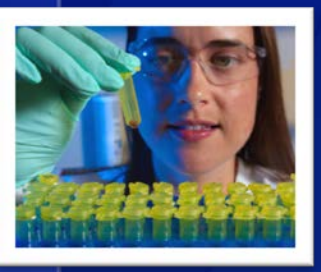
CDC's Program to Assure Laboratory Quality in Newborn Screening

Activities of the Newborn Screening and Molecular Biology Branch



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Division of Laboratory Sciences

National Center for Environmental Health

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Newborn Screening Saves Lives Reauthorization Act of 2014

SEC. 6. LABORATORY QUALITY AND SURVEILLANCE

SEC. 1113. LABORATORY QUALITY AND SURVEILLANCE

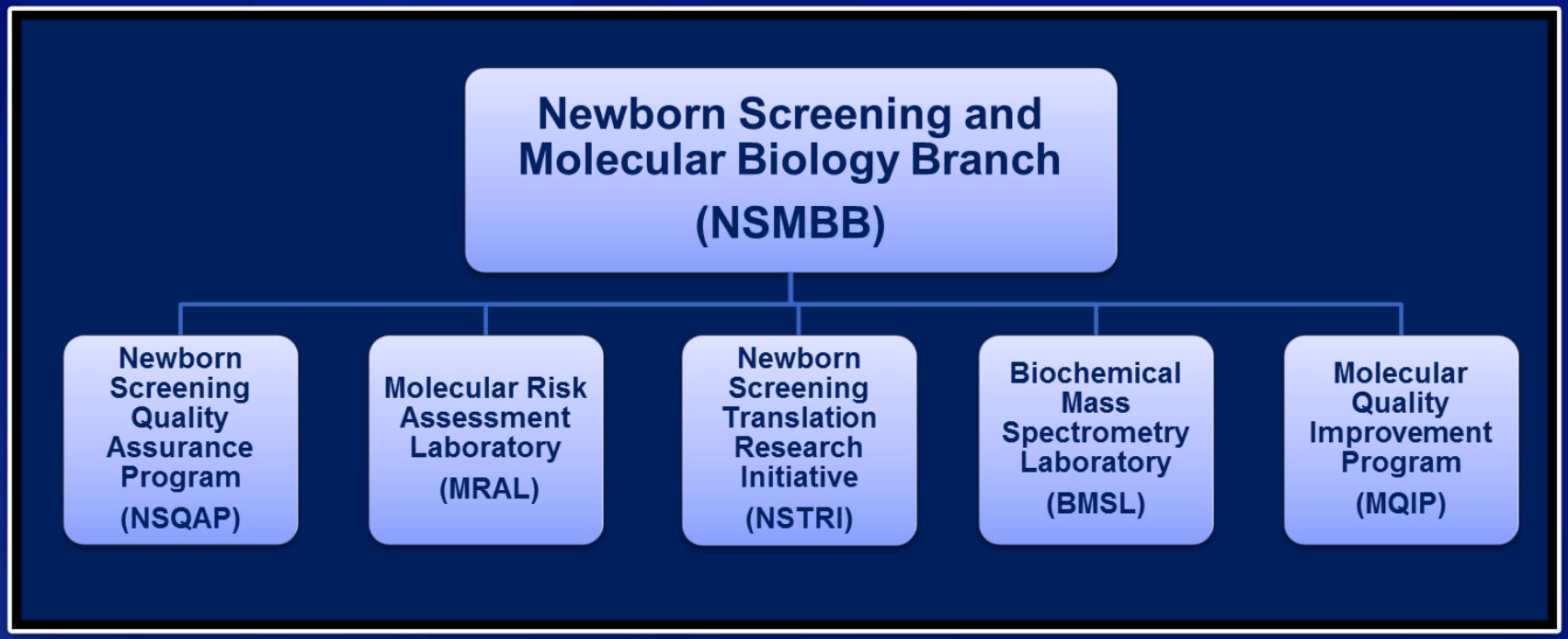
‘‘(a) IN GENERAL.—The Secretary, acting through the Director of the Centers for Disease Control and Prevention and taking into consideration the expertise of the Advisory Committee established under section 1111, shall provide for—

1) quality assurance for laboratories involved in screening newborns and children for heritable disorders, including quality assurance for newborn-screening tests, timeliness for processing such tests, performance evaluation services, and technical assistance and technology transfer to newborn screening laboratories to ensure analytic validity and utility of screening tests; and

2) appropriate quality control and other performance test materials to evaluate the performance of new screening tools.

Newborn Screening and Molecular Biology Branch

Goal: Assure the early and accurate laboratory detection of heritable disorders in newborns through dried blood spot testing



NSMBB Branch Priorities

1. Sustain and strengthen existing Quality Assurance Programs and services for Newborn Screening laboratories

2. Implement Quality Assurance Programs and provide technical support for both recent and anticipated additions to the Recommended Uniform Newborn Screening Panel (RUSP)

3. Improve the detection of inherited newborn disorders by public health laboratories through the use of molecular screening methods

4. Support national newborn screening initiatives through Federal collaborations and by working with State and other interested partners

Services Provided by CDC's Newborn Screening Quality Assurance Program

The only comprehensive quality assurance program using dried-blood spots

- Proficiency testing
- Quality Control Materials
- Method Development
- Training and consultation
- Filter paper evaluation

Preparation of whole blood pools

Reference Material Production

Certification of Blood Spots

Packaging and Shipment to Participating Labs

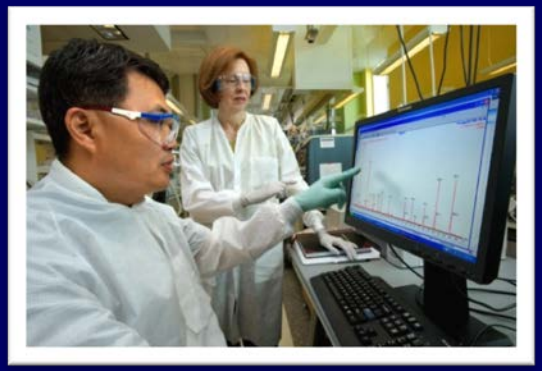
Quality Control Dried Blood Spot Materials for Newborn Screening

- Quality Control materials monitor method performance over time
  - Document trends in method performance
  - Identify problems so that corrective actions can be taken quickly
- *Kit QC:* Primary QC, comes with commercial reagents
  - Run on every plate or every assay
- *CDC QC* – EXTERNAL QC
  - Supplemental materials, not for every day use
  - Should be run periodically to assess method
  - QC Data is evaluated 2 times per year

Source: http://www.cdc.gov/labstandards/nsqap.html

Proactive Proficiency Testing Program

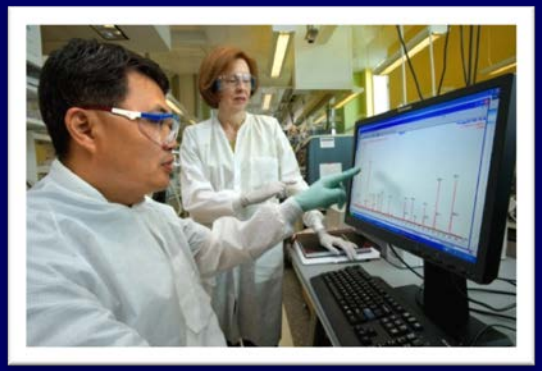
- **Proficiency Testing monitors laboratory performance for specific tests and measurements**
  - Similar to patient testing (or as close as we can get it)
- **Proficiency Testing – NBS State Assessments**
  - 100% of State NBS programs participate
  - Participating labs get 3 challenges of 5 blind-coded specimens per year
  - 80% Consensus (US labs) for graded specimens
  - Allows for accreditation of screening labs



Reference: https://wwwn.cdc.gov/nsqap/public/default.aspx

Proactive Proficiency Testing Program

- **Online reporting site**
  - Results posted and available to participating programs
    - Paperless PT report
  - Web location: http://www.cdc.gov/labstandards/nsqap_reports.html
- **Follow-up of False Negative (FN) results**
  - Proactive follow-up with NSQAP lab scientists
  - Additional challenge specimens are available
- **Technical assistance and technology transfer are available**
  - Assistance to ensure analytical validity and utility of screening tests



Reference: https://wwwn.cdc.gov/nsqap/public/default.aspx

NSQAP provides QA DBS materials for detection of screened conditions in the newborn period

Various Metabolic Conditions
Galactosemia
Biotinidase deficiency

Hemoglobinopathies
Sickle cell anemia
Hb S/C disease (Hb S/C)
HbS/Beta-thalassemia (Hb/Th)

Endocrinopathies
Congenital hypothyroidism
Congenital adrenal hyperplasia

Fatty Acid Oxidation Disorders
Medium chain acyl-CoA dehydrogenase deficiency
Long chain hydroxy-CoA dehydrogenase deficiency
Very long chain acyl-CoA dehydrogenase deficiency
Carnitine transporter deficiency
Trifunctional protein deficiency

Urea cycle disorders
Citrullinemia
Argininosuccinic aciduria
Argininemia

Amino acid disorders
Phenylketonuria
Maple syrup urine disease
Homocystinuria
Tyrosinemia, type I and type II

Organic Acid Disorders
Propionic acidemia
Methylmalonic acidemia
Multiple carboxylase deficiency
3-hydroxy 3-methylglutaric CoA lyase deficiency
3-methylcrotonyl CoA carboxylase deficiency
Isovaleric acidemia
Glutaric acidemia, type 1
Beta-ketothiolase deficiency

Cystic Fibrosis

SCID and T Cell Lymphopenias

Lysosomal Storage Disorders
Pompe Disease
Krabbe Disease

Peroxisomal Disorders
X-Linked Adrenoleukodystrophy

Processes involved in Newborn Screening Dried Blood Spot (DBS) Production

NSQAP prepares, certifies and distributes

~ 1,000,000 dried blood spots each year

1. DBS are cut into strips

2. QA panels packed into bags

3. Bags placed in Laboratory-coded packages

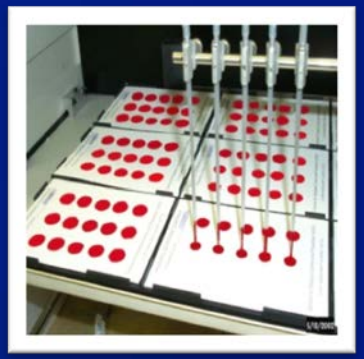
4. Preparation for shipment

Newborn Screening Quality Assurance Program Activities (2016)

- 100% States covered by the Program
  - Administers the distribution, data collection, and laboratory evaluations for 12 PT and 8 QC programs
- 654 Laboratories enrolled
- 78 Countries participated
- ~ 1,000,000 dried blood spots created and distributed
- Over 20 filter paper evaluation reports issued to manufacturers

CDC Provides limited Services to International Programs

- **International Laboratories can participate in NSQAP**
  - NSQAP is sensitive to the needs of non-domestic participants
- **As Newborn Screening Programs grow within countries, we encourage the development of national quality assurance programs to sustain and support domestic laboratories**



78 Countries Participated in NSQAP in 2016

Argentina
Armenia
Australia
Austria
Bahrain
Belgium
Bolivia
Brazil
Bulgaria
Canada
Chile
China
Colombia
Costa Rica
Cuba
Czech Republic
Denmark
Ecuador
Egypt
El Salvador
Estonia
Finland
France
Germany
Greece
Guatemala
Hungary
Iceland
India
Indonesia
Iraq
Ireland
Israel
Italy
Japan
Jordan
Kazakhstan
Kuwait
Latvia
Lithuania
Luxembourg
Macedonia
Malaysia
Malta
Mexico
Morocco
Netherlands
New Zealand
Norway
Oman
Pakistan
Panama
Paraguay
Peru
Philippines
Poland
Portugal
Qatar
Romania
Saudi Arabia
Singapore
Slovak Republic
South Africa
South Korea
Spain
Sir Lanka
Sweden
Switzerland
Taiwan
Tanzania
Thailand
Turkey
Ukraine
United Arab Emirates
United Kingdom
United States
Uruguay
Vietnam

Total # Participants N = 654

Filter Paper Quality Assurance

- **Provide Quality Control for Specimen "Filter Paper"**
  - **Monitor performance of new commercial lots**
  - **Special evaluations of paper / troubleshooting issues**
  - **Historical paper lot comparisons**
  - **Assure sustained performance criteria**

- **Protocol established in Clinical Laboratory Standards Institute (CLSI) Guidance Document "Filter Paper"**
  - **NBS01-A6 (replaces LA04-A5)—Blood Collection on Filter Paper for Newborn Screening Programs; Approved Standard—Sixth Edition (2013).**
    - Highlights specimen collection methods
    - Discusses acceptable techniques for applying blood drops or aliquots to the filter paper segment of the specimen collection device
    - Provides instructions on proper specimen handling and transport to ensure quality specimens are consistently obtained for newborn screening analysis

NSMBB Branch Priorities

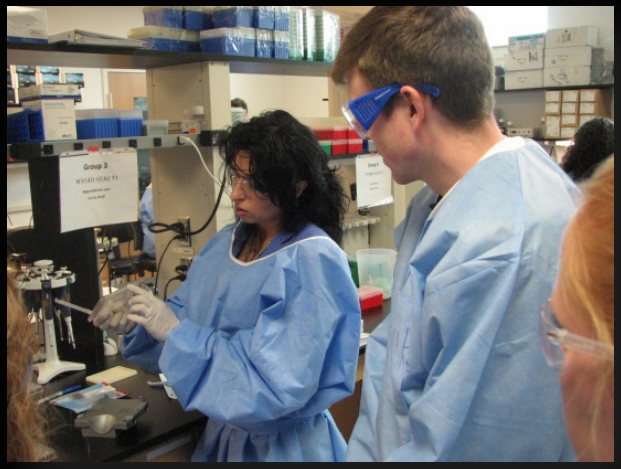
2. Implement Quality Assurance Programs and provide technical support for both recent and anticipated additions to the Recommended Uniform Newborn Screening Panel (RUSP)

- Provide funding to assist state programs in the implementation of new conditions
- In-house method development for recent/anticipated additions to the RUSP
  - Lysosomal Storage Disorders (LSDs), X-linked adrenoleukodystrophy (X-ALD)
  - Guanidinoacetate methyltransferase deficiency (GAMT)
  - Spinal Muscular Atrophy (SMA), Duchenne Muscular Dystrophy (DMD)
- Develop sustainable sources of quality assurance (PT/QC) dried blood spot materials for recent/anticipated additions to the RUSP
- Creation of unique dried blood spot resources to assist in new method development and validation for use in State Programs

Program Support for Domestic Labs

Provide Training and Support to Maintain Technical Expertise within NBS Labs

- National meetings*
- Laboratory-based Training*
- 1:1 Consultation
- Laboratory data review
- Site visits*
- Website Resources*



NSQAP Training and Technology Transfer

Mass Spectrometry Training and Education Updates

Newborn Screening by Tandem Mass Spectrometry (MS/MS):

A Hands-On Course in Understanding Lab Issues and Interpreting Test Results

- **One-week intensive hands-on training; 10 trainees; 5 lab instructors**

Training and Technology Transfer for Newborn Screening Professionals

"Newborn Screening Academy"

Development of 15 Education Modules for NBS Professionals

- Contracted with the Society for Inherited Metabolic Diseases (SIMD)
- Collaboration between SIMD's Metabolic Physicians and Biochemical Genetics Laboratory professionals together with the Newborn Community
- Deliverables include:
  - Website formatted content
  - Transcripts
  - Handouts/summaries and other reading materials

NSMBB Branch Priorities

3. Improve molecular detection of inherited newborn disorders by public health laboratories

- Develop in-house molecular methods and sustainable sources of extensively characterised QA materials for molecular NBS applications
- Identify gaps in molecular newborn screening and work collaboratively with State Labs to design and implement laboratory solutions
- Sustain and expand the “Molecular Assessment Program” which provides guidance and technical expertise to state public health laboratories
- Create hands-on and web-based educational tools to enhance molecular newborn screening laboratory personnel training

Support for Newborn Screening Tests using Molecular Technologies

- **Developed the NBS Molecular Resource Website***
  - Summaries and contacts for ongoing assays
  - Automation resources - incorporating robotics platforms
  - Developing Sequencing-specific resources
  - Training resources: Powerpoints and webinars
- **Hands-on NBS Molecular Training Workshop***
  - Ongoing for over 5 years (~14 participants for each session)
- **Molecular Assessment Program***
  - Ongoing since 2011
  - Expansion to support sequencing implementation

*** Done in partnership with the Association for Public Health Laboratories (APHL)**

Support for Newborn Screening Tests using Molecular Technologies

Quality Assurance for Molecular NBS Applications

- Molecular repositories of patient specimens for ongoing and future quality assurance
  - Cystic Fibrosis and other metabolic disorders (collaboration with CA PH Dept)
  - Congenital Adrenal Hyperplasia (collaboration with Univ of MN)
  - Galactosemia (collaboration with Emory Univ)
- Develop and validate DNA sequencing and large deletion reference methods
- Cooperative Agreement with NY NBS program for development of sequencing technologies for genes associated with SCID

NSMBB Branch Priorities

4. **Support national newborn screening initiatives through Federal collaborations and by working with State and other interested partners**

Federal Partners with Interest in Newborn Screening

CDC: Centers for Disease Control and Prevention

HRSA: Health Resources and Services Administration

NIH: National Institutes of Health

FDA: Food and Drug Administration

AHRQ: Agency for Healthcare Research and Quality

OHRP: Office for Human Research Protections

CDC's Partnership with APHL Supports NBS Laboratory Practice

- NSMBB has a cooperative agreement with APHL
- NSMBB supports the Newborn Screening and Genetics in Public Health Committee
  - QA/QC subcommittee
  - NBS Molecular Subcommittee
  - Other ad hoc workgroups and initiatives
- Other Program Activities
  - Guidance on policies, white papers, position statements
  - Training opportunities through courses, workshops, webinars, 1:1 training, on-line website resources
  - National Public Health Conversations & Initiatives to address current policy/practice issues

APHL: Association of Public Health Laboratories

Thank you for your attention!

Newborn Screening

***Saving* Lives.**

***Promoting* Healthier Babies.**

***Protecting* our Future.**

For more information please contact Centers for Disease Control and Prevention

1600 Clifton Road NE, Atlanta, GA 30333

Telephone: 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-6348

Visit: www.cdc.gov | Contact CDC at: 1-800-CDC-INFO or www.cdc.gov/info

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