational Research Network 14



Update on Informatics Tools and Resources

- ◆ **R4S – Laboratory Quality Improvement of Newborn Screening**
 - Analytical Validation
 - Clinical Validation
 - Pilots
- ◆ **Long-term and Effective Follow-up**
 - Common Data Elements
 - Disease Specific Data Elements
 - Standardization
 - Data Almanac
 - Data Capture Tool
 - Data Management
 - Pilots


Newborn Screening Translational Research Network 15



Two Resources

- ◆ **R4S**
 - Newborn screening tests are usually performed in public health laboratories using laboratory developed tests
 - The majority of conditions screened are rare and data aggregation is needed to enable analytical validation
 - Diagnosis of conditions in newborns who screen positive occurs within the clinical health environment and is a key component of clinical validation
- ◆ **Long-Term and Effective Follow-Up Data**
 - The majority of NBS conditions require lifelong treatment and clinical care management
 - There is no coordinated data collection to advance understanding of clinical outcomes, develop new treatments and technologies
 - Patients are seen in a variety of clinical settings including specialty care, family practice and pediatrics
 - Use of existing data standards is important to enable data sharing

Newborn Screening Translational Research Network 16



Two New Resources

Vision

To support newborn screening research through the development of new technologies, new conditions and new treatments

Objective

To facilitate analytical and clinical validation of new and existing technologies

Objective

To enable data collection, analysis and mining across the lifespan


Resource

A database and suite of analysis tools

Resource

Data sets, standards, capture tool and data resource

Newborn Screening Translational Research Network
17



R4S

Objective

To facilitate analytical and clinical validation of new and existing technologies

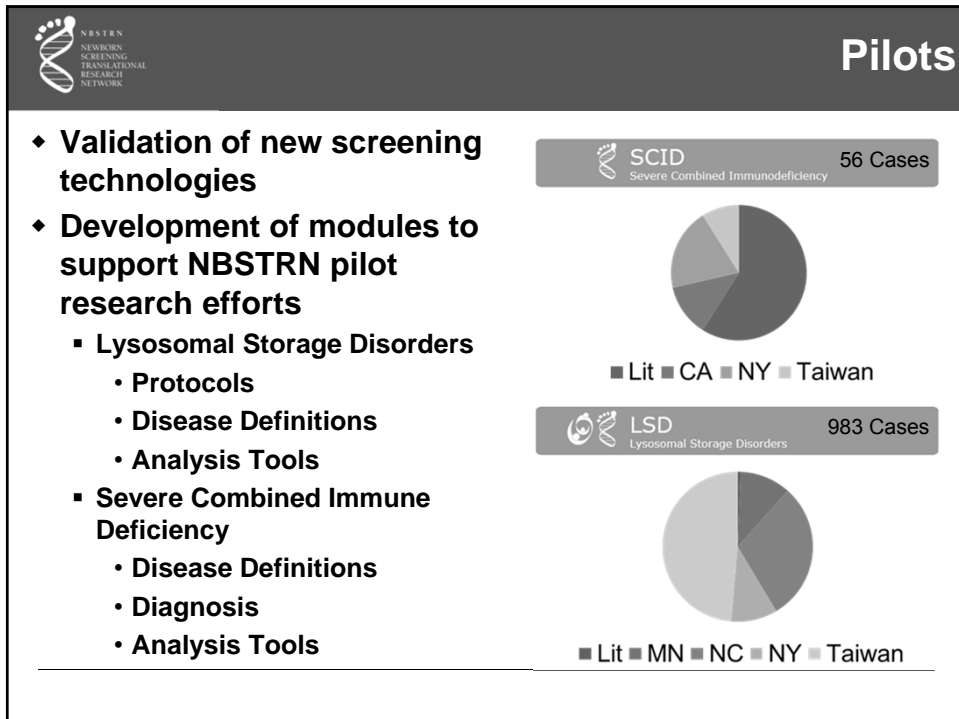
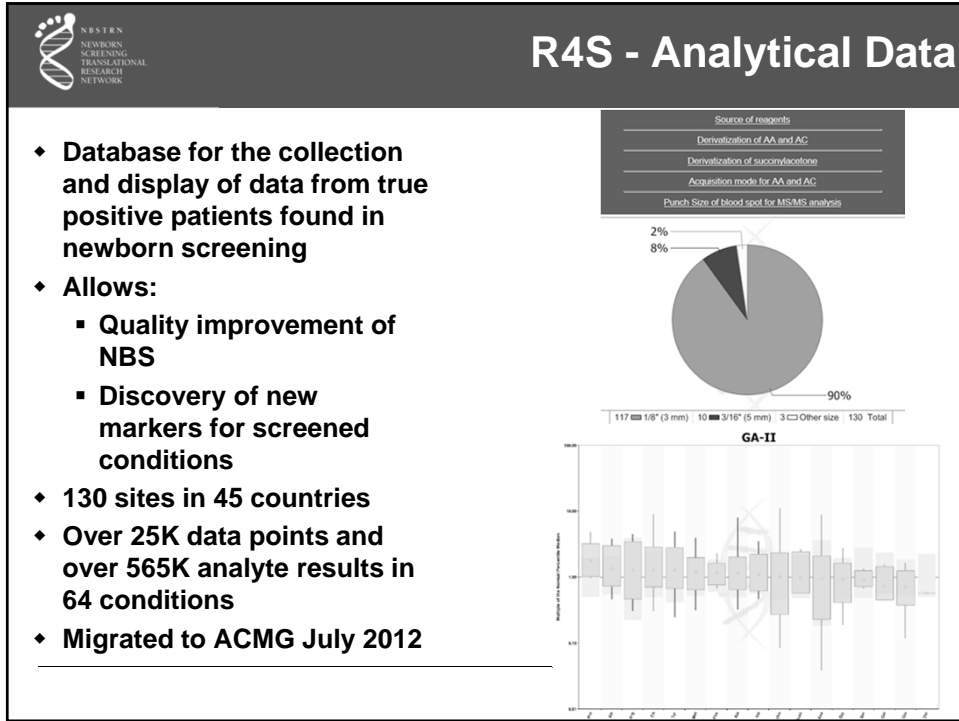
Resource


A database and suite of analysis tools

NEWBORN SCREENING COLLABORATIVE PROJECTS

Welcome to the Newborn Screening Domain

- MS/MS**
Amino Acids & Acylcarnitines by MS/MS
- CAH**
Congenital Adrenal Hyperplasia
- BIOT**
Biotinidase Deficiency
- MS/MS [2]**
Amino Acids & Acylcarnitines by MS/MS [2nd Sample]
- CH**
Congenital Hypothyroidism
- SCID**
Severe Combined Immunodeficiency
- LSD**
Lysosomal Storage Disorders
- ALD**
Adrenoleukodystrophy
- FRDA**
Friedreich Ataxia
- WD**
Wilson Disease






Clinical Centers Work Group

- ◆ **Datasets for condition in NBS nearing completion**
 - ◆ **Adapting data needs of new grantees to existing data sets**
 - ◆ **Ongoing facilitation of standardization of laboratory and clinical languages for grantees**
- ◆ **Shifting to data access, sharing, and use limitation recommendations and policies for NBSTRN**
 - ◆ **What all users must do**
 - ◆ **What all users must address for their projects**
 - ◆ **State public health authority and access to data**
- ◆ **Diagnostic confirmation requirements for research cohorts in VRDBS**


Newborn Screening Translational Research Network 21



Development of Data Capture Tool

- ◆ **Goal**
 - **Establish a network of centralized and institutionally-enabled infrastructure to support the capture and managed storage of longitudinal clinical data**
 - **This data will then be used by public health, clinicians and researchers to develop treatment programs and further newborn screening research**
- ◆ **Subcontract to CHOP – Dr. Pete White PI**

Newborn Screening Translational Research Network 22

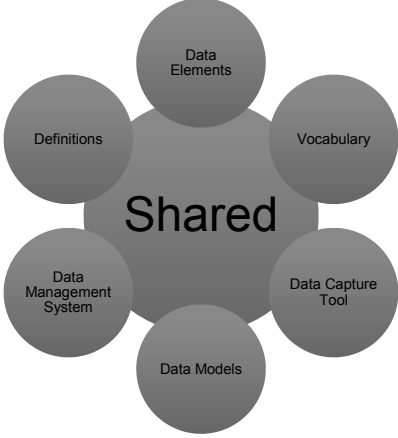
 **The LTFU Informatics Tools and Resources**

Objectives


- Determine the best course of treatment and disease management to maintain quality of life
- Enable data collection, analysis and mining across the lifespan by connecting research and clinical activities and data

Resource

- Data elements, definitions, data capture tool and management system with shared elements



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graph TD; Shared((Shared)); DataElements((Data Elements)); Vocabulary((Vocabulary)); DataCaptureTool((Data Capture Tool)); DataModels((Data Models)); DataManagementSystem((Data Management System)); Definitions((Definitions)); Shared --- DataElements; Shared --- Vocabulary; Shared --- DataCaptureTool; Shared --- DataModels; Shared --- DataManagementSystem; Shared --- Definitions;
```

 **LTFU Guiding Principles**

- ◆ **Researcher Focused**
 - Basic, Translational and Clinical Research
- ◆ **Clinician Driven**
 - What evidence and practices should advance understanding and inform screening, diagnosis, treatment and management of patients over their lifespan?
- ◆ **Multiple Stakeholders**
 - Public Health, Medical Home, Specialty Care, Patients
- ◆ **Adopt Relevant Standards**
 - Identify Areas Where Standards Would Be Helpful
- ◆ **Sustainable, Forward Looking Resource**
 - Both Evidence-based and Discovery-based
 - Linkage to NIH Resources

Standardization

NBSTRN
NEWBORN
SCREENING
TRANSLATIONAL
RESEARCH
NETWORK

NON STATE-OF-THE-SCIENCE CONFERENCE
FAMILY HISTORY
and Improving Health

NNSGRC
NATIONAL NURSING SCREENING & ANALYSIS RESOURCE CENTER

NATIONAL INSTITUTES OF HEALTH

U.S. National Library of Medicine
National Institutes of Health

FDA
U.S. Food and Drug Administration
Protecting and Promoting Your Health

U.S. National Library of Medicine
National Institutes of Health

U.S. Food and Drug Administration
Protecting and Promoting Your Health

IMPROVING THE HEALTH OF AMERICA'S CHILDREN

THE NATIONAL CHILDREN'S STUDY
HEALTH, BEHAVIOR, ENVIRONMENT

NATIONAL INSTITUTES OF HEALTH
Office of Rare Diseases Research

U.S. Department of Health and Human Services
HRSA
Health Resources and Services Administration

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

Newborn Screening Translational Research Network 25

Data Capture Screen Shot

NBSTRN
NEWBORN
SCREENING
TRANSLATIONAL
RESEARCH
NETWORK

Uniform Dataset | REDCap

https://research.chop.edu/redcap_uniform_dataset_entry.php?pid=98&id=3&event_id=22&page=demographics

REDCap

Uniform Dataset

Demographics

Editing existing Participant ID 1 (Study ID PAC10001)

Event Name: Intake

Participant ID: PAC10001

Study ID: (Secondary survey field)
NOTE: Modifying this value will also change the value and corresponding instances of this field in other Events when this form is saved.

Consent obtained: Yes No Not Needed Not Applicable Not Specified

Assent obtained: Yes No Not Needed Not Applicable Not Specified

Permission to recontact: Yes No

Type of Visit:

Demographics Information

Date of Birth: (07-25-1986) (MM/DD/YYYY)

Age: (Enter age in days of birth to not available)

Current Age (calculated): (View details) (Include)

Generational age:

Sex: (Female)

Biological mother's maiden name: (Enter NA if not available)

Condition Follow-up Status: Active Inactive

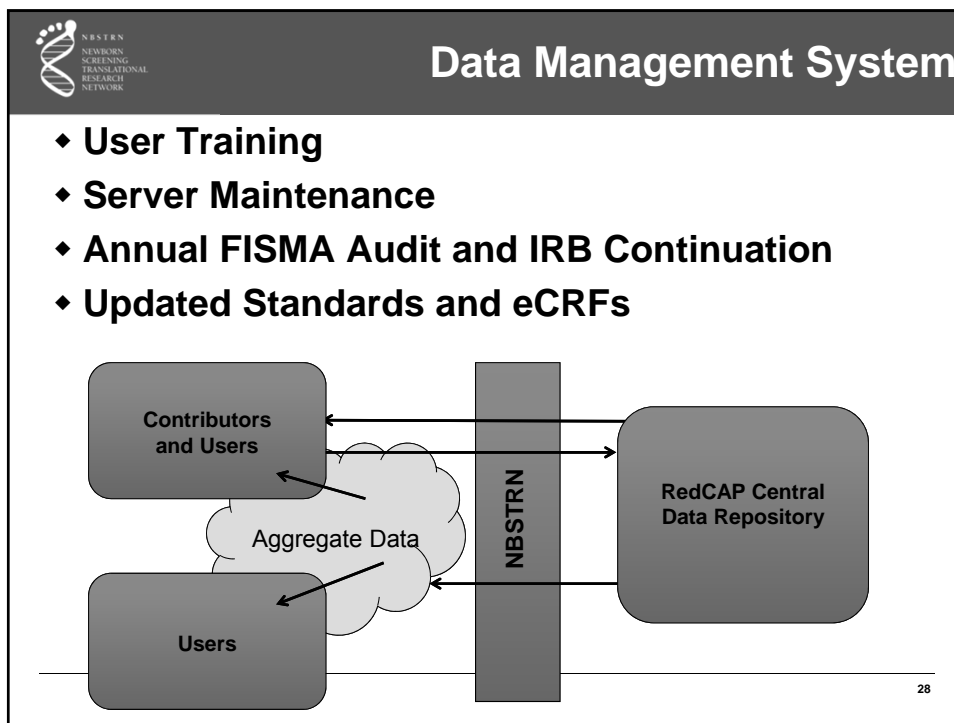
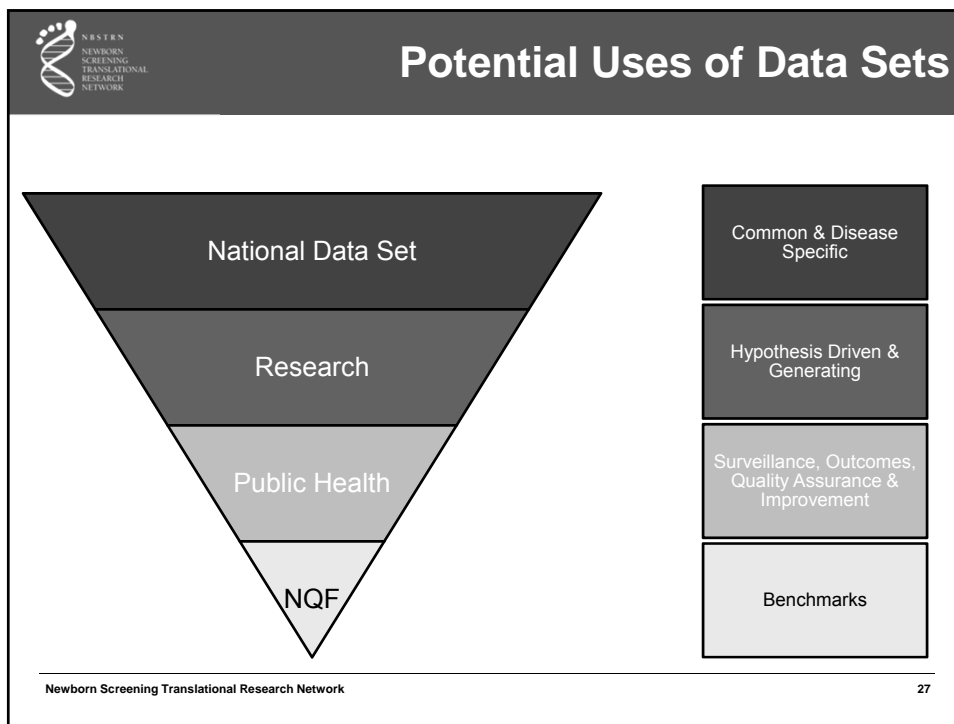
If inactive, why? (Moved to another center not participating)

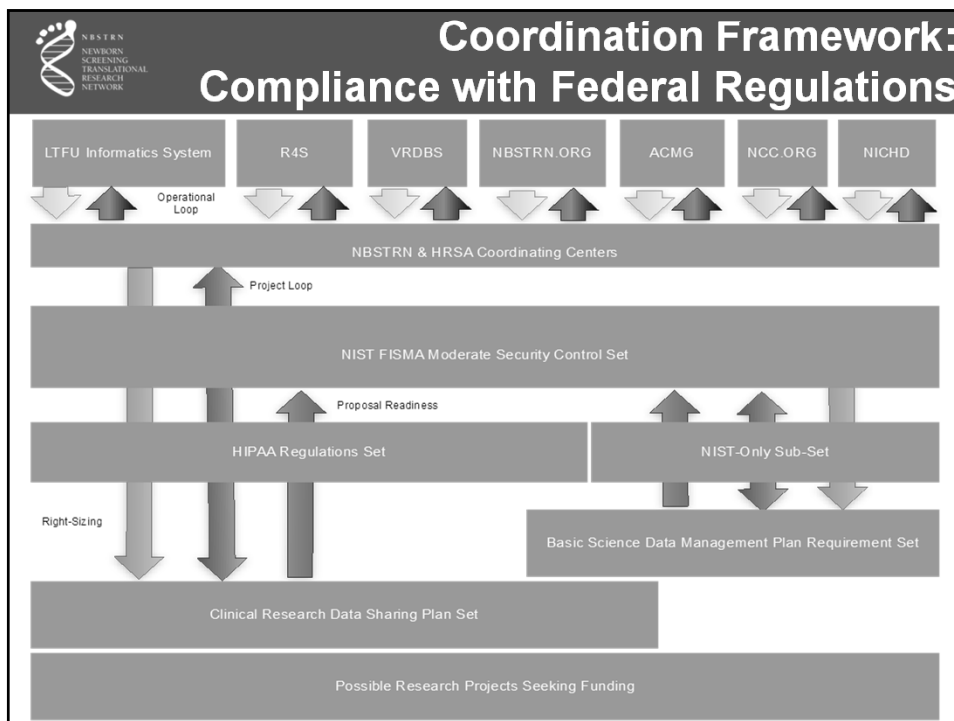
Followed by more than one center: Yes No

Permission to share data: Yes No Unknown

Name of additional center: (Select the name of the center from the dropdown list or specify a new center in the dropdown list.)

Newborn Screening Translational Research Network 26











NBSTRN Data Access and Sharing Policies

- ◆ **NIH policies**
 - Applicability
 - Timeliness
- ◆ **NBSTRN policies**
 - Investigators drive individual project policies
 - NBSTRN indexing of data available in repository
 - Publication related data should be open
 - Investigators designate open non-PHI data
 - Post-project data retention
- ◆ **NBSTRN Data Access Committee (DAC)**

Newborn Screening Translational Research Network 30

 Research Pilots Utilizing NBSTRN				
Pilot		New Test	New Condition	New Treatment
Severe Combined Immune Deficiency		√	√	
Spinal Muscular Atrophy		√	√	√
Inborn Errors of Metabolism				√
Lysosomal Storage Disorders		√	√	√

 Grantee Update
<ul style="list-style-type: none"> ◆ NIH Awarded Grantees <ul style="list-style-type: none"> ▪ Cynthia Cameron and Susan Berry – Clinical history of metabolic diseases in NBS ▪ Kathy Swoboda – Clinical history of SMA ▪ Shunji Tomatsu – NBS for mucopolysaccharidoses ▪ Eric Vilain – Clinical history of disorders of sexual development (includes CAH) ◆ NIH Awarded Contracts <ul style="list-style-type: none"> ▪ Steven Dobrowolski –Application of calibrated molecular melting curve analysis to SCID and SMA ▪ Dietrich Matern – Comparative assessment of technologies for LSD NBS
<p>Newborn Screening Translational Research Network 32</p>




Grantees: Kathy Swoboda – NBS for spinal muscular atrophy to develop clinical history

- ◆ **Screening for SMA in Utah and Colorado**
 - ◆ **Diagnosis and follow-up among providers in Utah and Colorado**
 - ◆ **Project started in April 2011**
 - ◆ **Screening planned to begin in April 2012**
 - ◆ **Developing policies with NBSTRN on recommendations for modes of consent for research involving conditions that are neither part of NBS nor immediate candidates for NBS**
 - ◆ **Utilizes NBSTRN repository system and patient data capture tools**



Grantees: Cynthia Cameron and Sue Berry - Clinical Histories of Metabolic diseases in NBS


- ◆ **Clinical history development in diagnosed cases**
 - ◆ **Involves 13 clinical centers in 10 states**
 - ◆ **Project started in April 2011 with prior history in Regional Collaborative project**
 - ◆ **Utilizes NBSTRN patient data capture tools**



Grantee: Melissa Wasserstein Newborn Screening Pilot for 5 LSDs

- ◆ **Screening**
 - in collaboration with New York State Lab/Program
 - 4 large hospitals in NYC
 - 80,000 babies over 4 years
- ◆ **Diagnosis and evaluation/management**
 - Using NBSTRN infrastructure


Newborn Screening Translational Research Network 35



Contractor: Dietrich Matern – Comparative Assessment of NBS Screening Technologies for LSDs

- ◆ **Utilizing R4S web resource**
- ◆ **Curating LSD pilot study data in R4S**
- ◆ **Dealing with complications in accessing NBS specimens in Minnesota**


Newborn Screening Translational Research Network 36



Contractor: Steve Dobrowolski – Application of calibrated molecular melting curve analysis to SCID and SMA

- ◆ **Development of melting curve assays for SMA, SCID, CMV....**
- ◆ **Needs research cohorts**


Newborn Screening Translational Research Network 37



Pilot Project - LSDs

- ◆ **NY, IL, MO, NM initiating screening**
- ◆ **Working with Lysosomal Disease Network (ORD-RDCC)**
- ◆ **Data collection slowed by Illinois' need to validate an alternative testing platform**


Newborn Screening Translational Research Network 38



Grants in Process

- ◆ **Natural History of Disorders Identifiable by Newborn Screening - LSDs**
- ◆ **Fragile X Newborn Screening Technology**
- ◆ **Several prior applicants resubmitting**
 - **A Prospective Delineation of the Adult Galactosemic Phenotype: The Impact of Newborn Screening**
 - **Whole genome analysis in NBS**
- ◆ **How will the NBSTRN need to be modified for upcoming projects?**
 - **Newborn Screening and Whole Genome Sequencing RFA now open**

Newborn Screening Translational Research Network 39



Next Steps

- ◆ **NBSTRN Annual Meeting**
- ◆ **Whole genome sequencing with integration with LTFU data capacity development**
 - **?Other whole genome issues**
- ◆ **Research cohort development**

Newborn Screening Translational Research Network 40



Thank You and Acknowledgments

NBSTRN is funded by a contract to the American College of Medical Genetics and Genomics from the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, National Institutes of Health (HHSN27520080001C)

LTFU Data Sets:

- ♦ **Inborn Errors Of Metabolism Collaborative (IBEMC)**
- ♦ **National Institute of Neurological Disorders and Stroke (NINDS)**
- ♦ **National Library of Medicine (NLM)**
- ♦ **National Coordinating Center for Regional Genetics and Newborn Screening Service Collaboratives (NCC)**

Center for Biomedical Informatics, Children's Hospital of Philadelphia

QUESTIONS?