Laboratory Standards and Procedures Subcommittee Report

May 30, 2014

Susan Tanksley, Ph.D. – Co-chair
DACHDNC Organizational Representative

Priorities for Lab Subcommittee

- **Priority A:** Review new enabling/disruptive technologies
  - SUAC Implementation Survey Update
- **Priority B:** Provide guidance for state NBS programs in making decisions about lab implementation, integration, follow-up (FU), and quality assurance (QA)
  - SCID Slide Deck
  - Timeliness of specimen transport and newborn screening
- **Priority C:** Establish process for regular review and revision of the Recommended Uniform Screening Panel (RUSP)
  - No update at this time

Subcommittee Roster

Stanton Berberich
Robert Zori
Fred Lorey
Carla Cuthbert
Clem McDonald
Harry Hannon
Bill Slimak
Mei Baker
Swapna Abhyankar
Michele Caggana
Dieter Matern
Jane Getchell
Michael Watson
George Dizikes

Ad Hoc Experts: Koon Lai, Joann Bodurtha, Jelili Ojodu, Ed McCabe

Chair: Kellie Kelm
Co-chair: Susan Tanksley
HRSA staff: Tina Turgel and Debi Sarkar

Priority B - SCID Slide Deck

- Presented by Amy Brower
- Content built from workgroup discussions – Amy Brower, Jane Getchell, Michele Caggana, Mei Baker & Fred Lorey
- Audience: administrators, lab personnel, etc., to use as a tool as a state would consider whether to add a condition for testing in that state
- Concept: assortment of slides provided (based on requests of information/feedback from states) and then the user can pick and choose the slides to use in their own presentation

Overview of Slide Deck Content

- Background on the condition
- Addition to the Recommended Uniform Newborn Screening Panel (RUSP)
  - SCID Newborn Screening Pilots
  - Federal Partner Efforts
- State Implementation
  - Tools and Resources
  - SCID National Monthly Conference Call
- Ongoing Efforts
- Publications

Timeliness of newborn screening

Background for report

In order to effectively reduce mortality and morbidity, NBS must occur in a timely manner. Based on a public comment during the September 2013 meeting of the DACHDNC that raised the issue of timely NBS, the DACHDNC decided to review current policies and practices relating to timeliness of NBS in the US.

Background for report, continued

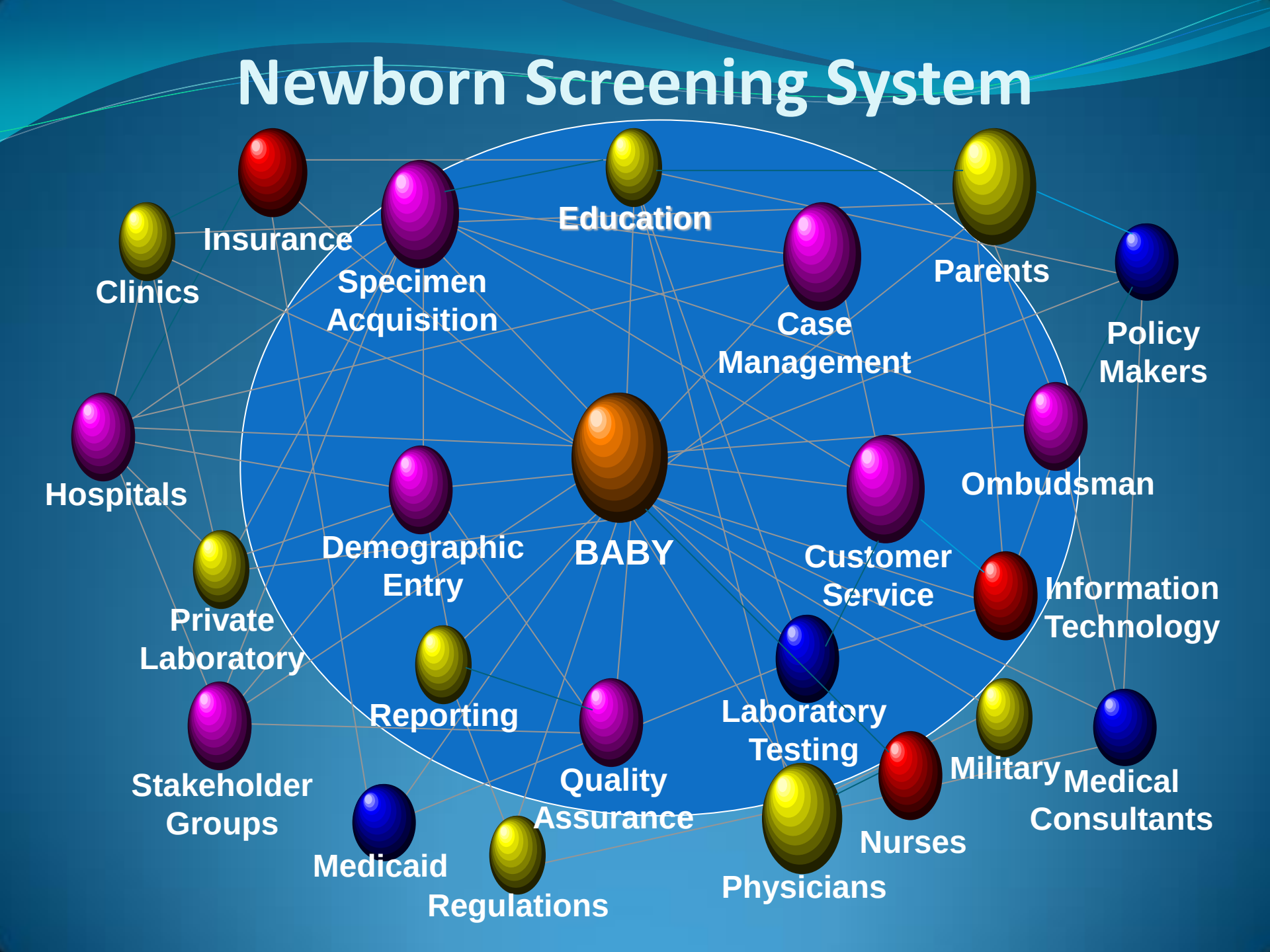
After an initial report in January 2014 based on survey data, discussions and review of pertinent literature, the DACHDNC recommended the following timeframes related to NBS:

- Initial NBS specimens should be collected at 24 to 48 hours of life.
- NBS specimens should be received at the Laboratory within 24 hours of collection.
- Newborn screen results for time-critical conditions should be available within 5 days of life.
- All NBS results should be available within 5 days of collection.

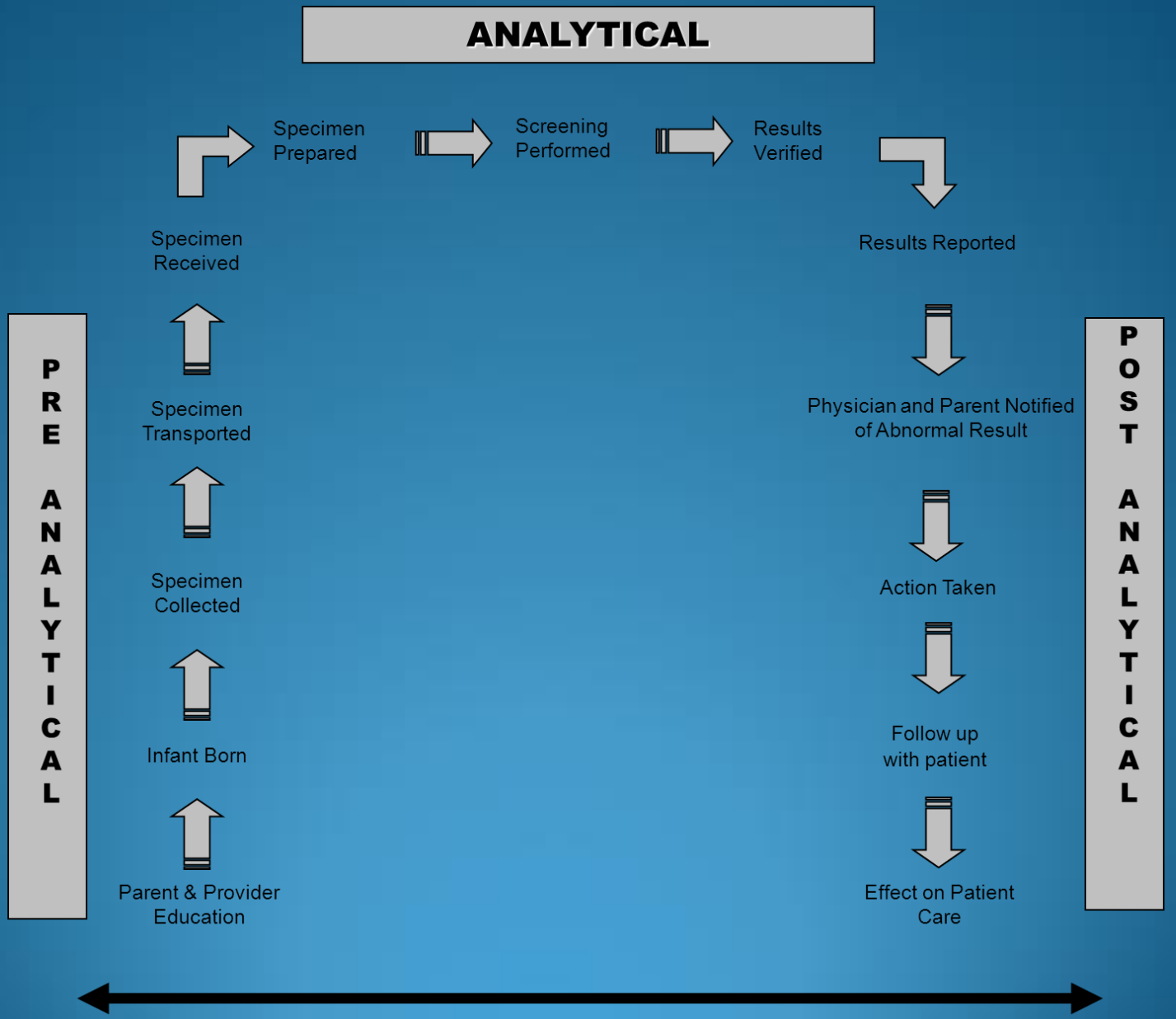
Lab Subcommittee Tasks

1. Outline the NBS system
2. Investigate existing gaps and barriers in NBS systems
3. Identify best practices to achieving these goals
4. Develop a list of critical conditions that require urgent follow-up
5. Review the recommendations in light of new technologies
6. Suggest revisions, if needed.

Newborn Screening System



NBS System Processes



Activities January through May 2014:

- Recruited a small workgroup from the Subcommittee: D. Matern, B. Slimak, S. Berberich, M. Baker, G. Dizikes, M. Caggana, E. McCabe* (K. Kelm, S. Tanksley, APHL)
- Submitted an abstract to the APHL NBSGT Symposium
- Working with an SIMD workgroup to assess the metabolic disorders that have the most urgent timelines for screening result reporting
- Working with APHL to generate a survey with accompanying webinar to gather gaps, barriers and best practices for timely screening

Next Steps

- Data Collection – Webinar & Surveys
  - Survey followed by webinar, FAQs and other documents to help survey takers
- Involvement with other stakeholders
  - Participation in survey (e.g. genetic counselors, follow-up staff)
  - Participation with other workgroups to work with hospitals
- Assessment of non-metabolic conditions that require urgent follow-up

September 2014 DACHDNC Meeting

- First draft report due to Committee in September 2014.

Priority A:

SUAC Implementation for Tyrosinemia Type I

Succinylacetone as Primary Marker to Detect Tyrosinemia Type I in Newborns and its Measurement by Newborn Screening Programs

V De Jesús, BW Adam, D Mandel, CD Cuthbert and D Matern

For the Laboratory Standards and Procedures Subcommittee
Secretary's Discretionary Committee on Heritable Disorders in Newborns and Children

Thursday, May 29, 2014

MAYO CLINIC

CDC

The Problem of Newborn Screening for Tyrosinemia Type I

- Tyrosine is not a specific marker for TYR I, but also elevated in other conditions
- Succinylacetone is a specific marker for TYR I, but not detectable by all NBS methods.

- 50 of 51 NBS programs in the US screen for TYR I

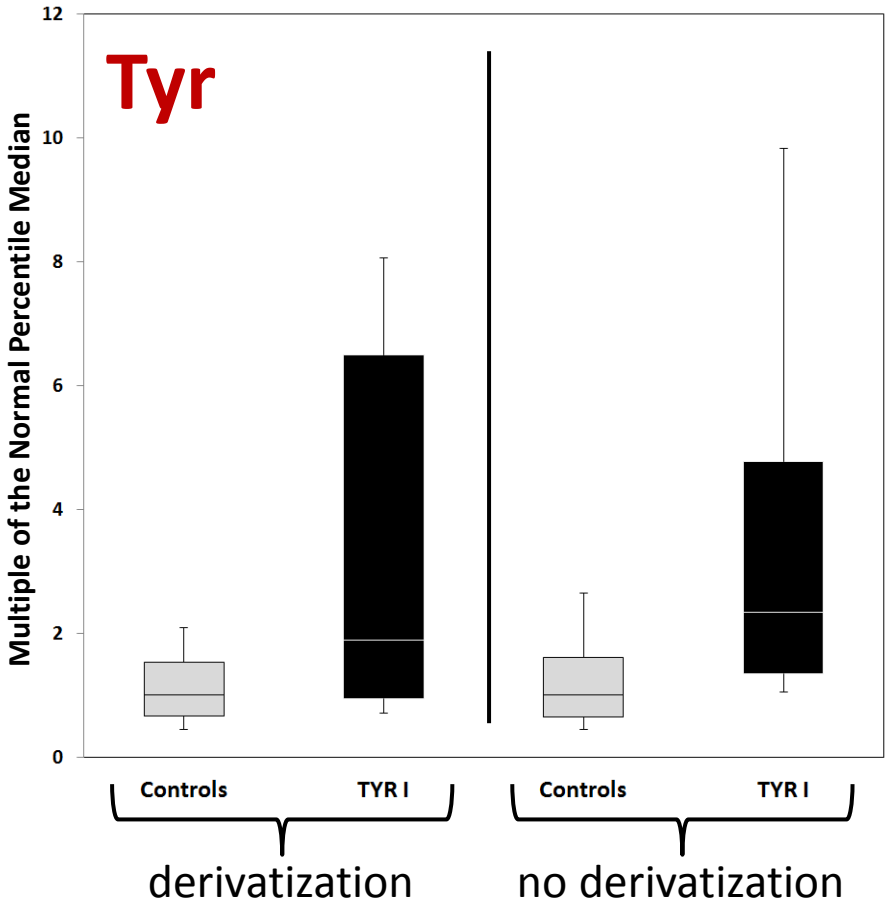
  (http://www.babysfirsttest.org)

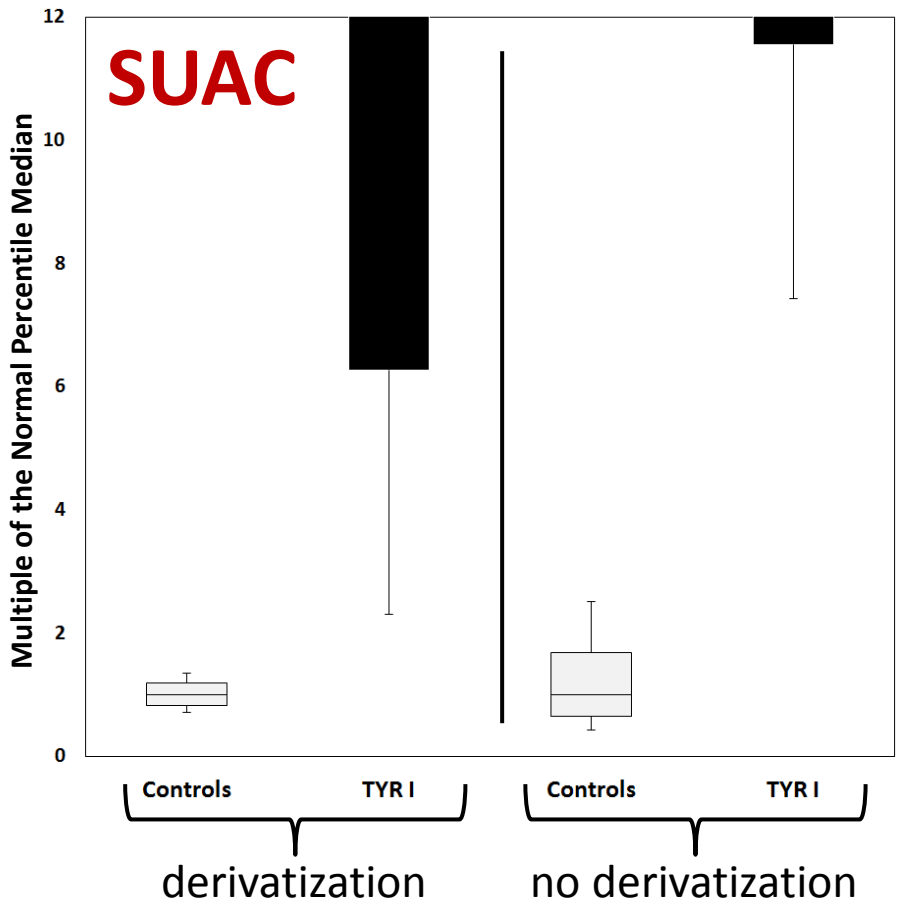
- 38 NBS programs in the US use SUAC to screen for SUAC

Methods for SUAC applied to NBS in the USA

- **MS/MS-based laboratory-developed tests (LDTs)**
  - Derivatization
  - No derivatization
  - LDTs are fully validated by each user lab, but not FDA approved
- **NeoBase™ Non-derivatized MS/MS kit (PerkinElmer)**
  - Has poor extraction efficiency for SUAC
  - FDA approved
- **Concerns:**
  - Some labs have to use FDA approved kits (state law)
  - Some labs concerned about accuracy of NeoBase kit
  - **Are assays sufficient to detect newborns with TYR I?**

Tyr and SUAC as Markers for TYR I





Data are based on information provided by 15 NBS programs (including 9 US programs) using derivatization and 14 programs (including 6 US programs) that do not derivatize.

Summary

- **TYR I should remain in RUSP**
- **SUAC is currently the best NBS marker for TYR I (independent of analytical method)**
- **CDC provides QA/QC/PT for TYR I (incl. SUAC)**
- **Surveys of NBS labs were conducted:**

  13 of 51 US NBS programs screen for TYR I with an unreliable marker (Tyrosine). *WHY?*

  - **perception that FDA assay not good enough**
  - **lack of money, space, staff, equipment**

Next Steps

- **Manuscript written (included in Briefing Book, comments welcome)**
- **Input from Committee:**
  - **Should DACHDNC/HHS recommend to the Secretary that the use of SUAC is a more appropriate NBS marker for TYR I? *or:***
  - **Should DACHDNC acknowledge the value of the article and add the article to the website?**
- **The subcommittee is interested in educational opportunities (via APHL) to reach out to the 12 programs still using TYR**