LABORATORY STANDARDS AND PROCEDURES WORKGROUP

August 3, 2017

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

Agenda

1. Intro and roll call (10 min)
2. Review priority projects for Lab Workgroup (10 min)
3. Best Practices for State NBS Labs and Programs on Cutoffs and Discussion (60 min)
4. Ideas for New Topics (15 min)
5. Wrap-up and adjourn (5 min)

Workgroup Roster

Mei Baker
Stanton Berberich
Carla Cuthbert
Patricia Hall
Koon Lai
Holly Winslow
Fred Lorey
Joann Bodurtha
George Dizikes
Harry Hannon
Jelili Ojodu
Roberto Zori
Dieter Matern
Michele Caggana
Rebecca Goodwin
Travis Henry
Michael Watson

- 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

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NBS QA/QC Subcommittee: Guidelines for Determining "Cutoffs"

Presentation to ACHDNC Laboratory Standards and Procedures Workgroup

August 3, 2017

Presenters:

Joseph Orsini, Ph.D.

Patricia Hunt

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Background

- Following discussion of cutoffs at the national level, the APHL NBS QA/QC Subcommittee has been tasked with developing a draft guidance document on how to determine cutoffs used in newborn screening.
- Only a subset of the NBS QA/QC Subcommittee has contributed thus far, others are now reviewing.
- To follow is a draft outline of the document.

QA/QC Subcommittee members:

- Adrienne Manning, CT
- Amy Hietala, MN
- Carla Cuthbert, CDC
- Eleanor Stanley, MI
- Hari Patel, NC
- Inderneel Sahai, MA
- Joanne Mei, CDC
- Joseph Orsini, NY (co-chair)
- Kostas Petritis, CDC
- Mike Ramirez, IA
- Patricia Hunt, TX (co-chair)
- Santosh Shaunak, WA
- Laura Russell, APHL (staff liaison)

First Draft: Outline

I. Purpose

This document provides an overview of some of the approaches newborn screening programs may take in determining a “cutoff” between abnormal and normal test results. This is not meant to cover all possible methods of determining if a sample is screen positive; other resources are also available.

First Draft: Outline

II. Overview of Cutoff Determination

A cutoff can be either at the low end or the high end of the marker(s) reference range depending upon what the test method is intended to identify. Generally, a cutoff can be determined by completing the following steps:

A. Perform a small population study
B. Evaluate demographic factors that may impact the reference range
C. Determine the normal or reference range of the population graphically by creating a frequency histogram or probability density function.

First Draft: Outline (Contd.)

E. Determine the normal or reference range of the population statistically.

F. Conduct a literature search to identify prevalence and incidence of the disorder, and any published reference ranges and cutoffs.

G. Contact other states that are running the test and ask for their cutoffs for comparison

H. Evaluate results of the population study compared to true positives

First Draft: Outline

III. Cutoffs for Specific Newborn Screening Disorder Categories (Considerations for AA/AC, endocrine, LSDs, etc.)

IV. Challenging the preliminary cutoff (running known positives from other states, for positive controls, use of PT specimens if available, comparison to other programs)

V. Special considerations (first laboratory to set up screening, age, birthweight dependencies)

VI. Monitoring and evaluating the cutoff

VI. References

Next Steps and Estimated Timeline

1. APHL NBS QA/QC Subcommittee review (August 2017)
2. Incorporate Subcommittee feedback (September 2017)
3. Submit draft document to APHL Newborn Screening and Genetics in Public Health Committee (October 2017)

Brainstorming New Topics

- Two projects on detection of hearing loss using a molecular first line test
  - Picks up the late onset hearing loss cases not detected by the hearing screen (usually onset between birth and school age)
  - Extension of current condition on the RUSP?
- Update on the NSIGHT Projects, especially the projects comparing NGS to traditional NBS
- National data aggregation, outside of CLIR and NBSTRN
- Second tier testing for the new conditions added to the RUSP
  - NewSTEPs Peer Network
  - NY NGS for SCID second tier testing
- Report on the NICHD pilot studies for the LSDs