CDC's Program for Laboratory Quality in Newborn Screening

The Role of the Newborn Screening and Molecular Biology Branch

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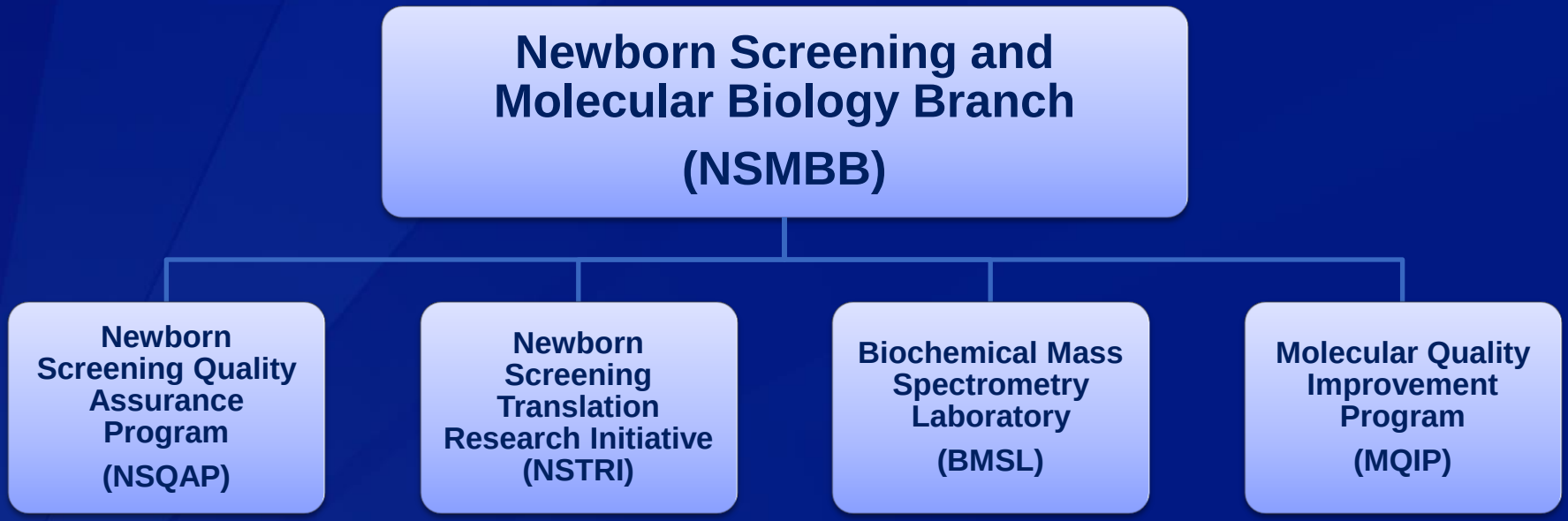
Mandate from Congress: Provide Quality Assurance Materials for NBS Laboratories

Provide for:

- Quality assurance for laboratories involved in screening newborns and children for heritable disorders
  - Quality assurance for NBS tests
  - Performance evaluation services
  - Technical assistance and technology transfer to NBS laboratories
  - Assistance to ensure analytic validity and utility of screening tests
- Appropriate quality control and other performance test materials to evaluate the performance of new screening tools

Newborn Screening and Molecular Biology Branch Organization



The Newborn Screening Quality Assurance Program

The only comprehensive quality assurance program using the dried-blood spots

Laboratory Services Provided by NSQAP

1. **Filter paper evaluation**
2. **DBS reference and quality control materials**
3. **Proficiency Testing**
4. **Internet reporting site for laboratories**
5. **Follow-up of False negative results**
6. **Training, consultation, network resources**

Newborn Screening Quality Assurance Program Statistics in 2010

100% participation of US states

67 countries participated

717,255 DBS produced

28 employees

36 new enrollments

463 labs enrolled at year end

456 labs reported data

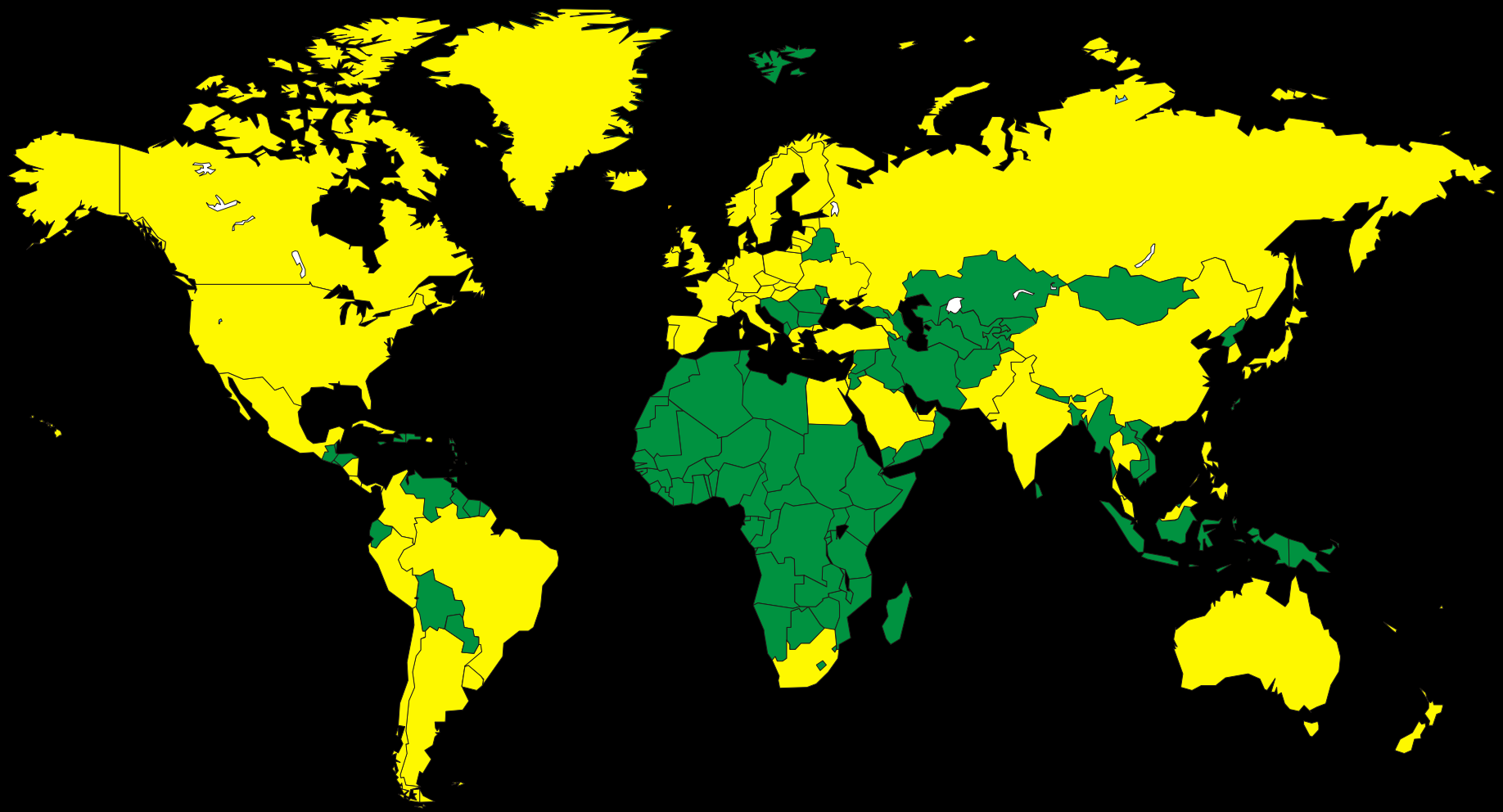
391 labs participated in PT

337 labs participated in QC

17 reports to participants

4 filter paper lots evaluated

Sixty-seven Countries Participated in the Newborn Screening Quality Assurance Program in 2010



NSQAP provides QA materials in dried blood spots for Newborn Screening Disorders

Inborn Errors of Metabolism

Galactosemia

Glucose-6-phosphate dehydrogenase deficiency

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 3 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 (PKU)

Maple syrup urine disease

Homocystinuria (cystathionine synthase deficiency)

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

Translation Research Initiative

Mission:

Assure that the translation of research methods into routine laboratory tests for newborn screening leads to sustainable high-quality testing and healthier babies worldwide

- Develop new screening methods for specific diseases
- Integrate State Public Health Laboratories into the translation process through collaborative field studies
- Expand global reach of newborn screening
- Adapt innovative technologies for screening and quality assurance

Ongoing collaboration between the CDC Foundation and NSMBB

Ongoing Newborn Screening Translation Research Initiative Laboratory Projects

- **Severe Combined Immunodeficiency (SCID)**
  - Produces PT materials for TREC assay
  - Developed *in situ* qPCR TREC assay specific for DBS
  - Trains laboratory personnel and provides technical support
- **Lysosomal Storage Disorders**
  - Produces QC and PT materials for five disorders: Fabry, Gaucher, Krabbe, Niemann-Pick and Pompe and distributes Genzyme reagents to participating programs
  - Trains laboratory personnel and provides technical support
- **New and emerging technologies in NBS**

TREC: T-Cell Receptor Excision Circle

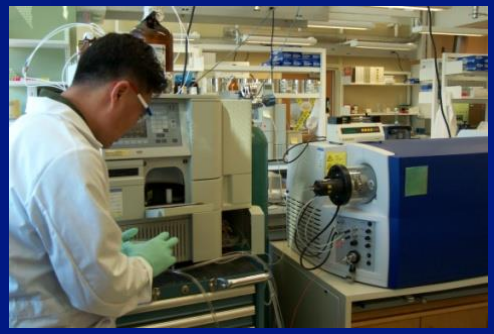
Biochemical Mass Spectrometry Laboratory

Mission Statement:

Work with public health partners to develop ***new mass spectrometry-based assays*** to detect and monitor metabolic disorders, and ***enhance newborn screening laboratory performance*** through innovative approaches to biochemical marker detection.

Selected Priorities:

- Develop new methods for the analysis of dried-blood for metabolic screening and diagnosis of selected inborn errors of metabolism
- Pilot program for MS/MS analyte ratios analysis for metabolic disorders to improve specificity of existing MS/MS-based newborn screening assays



Mass Spectrometry Quality Assurance Helps Laboratories Achieve High Proficiency

Public health impact:

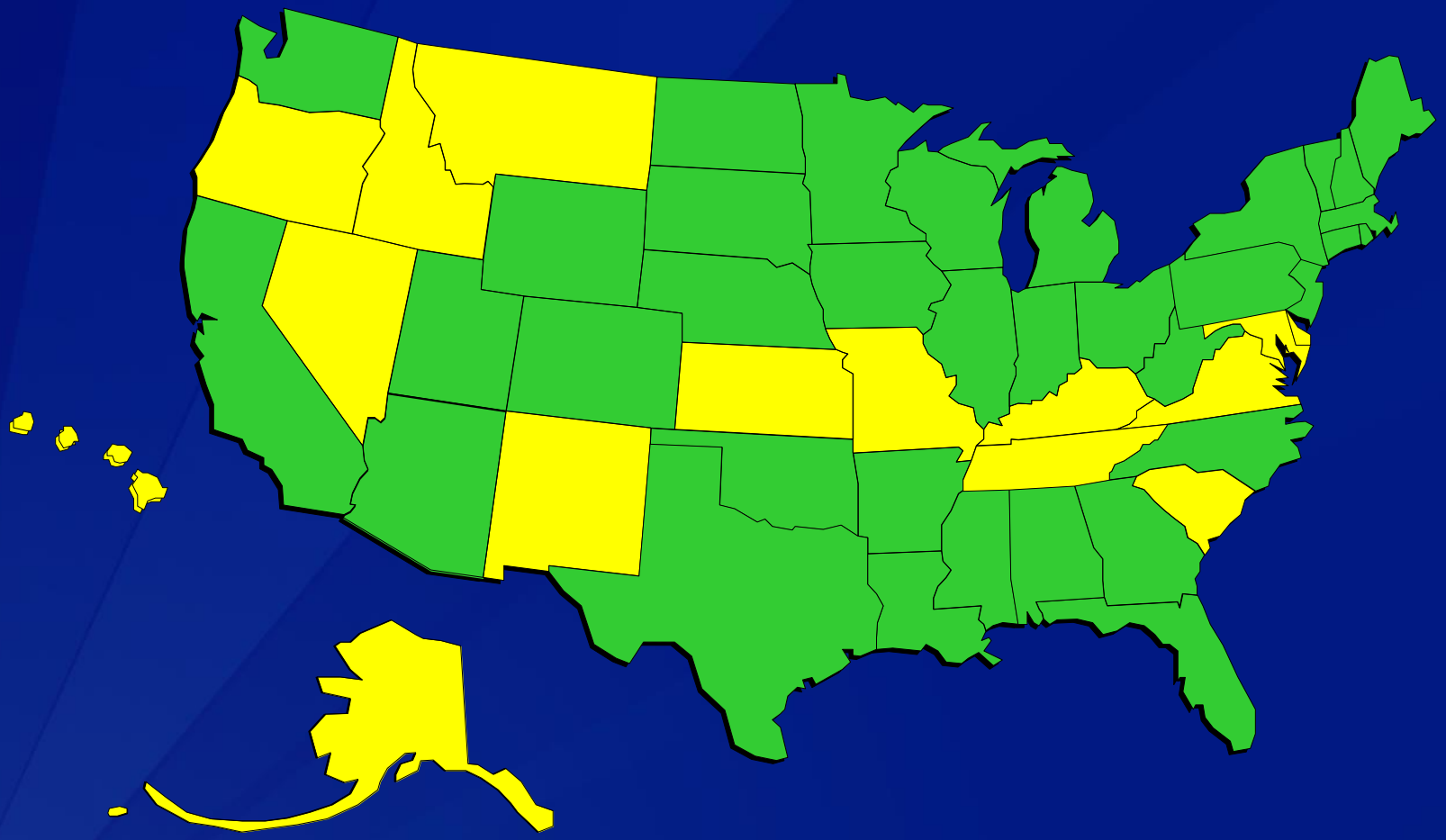
- **100% coverage of primary biomarkers for simultaneous, high-throughput detection of 43 disorders - *high impact, cost-efficient***
- **QC program for lysosomal storage disorders screening - *pioneering QA for emerging newborn screening activities***
- **QA materials to enhance analytical specificity through second-tier tests - *technical expertise and leadership expands disease diagnosis***

Molecular Quality Improvement Program

Mission:
Work with public health laboratories to detect newborn disorders with molecular methods, and provide a public health forum to exchange molecular best practices, quality improvements and educational resources to enhance laboratory performance.

- Second tier and primary molecular methods are now being used by a number of newborn screening laboratories
- Molecular screening brings new and different technologies into the NBS laboratory creating a need for newborn screening laboratory resources

NBS Molecular Testing Status: 2010

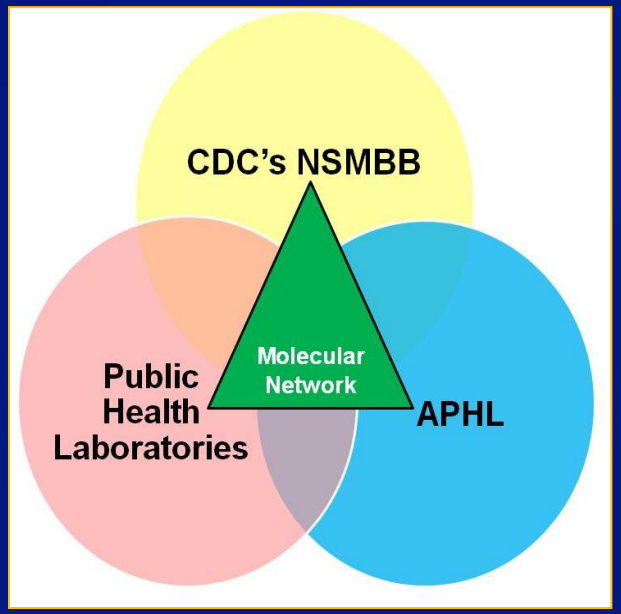


36 state labs (denoted in green) offer a molecular test

84% of babies born/year

Molecular Quality Improvement Activities

- Establishment of the NBS Molecular Network
- Implementation of NBS Molecular Assessment Program (MAP)
- Quality assurance research to identify and develop quality molecular methods for the DBS matrix
- Molecular characterization of quality assurance materials (*e.g*. cystic fibrosis and hemoglobinopathies)
- Translational research to address NBS community identified needs and quality assurance protocols



Newborn Screening and Molecular Biology Branch FY2011 Priorities

- Sustain and strengthen existing Quality Assurance programs
  - Involved in several active collaborations to expand existing proficiency testing materials and resources for Cystic Fibrosis
  - Ongoing collaboration with Ghana to establish a mutually beneficial program to expand NBS proficiency testing for hemoglobinopathies
    - Ghana has one of the highest incidences of Sickle Cell world wide

Country	Population (millions)	Birth Rate	Total Births	SCD Birth Rate	Total SCD Births
Ghana	23.8	29.6	705,575	1:55	12,829
USA	308.8	14.0	4,323,634	1:2,474	1,748

Newborn Screening and Molecular Biology Branch FY2011 Priorities cont.

- Implement quality assurance programs for recent additions to the newborn screening panel (*e.g.* SCID)
  - NSMBB, as early advocates of SCID NBS, provided greater than $3 million over 3 years to support SCID screening in Wisconsin and Massachusetts NBS laboratories and in the Navajo Population
  - In September 2011, new funds will support two new states implement SCID screening for 2 years
  - Ongoing SCID proficiency testing program - TREC Model Performance Evaluation Survey (MPES) - currently 11 participants
  - CDC developed *in situ* qPCR assay to detect TREC in dried blood spots

Newborn Screening and Molecular Biology Branch FY2011 Priorities cont.

- Identify gaps and address laboratory needs as NBS laboratories introduce routine molecular testing
  - Creation of the Molecular Quality Improvement Program (MQIP)
  - NBS Molecular Network
  - Molecular Assessment Program (MAP)
  - Collaborative laboratory research to assure quality molecular testing

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