Virginia Newborn Screening Advisory Committee
Meeting Minutes
June 29, 2017

Attendees:

Members: Dr. Bill Wilson (UVA), Willie Andrews (DCLS), Jennifer Macdonald (VDH), Abraham Segres (VHHA), Christy Keppel (for Marie Pokraka-MOD), Jana Monaco (by phone- Parent)

Interested Parties: Eileen Coffman (CHKD), Laura Duncan (VCU), Dr. Hind Al-Saif (VCU), Virginia Pallante (VCU), Dr. Brook Vergales 9UVA), Sarah Viall (CNMC), Kim Pekin (Premier Birth Center), Becky Bowers-Lanier (VMA), Christina Owens (VMA), John Gibson (Biogen), Candice Brennan (Baebies), Vamsee Pamula (Baebies), Brianna Murray (CHKD), Amy Kenney (CHKD)

VDH/DCLS NBS Staff: Dr. Denise Toney (DCLS), Dr. Andrea Fritzinger (DCLS), Dr. Cornelia Deagle (VDH), Christen Crews (VDH-NBS), Kim Turner (DCLS-NBS), Lillie Chandler (VDH-NBS), Katie Duni (VDH-NBS), Marcus Allen (VDH_CYSHCN), Shamaree Cromartie (VDH-Blood Disorders), Richard Haughton (DCLS-NBS), Chris Nixon (DCLS-NBS), Rhonda West (DCLS), Katherine Crawford (VDH- Zika Birth Defects), Shea Browne (VDH-Zika Pregnancy Registry), Chris Patrick (DCLS-Contractor)

I. Welcome:
   a. Dr. Denis Toney welcomed everyone to DCLS
   b. All present introduced themselves.
   c. Agenda was reviewed. No additions noted.
   d. Membership was reviewed.
   e. Vote to approve 2/25/16 meeting minutes: Y-6 N-0 Absent 2

II. Public Comment Period
   a. John Gibson from Biogen spoke on the status of the nomination of Spinal Muscular Atrophy (SMA) as an addition to the national Recommended Uniform Screening Panel (RUSP) and Biogen's contributions to treatment for SMA.

III. Committee name change
   a. *Proposed name change: THE VIRGINIA NEWBORN SCREENING ADVISORY COMMITTEE*
      i. Reflects the evolution and changing business of newborn screening, nationally and in Virginia
      ii. A committee under the name *Virginia Genetics Advisory Committee* will be spearheaded by Office of Family Health Services to address and learn about genomic practices in Virginia
      iii. The Virginia Newborn Screening Advisory Committee will be a stand-alone committee, not a subcommittee of the Virginia Genetics Advisory Committee
      iv. Member Vote- unanimous in favor of name change Y-6 N-0 Absent 2
   b. Committee Infrastructure and By-Laws (*Attachment- Virginia Newborn Screening Advisory Committee Bylaws)*

i. Last updated Oct 2009
ii. Review of updated document
    1. Changes to Note:
        a. Updated Format
        b. Expanded Membership
    2. Discussion
        a. Add representative from the American College of Obstetricians and Gynecologists
        b. Change "certified practicing midwife" to "Certified Professional Midwife (CPM)"
        c. Add "certified" before Genetic Counselor
        d. Change "nutritionist" to "Registered Dietician"
        e. Add representative from the American College of Nurse Midwives- Virginia Affiliate
    3. Vote to Adopt Virginia Newborn Screening Advisory Committee By-Laws with changes: Y-6 N-0 Absent 2

IV. Periodic Regulation Review – Virginia Administrative Code
a. Last updated with CCHD regulations (current) & addition of SCID to panel
b. Last full review of dried blood spot regulations was in 2011
    i. No major changes made
c. What has happened since then?
    i. National timeliness recommendations
    ii. Three new disorders added to RUSP
    iii. LBW/Sick infant guidelines published
    iv. 21 day comment period of current regs in April – May 2017
        1. 1 comment in regards to support for CCHD screening
d. Please review *Regulations Governing Virginia Newborn Screening Services (12 VAC 6-71)* and provide comments for workgroup to look at during the regulatory process
e. What now??
    i. Comprehensive Review by Work Group of Committee
    ii. Areas that need addressing:
        1. Committee name change
        2. More details re: process of adding new disorders to Virginia's panel
        3. Ascertaining PCP name before discharge
        4. LBW/Sick infants protocols
        5. HL-7 messaging
f. Workgroup representation needed
    i. List
        1. Program staff
        2. Hospital well-baby nursery and NICU staff to include neonatologists and nursing

3. Community Pediatrician
4. Midwives
5. Genetic Counselor
6. Parent advocate
7. Specialists from disorders branches (Metabolics, Endocrine, CF, SCID, Sickle Cell)
8. DMAS
9. VHHA
10. MOD
11. Others??????

ii. Formal invite will be sent to interested parties

iii. Review slated for Fall 2017 via webinar to accommodate scheduling

1. Will likely need to meet often- monthly, over a period of ~1 year

V. CCHD Screening Program

a. Since coming to the end of the grant period, there have been limited resources available for CCHD activities

b. Recently hired nurse to assist in CCHD follow-up

i. Will perform quality assurance on CCHD diagnosis data

c. Question- How do low birth weight and premature babies, who don't get identified with CCHD through the newborn screening, get into the EBC?

i. Answer- They likely do not. This will be a topic during the regulation review.

ii. Currently EBC notes if a baby was not screened

d. VA midwives alliance has been engaged in all NBS practices

i. Education provided

ii. Feedback solicited on CCHD process from midwives

iii. NBS program is applying for a grant to provide pulse oximeters free or at low cost to midwives

VI. EHDI

a. Advisory committee had their last meeting on June 3, 2017

i. Committee must be 25% parents

b. Program funding received through 2020 via CDC and HRSA

c. Grants focusing on increasing family engagement, development of regional learning communities and Early Intervention (EI) documentation.

d. EHDI team received two ABR machines from Henrico Doctors Hospital which were gifted to midwives in Lynchburg and Winchester.

e. EHDI team attended the following:

i. May 2017 Virginia Otolaryngology Association conference

ii. June 2017 Virginia Hands & Voice event and Opening Doors, Unlocking Potential conference

iii. July 2017 Shining Stars conference

VII. Birth Defects

a. Zika Surveillance Program
    i. Currently a passive surveillance
    ii. Funding available through 2019
    iii. Zika pregnancy registry fully implemented in Virginia
        1. 65 women currently enrolled in VA as of June 29, 2017

VIII. Children and Youth with Special Health Care Needs (CYSHCN)

a. Title 5 funded
    i. State provides match of funding
b. Sub programs:
    i. Care connection for children
        1. 6 centers
        2. Private/public partnership with health systems
        3. Code requires follow-up to refer long-term physically affected children to care coordination
        4. Care coordination- More than just case management
    ii. Sickle Cell Disease Program
    iii. Hemophilia Program
c. Medical Neighborhood initiative
    i. Medical neighborhood collaborative in Blue Ridge area
    ii. Initiative to provide training on importance of a medical home
        1. Specifically, for the transition from pediatric to adult care for affected children

IX. Sickle Cell program update

a. In process of rebranding to bring sickle cell awareness
b. Working with four centers to approve materials before they are released to the public

X. Newborn Dried Blood Spot Program

a. National Issues update
    i. Milwaukee Journal-Sentinel– Article *The Price of Being Wrong 12/9/16*
        1. Challenging NBS Programs on the use of cut-offs for result interpretation
            a. APHL has launched a national survey to gather current practices
            b. Survey results to be presented to the Secretary's Advisory Committee on Heritable Disorders in Newborns and Children (SACHDNC)
        2. Milwaukee Journal-Sentinel article previously released in 2013, focused on lack of timeliness of NBS
            a. Targeted hospitals who were batching samples
    ii. SACHDNC – May Meeting (May 11-12, 2017)
        1. Presentations from NBS Programs regarding validations and cut-offs
        2. Dr. Piero Rinaldo spoke on the use of R4S/CLIR as a web-based tool
        3. Spinal Muscular Atrophy(SMA) was moved to full evidence review after report out by the Nomination & Prioritization Workgroup

4. Next SACHDNC meeting August 3-4, 2017

b. NBS LIMS – V10 Implementation
    i. June 23, 2016 – V10 LIMS moved into production **A HUGE EFFORT!!**
    ii. For the Lab – V10 provides greater traceability, automates QC functions and ties the instrument system into the LIMS
    iii. For the Follow-up team- V10 provides more report generation capabilities, enhanced functionality to capture nurses notes and greater flexibility in extracting data needed to track pending and diagnosed cases
    iv. For Program & Partners – V10 enable us to bring HL7 messaging to NBS – to receive electronic sample submissions and send electronic results
c. 2nd Tier CAH Update
    i. Main Goal: Reduce CAH False Positives
    ii. MS/MS and HPLC Parameters Optimized
        1. Approx. 5min per injection
    iii. Utilize Existing Instrumentation
    iv. DBS Materials for Cal. and QC
        1. Produce in-house
        2. CDC Materials
    v. Optimize Extraction Procedure
    vi. Validation and IT Build-out
    vii. Proposed Implementation Q1 2018
d. Follow-up updates
    i. Co-location of NBS Follow-Up team with Laboratory
        1. Enhanced communication
        2. Improve operations
    ii. Automation of completion of critical report forms
        1. Improve efficiency
        2. Decrease administrative demands of nursing staff during period of staffing issues
    iii. New part-time follow-up nurse
        1. Reduce workload of follow-up
        2. Focus on special projects
e. Midwife Engagement
    i. Identified 15 Midwifery Birth Centers in VA
        1. Established daily pickup UPS services at 13 centers to insure timely delivery and preserve sample integrity
        2. Training webinar held June 13, 2017
    ii. Now offer a separate NBS collection kit for Midwives
        1. Allows midwives to order between 1 and 9 collection cards, as needed
f. Celebrating and Educating
    i. Oct 1 2016 – 50th anniversary of NBS in Virginia
    ii. Celebrated by setting up a booth at the state fair

1. Spoke with the public about Newborn Screening (and other testing at DCLS)
2. ~3500 people

iii. 50th Anniversary Conference
1. Offered continued education
2. Keynote speaker- Dr. Berry Wolf
a. 1984 Dr Wolf and NBS program developed first screening test for BIOT deficiency
3. http://vanbsfiftyyears.virginia.gov/index.html

g. Preliminary 2016 data
i. 100,431 infants screened
ii. 108,413 samples received
iii. 3,143,977 tests run
iv. 20,842 abnormal
v. 1,182 critical
vi. 3,323 diagnosed (includes carrier statuses)
vii. 228 lost to follow-up
viii. *See Attachment 1*

h. NBS Timeliness Initiatives
i. Year 4 of this project
ii. National recommendations from SACHDNC
iii. 1st area of focus in VA – Reduce Transit time
1. Added courier sites to 13 hospitals
2. Added Sunday pickups to all hospitals
3. Monitor and visit "top offenders"
4. Distribute quarterly report cards

iv. Report Card
1. Diagnosed cases added on to show impact of NBS and that babies from their facilities are affected

v. Emphasis- DON'T CALL IT "THE PKU TEST"!
1. Health of babies affected by this misnomer

vi. Next Steps
1. The Virginia Newborn Screening timeliness workgroup needs more perspective from professionals outside of the program
2. Email request will be sent for volunteers

XI. DCLS/UVA Capstone Project

a. Partnered with two students through the UVA Data Science Institute
i. Project goals – to automate and improve data analysis and data queries

b. Accomplishments -
i. Automated and enhanced hospital report card generation & distribution process
ii. Developed automated queries to gather and upload quality
iii. indicator data to NewSTEPs

iv. Developed queries and introduced visualization tools to look
v. at program data, such as:
    1. Incidence and prevalence of disorders
    2. False positive rates
    3. And more…
vi. Provided training to the DCLS Informatics team to build new queries in R Studio (and this effort is ongoing…)

XII. NewSTEPs360 Grant Projects

a. NYMAC Collaboration
    i. Focused on education – collection and timeliness
    ii. Aug 2016 Publication in American Nurses Association magazine (circulation 102,000 in Virginia)
    iii. Fall 2016 - present Blood specimen collection video pilot testing
        1. 14 Virginia Hospitals participated in pilot testing
            a. pre and post testing
            b. correlating hospital unsats and transit time for 18 month time period
    iv. Winter 2017 – present Electronic Messaging Capability Survey
b. Electronic Messaging
    i. VA was awarded a 3 yr grant in 2016 -
    ii. "*Using Health Information Technology to improve timeliness through electronic demographic and order submission and result reporting"*
        1. Manual data entry
            a. Manual errors are always a possibility
            b. Handwriting
            c. Missing data
        2. Paper reporting process is not time efficient
            a. Returned by mail to providers and by courier to hospitals
            b. Long printing and envelope process
    iii. Currently working with 12 Hospital Pilot Sites
    iv. Partnering with OZ Systems to expedite hospital implementation
    v. HIE provides a pipeline and is already used by hospitals for reportable diseases
    vi. Pull as much data from Electronic Health Record into a module, key in missing data
    vii. On target to establish sample order messaging in Yr 2 and result messaging in Yr 3 of pilot project
        1. VCU and UVA will be first to send NBS order messages
    viii. Goal is to establish electronic messaging with <u>all</u> VA's hospital systems

XIII. Adding New Disorders to Virginia's Panel

a. LSD workgroup convened on 2/24/2017
b. Focuses of Review
    i. Pompe Disease

ii. MPS-1

c. NBS Programmatic Staff Preparation:
    i. Nov 2015 NBS for Pompe and MPS-1 Screening
    ii. Feb 2017 Gene Sequencing in Public Health Newborn Screening
    iii. June 2017 National NBS Meeting on New Disorders
    iv. July 2017 NYMAC New Disorders Training (Lab and Follow-Up)
d. Review process
    i. Review of ACHDNC Disorder Review
    ii. Review of Current Scientific Literature
    iii. Review of Other State Screening Data
    iv. ID Infrastructure Needs
    v. Economic Evaluation
    vi. ID Benefits & Risks
    vii. Summary of Findings
e. Post Review
    i. Workgroup and Advisory Committee Review
    ii. Commissioner Report
    iii. Commissioner Response
    iv. BOH
    v. Regulatory Process
    vi. Planning & Implementation
f. Workgroup review entails…
    i. Disease Definition
    ii. Treatment Options
    iii. Screening Methodology
    iv. Other State Perspectives and Experience Thus Far
    v. Scientific Literature Review
    vi. Initial Cost Assessments
    vii. Discussion: Risks vs. Benefits
g. This process was used for the review of Krabbe
    i. recommendation is on the general assembly website
h. Pompe discussion notes – *see Attachement 2 from Feb 2017 session*
    i. No clear-cut recommendations on when to treat
        1. Insurance companies do not support giving treatment early treatment (very costly)
    ii. There are secondary testing besides molecular
    iii. Virginia Newborn Screening Lab is not a diagnostic lab, but would like to provide doctors with as much information as possible
    iv. Presence of pseudogene and pseudodeficiencies
    v. No consensus on long term follow-up process
    vi. A webinar will be scheduled to revisit this topic prior to next meeting

vii. Some concern that border states are testing for Pompe and Virginia is not – screening can depend on where you live
viii. All in agreement to implement screening of Pompe, question of how
1. Need to come to an agreement about second tier testing.
ix. NY has shown success with DNA sequencing for Pompe
x. Missouri false positive rate is 0.035
xi. Suggestion: look at other states to choose an algorithm
xii. Suggestion: How we phrase our recommendation can be done in a way that allows us to look at the algorithm later. Exclude specifics of the technology because it changes rapidly
1. Revised recommendation will be brought forth to next meeting for vote

i. MPS-1 – *see Attachment 3 from Feb 2017 session*
i. Suggestion: How we phrase our recommendation can be done in a way that allows us to look at the algorithm later. Exclude specifics of the technology because it changes rapidly
1. Revised recommendation will be brought forth to next meeting for vote

j. Review of X-ALD
i. Will attempt to schedule for September
ii. Need to expand stakeholders
1. Endocrine specialist
2. Neurology specialist
3. parent

XIV. 2017 Planning/Future Dates

a. July Periodic Cystic Fibrosis Screening Review
b. August Annual SCID Screening Review
c. September X-ALD review (tentative)
d. October Periodic Galactosemia Screening Review
e. Fall 2017 Regulation review workgroup meets
f. December 7 Next Advisory Meeting (tentative)

The meeting was adjourned at 2:30 PM.

Attachment 1

2016 Diagnosed Cases – Preliminary Data

Metabolic Conditions	
3-Methylcrotonyl-CoA carboxylase deficiency (3-MCC)	1
Argininosuccinic aciduria (ASA)	1
Biotinidase deficiency (BIO)	3
Biotinidase deficiency, partial (BIO partial)	3
Galactosemia (GALT)	6
Galactosemia, non-classical	21
Galactosemia carrier (GALT carrier)	47
Long-chain L-3-Hydroxy acyl-CoA dehydrogenase deficiency (LCHAD)	1
Maple syrup urine disease (MSUD)	1
Medium-chain acyl-CoA dehydrogenase deficiency (MCAD)	4
Medium-chain acyl-CoA dehydrogenase deficiency carrier (MCAD carrier)	1
Classic Phenylketonuria (PKU)	5
Hyperphenylalaninemia	10
Tyrosinemia	2

Severe Combined Immunodeficiency	
DiGeorge Syndrome (Thymic Hypoplasia)	1
Partial DiGeorge syndrome /22q11.2 deletion syndrome (Thymic Aplasia)	1
Thyroid-binding globulin deficiency (TBG)	7
Severe Combined Immunodeficiency Deficiency	1
Other Lymphopenia	6

Cystic Fibrosis	
Cystic fibrosis (CF)	15
Cystic fibrosis carrier (CF carrier)	84

Congenital Adrenal Hyperplasia	
Congenital Adrenal Hyperplasia	1

Hemoglobinopathies	
Sickle Cell Disease	50
Sickle Cell Disease Carrier	1700
Hemoglobinopathies	11
Hemoglobinopathy Carrier	1318

Congenital Hypothyroidism	
Primary Congenital Hypothyroidism (CH)	20
Hypothyroidism	1
Hyperthyroidism	1
Thyroid-binding globulin deficiency (TBG)	7

Attachment 2
Pompe Workgroup Review Discussion Notes

Referral Sites

- 4 sites CNMC, VCU, UVA, CHKD
    - *Provide management report on # referrals/disorder per site
- Concerns about volume of referrals affecting current caseload
    - Estimate 1-2/week per disease across sites
    - False positives

Education

- Known patients in Virginia with missed timely diagnosis due to provider knowledge, can take years to receive appropriate diagnosis
- Concerns of parent education for late-onset diagnosis through NBS, different approach needed

Research

Taiwan- started screening around 2007/2008

- Babies started treated prior to 2 weeks of age, at 3 years normal development
- Unknown long term outcomes of treated infants

Early treatment has better outcomes, decreased risk of respiratory complications

Consider cost of undiagnosed child vs early diagnosed via NBS

- Not implementing would result in more undiagnosed children with Pompe to undergo unnecessary testing or delay in treatment, resulting in potential negative outcomes, would be difficult for family to understand why disorder was not added to panel

Projected to have increased percentage of late-onset diagnosed cases once NBS starts

Methodology/False positives

- Enzyme sensitivity due to storage, heat, humidity may cause false positives
    - Consider promoting overnighting samples to decrease concerns of environmental exposure
- Utilizing method of having 2 disorders flagged in one sample to be unsat to decrease FP rate
- Evaluate streamlining algorithm for multiple abnormal/unsats for moving to diagnostics (i.e. GALT)
- Emotional and financial impact on families with false positives, molecular testing would reduce

Long Term Follow-Up

- How to follow- when start treatment, how to educate parent
    - Taiwan follows patients by annual CK and physical exam and being ERT treatment when clinical presentation arises
    - Who will do annual diagnostics, follow patient
- Long term follow-up
    - *Need more information from other states who have programs in place for late-onset disorder
- Emotional impact on families with knowledge of late-onset

Legal implications

- Milwaukee Sentinel Journal
- Healthcare, life insurance increase for future late-onset conditions

Molecular testing

- P&E ~$400/sample for LSD panel
- Reduce false positives, decrease emotional anxiety on families
- Current program (Duke?) offers molecular testing/CRIM status at no cost, unsure of longevity

Financial Support

- Consider requesting GF to supplement fee for service, possible help from NORD or other advocates to request supplemental funds to implement disorders without increasing screening fee
- Consider start-up grant from APHL or CDC for implementation

Careful planning and implementation needed, additional information from other states on algorithms and follow up for long-term onset

Other states's status
DC has approved Pompe, MPS-I, and X-ALD
Maryland approving Pompe, not MPS-I

Recommendations of Workgroup: POMPE
Recommendation:
Virginia shall implement newborn screening for Pompe Disease. Screening methodology shall include:

- *1st tier screening in conjunction with 2nd tier gene sequencing*

Acknowledgement:
Performing molecular testing in-house would require 4-5 years. Additional investigation is necessary to outsource 2nd tier testing until this capability is reached.

Vote: <u>All in favor</u>

Attachment 3
MPS-I Workgroup Review Discussion Notes

Concerns about positive predictive value (PPV) methodology
Low incidence (1:100,000)
Similar concerns to Pompe about false positive, effect on families, long term follow-up
No current molecular testing methodology available (NY available)

- Reduce/eliminate psuedodeficiencies from 1st tier positives resulting with carriers or confirmed cases from referrals
- Fiscal impact of testing for both disorders

Limited facilities for BMT, limitations on insurance coverage
*Assess which centers/hospitals can do BMT in state/border states
If do not recommend MPS-I, unable to use false- positive elimination methodology by 2 disorders being flagged resulting in unsat

- Consider using GALT/BIOT to flag as an unsat if only Pompe recommended

Recommendations of Workgroup: MPS-I

Recommendation:
Virginia shall implement newborn screening for MPS-1 Disease. Screening methodology shall include:

- *1st tier screening in conjunction with 2nd tier gene sequencing*

Acknowledgement:
Performing molecular testing in-house would require 4-5 years. Additional investigation is necessary to outsource 2nd tier testing until this capability is reached.

Vote: <u>All in favor</u>