NewSTEPs

A Program of the Association of Public Health Laboratories™

Second National Newborn Screening Meeting on New Disorders

Pompe, MPS I and X-ALD

Meeting Summary and Notes

June 20-21, 2018

Washington, DC

This project is supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) under grant number # UG9MC30369 New Disorders Implementation Project for $4,000,000.This information or content and conclusions are those of the author and should not be construed as the official position or policy of, nor should any endorsements be inferred by HRSA, HHS or the U.S. Government.

TABLE OF CONTENTS

ACKNOWLEDGEMENTS

The Association of Public Health Laboratories would like to recognize the National Newborn Screening Meeting on New Disorders Planning Committee members who generously donated their time and input for the development of the meeting agenda.

Mei Baker, MD, FACMG, Wisconsin State Laboratory of Hygiene
Michele Caggana, ScD, FACMG, New York State Department of Health
George Dizikes, PhD, HCLD/CC(ABB), Tennessee Department of Health
Amy Gaviglio, MS, CGC, Minnesota Department of Health
Patrick Hopkins, Missouri Newborn Screening Laboratory
Amelia Mulford, Baby's First Test, Genetic Alliance
Jelili Ojodu, MPH, Association of Public Health Laboratories
Kimberly Piper, RN, BS, CPH, CPHG, Iowa Department of Public Health
Sikha Singh, MPH, PMP, Association of Public Health Laboratories
Staff Liaison: **Kshea Hale**, MPH, Association of Public Health Laboratories
Staff Evaluator: **Yvonne Kellar-Guenther**, PhD, Colorado School of Public Health

We also would like to thank our presenters and speakers who shared their experiences.

Mei Baker, MD, FACMG, Wisconsin State Laboratory of Hygiene
Michele Caggana, ScD, FACMG, New York Department of Health
Suzanne Canuso, MSN, RN, New Jersey Department of Health
Adrianna Evans, MPH, Genetic Alliance
Amy Gaviglio, MS, CGC, Minnesota Department of Health
Scott Grosse, PhD, Centers for Disease Control and Prevention
J. Austin Hamm, MD, FACMG, East Tennessee Children's Hospital
Patrick Hopkins, Missouri Department of Health
Amelia Mulford, Baby's First Test, Genetic Alliance
Robert Paul, Utah Public Health Laboratory
Kimberly Piper, RN, BS, CPH, CPHG, Iowa Department of Public Health
Nisha Quasba, MPH, Association of Public Health Laboratories
Gerald Raymond, MD, Penn State Children's Hospital
Andreas Rohrwasser, PhD, MBA, Utah Public Health Laboratory
Marci Sontag, PhD, Colorado School of Public Health
Tomi Toler, MS, CGC, Washington University School of Medicine
Beth Vogel, MS, CGC, New York State Department of Health
Careema Yusuf, MPH, Association of Public Health Laboratories

We would like to extend a special thank you to the parent presenters for sharing their experiences with MPS I, Pompe and X-ALD.

Kerri DeNies
Amanda Java
Kenneth Jarrell

BACKGROUND

Pompe was added to the Recommended Uniform Screening Panel (RUSP) in March 2015, and X-Linked Adrenoleukodystrophy (X-ALD) and Mucopolysaccharidosis type I (MPS I) were added in February 2016. State newborn screening programs pursuing universal implementation of these three new disorders encounter laboratory, staffing, clinical follow-up, personnel, equipment, education and legislative challenges.

MEETING PURPOSE

The purpose of the National Newborn Screening Meeting on New Disorders was to convene newborn screening personnel, as well as pertinent partners and stakeholders who have experience with implementing new disorders to discuss the status of newborn screening for new disorders added to the RUSP.

MEETING OBJECTIVES

1. Discuss current status of as well as future for Pompe, MPS I and X-ALD newborn screening in the United States.
2. Discuss decision points, barriers, unintended consequences to address in preparing for and implementing population screening for new disorders.
3. Identification and sharing of tools/resources used by newborn screening programs to prepare for and conduct screening for new disorders.

STATE OF NEW DISORDERS NEWBORN SCREENING

Figures 1, 2 and 3 depict the states who are offering universal newborn screening for Pompe, MPS I and X-ALD, respectively, in the United States as of July 2018.

Pompe is currently universally screened for in 13 states- District of Columbia, Illinois, Kentucky, Minnesota, Massachusetts, Michigan, Missouri, Nebraska, New York, Ohio, Pennsylvania, Tennessee and Wisconsin.

MPS I is currently universally screened for in 11 states- District of Columbia, Illinois, Kentucky, Minnesota, Massachusetts, Michigan, Missouri, Nebraska, Ohio, Pennsylvania, and Tennessee. New York is offering MPS I newborn screening to select populations.

X-ALD is currently universally screened for in 11 states- California, Connecticut, District of Columbia, Florida, Massachusetts, Minnesota, Nebraska, New York, Pennsylvania, Tennessee and Washington.

Figure 1: Pompe Newborn Screening Status in the United States as of July 2018

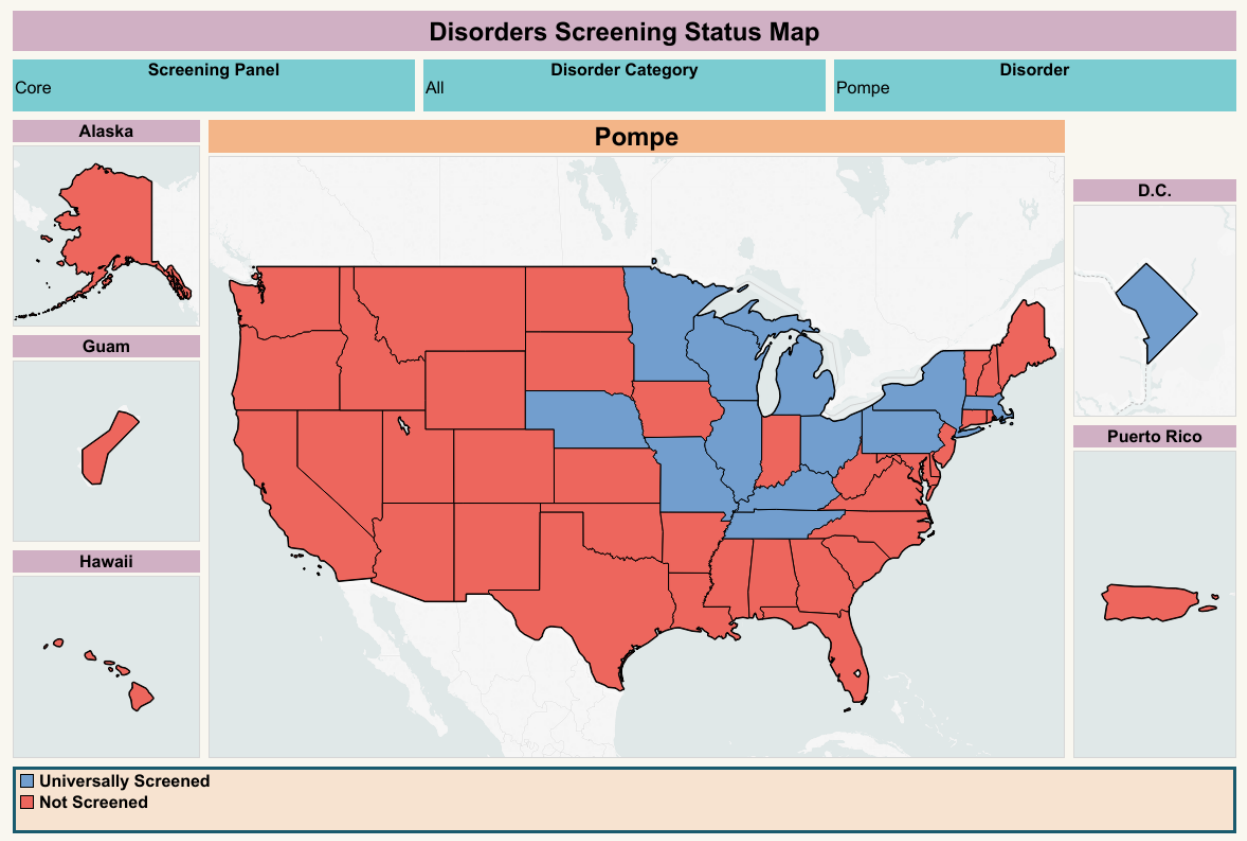


Figure 2: MPS I Newborn Screening Status in the United States as of July 2018

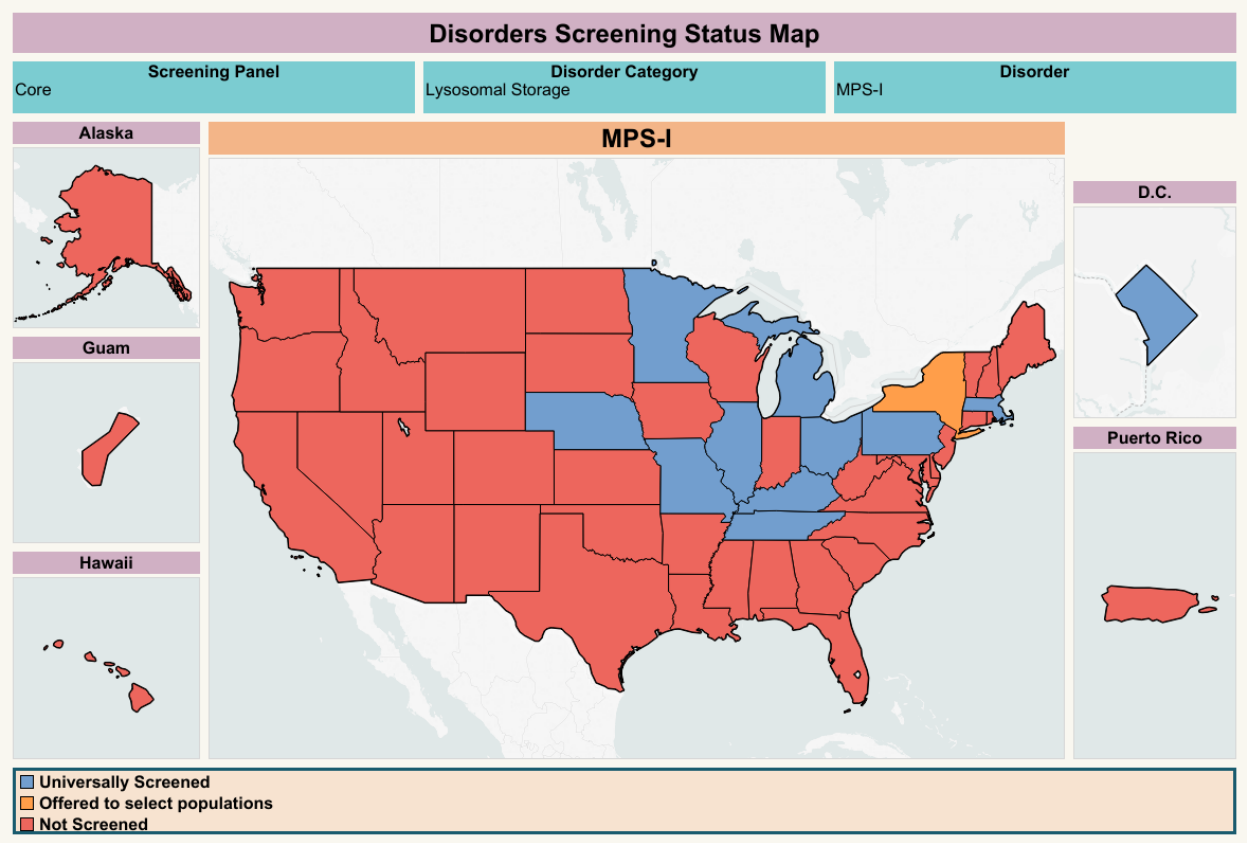
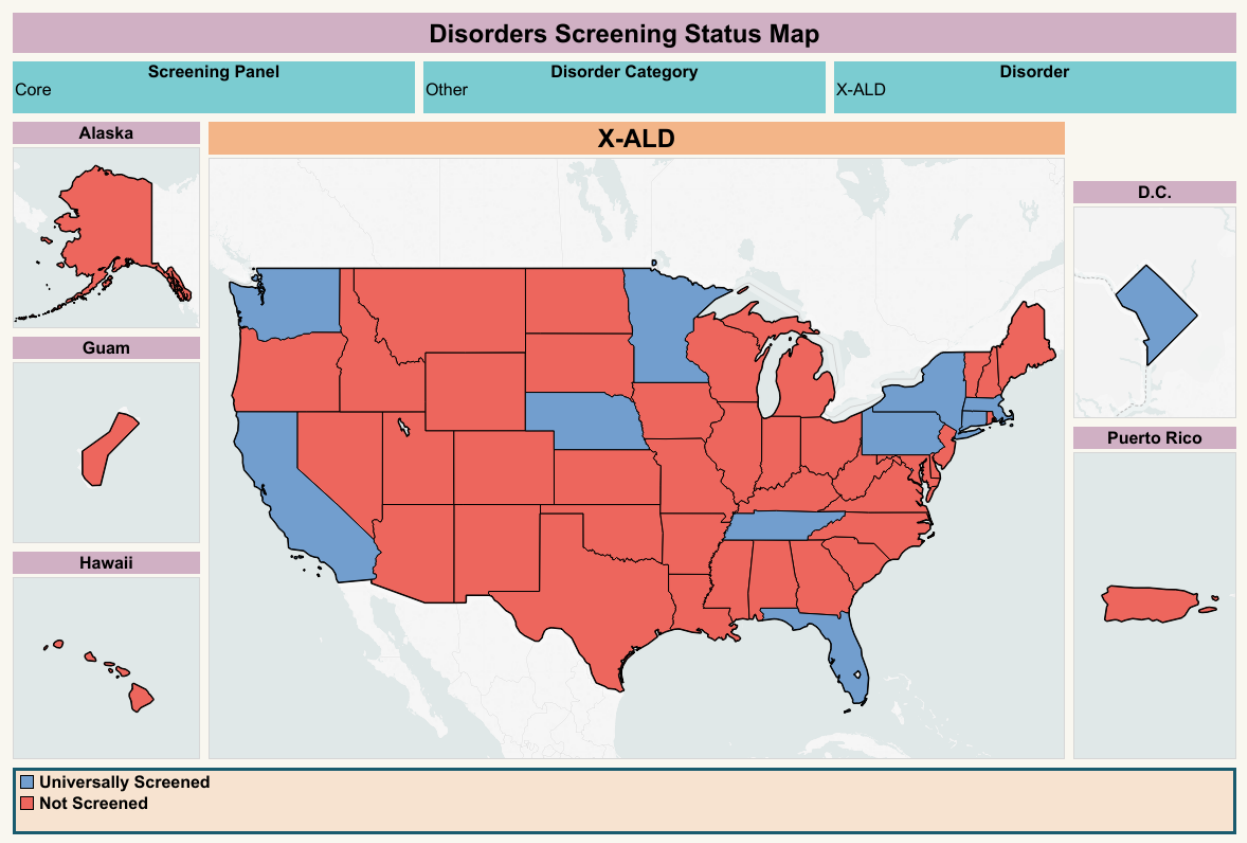


Figure 3: X-ALD Newborn Screening Status in the United States as of July 2018



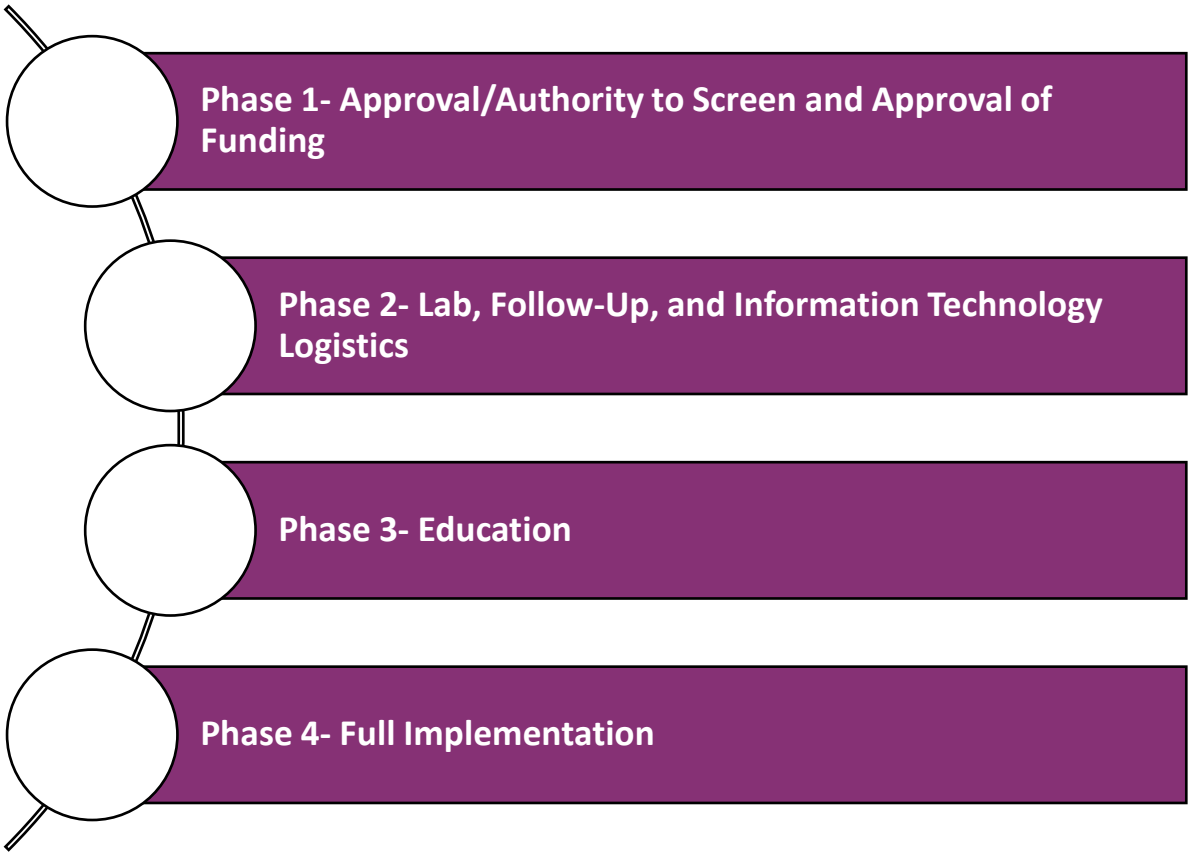
READINESS TOOL RESULTS

In spring 2018, NewSTEPs issued a request for all states attending the New Disorders National Meeting to complete or update the New Disorder Readiness Tool (Figure 4). The purpose of this tool is to capture and track over time the resources, tools and activities required by newborn screening programs for implementation of a new disorder during all stages of implementation (Figure 5). The tool results help identify variations in readiness for population screening in each state and can be used to connect states to one another for experience sharing purposes. A detailed summary of the Readiness Tool results can be found linked here.

Figure 4: Status of State New Disorder Newborn Screening, Readiness Tool- June 2018

State	MPS I					Pompe					X-ALD					SMA				
	Phase 1	Phase 2	Phase 3	Phase 4	Universal	Phase 1	Phase 2	Phase 3	Phase 4	Universal	Phase 1	Phase 2	Phase 3	Phase 4	Universal	Phase 1	Phase 2	Phase 3	Phase 4	Universal
Arizona	•					•					•					•				
Arkansas	•					•					•					•				
California		•													•					
Colorado	•					•					•					•				
Connecticut		•					•								•					
Delaware	•					•					•									
Florida		•			pilot		•					•			•					
Georgia				pilot					pilot		•									
Hawaii	•					•					•					•				
Illinois					•					•		•								
Indiana	•					•					•					•				
Iowa			•				•					•					•			
Kansas																				
Kentucky	•									•										
Louisiana																				
Maine	•					•					•									
Maryland			•				•					•								
Massachusetts			•					•		•			•		•					•
Michigan				pilot	•					•		•								
Minnesota					•					•					•					
Mississippi																				
Missouri			•		•					•	•									
Nebraska					July 1					July 1					July 1	•				
Nevada	•					•					•									
New Hampshire	•					•					•								pilot	
New Jersey				pilot					pilot			•								
New York					•					•					•					
North Carolina							•							pilot						
North Dakota																				
Ohio					•					•	•									
Oklahoma	•					•					•					•				
Oregon		•					•					•				•				
Pennsylvania					•					•					•					
Puerto Rico	•					•					•									
Rhode Island			•		July 1					July 1		•			July 1					
South Carolina		•					•					•								
Tennessee					•					•					•					
Texas		•					•					•								
Utah		•					•					•								•
Vermont	•										•									
Virginia			•					•			•					•				
Washington			•				•						•		•					
Wisconsin					•					•										

Figure 5: New Disorders Implementation Readiness Phases



At the time of the meeting, 39 states had provided data for the Readiness Tool. The data revealed that there was an increase in the number of states implementing full statewide screening and completing pilot testing for Pompe and MPS I over the last year (Figures 6 and 7). The Readiness Tool data also revealed that there was an increase in the percentage of states who completed a budget in the Approval/Authority to Screen Phase (Figure 8). There was little to no growth over the past year in the percentage of states who developed Long-Term Follow-Up protocols in the Laboratory/Follow-Up/Information Technology Logistics Phase. Only a few states had initiated educational activities for family, providers, and the general public. There was an increase in the percentage of states that had identified/modified general public educational materials for Pompe (Figure 9). There was also an increase in the percentage of states that had initiated a strategy for family education materials/created own materials for MPS I (Figure 10).

Figure 6: States Implementing Screening for Pompe Disease in 2017 and 2018

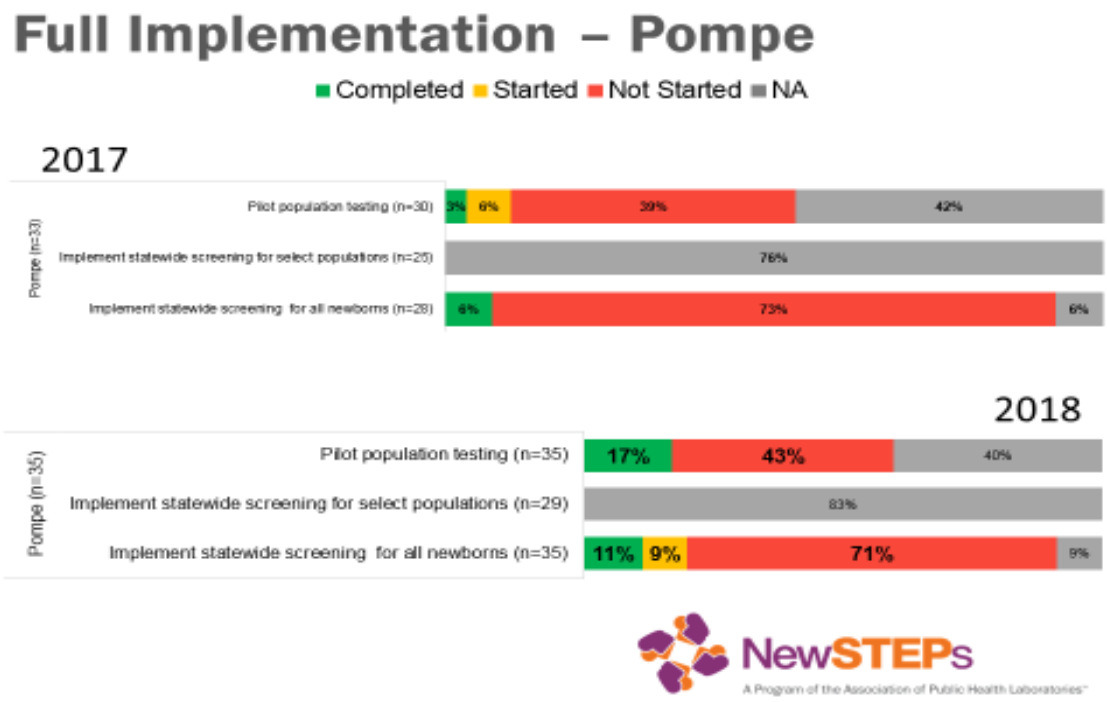


Figure 7: States Implementing Screening for MPS I in 2017 and 2018

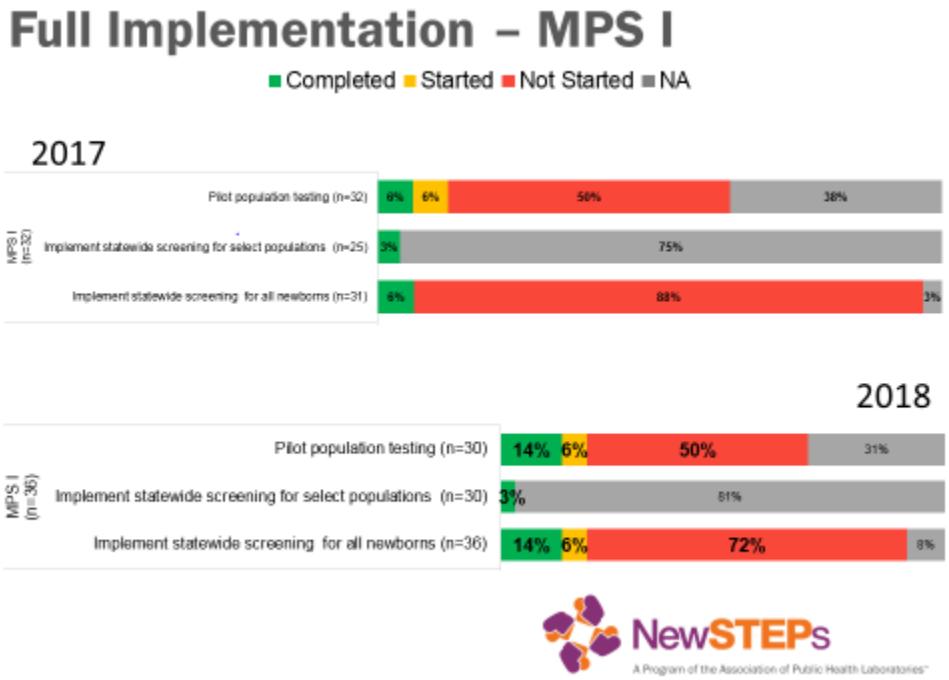


Figure 8: Phase 1- Approval/Authority to Screen

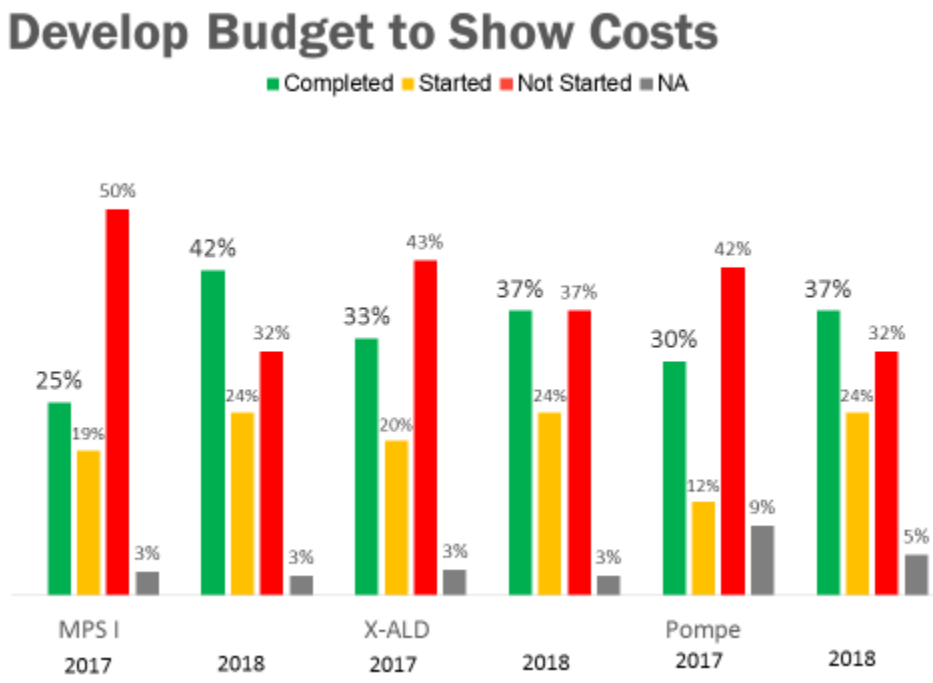


Figure 9: Phase 3- Education Data- Pompe 2018

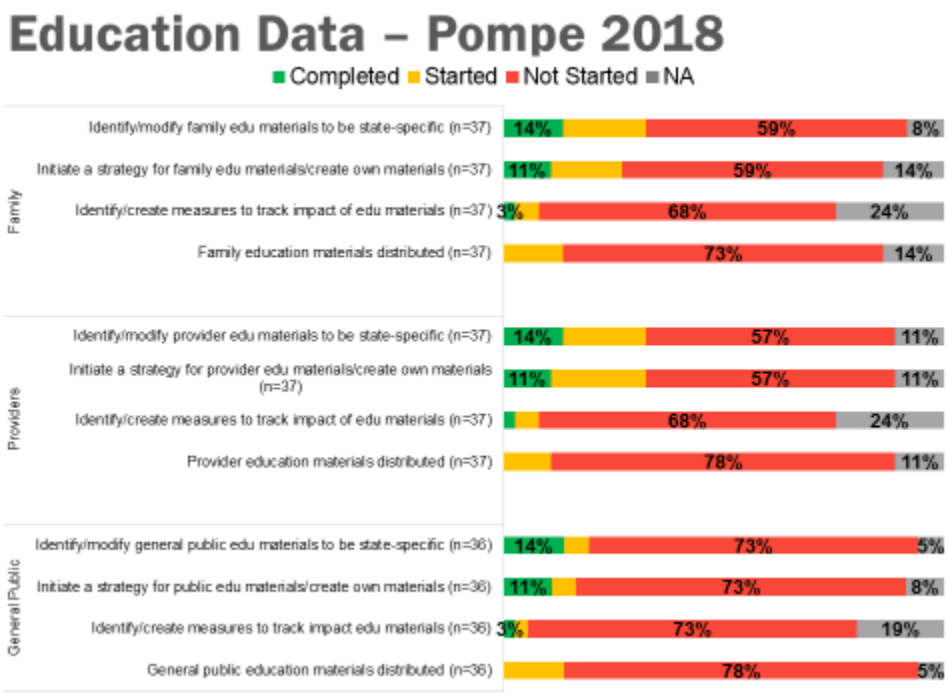
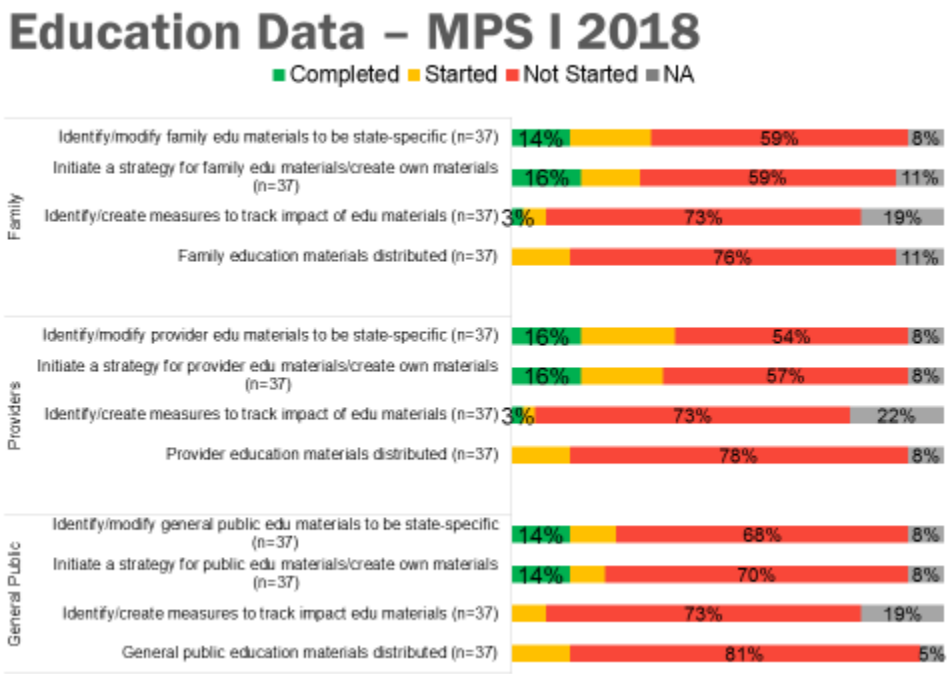


Figure 10: Phase 3- Education Data- MPS I 2018



MEETING SUMMARIES

In June 2017, NewSTEPs hosted the first National New Disorders Meeting. The first national meeting focused on providing insight on considerations and practices around implementation of newborn screening for Pompe, MPS I and X-ALD. Building upon the first meeting, the purpose of the 2018 National New Disorders Meeting was for newborn screening program personnel to: (1) Discuss current status of as well as future for MPS I, X-ALD and Pompe newborn screening in the United States (2) Discuss decision points, barriers, unintended consequences to address in preparing for and implementing population screening for new disorders, (3) identify and share tools/resources used by newborn screening programs to prepare for and conduct screening for new disorders.

The agenda for the second national meeting focused on providing insight around cost analysis considerations, APHL public policy tools and resources, surveillance case definitions, long-term follow-up (LTFU) clinical guidelines, and education for staff, clinicians, and families. The meeting also featured presentations and discussions from parents of children living with MPS I, Pompe, and X-ALD and clinicians providing treatment for these disorders.

The surveillance case definitions were presented by NewSTEPs staff for each disorder. Following each presentation around surveillance case definitions there was a presentation from a clinical specialist to provide insight on long-term follow-up clinical guidelines for Pompe, MPS I, and X-ALD.

Below are the highlights from those presentations as well as links to the speaker's PowerPoint presentations, when available. NewSTEPs will continue to collect and share practices to address the considerations and needs identified by the speakers. Please reach out to Kshea Hale at Kshea.Hale@aphl.org if you would like additional information from a particular newborn screening program or more detailed information regarding any of the considerations highlighted below.

Meeting Presentation and Summaries

Building a Cost Analysis and APHL Policy Tools

The first presentations centered on building a cost analysis and APHL public policy tools, with the speakers offering distinct perspectives- from a national and state laboratory perspective. These are summarized below.

Calculating the Cost of Adding New NBS Disorders: ***Scott Grosse, PhD, Centers for Disease Control and Prevention***

- Summary notes:
  - Establish a relationship with financial decision makers and understand all costs related to screening including economic, financial or accounting, variable and fixed, marginal, and incremental.
  - Understand how to estimate costs for health care
    - Direct: used for services performed in-house.
    - Indirect: used for purchased services.
    - Direct or indirect costs vary by laboratory model.
  - Key factors impacting **economic** costs to add a new condition include testing volume at screening lab, number of specimens tested per infant, and testing method.
  - Key factors impacting the **accounting** costs to add a new condition include use of commercial assays vs. laboratory-developed tests, use of rental agreement vs. purchase depreciation, fixed costs, and downstream clinical services.
  - Lessons learned from case studies include:
    - Unit cost of confirmatory testing is high, but it is low relative to the number of infants screened because of low referral rates from first tier screening.
    - Cost estimates vary. Average direct cost of laboratory testing may be $5-7 per infant per LSD tested in labs with at least 50,000 annual testing volume.
    - Accounting costs may exceed the economic estimates.
    - Early adopters sometimes report low cost estimates (e.g. ~$1 per infant for MPS I using MS/MS).

Building a Cost Analysis: ***Andy Rohrwasser, PhD, MBA, and Robert Paul, Utah Public Health Laboratory***

- PowerPoint slides linked here
- Summary notes:
  - 52,000 births annually in Utah. 99% of total baby population screened (two-screen state).
  - Utah NBS program operates on kit fee alone. Kit fee is $112 ($7 for hearing and CCHD and $105 for NBS).

- Strategic prioritization will help understanding of cost benefit.
- Key problems include cash accounting, lack of proper depreciation accounting instruments, non-lapsing mechanisms (motivated them to engage in innovation and new initiatives), and resource utilization/capacity.
- Key factors to consider when framing the Cost Analysis:
    - Know your audience. Who is the cost being summarized for?
    - What is the study question? Is it disorder specific? Is it analyzed between corporate partners' instrumentation? Reagent rental vs purchase?
    - What is the time frame? Timing of cash outflow and inflows?
    - What is the method of evaluation?
    - Measuring costs and measuring outcomes.
    - Discounting rates and costs.
    - Reporting and impact.
- Establish relationship with the financial decision maker and understand all costs to the $100 increment.
- Importance of stress testing assumptions through uncertainty and scenarios analysis.
- Sensitivity analysis helps with informed decision-making.
- Need for state-specific cost estimates. One size does not fit all.

APHL Public Policy Tools: ***Nisha Quasba, MPH, Association of Public Health Laboratories***

- PowerPoint slides linked here
- Summary notes:
    - APHL State Legislative Tracking/CQ Tracker provides real time report to track newborn screening legislation in progress.
    - APHL Policy team can assist in helping connect states to other similar NBS programs and key stakeholders within their state.

Pompe Disease

Pompe was the first disorder presented during the national meeting, with the speakers discussing surveillance case definitions around Pompe and clinical and long term follow up considerations. These are summarized below.

Surveillance Case Definition around Pompe: ***Marci Sontag, PhD, Colorado School of Public Health and Careema Yusuf, MPH, Association of Public Health Laboratories***

- PowerPoint slides linked here
- Summary notes:
    - Definitions created by panel of experts between July 2017 and June 2018.
    - Uniform criteria for disease reporting.
    - Classifications include Definite, Probable, Possible
    - Based on answers provided to set criteria.
    - Pompe Case Definitions Table (May 2018) available here.

- Pompe Worksheet available here.

Long Term Follow-Up Clinical Guidelines for Pompe: ***Austin Hamm, MD, FACMG, East Tennessee Children's Hospital***

- PowerPoint slides linked here
- Summary notes:
  - Pompe Disease is caused by a lysosomal acid maltase deficiency.
  - Defective function of lysosomal acid maltase leads to accumulation of glycogen within lysosomes.
  - Incidence rate is 1:15,000 – 1:100,000.
  - Infantile Onset Pompe Disease (IOPD) symptoms include larger heart, floppiness, feeding problems, respiratory problems. Onset of symptoms prior to 12 months.
  - Cardiomyopathy must be present to be diagnosed with "classic" IOPD.
  - Late Onset Pompe Disease (LOPD) symptoms include wasting of musculature. Cardiomyopathy may or may not be present. Onset of symptoms after 12 months old and may not present until late adulthood.
  - Primary treatment is enzyme replacement therapy (ERT). Other specific therapies have limited impact. LOPD patients may benefit from dietary treatment and Albuterol.
  - Bone marrow transplant has not been proven to be effective.
  - Early ERT studies demonstrated prolonged life expectancy, improvement in cardiomyopathy and decreased need for assistive ventilation.
  - Determine Cross-Reactive Immunologic Material (CRIM) status to guide immune tolerance induction (ITI) therapy:
    - CRIM positive (+) patients have residual GAA protein production. Generally associated with 1 or 2 missense variants in GAA.
    - CRIM negative (–) patients have undetectable GAA protein production. Generally associated with nonsense or frameshift GAA variants with multi-exon deletions.
    - CRIM (–) patients have poorer response to ERT.
  - Guidelines for Short-Term Follow-Up (STFU) of positive NBS:
    - Determine clinical status and differentiate IOPD from LOPD. Symptomatic newborns need to be evaluated immediately.
    - What information does your state program provide and what is the turnaround time for results?
    - What information is helpful in the diagnostic stage?
  - Clinicians should assess for clinical symptoms (muscular disease and cardiac disease) and identify IOPD patients in need of treatment during the first clinical visit.
  - Detection of LOPD "Patients in Waiting" can result in early treatment of LOPD and avoidance of diagnostic odyssey and associated costs.

- Families may experience psychological burden due to uncertain long term course of disorder and medicalization or stigmatization of LOPD children.
- Recommended Follow-up and treatment guidelines for **asymptomatic** LOPD patients:
    - Do not initiate ERT.
    - Evaluate patients every 3 months during first year post-diagnosis.
    - If symptom free for 12 months, evaluate every 3-12 months as clinically indicated. Start ERT if signs/symptoms of Pompe disease emerge.
- Recommended Follow-up and treatment guidelines for **symptomatic** LOPD patients:
    - Evaluate for signs/symptoms of muscle weakness, challenges with breathing and subtle developmental delays (per recommended schedule of assessments).
    - Start ERT at first sign/symptom of Pompe disease based on test results.
    - Evaluate monthly until 4 months and then every 3 months from 4-12 months.
- Advice to healthcare providers:
    - Faster diagnostic process
    - Find better ways to communicate results
    - Support for families
    - Education for parents and providers

MPS I

MPS I was the second disorder presented during the national meeting, with the speakers discussing surveillance case definitions around MPS I and clinical and long term follow up considerations. These are summarized below.

Surveillance Case Definition around MPS I: ***Marci Sontag, PhD, Colorado School of Public Health and Careema Yusuf, MPH, Association of Public Health Laboratories***

- PowerPoint slides linked here
- Summary notes:
    - Definitions created by panel of experts between July 2017 and June 2018.
    - Classifications- Definite, Probable, Possible
    - Based on answers provided to set criteria.
    - MPS I Case Definitions Table (May 2018) available here.
    - MPS I Worksheet available here.

Long Term Follow-Up Clinical Guidelines for Pompe: ***Tomi L. Toler, MS, CGC, Washington University School of Medicine***

- Summary notes:
    - MPS I is caused by pathogenic variant in IDUA gene.
    - MPS I-H is classified as Severe MPS I.
    - MPS I-Hurler/Scheie (MPS-HS) and MPS I-Scheie (MPS I-S) are classified as Attenuated MPS I.

- Severe MPS I often due to homozygosity or compound heterozygosity of the common pathogenic variants; usually causes complete loss of enzyme activity.
- Attenuated MPS I usually associated with one severe variant and a second pathogenic variant; usually has some residual enzyme activity.
- No biochemical differences exist between MPS I-H, MPS I-HS and MPS I-S.
- Clinical symptoms occur very early on. Attenuated MPS I less obvious early on and less severe.
- Pseudodeficiencies account for approximately 50% of all NBS referrals. No correlation between the original NBS levels and likelihood of a pseudodeficiency. Glycosaminoglycan levels were normal in all patients.
- Wide range of enzyme levels for all pseudodeficiencies. Genetic testing is important.
- Treatment for MPS I includes Enzyme Replacement Therapy (ERT) (Aldurazyme) and Hematopoietic Stem Cell Transplantation (HSCT). HSCT is the standard of care for patients with severe MPS I. Intrathecal ERT is in clinical trials.
- Outcomes correlate with age at treatment.
- Missouri NBS Follow up Criteria:
    - Severe MPS I
        - IDUA enzyme activity within affected range
        - Elevated urine GAGs
        - 2 mutations associated with severe disease, 1 severe mutation & 1 or more variants of unknown significance, or 2 variants of unknown significance
        - Clinical presentation may include course facial features, macrocephaly, corneal clouding, enlarged liver, enlarged spleen
    - Attenuated
        - IDUA enzyme activity within affected range
        - Urine GAGs within normal limits or elevated
        - 2 mutations associated with attenuated disease, 1 attenuated mutation and 1 or more variants of unknown significance, or 2 variants of unknown significance
        - Clinical presentation within normal limits at birth
    - Pseudodeficiency
        - Decreased IDUA enzyme activity
        - Urine GAGs within normal limits
        - 2 pseudo-deficiency alleles
        - Clinical presentation within normal limits
    - Genotype of unknown significance
        - Decreased IDUA enzyme activity
        - Urine GAGs within normal limits
        - 1 severe mutation and 1 or more variants of unknown significance, 1 attenuated mutation and 1 or more variants of unknown significance, or 2 or more variants of unknown significance
        - Clinical presentation within normal limits at birth

- NBS Follow-Up Best Practices for MPS I:
    - Repeat urine GAGs
    - Evaluate at 3-6 months of age and as clinically indicated
    - Test parents and siblings
    - Provide genetic counseling
    - Send the families a letter summarizing the results for patients with pseudodeficiencies.
- Genetic testing is critical to differentiating the recommended treatment and follow up.

X-ALD

X-ALD was the last disorder presented during the national meeting, with the speakers discussing surveillance case definitions around X-ALD and clinical and long term follow up considerations. These are summarized below.

Surveillance Case Definition around X-ALD: ***Marci Sontag and Careema Yusuf, NewSTEPs***

- PowerPoint slides linked here
- Summary notes:
    - Definitions created by panel of experts between July 2017 and June 2018.
    - Classifications- Definite, Probable, Possible. Differences in males and females
    - X-ALD Worksheet available at here.

Long Term Follow-Up Clinical Guidelines for X-ALD: ***Gerald Raymond, M.D., Penn State Medical Center***

- PowerPoint slides linked here
- Summary notes:
    - X-ALD is a peroxisomal disorder resulting from a defect in peroxisomal beta oxidation.
    - Incidence rate is 1:17,000, all races are affected.
    - Over 2,000 variants that can result in disease (whole exons deleted or other variants).
    - Phenotypes important in understanding ALD. Phenotypes include Cerebral, Adrenomyeloneuropathy (AMN), Addison Disease, and Asymptomatic.
    - Childhood Cerebral ALD (CCALD) has an onset between 4-10 years of age (peak at 7 years). Initial normal development and subtle presentation. Progresses rapidly to vegetative state. 35% of at risk males will develop CCALD
    - Hematopoietic stem cell transplant (HSCT) is the treatment for CCALD. Gene therapy is on the horizon.
    - AMN has an adult onset with gradual progression. Consistent with normal life span, but cerebral disease occurs in 20% of patientes. Greater than 50% of heterozygous women develop AMN in adult years.
    - 20-50% of women who are carriers will develop symptoms in adult years (Heterozygotes).

- Addison disease is caused by a primary adrenal cortical dysfunction. Leading cause of adrenal insufficiency in males.
- 90% of at risk males will develop Primary Adrenal Insufficiency. The symptoms include difficultly fighting infections, hyperpigmentation, dehydration, and hypoglycemia.
- Recommendations for follow-up:
    - Confirmation through biochemical and gene testing (ABCD1), genetic counseling, etc.
    - Adrenal function monitoring starting at 3 months of age and monitoring every 3-6 months.
    - Surveillance of cerebral ALD.
- Surveillance for childhood cerebral ALD:
    - MRI precedes disease. Neurologic findings are late manifestations.
    - Start MRI surveillance at 12 months. This will occur yearly until 3 years and every 6 months until 13 years.
    - After 13 years continue MRI yearly and endocrine care.
- Neuropsychological testing not recommended routinely.
- Get a second opinion if there is a questionable spot on the MRI. Refer to BMT center if there is an MRI lesion.

Breakout Session: Readiness Scale Phases

The objective of the breakout session was to discuss the NewSTEPs New Disorders Readiness Scale and identify the needs of states as well as any resources or approaches that can be shared. These are summarized below.

- Summary notes:
    - **Group 1- Phase 1: Authority to Screen**
        - What challenges have you faced obtaining approval/authority to screen?
            - Unable to obtain authority to screen unless there is an FDA-approved kit.
            - General revenue
            - Difficulty funding current disorders, which prevents from adding future disorders.
            - Advisory committee missing members to vote on adding new disorders.
        - What unique challenges did you face for MPS I or Pompe? Would these challenges translate to other disorders such as SMA?
            - No fee to support screening for new conditions.
            - Exceeded the amount of state funding without adding new conditions.
        - Have you found any unique solutions to the challenges identified?
            - Obtain budget tools from other states.
            - Invite parent advocates to the lab for a tour/walk through of the process.
            - Develop a strategic plan to assess which conditions to bring on first.

        - Refer to the legislative fact sheet developed by the APHL Legislative Workgroup, and make an effort to educate legislators.
    - How can APHL and NewSTEPs help your program address these challenges?
        - Provide a tool that shows families how long the "approval to screen" process will take and the steps that it entails.
        - Provide guidance around conversations with advocacy groups.
        - For reporting out, it would be helpful to have scripts for responding to advocates, parents and families.
        - Send periodic reminders on navigating website.

- **Group 2- Phase 2: Laboratory & Follow-Up Logistics**
    - What challenges/barriers have you encountered with regards to facility/infrastructure readiness for new disorders? What are the proposed or implemented solutions?
        - Barriers:
            - Acquisition of new space and remodeling.
            - Timeline for planned renovations compressed by legislation.
            - Time to dedicate to evaluate needs.
            - Health information technology (HIT) reporting.
            - Acquisition of equipment and depending on the corporate partner.
            - Merging LIMS and accessioning alignment of timelines.
            - Working with IT department for buy-in.
            - Lack of staff and project manager.
            - Coordinating corporate partners and LIMS upgrades.
        - Solutions:
            - Ask Department of Health for project management assistance.
            - Acquire unfinished lap space.
            - Allow for telework of follow-up staff.
            - Incorporate a hot-desk (multiple people rotate/share desk).
            - Take over conference room space.
            - Communication with legislators about needed time.
            - Include timelines in budget request with needed components.
            - Stakeholder meetings with IT personnel.
            - Develop relationships with legislative staff in state.
            - Develop detailed timeline.
            - Involve corporate partners.
            - Incorporate future needs into requests.
            - Reassess resources and reallocate as needed.

- What are your concerns regarding long-term follow-up (LTFU)?
  - What information should be collected
  - Who should handle late-onset cases
  - Long term outcomes for pathogenic variances
  - Data ownership, multiple repositories
  - Coordinating care, surveillance with specialists out of state
  - Blurred lines between NBS & LTFU
  - Sustainability and feasibility of screening family members
- What are the challenges for SMA?
  - Treatment cost and availability
  - There will be false negative results based on ACHDNC recommendations to screen for deletions
  - How to communicate false negative results
  - How to communicate what exactly we are screening for
  - New class of specialists
  - Frequency of the condition, follow-up case load
  - Complications of therapy & LTFU (renal toxicity)
  - Complications from other new therapies

- **Group 3- Phase 3: Education**
  - Which audiences have been most difficult to create and disseminate education materials for?
    - Challenges in creating materials for pseudodeficiencies
  - Geographic/Cultural/Language barriers?
    - Disproportionate number of pseudodeficiencies in African American population. Culturally appropriate materials are needed.
    - Refugee and immigrant families are skeptical of medicine and follow up, especially with pseudodeficiencies that do not require treatment.
    - Mistrust and disbelief of translated information.
    - Patients may not want a live interpreter if they are from within the community. Use anonymous phone interpreter. Ensure phone interpreters are not from the same area.
  - Challenges in communication and education for new disorders?
    - Industry representatives offering biased educational materials. Families gravitate toward industry materials.
    - Expected immediacy of genetic test results. Correcting misinformation and managing expectations regarding genetic tests.
    - Surveys indicate the best place for prenatal NBS education is in the Obstetrics (OB) office. OB office does not have time to address education and answer questions. Important to provide information to OBs during residency through didactic lectures.

- How can Babies First Test and NewSTEPs help?
    - Provide access to high level resources in multiple languages other than Spanish.
    - Provide resources that define the following: What is a pseudodeficiency? What is autosomal recessive inheritance? What does an abnormal result mean?
    - Reuse resources from other states and Babies First Test. Obtain information from multiple resources to customize letter to parents based on results. Can APHL compile these resources on the website (i.e. paragraphs about NBS, genetics, and specific disorders in multiple languages that follow up can cut and paste into letters and other communications as needed)?

- **Group 4- Phase 4: Full Implementation**
    - What is biggest lesson learned so far for full implementation?
        - NBS programs should be as inclusive as possible during the planning process and engage all stakeholders (e.g. IT, clinicians, dentists).
        - Meet with clinicians to discuss diagnostic testing and set up a plan.
        - Ensure funding is taken care of for pilots. Prepare/ protocols (share hospital specific protocol).
        - Make sure referral centers are prepared.
        - Talk to legislator/ board of health. Invite them to visit the NBS program and provide them with information/ pictures/ family stories. Advocate for the need for screening.
        - Consider 2 timelines: What to do if you are up against timeline? How to get things done in restricted time?
        - Connect with partnering states.
        - For pilot studies, add a disclaimer on the lab report.
        - Timeline of LIMS validation may not coincide with go live date.
        - Reserve funding for second tier testing.
    - Successes/ accomplishments of any of the 3 disorders?
        - TN: Implemented screening for all 3 disorders and identified first case. Established a better relationship with specialists/more inclusion from the beginning; received more feedback/ established more trust. Asked specialists to be on workgroup.
        - NJ: Success in sharing information across states to grow and learn from each other.
        - MI: Implemented second tier testing for MPS I. Looking to implement second tier testing for Pompe.

Facilitated Group Discussion

This section includes the questions and considerations that were brought up during the facilitated group discussion.

- Summary notes:
  - What has been the biggest success of any state in your group so far in getting ready for or screening statewide for MPS me, Pompe, and/or X-ALD?
    - Detecting positive cases
    - Building relationships with clinicians/treatment centers
  - In your view, what is the biggest need for the NBS community in getting ready to or screening statewide for these conditions?
    - Analysis of false positives
    - Limited insurance coverage for treatment services
    - Expectations/recommendations for STFU vs. LTFU
    - Pseudodeficiency education
    - Costs for diagnostic testing
    - More information on clinical outcomes
    - Defining end line for public health

Education for Staff, Clinicians, and Families

The second day of the meeting focused on education, with speakers sharing recommendations and resources to aid laboratory and follow-up staff in communicating with clinicians and families. These are summarized below.

Educating Newborn Screening Staff (Lab): ***Mei Baker, M.D., Wisconsin Newborn Screening Laboratory***

Educating Newborn Screening Staff (Follow-up): ***Suzanne Canuso, MSN, RN, New Jersey Department of Health***

- PowerPoint slides linked here
- PowerPoint slides linked here
- Summary notes:
  - NBS Staff need education regarding etiology, pathophysiology, clinical presentation, treatment for new disorders and testing methods before educating /communicating with others.
  - Education materials include letter to primary care providers, opt-out letter, website information and additional information for families with screening positive infants.
  - Tools for educating newborn screening follow up staff:
    - Orientation; lab tour; point person; binder/ protocols/ contacts/ ACT sheets; shared drive access to disease specific information; specialty group meetings biannually; lab/follow-up meetings monthly; weekly Monday huddles.

Educating Clinicians, Genetic Counselors & Providers: *Amy Gaviglio, MS, CGC, Minnesota Department of Health*

- PowerPoint slides linked here
- Summary notes:
  - NBS staff should provide clinicians with screening knowledge (what are we doing, what are we not doing), disorder-specific knowledge, communication tools, and Pre- and Post-diagnostic action plan.
  - Effective communication between provider and family foster great relationship, higher quality of care, autonomy of patient/ adhering to recommendations for treatment.
  - What do we need to talk about with providers?
    - Basics and process of screening
      - What have you/ state already done?
      - What are we looking at to get result and what does this mean?
      - What is the screening process?
    - Disorder specific information
      - Providers want to know information regarding next steps, clinical summary and treatment options, what to review with family, differential diagnoses, race/ethnic-specific findings/ increased incidences
      - ACT sheets are available for providers
  - New Disorder specific considerations
    - Potentially higher and longer rate of ambiguity for family and provider (VOUS/ Pseudodeficiency/ Late-Onset).
    - Molecular testing does not equal a black and white answer due to low genetic literacy amongst primary care providers.
    - Newly screened conditions equal higher concern for older siblings.
  - Have specialists consider forming a "Center of Excellence" or "Multi-disciplinary clinic"
  - Discuss the importance of reporting outcomes back to program with clinicians.
  - Need clinical guidelines for presymptomatic infants/children. Providers should be informed of new clinical guidelines.
  - Recommend regular meetings with specialty centers to define role of public health LTFU/ data collection versus clinical follow-up and clinical patient registries

Family Education for New Conditions: *Amelia Mulford, Baby's First Test and Kimberly Piper, RN, BS, CPH, Iowa Department of Public Health*

- PowerPoint slides linked here
- Summary notes:
  - Baby's First Test houses the nation's newborn screening clearinghouse. Provides numerous services and resources: state work group, annual outreach to states, Beyond

the Bloodspot Education and Engagement Summit, interactive national maps, public square, family stories, Spanish website, and resource center.

- Continuum of NBS Education Touchpoints. Important to define which of these we are focusing on:
    - Awareness: Exposure to information
    - Education: Imparting fundamental knowledge and tools that can be used to grow and expand the concept
    - Training: Imparting "how to" or technical knowledge
    - Engagement: Bidirectional process of collaboration
- Connect and hear from families and the public through community engagement and condition specific work groups. Examples include:
    - Iowa Deliberative Community Engagement Event
        - Model where you bring individuals together to deliberate a topic and share their own perspectives/come to a consensus.
        - Charged with making recommendations for Iowa NBS Program about *how* to add conditions and how to best communicate information to families and providers. The program will consider these recommendations moving forward and share them with the rest of the NBS community.
    - Minnesota phone interviews with families affected by X-ALD, Pompe, and MPS I
    - Condition-specific work groups
        - Facilitating condition-specific work groups bi-monthly
        - Includes family members of those affected by new disorders and clinicians
        - Have ties to advocacy organizations
- Themes and needs from families & community members include:
    - Information on opt-out/consent process
    - Latest knowledge about late onset variants and carrier status
    - Direction for pursuing screening if condition was not on panel at birth
    - Clearly defined screening status and start date for that state and condition
    - Support for healthcare professional/provider education
    - Connection with support groups and other families
    - Screening vs. diagnostic test distinction
    - Current information on effective/promising treatments
    - Roadmap for monitoring and treatment/what to expect
- What is available to meet NBS educational needs:
    - Condition-specific template materials (coming soon)
    - Baby's First Test Resource Center
    - Ask an Expert tool on BabysFirstTest.org
    - State disease-specific fact sheets
    - Plain language NBS results document (coming soon)
    - TA for strategy and development of educational content

- NBS educational plan next steps and future needs:
    - Education on new testing technology
    - Education on carrier status
    - Changes in Common Rule
    - Provide clear info about opt-out/consent procedures as appropriate
    - Strengthen relationships between FU program and clinical specialists
    - Increasing reliance on strategic planning and implementation for late onset
    - Maintaining NBS as a system of care
    - Thwart misinformation and evaluate sources
    - Monitoring internal consistency in communications
    - Bolster educational feedback loops to support clinician and parent

Educating Providers: Clinician and Families Panel

This section provides a summary of the stories and considerations shared during the Clinician and Families Panel.

- Summary notes:
    - **Pompe- J. Austin Hamm, MD, FACMG (clinician perspective)**
        - Presented two case studies on experiences with Pompe. Summary linked here.
        - Communication tips in the diagnosis period:
            - Families should be notified by NBS staff familiar with the disease.
            - Reason for repeats should be explained to the family.
            - Be disease specific.
            - Acknowledge the possibility of ambiguous results on the front end, if possible.
            - There are unique features in dealing with an asymptomatic vs symptomatic child.
    - **Pompe- Amanda Java (parent perspective)**
        - Has 4 children all of which were diagnosed with Pompe (Twins- 10 years, 7 year old, and 9 month old).
        - 9 month old screened positive. This case was identified by the Wisconsin NBS program (detected through pilot study). The other children were screened and also screened positive.
        - Recommended that the medical board updates information so that they do not give worst case scenarios to parents.
    - **MPS I- Tomi Toler, MS, CGC (clinician perspective)**
        - Presented first positive case that was not a pseudodeficiency. The process went well due to coordination of care.
    - **MPS I- Kenneth Jarrell (parent perspective)**
        - Daughter diagnosed with MPS I, son is a carrier.
        - 42 days elapsed from birth to first enzyme treatment.

    - Not every child is the same; early treatment is the best; cannot justify waiting 4-6 months when you can get tested the day of birth; want more states to test for MPS I. Facebook groups/ social groups are important for support
    - Important to improve education to parents.
    - Helpful to know carrier status.
- **MPS I- Gerald Raymond, MD (clinician perspective)**
    - Dr. Raymond involved in 2 state rollouts of X-ALD.
    - Important to make sure that parents get the best information quickly and explanation of next steps.
    - First MRI should occur at 12 months.
- **MPS I- Kerri DeNies (parent perspective)**
    - Son was diagnosed with X-ALD at 9 months due to California retro-testing for X-ALD.
    - Received a call from family doctor; visited doctor who had limited information regarding X-ALD and provided only worst case scenarios. Left with no pamphlet or information about the disease. PCP gave diagnosis without any resources/materials.
    - Geneticist was unaware of treatment options for X-ALD and testing.
    - Received support from another X-ALD mom who referred her to Dr. Eichler.
    - Son received first MRI at 2 years of age.
    - All 50 states should screen for X-ALD. Add to prenatal testing.
    - Establish a uniform standard of care among medical field
    - Develop a universal pamphlet for doctors and schools nurses to provide to parents. Include information on female carriers and disease and treatment in the pamphlet.

APPENDIX 1:

Meeting Participants

Name	State/Organization	Email Address
STATE NEWBORN SCREENING PROGRAM REPPRESENTATIVES		
Glenda Matthews	Arkansas	glenda.matthews@arkansas.gov
Pat Purifoy	Arkansas	Patricia.Purifoy@arkansas.gov
Sonal Bhakta	Arizona	Sonal.Bhakta@azdhs.gov
Ward Jacox	Arizona	ward.jacox@azdhs.gov
Tracey Bishop	California	Tracey.Bishop@cdph.ca.gov
Rasoul Koupaei	California	Rasoul.Koupaei@cdph.ca.gov
Darren Michael	Colorado	darren.michael@state.co.us
Emily Reeves	Florida	Emily.Reeves@flhealth.gov
Dusty Edwards	Florida	Dusty.Edwards@flhealth.gov
Arthur Hagar	Georgia	Arthur.hagar@dph.ga.gov
Judith Kerr	Georgia	Judith.kerr@dph.ga.gov
Sylvia Mann	Hawaii	sylvia@hawaiigenetics.org
Gwen Palmer	Hawaii	gwen.palmer@doh.hawaii.gov
Laura Ashbaugh	Illinois	laura.ashbaugh@illinois.gov
Christina Knepler	Illinois	christina.knepler@illinois.gov
Megan Griffie	Indiana	MGriffie@isdh.IN.gov
Barbara Lesko	Indiana	bglesko@iupui.edu
Kimberly Noble Piper	Iowa	Kimberly.piper@idph.iowa.gov
Sarah VanGorp	Iowa	Sarah.VanGorp@idph.iowa.gov
Shawn Manos	Kansas	shawn.m.manos@ks.gov
Caryn Masters	Kansas	Caryn.masters@ks.gov
LaShawn Marks	Louisiana	LaShawn.Marks@LA.GOV
Megan Dumas	Maine	mdumas@mmc.org
Wendy Smith	Maine	smithw@mmc.org
Fizza Majid	Maryland	Fizza.Majid@maryland.gov
Johnna Watson	Maryland	johnna.watson@maryland.gov
Kerri-Lynn Lockwood	Michigan	lockwoodk@michigan.gov
Mike Sarzynski	Michigan	SarzynskiM@michigan.gov
Mary Seerterlin	Michigan	SeeterlinM@michigan.gov
Kristi Bentler	Minnesota	kristi.bentler@state.mn.us
Amy Gaviglio	Minnesota	amy.gaviglio@state.mn.us
Elise Holmes	Minnesota	elise.holmes@state.mn.us
Tracy Klug	Missouri	Tracy.Klug@health.mo.gov
Patrick V. Hopkins	Missouri	Patrick.Hopkins@health.mo.gov
Sharmini Rogers	Missouri	Sharmini.Rogers@health.mo.gov
Krystal Baumert	Nebraska	Krystal.Baumert@nebraska.gov

Karen Eveans	Nebraska	Karen.Eveans@nebraska.gov
Jasmin Torres	Nevada	jasmint@med.unr.edu
Suzanne Canuso	New Jersey	Suzanne.canuso@doh.nj.gov
Sarah Eroh	New Jersey	Sarah.Eroh@doh.nj.gov
Michele Caggana	New York	michele.caggana@health.ny.gov
Beth Vogel	New York	beth.vogel@health.ny.gov
Joe Orisini	New York	joseph.orsini@health.ny.gov
Hari Patel	North Carolina	hari.patel@dhhs.nc.gov
Carol Johnson	Iowa (on behalf of North Dakota)	carol-johnson@uiowa.edu
Rosemary Hage	Ohio	Rosemary.Hage@odh.ohio.gov
Sharon Linard	Ohio	Sharon.Linard@odh.ohio.gov
Tonya D. McCallister	Oklahoma	TonyaJ@health.ok.gov
Sara Denniston	Oregon	SARA.DENNISTON@dhsoha.state.or.us
Stacey Gustin	Pennsylvania	sgustin@pa.gov
Justin White	Pennsylvania	justinwhit@pa.gov
Sandi Hall	South Carolina	Hallss@dhec.sc.gov
Tanya Spells	South Carolina	spellsty@dhec.sc.gov
M. Christine Dorley	Tennessee	M.Christine.Dorley@tn.gov
Ashley Porter	Tennessee	Ashley.M.Porter@tn.gov
George Dizikes	Tennessee	george.dizikes@tn.gov
Karen Hess	Texas	Karen.Hess@dshs.texas.gov
Patricia Hunt	Texas	patricia.hunt@dshs.state.tx.us
Robert Paul	Utah	rpaul@utah.gov
Andreas Rohrwasser	Utah	arohrwasser@utah.gov
Nicole Schultz-Ruiz	Utah	nruiz-schultz@utah.gov
Cindy Ingham	Vermont	Cindy.Ingham@vermont.gov
Chris Nixon	Virginia	christopher.nixon@dgs.virginia.gov
Christen Crews	Virginia	christen.crews@vdh.virginia.gov
Gretchen Wilson	Virginia	gretchen.wilson@dgs.virginia.gov
Richard Haughton	Virginia	richard.haughton@dgs.virginia.gov
Jennifer O. Macdonald	Virginia	Jennifer.Macdonald@vdh.virginia.gov
Aaron Boyce	Washington	Aaron.Boyce@DOH.WA.GOV
Gauri Gupta	Washington	Gauri.Gupta@DOH.WA.GOV
Carol Nucup-Villaruz	Washington	Caroline.Nucup-Villaruz@DOH.WA.GOV
Mei W. Baker	Wisconsin	mei.baker@slh.wisc.edu
PARTNERS		
Natasha Bonhomme	Genetic Alliance	nbonhomme@geneticalliance.org
Annie Evans	Genetic Alliance	aevans@geneticalliance.org
Amy Brower	ACMG	abrower@acmg.net
Danielle Ekoma	ACMG	dekoma@acmg.net

Sanjyot Sangodkar	ACMG	ssangodkar@acmg.net
STAFF		
Oluwafunke Akinsola	APHL	Oluwafunke.Akinsola@aphl.org
Sari Edelman	APHL	sari.edelman@aphl.org
Erin Darby	APHL	erin.darby@aphl.org
Kshea Hale	APHL	kshea.hale@aphl.org
Precious Kolawole	APHL	precious.kolawole@aphl.org
Jelili Ojodu	APHL	Jelili.Ojodu@aphl.org
Nisha Quasba	APHL	nisha.quasba@aphl.org
Ruthanne Sheller	APHL	ruthanne.sheller@aphl.org
Sikha Singh	APHL	sikha.singh@aphl.org
Kayana Walters	APHL	kayana.walters@aphl.org
Careema Yusuf	APHL	careema.yusuf@aphl.org
Guisou Zarbalian	APHL	guisou.zarbalian@aphl.org
Yvonne Kellar-Guenther	University of Colorado	Yvonne.Kellar-Guenther@ucdenver.edu
Sarah McKasson	University of Colorado	sarah.mckasson@ucdenver.edu
Marci Sontag	University of Colorado	Marci.Sontag@ucdenver.edu
CLINICIANS		
Austin Hamm	East Tennessee Children's Hospital	JAHamm@etch.com
Catherine Long	Children's Minnesota	Catherine.Long@childrensmn.org
Dietrich Matern	Mayo	Matern@mayo.edu
Gerald Raymond	Penn State Children's Hospital	graymond@pennstatehealth.psu.edu
Tomi Toler	Washington University School of Medicine	ttoler@wustl.edu
Sarah Viall	Children's' National	SViall@childrensnational.org
PARENTS		
Kerri DeNies	X-ALD	kerridenies@gmail.com
Amanda Java	Pompe	amanda.java@yahoo.com
Kenneth Jarrell	MPS I	tinajarrell18@gmail.com
CORPORATE PARTNERS		
Sean Romigh	PerkinElmer	Sean.Romigh@PERKINELMER.COM
Jodi Vaughn	PerkinElmer	Jodi.Vaughn@perkinelmer.com
Jon Washburn	Baebies	JWashburn@baebies.com
Candice Brannen	Baebies	cbrannen@baebies.com