CDC’s Role in the Implementation of Newborn Screening Pilot Programs

Activities of the Newborn Screening and Molecular Biology Branch

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Newborn Screening and Molecular Biology Branch

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

Newborn Screening and Molecular Biology Branch (NSMBB)

Newborn Screening Quality Assurance Program (NSQAP)
Newborn Screening Translation Research Initiative (NSTRI)
Biochemical Mass Spectrometry Laboratory (BMSL)
Molecular Quality Improvement Program (MQIP)

Established in 2011
CDC Funding Opportunities for SCID

- Funding and administration of FIRST public health pilot studies of newborn screening for SCID
  - Public Health Labs: Massachusetts and Wisconsin (~ $500K/yr)
  - Three Years: Fall 2008, Fall 2009, Fall 2010

- Funding and support of SCID Newborn Screening pilot study among Native Americans
  - Pilot studies: Fall 2008, Fall 2009 (~ $100K/year)

- Additional 2 year SCID NBS implementation funding
  - Fall 2011, Fall 2012 .... Michigan and Minnesota (~$400K/yr)
  - Fall 2013, Fall 2014 .... Oklahoma, Virginia and Georgia (~$200-$300K/yr)
  - Fall 2015?
SCID NBS Funding Opportunities

- Early Research Pilot Objectives:
  - Develop, Evaluate, and/or Improve newborn bloodspot screening tests for SCID to increase sample throughput, positive predictive value, multiplexing capacity
  - Develop and/or evaluate second tier tests to confirm primary tests and reduce false-negative results
  - Develop and/or evaluate novel approaches for data analysis and statistical algorithms that can improve the predictive values of primary SCID NBS tests
  - Increase the pool of laboratory scientists with knowledge and skill in conducting NBS for SCID
  - Provide training for the public health community ….. to foster their integration into the standard of care for communities
CDC activities that support sustainability of Pilot Programs and Implementation of Screening for Newborn Conditions
1. Newborn Screening Quality Assurance Program supports quality testing

The only comprehensive quality assurance program using dried-blood spots

- Quality Control Materials
- Proficiency testing
- Filter paper evaluation
- Translational Research

Preparation of whole blood pools
Reference Material Production
Certification of Blood Spots
Packaging and Shipment to Participating Labs
Development of Quality Control Materials for new programs

- Quality Control materials: provide a high degree of confidence that testing results are ACCURATE for the batch of samples tested

- Quality Control materials monitor method performance over time
  - Document trends in method performance
  - Identify problems so that corrective actions can be taken quickly

- 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
Proficiency Testing Dried Blood Spot Materials for Newborn Screening

- Proficiency Testing: Lab is evaluated for its ability to get same results on a set of samples
  - Assessment at one point in time
  - Similar to patient testing (or as close as we can get it)

- CDC Proficiency Testing Programs
  - 3 times per year for US and International participants
  - One-month data turnaround to receive results

NSQAP Analyte Implementation Timeline

- 1978 - Congenital hypothyroidism (T4, TSH)
- 1980 - Phenylketonuria (Phe)
- 1988 - Galactosemia (TGal); HIV antibodies
- 1990 - Congenital Adrenal Hyperplasia (17-OHP)
- 1991 - Sickle Cell Disorders
- 1992 - Maple Syrup Urine Disease (Leu, Val)
- 1994 – DNA Confirmatory methods for Hb S, A, C, E D
- 1995 - Homocystinuria (Met)
- 1997 - Biotinidase; Cystic fibrosis F508del
- 2001 - MS/MS Analytes (Tyr, C3, C4, C8, C14, C16); GALT
- 2002 - Cystic Fibrosis (IRT); Cit, C6, C10
- 2003 – C5, C5DC
- 2005 - Toxoplasmosis gondii PT

- 2006 - 2nd tier Congenital Adrenal Hyperplasia by MS/MS (17-OHP, androstenedione, cortisol, 11-deoxycortisol, 21-deoxycortisol)
- 2007 - Cystic Fibrosis DNA Mutation Panel; C0, C2, C10:1, C14:1
- 2008 - Succinylacetone
- 2008 - Lysosomal Storage Disorders (Krabbe, Pompe, Gaucher, Niemann-Pick A/B, Fabry, MPS-1)
- 2009 - 2nd tier Maple Syrup Urine Disease (Alloisoleucine, Isoleucine); C5OH, C18
- 2010 – Arg, C4OH, C5:1, C12, C16OH
- 2011 – SCID (TREC); C18:1
- 2012 – Ala, C10:2
- 2013 – C18OH
- 2015 – XALD, G6PD
NSQAP Quality Assurance Programs

- Quality Control
  - 17-OHP
  - T4
  - TSH
  - Amino acids, SUAC and TGal
  - Acylcarnitines
  - IRT
  - X-ALD
  - GALT

- Proficiency Testing
  - Hormones (T4, TSH, 17-OHP, TGal)
  - Amino acids, SUAC
  - Acylcarnitines
  - IRT
  - CF DNA
  - *Toxoplasmosis gondii*
  - Hemoglobinopathies
  - 2nd tier CAH
  - LSD
  - TREC
  - Biotinidase
  - GALT
  - G6PD*
  - X-ALD*  
  *starting July 2015
Processes involved in Newborn Screening Dried Blood Spot (DBS) Production

NSQAP prepares, certifies and distributes over 850,000 DBS each year
Key Point:

Critical that CDC be involved in early stages of any NBS condition* that is being considered for nationwide implementation.

Development of robust QA materials is not trivial and requires iterative evaluation with early adopting programs to assess performance and to document proper certification of materials.

* conditions identified through dried blood spot evaluation
2. Method Development: New targets and Quality Improvement for Existing Targets

- Important to have expertise in Newborn Screening Methods
  - Evaluation of QA materials
  - Troubleshooting with State labs
  - Opportunities for training state program lab personnel

Each Laboratory within the Branch is actively engaged in method development using dried blood spots for anticipated conditions
On-card real time PCR compared to Extracted DNA real time PCR

- Developed on-card real-time PCR TREC assay for SCID using DBS
- Development of digital PCR technology: Absolute TREC copy number

Digital PCR: The Next Generation of Quantitative PCR

- Allows for absolute copy number quantification
- No standard curve needed
- Greatly improved precision over real time PCR (< +/- 10% error)
- Greater sensitivity – lower limit of quantification

Ideal platform for measuring calibrators and reference material
3. Technical Program Support

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
National Meetings and Discussions

- National conversations give States the opportunity to share best practices and address areas of concern with Program-based solutions

Newborn Screening for Severe Combined Immunodeficiency: *Implementation, Challenges, and Successes*

- Outline basic information regarding SCID and its detection through the newborn screening process
- Describe the basic testing methodologies of SCID testing and state implementation experiences
- Discuss the treatment and clinical management of patients with SCID

Target Audience:
- State Newborn Screening Laboratorians
- Newborn Screening Follow-up Program Personnel and Physicians
- Newborn Screening Stakeholders

*Hosted by APHL and NNSGRC in October 2010*
Workshops and Technical Meetings

- Scientific Workgroups and meetings addressing technical details of methods implementation
- Workshop on SCID testing and TREC Reference Materials
- Public Health Laboratory representatives from CA, CT, GA, MA, MN, WI, NY, TX
Laboratory-based Courses: Using Mass Spectrometry and Molecular Biology platforms

- In a climate where there may be high staff turnover, it is important to provide opportunities to support staff competency
- Intensive lectures and hands-on laboratory training
- Offered once or twice a year as needed
Site Visits to Evaluate Laboratory Workflow and Assist with Troubleshooting

NBS Molecular Assessment Program (MAP)

- Helps laboratories gauge current quality assurance practices and identify potential improvements to testing quality or efficiency
- MAP can provide support for determining how to fit molecular testing into the laboratory given existing program resources and application needs.
- The MAP guidance covers numerous laboratory processes including documentation, workflow, assay validation and results reporting.
- Feedback from the visit is provided in an exit discussion and a confidential written report to the program.

MAP: Non-regulatory site visit of molecular biologists from CDC and State Public Health newborn screening programs. 14 visits to date.
4. Support of NBS Laboratory Practice through Partnerships

- CDC has a cooperative agreement with APHL that supports:
  - Newborn Screening and Genetics in Public Health Committee
  - QA/QC subcommittee
  - NBS Molecular Subcommittee
  - Other ad hoc workgroups and initiatives

- Partnerships enable:
  - Guidance on policies, development of white papers, position statements
  - Facilitate training opportunities through courses, workshops, webinars, 1:1 training, on-line website resources
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
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Telephone, 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-6348
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The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.