LABORATORY STANDARDS AND PROCEDURES WORKGROUP

November 2, 2018

Co-chairs: Kellie Kelm, PhD & Susan Tanksley, PhD

Agenda

1. Welcome and roll call (5 min)
2. Workgroup membership (10 min)
3. APHL Guidance Document NBS Risk Assessment and Cutoffs update (10 min)
4. Ad hoc workgroup introduction (10 min)
5. Brainstorming new topics (75 min)
6. Wrap up (10 min)

Workgroup Roster

Mei Baker	Stan Berberich	Michele Caggana
Carla Cuthbert	George Dizikes	Rosemary Hage
Tricia Hall	Travis Henry	Scott McCandless
Jelili Ojodu	Scott Shone	Bonnie Taffe
Michael Watson	Holly Winslow	Roberto Zori

- Chair: Kellie Kelm
- Co-chair: Susan Tanksley
- HRSA staff: Ann Ferrero

Workgroup Charge

Define and implement a mechanism for the periodic review and assessment of

1. The conditions included in the uniform panel
2. Laboratory procedures utilized for effective and efficient testing of the conditions included in the uniform panel.
3. Infrastructure and services needed for effective and efficient screening of the conditions included in the uniform panel

Project 1

- Laboratory procedures: Explore the role of next generation sequencing in newborn screening
  - Screening is currently based on phenotypic data. How do we accumulate the data to identify correlation between phenotypic & genotypic data?
  - Are there conditions for which sequencing is the only screening method?
  - What do you gain/lose from NGS?
  - Which data do you report?
    - What do you do with variants of unknown significance?
    - When do you report carrier status? Are there particular conditions where reporting carrier status is important?
  - What new infrastructure needs to be built for NGS?

Project 2

- Infrastructure and services: A portion of the timeliness initiatives fits here:
  - Review data related to testing (Timeliness 1.0)
  - What are the implications of earlier specimen collection (<24 hrs)?
  - What are the unforeseen consequences and costs of timeliness?

Risk Assessment/Cutoffs

- Overview of Cutoff Determinations and Risk Assessment Methods used in Dried Blood Spot Newborn Screening - Role of Cutoffs and Other Methods of Data Analysis
- Feedback from multiple parties has been gathered, discussed and incorporated
- The living document has been posted to APHL's website
- Will be reviewed as needed in the future

Brainstorming

- Topic 1: Improving specificity. Could include:
  - Assess adding variables (e.g. weight, age) into our risk assessment/primary screen to improve specificity
  - New second tier tests (molecular and MS based)
  - Use of reference labs for second tier?

- Topic 2: Unifying definitions for NBS
  - Ad hoc workgroup discussed need for unified terms for describing NBS results
    - Is it normal vs. Negative vs. In-range?
    - Should it be a risk-based description?

Brainstorming

- Topic 3: What is the target of screening?
  - What are we likely to find in addition to what we're screening for?
  - Core conditions vs. Secondary targets
  - Transparency
  - Define the target and then economize screening for the target
    - E.g. appropriate methods, cut-offs/risk determinations

- Topic 4: Impact of broad phenotypes on laboratories
  - Share lessons learned on identifying late onset Pompe disease, SMA cases with 2, 3, or 4 copies of SMN2, etc.
  - Use information to refine the target of the RUSP condition?