

Illinois Department of Public Health  
Newborn Screening Laboratory Subcommittee  
Conference Call Meeting Minutes: May 18, 2011

Subcommittee Members Attending:

Dr. George Hoganson-University of Illinois at Chicago - Chair  
Dr. Gopal Srinivasan- Mt. Sinai Hospital  
Dr. W. Patrick Zeller- Pediatric Endocrinologist  
Sunetra Reddy- University of Chicago

IDPH Staff:

Dr. George Dizikes	Dr. John Nawrocki	Claudia Nash	Dr. Khaja Basheeruddin
Dr. Mike Petros	Barbara DeLuka	Margie Nelson	Karen Devine
Dr. Rong Shao	Heather Shryock	Angela McCauley	Laura Harris

The meeting was called to order at 9:05 AM, and introductions were made. The minutes of the December 15, 2010 meeting were approved.

**New Business**

Staffing and Laboratory Resources

Dr. Dizikes is Acting Chief of the Newborn Screening Laboratory.

In the laboratory, Dr. Khaja Basheeruddin has been transferred to the lysosomal storage disease (LSD) pilot screening initiative full-time. Dr. Rong Shao has been working on the LSD Pilot since November.

On the follow up program side, one follow-up vacant position will be filled, and two other new positions for LSD follow-up have been posted. Three administrative positions remain vacant and the workload is currently covered by one full-time employee who manages grants and the SIDS Program. Follow up staff are currently covering multiple program responsibilities.

Data System/Reports

The Perkin Elmer data system is now being utilized by both the laboratory and follow up components of the Newborn Screening Program. Basically the system is functioning well with minor adjustments still being made. Laboratory quality assurance unit staff continue to review all of the reports prior to issuance to the hospitals as there have been some discrepancies noted between the first and second pages of the new laboratory reports. The laboratory plans to transition to a single page report, although the second page detailed test results and normal values will still be available on request. Perkin Elmer, the data system vendor, will begin work to place the one page report into production.

Follow up program is utilizing the Perkin Elmer system for all reporting with the exception of LSD results which currently must be reported through the old data system. In addition, the old data system is still utilized for formula orders and some long-term follow up activities, but these will be transitioned to Perkin Elmer data system. Preparations are being made to introduce HL7 data transfers between the Northwestern Memorial Prentice Women's Hospital data system and the IDPH data system. System developments will allow inbound transfers of demographic data and specimen information from the hospital, and outbound test result data from the Newborn Screening laboratory back to the hospital data system.

### Lysosomal Storage Disorders Pilot

Since November 2010 when the LSD pilot began, approximately 8,000 samples from Northwestern Memorial and the University of Chicago have been screened for Pompe, Fabry and Gaucher disease. Thus far there have been 25 positive screens for Gaucher, 2 for Pompe and 12 for Fabry, and 2 cases have been reported with decreased activity for all three enzymes (Gaucher, Pompe, Fabry). There have been 3 confirmed cases of Gaucher, 4 confirmed cases of Fabry, and no cases of Pompe confirmed. Several additional cases of Fabry are still pending final diagnosis by DNA testing. Currently LSD testing is performed using Advanced Liquid Logic (ALL) 10-specimen cartridges, and approximately 90 samples per day are received for LSD testing. Dr. Shao and Dr. Dizikes reported there have been problems with some of the cartridges, and the company is attempting to address these problems. In addition, the capacity for volume testing is very limited with these smaller cartridges, and manual pipetting of samples for the assays make the ALL microfluidic process very labor and time intensive. Variability of results and a lack of reproducibility of results, especially for Gaucher testing were also reported as serious concerns. Issues concerning the LSD pilot were previously discussed during a conference call by the LSD ad hoc subcommittee on May 11<sup>th</sup>. Although the manufacturer was to provide newly developed 40-specimen cartridges on May 17<sup>th</sup>, the company later acknowledged that these new higher capacity cartridges are not yet ready for use. The company continues to work to improve the performance quality for the Gaucher assay, and may add a newly developed enzyme purification step for all LSD microfluidic assays.

Statewide screening for the LSD disorders using the ALL microfluidic assays will not be possible by June 2011, as was previously legislated. Dr. Dizikes informed the members that the LSD microfluidic assay pilot has been suspended until further notice, and that the hospitals included in the LSD pilot will be notified of the suspension. Concerns were voiced that IDPH is effectively validating the assays for the manufacturer in development of this testing process. There was also discussion about the need for an IRB review and possibly an informed consent requirement for further continuation of the LSD pilot using the ALL microfluidic process. (See note)

Dr. Dizikes indicated the laboratory is poised to explore tandem mass spectrometry (MS/MS) testing for LSD under the current Illinois mandate, and that testing for all LSD disorders in the mandate could be available through MS/MS with the exception of Niemann-Pick. Although no other state currently screens for all of the LSD disorders in the Illinois mandate by using MS/MS, New York has proposed a multiplex assay (not yet published or peer reviewed), and CDC has developed reagents and controls for Fabry, Pompe, Gaucher, Krabbe and MPS1 using MS/MS. The Newborn Screening laboratory has a sufficient number of MS/MS instruments to proceed with a pilot by the fall of 2011.

There was further discussion about the IRB and consent issues. It was felt that the continuation of the current LSD pilot would require informed consent and a data sharing agreement between the company and IDPH as ALL would need the results of the pilot to further test development. Any agreement would need to be clear, transparent and approved by IDPH legal department. It was also felt that an IRB for MS/MS pilot testing for LSD may not be needed. This method could be validated "in house" utilizing reagents provided by CDC. This pilot process would meet Clinical Laboratory Improvement Amendment (CLIA) requirements for the IDPH laboratory.

It was decided that while consent for testing has never been an issue for Illinois newborn screening in the past, additional research and discussion on this issue in relation to pilot testing is probably warranted, with the distinctions between "opt in" and "opt out" consents reviewed. One state that utilizes an informed consent process is Massachusetts.

### Galactosemia Screening

Effective February 1, 2011, new testing for galactosemia was implemented that includes a two channel process for both total galactose and galactose-1-phosphate uridylyltransferase (GALT) enzyme activity testing on all samples. Previously GALT testing was performed only as a second tier test for samples with elevated total galactose and those marked "soy" or "NPO" feeding status. Total galactose results will continue to be reported as quantitative values, and GALT testing will continue to be reported as qualitative values (activity present, reduced or absent). While the testing implementation has been successful, there have been concerns that a high number of borderline abnormal results (reduced enzyme activity with normal total galactose) are being reported. It is anticipated that this will intensify during the summer months since the GALT enzyme is sensitive to heat degradation. While the number of elevated total galactose cases has not changed, the number of positive screens for reduced GALT enzyme activity has increased. GALT activity is currently reported as borderline abnormal when activity is less than 50uM/L and a retest sample is requested, or positive (recommending referral to a metabolic specialist) when activity is less than 30uM/L. The laboratory report and the follow-up abnormal reports currently do not record quantitative results for GALT activity.

A conference call with interested metabolic specialists will be arranged in the near future to discuss galactosemia testing, quantitative reporting of results, and revisions to the recommendations on follow up and laboratory reports for abnormal galactosemia screens.

### NICU Newborn Screening

Additional information will be obtained from Dr. Kumar and the Perinatal Advisory Committee regarding the issue of changing the specimen collection requirements for newborn screening in the NICU population. Thus far no new information on this issue has been reported. It was acknowledged that most low birth weight infants (less than 2500 Gms) remain in the NICU a minimum of 10-20 days prior to discharge, while very low birth weight infants (less than 1500 Gms) may remain in the NICU for several months. There has been past discussion about changing the Illinois requirement for a routine second specimen on day 14 to day 28-30, or prior to discharge, or adding a third specimen at 30 days, in an effort to better detect late onset hypothyroidism among this population. Data on birth weights and NICU admissions from Vital Records and the Perinatal Networks will be collected and distributed prior to the next meeting. Clinical Laboratory Standards Institute (CLSI) has recommended that a third sample be collected at day 28 or prior to discharge for babies weighing less than 2000 Gms and/or born at less than 34 weeks gestation.

### SCID Newborn Screening

Legislation for the addition of SCID testing to the Illinois newborn screening panel is anticipated and in preparation, Dr. Nawrocki of the IDPH Molecular lab will be working on validation studies, setting up quality assurance, and cut-off values for this testing. Dr. Nawrocki is working with Dr. Mei Baker in Wisconsin and CDC, which has provided quality control materials, as well as working to secure necessary equipment, staff and training. Plans include use of high through-put DNA technology that can be applied to other screening tests, such as cystic fibrosis. The time-line for implementation of SCID pilot testing could be 3-4 months after adoption of the revised Administrative Rule.

Claudia Nash mentioned that in preparation for SCID screening, follow up staff have participated in several SCID Webinars provided by the Association of Public Health Laboratories, and she has also been in contact with Dr. Ramsey Fuleihan, a pediatric immunologist at Children's Memorial. Dr. Fuleihan has assisted in development of educational materials and in drafting the Administrative Rule requirements for medical specialists designated by IDPH to provide follow up care for newborns with abnormal

screens for SCID. The Administrative Rule for the addition of SCID will be presented to the State Board of Health at their meeting on June 9, and then published in the Illinois Register which opens a public comment period.

Questions were asked about the need for an IRB to pilot SCID testing and Dr. Dizikes is discussing this with the IDPH IRB board chairman. It was noted that the addition of SCID could provide a good example for future additions, since this was based on the recommendation of the IDPH Director and the Genetics and Metabolic Diseases Advisory Committee following a national recommendation by the Secretary's Advisory Committee on Heritable Diseases in Infants and Children.

#### Cystic Fibrosis Screening

Dr. Nawrocki announced there will be changes to the CF DNA mutation test panel that will also utilize high through-put DNA technology, and the Cystic Fibrosis Collaborative will be informed of these changes. The new CF DNA panel will include 46 DNA mutations and this new process will be much less labor intensive than the current DNA extraction method.

#### Additional Business

Recently four late diagnosed cases of congenital adrenal hyperplasia were reported to the Follow up program and available information about these cases was discussed. Additional de-identified diagnostic data regarding these cases will be collected and distributed for review at the next Subcommittee meeting.

The meeting was adjourned at 10:30 AM. The next meeting is set for September 28, 2011 from 9-11AM.

#### Note:

The IDPH later decided that storage of samples from pilot hospitals for subsequent LSD testing using the microfluidic process was not an option as no informed consent was obtained for this purpose. Both participating hospitals, University of Chicago and Northwestern Memorial Prentice Women's Hospital will be notified that the LSD phase-in pilot has been temporarily suspended until further notice.