Virginia Newborn Screening Advisory Committee
Thursday, November 15, 2018
10:00 a.m. – 2:00 p.m.

The Division of Consolidated Laboratory Services (DCLS)
600 North 5th St. Room T21/T23
Richmond, VA 23219
Conference call-in phone number: 1-866-842-5779 Code: 804-648-4480

AGENDA

Members (check = present):

- ■ Dr. Bill Wilson, UVA, Chair
- ☐ Abraham Segres, VHHA
- ■ Sarah Viall, NP, CNMC
- ☐ Julie Murphy, Parent
- ■ Karen Shirley, HCA-Va, Chippenham Hospital
- ■ Lisa Shaver, Children's Hospital of Richmond at VCU (phone)
- ■ Amber Price, ACNM
- ☐ Rachel Gannaway, Genetic Counselor, VCU
- ■ Dr. Christian Chisholm, UVA, Virginia Chapter ACOG
- ■ Dr. Michael Martin, Virginia Chapter AAP
- ☐ Pediatrician, TBD

VDH & DCLS Staff

- ■ Willie Andrews
- ■ Jennifer Macdonald
- ■ Marie Pokraka, MOD (phone)
- ■ Jana Monaco, NORD, OAA, Parent (phone)
- ■ Dr. Hind Al Saif, VCU
- ■ Dr. Samantha Vergano, EVMS/CHKD
- ■ Dr. Brooke Vergales, Neonatologist, UVA
- ☐ Kim Pekin, CPM
- ☐ Barb Goodin, Dietician, UVA
- ☐ DoD, TBD
- ☐ INOVA, TBD

Interested Parties: Eileen Coffman (CHKD), Kelly Jones (CHKD), Amy Kenney (CHKD), Chris Nixon (DCLS), Richard Haughton (DCLS), Jacqueline Schools (DCLS), Denise Toney (DCLS), Angela Fritzinger (DCLS), Gretchen Cole (DCLS), Rob Comia (DCLS), Jennifer Brickey (VDH), Lillie Chandler (VDH), Christen Crews (VDH), Daphne Miller (VDH), Marcus Allen (VDH), Shamaree Cromatrie (VDH), Sylvia Lee (DOD, Pediatrician), Virginia Pallante (VCU), Debra Schaefer (Cure SMA), Peter Grab (Cure SMA, parent), Amanda Grab (Cure SMA, parent), Lauren Sullivan (by phone-Cure SMA, parent), Marta Bitterman (phone - Geneticst, INOVA), Dr.Reuben Rohn (by phone- Endocrinologist, CHKD), John Gibson (phone - Biogen); Jaimie Vickery (phone – CureSMA)

10:00 – 10:20	Welcome: Dr. Bill Wilson, Chair A. Welcome to Division of Consolidated Laboratory Services (DCLS): Dr. Denise Toney a. Dr. Wilson opened session and introduced Dr. Denise Toney. Dr. Toney welcomed everyone. Dr. Toney is glad to have the meeting to share the work that DCLS is doing in collaboration with the Virginia Department of Health (VDH), and many changes are expected in the next few months. The need to expand is important, as we need to protect our babies. Dr. Toney reviewed safety procedures and protocols with the attendees. Dr. Angela Fritzinger, Deputy Director was introduced. B. Role Call – Quorum present C. Introductions of Members and Interested Parties

	D. Review of Agenda E. Approval of June 7, 2018 Meeting Minutes a. Minutes were approved unanimously by voting members. F. Travel Reimbursement (members only)
10:20 – 10:35	Public Comment: a. Debbie Schaefer (CureSMA, parent): showed picture of granddaughter Madison and Bailey, both have Type 1 Spinal Muscular Atrophy (SMA). Madison would have been 7 years old, but she passed away at 7 months shortly after being diagnosed with SMA. When she was a few months old they noticed floppiness, difficulty swallowing, unable to move arms- and she never was able to hold head up. After multiple doctor appointments and testing, she was diagnosed at Children's National Medical Center (CNMC) with SMA. At that time, there were no treatment and palliative care was recommended unless choose to do invasive interventions. Madison passed away at 7 months. About 5 years ago, her other granddaughter Bailey was diagnosed prenatally with SMA and was entered into Phase II of the clinical trial that resulted in the FDA treatment of SMA. Bailey can move her arms and legs, she can move her manual wheel chair, she can talk, and she will be 5 in January. It is unknown if she will ever walk, but there is hope as others in her trial group have started walking with assistive devices.Ms. Schaefer stated that babies given the treatment, Spinraza, within 7-10 days of birth are meeting developmental milestones. Early diagnosis and intervention profoundly improve life. The entire family is impacted with a child with special needs, becoming a 24/7 caregiver. The early detection and early treatment is incredibly important because biological effects are happening that can't be recovered. Bailey is receiving Spinraza- not only did it slow progression, but it has also reversed some things that did occur with her disease progression. She also shared that a company, AveXis, is working on a gene therapy treatment which would require a one-time application. Bailey has to currently receive treatment every 4 months. Ms. Schaefer said it is expected 9 babies diagnosed every year with SMA. b. Lauren Sullivan (CureSMA, parent): daughter has SMA type unknown, asymptomatic, poster child of early detection and intervention- diagnosed prenatally through routine carrier testing and confirmed amniocentesis, has 4 or more copies of SMN2, received first dose of Spinraza at about a month old, she has had 6 doses and is on time for milestones and ahead developmentally. c. Peter Grab (CureSMA, parent): daughter was born in 2014 – no complications at birth, around 2 months of life not meeting milestones (sitting up, rolling over, etc). Pediatrician suspected low

	muscle tone- referred to neurologist- appointment scheduled for 3 weeks out. The neurologist suspected SMA; however, Tricare refused genetic testing. Kinsley continued to get weaker and not gain weight. With her weight declining, her mother took a leave of absence without pay to provide care. They went to another neurologist who fought to get geneticist testing approved. She received G tube and respiratory treatments every 2-3 hours to clear airway. This made it difficult to leave house due to potential risk of choking. Kinsley needed BiPAP at night; however, no masks approved in US for pediatrics so had to be ordered overseas. They requested overnight care and insurance denied due to lack of official diagnosis. She received the official diagnosis and insurance approved additional care 3 days before her lung collapsed. If she had been identified through newborn screening, she could have been diagnosed earlier.
10:35-11:35	Virginia Newborn Screening (NBS) program updates: Willie Andrews, Jen Macdonald A. Secretary's Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC) meeting updates i. August 2- reviewed agenda and discussion on August 2nd meeting 1. Risk assessment in NBS 2. Improving timeliness in NBS 3. Workgroup updates: Education and Training, Laboratory Standards and Procedures, Follow-up and Treatment 4. Report on Long Term Follow-up in NBS 5. Report on Technology in NBS ii. November 1-2- reviewed agenda and discussion on November meeting 1. Condition Nomination for Cerebrotendinious Zanthomatosis (CXR)- need more information before nominated 2. Baby's First Test 3. Education Activities in NBS 4. Genomic Sequencing in NBS: Ethical, Legal, and Social Implications 5. Ethical Legal Social and Policy Considerations in NBS Pilot Studies 6. Workgroup Updates: Education and Training, Laboratory Standards and Procedures, Follow-Up and Treatment, Interpreting NBS results B. Virginia Programmatic Updates

i. Early Hearing Detection Intervention (EHDI): Daphne Miller
    a. In 2018, 137 children who have been diagnosed with hearing loss- normal amount is about 300- decreasing amount of time to get babies diagnosed
    b. n process of purchasing OAE machines around the state- for midwife birthing facilities- to receive hearing screening prior to leaving
    c. 4 learning communities across state- Central, Roanoke, Southwest, NOVA
    d. Created to provide unique opportunities for parents and providers to connect
    e. Started texting to parents – took 2 years to receive final approval to implement- will work on improving quality improving- pushing time back, trials to see if improve responses
    f. Working with WIC, VIIS, and Home visiting to provide educational materials

ii. Sickle Cell Screening/Program Update: Shamaree Cromartie
    a. Rebranded program last year- new logo, brochure, very popular in community
    b. In process of updating material for providers and educational fact sheets
    c. Works closely with sickle cell centers to make sure that babies are in care and receiving treatment or documentation if family decides against penicillin

iii. Children & Youth with Special Health Care Needs (CYSHCN) Updates: Marcus Allen
    a. Part of federal Title V block grant- maternal child health, CYSHCN receives largest portion of funding.
    b. 4 programs- Child development center, Care connection for Children, Blood Disorders Program (Sickle Cell and Hemophilia)
    c. Care Connection for Children (CCC)
        1. Every child diagnosed through newborn screening is automatically referred and offered services to CCC
        2. Provide care coordination for children- UVA, Carilion, VCU, CHKD, Southwest (UVA)
    d. Working on updating assessment tool

iv. Critical Congenital Heart Disease (CCHD): Jen Macdonald
    a. Recently engaged a contractor to focus on QA and confirming cases to refer to CCC

v. Dried Blood Spot (DBS): Christen Crews
   a. Hired 2 new nurses (1 FT, 1 wage) to replace staff lost over the summer
   b. Currently seeking a third employee- attempting to recruit a Genetic Counselor to assist follow-up with expansion of disorders with gene sequencing
   c. Actively creating health care manual with updated information on collection, disorders, contacts, and "just-in-time" education fact sheets

vi. Virginia Commonwealth University (VCU) Capstone Project:Willie Andrews
   a. Capstone students have helped by developing a list to identify midwives and if associated with a birthing center
   b. Provided survey to midwives to identify needs and address issues- ask if report card would be beneficial and what would the like to see

vii. NewSTEPS 360 grant updates: Willie Andrews
   a. HL-7 Messaging Project
      1. Initially identified 13 hospitals interested in serving as pilot sites, 5 hospitals are actively sending demographics and printing labels, 2 hospitals are in test phase of receiving results back. 4 hospitals in test phase with e-orders, and 8 additional hospitals in development phase. The pilot will capture about 44% of samples coming in (proposal was only 25%). Goal is to roll out to all hospitals
      2. Early project wins
         a. Improved quality:
            i. Average # samples received missing data:
               1. Before e-orders: 3.6%
               2. After e-orders: 0.4%
         b. Efficiencies gained by DCLS
            i. Average sample processing time from accessioning to data verification in LIMS
               1. Before E-orders: 6 hours
               2. After e-orders: < 1 hour
         c. Improved Transit time (1 pilot site)
            i. Before e-orders: 2.37 days
            ii. After e-orders: 1.33 days

viii. DBS Data Review: Willie Andrews
   a. Reviewed 2018 Q1-Q3 data and diagnosis for the last few years

	a. Transit time has improved dramatically over the past few years- at 1.72 days as of 2018 (Q1-Q3) and started with 2013 at 2.96 days b. Question about time period for reporting out within 7 days- clarified all results, not just critical results (reported via phone call) 1. Mentioned looking at ways to getting the results to the right person- the correct PCP isn't always listed, timeliness of US mail is concern, Portal will hopefully available by March of 2019 for PCP to receive electronic results
11:35 – 12:00N	Old Business A. Congenital Adrenal Hyperplasia (CAH) screening-2nd tier screening update: Chris Nixon, DCLS i. Main goal: reduce CAH false positives ii. Updates: Optimized DBS extraction procedure, hired new senior scientist, other developments on-hold – delayed due to accelerated implementation of Lysosomal Storage Disorders (LSD)- will resume ASAP in 2019 B. LSD Screening implementation update: Jen Macdonald and Willie Andrews i. Prior to 2018 GA session, VA NBS was already in process of implementing Pompe and MPS-1 ii. 2-3 hour weekly meeting of VDH and DCLS staff iii. Association of Public Health Laboratories (APHL) Funding for LSD implementation- 1 year grant 1. Lab activities: a. Develop computer infrastructure needed b. Design/implement a database for variant classification/reclassification i. Travel to other states to observe current processes and practices c. Primary screening method identified- digital microfluidics d. Secondary screening- sequencing analysis- hiring additional staff, recruiting for genetic counselor 2. Follow-up activities a. Travel to other states b. Convene statewide workgroup c. Creation of education materials i. New module

	ii. Webinars iii. Healthcare provider manuals- distributed January/February C. Expansion to 7 days/week: Willie Andrews i. Been in process for increasing staffing – will start January 2019, already working all Saturdays and holidays ii. All time-critical disorders on holidays and weekends iii. Time-critical disorders identified on national level iv. 8 data entry, 5 person in lab, 1 VDH/Follow-up v. Dr. Wilson shared concerns with reporting to Primary Care Physicians (PCP) on weekends- follow-up agreed with challenges and will continue to implement strategies to assist in the effort vi. Fee Increase to support expansion of hours and disorders 1. Fee increased to $101.20 and was implemented on August 1, 2018 Discussion/Questions: • Education: Webinars for all providers that will be recorded and be available on website, module for professionals – relationship with hospitals, monthly report cards, will use relationship with AAP • Dr. Wilson encouraged parents to advocate for general funds to help support newborn screening operations to lessen burden on parents and hospitals • Jana: recently met with a delegate who is becoming a champion for Rare Disease day, one of the items to work on is funding for newborn screening
12:00 N – 12:15 PM	Break and Lunch Set-up
12:15 – 12:45	Working Lunch Guest Speaker: Gretchen Wilson – Introducing Bioinformatics to Virginia Newborn Screening a. Bioinformatics Master's Degree from VCU i. Human Genome 1. 99.5% is shared between individuals a. 0.5% is what makes us who we are- distinguishes us 2. Reference sequences are curated on multiple levels- important to look at changes at multiple levels a. Chromosomes b. Gene (local reference) c. Transcript d. Protein

ii. What are variants?
    1. Differences in a genomic sequence identified by comparing an individual genome to a select reference sequence
        a. Inherited or de novo
        b. Size ranges from a single nucleotide to entire chromosome
            i. Focusing on gene level variants

iii. Variant Identification
    1. Variant Calling- Variant Reporter (proprietary software)
    2. Analyst role is limited to reviewing and verifying software calls

iv. Variant effects
    1. Can have varying effects depending on where they occur
    2. What is the ultimate effect on the function of a protein?
        a. No Mutation
        b. Missense
        c. Nonsense
        d. Silent

v. Reviewed variant interpretation processes at NY, MA, and WI
    1. 2 approaches:
        a. Manually visit each data source of interest- Follow ACMG guidelines
        b. Manually visit each data source- Report only what is listed
    2. Time intensive and prone to human error and misinterpretation
    3. Does not account for changes over time in the content of data sources
    4. Alternative: outsource entire second tier assay
    5. Concerns about re-classification of variants (i.e. VOUS to known pathogenic)

vi. Difficulties of the Interpretation Process
    1. Complex naming schemes
    2. Widely-dispersed resources
    3. Duplicate information among data surces
    4. Inconsistencies among data sources
    5. Varying levels and schedules of curation

vii. Newborn Screening Variant Interpretation (NBSVI)

	1. Assist with the variant interpretation process by performing: a. Real-time variant nomenclature conversion b. Annotation c. Report generation d. Aid the clinical significance calculations i. Accepts criteria and comments ii. Calculates and reports the significance viii. Path to going live 1. Built a solid but flexible resource on which we will expand 2. Moving forward: a. Validation will begin in the next few weeks b. Begin the interpretation process prior to Jan 1 c. Increase data resources
12:45 – 2:00	New Business A. NBS Reporting to PCPs: Dr. Martin, Virginia chapter AAP a. DCLS and NBS program staff are engaged in discussions with AAP reps b. Looking for opportunities to reduce the number of requests c. Need PCPs name on the collection card so report goes to the right place i. Need to work with hospitals and prenatal educators to assist d. Need faster ways to get results to PCPs (USPS very slow) i. Electronic data transmission will help e. Building a web portal to enable PCPs to acquire results without submitting faxed request i. Expected to be available by March 2019 f. Surveyed other PCPs i. Received majority NBS results after 2 weeks ii. Receive fax request returned with results within 48 business hours g. Consider back notification to mother's care provider of positives for appropriate genetics- huge issue- communicate with OBGYN- may need to provide counseling to mom for future pregnancies i. Dr. Toney has concerns with sharing data with OBGYN- will have to explore further with HIPAA- may have to provide to mom to provide to OB B. Adding new disorders: Jennifer Macdonald a. recap of process with expert review recommendation, if approved through both through workgroup and full voting members, then will start process to add to regulations- takes approx. 12-18 months C. X-ALD Workgroup: recap of workgroup meeting, unaminous recommendation by all workgroup members to recommend addition of X-ALD; methodology was tabled and will be left to X-ALD implementation workgroup

	a. Recommendation: Add X-ALD to Virginia's Core Newborn Screening Panel b. Roll call of Advisory Committee voting members: 12 Yes 0 Nays D. SMA Workgroup: recap of workgroup meeting, only handful of states currently screening, screening will be multiplexed with SCID, possible future testing of number of SMN2 copies may assist in insurance approvals (will it satisfy insurance approval?), cost of treatment and hard to navigate insurance approvals (if equitable)- there are patient assistance programs. Unanimous recommendation by workgroup members to recommend addition of SMA; methodology was tabled and will be left to SMA workgroup. a. Recommendation: Add SMA to Virginia's Core Newborn Screening Panel b. Roll call of Advisory Committee voting members: 12 Yes 0 Nays E. 2019 meeting dates: June 13th 2019 & November 14th 2019 F. Annual specialists calls will be scheduled a. Jan – March 2019: Metabolic Geneticists (LSD implantation & metabolic disorders) b. Spring 2019: Pulmonologists -Cystic Fibrosis c. Summer 2019: Endocrinologists – CAH, CH d. Fall 2019: Immunologists – SCID e. X-ALD and SMA workgroups to meet throughout year.
2:00	Adjournment