Illinois Department of Public Health (IDPH)
Genetic and Metabolic Diseases Advisory Committee (GMDAC)
Newborn Screening Laboratory Subcommittee
Minutes – May 26, 2010
2121 W. Taylor St., Rm. 139E, Chicago, Illinois
Conference Call Site – 500 E. Monroe St., Springfield, Illinois

Attendance
Dr. George Hoganson (Subcommittee Chair), University of Illinois at Chicago
Attendance by Audio Conference
Dr. Barbara Burton, Children's Memorial Hospital
Kristin Culp-Clemenz, Children's Memorial Hospital
Sunetra Reddy, University of Chicago
Dr. Gopal Srinivasan, Mt. Sinai Hospital
Dr. Patrick Zeller, Pediatric Endocrinologist
Barbara Haller, Illinois Hospital Association (Guest)

IDPH Staff
Dr. David Jinks, Newborn Screening Laboratory
Tom Johnson, IDPH Division of Laboratories
Mike Petros, Newborn Screening Laboratory

Attendance by Audio Conference
Barbara DeLuka, Genetics/Newborn Screening Follow-up Program
Heather Gardner, Genetics/Newborn Screening Follow-up Program
Claudia Nash, Genetics/Newborn Screening Program
Kate Seymore, Genetics/Newborn Screening Follow-up Program

Call to order by Dr. Hoganson at 9:02 AM
Introductions
Minutes of January 6, 2010 meeting were approved.

IDPH Report and Discussion
Confirmed Cases
Dr. Jinks presented the list of diagnosed cases with discussion about several cases with normal initial newborn screens. There was additional discussion regarding the value and problems associated with MS/MS second tier screening for succinyl acetone (SA) in detection of tyrosinemia type 1. Second tier screening of all samples would require additional laboratory staff and supplies and the results (additional cases of tyrosinemia detected) would be questionable. This may be a future consideration that will be discussed further, although tyrosinemia type 1 is extremely rare and IDPH literature acknowledges that detection in newborn samples collected at 24 hours of age is limited.

Screening for carbamoylphosphate synthetase deficiency (CPS) and ornithine transcarbamylase deficiency (OTC) disorders by using citrulline and glutamine levels, along with phenylalanine/citrulline, glutamine/citrulline, valine/citrulline and alanine/citrulline ratios was discussed. Several CPS cases and one mild variant form of OTC in a male newborn have been identified in Illinois as by-products of MS/MS screening using these analytes.

Reflex DNA testing for cystic fibrosis (CF) was recently changed to due to the unavailability of the Tepnel test kits. The new kits contain a panel of 38 CFTR mutations that are similar to those in the original kits, although there are some individual differences between the two panels. The CF specialists have been informed of this change.

There were questions and discussion about screening for alpha thalassemia using the newly adopted Primus high performance liquid chromatography system. Three cases of alpha thalassemia have been confirmed since the testing began in June 2008. The new system allows reflex testing that separates Bart's hemoglobin into a relative percentage, and this has reduced the number of false positive results for alpha thalassemia. There was discussion about the possibility of sending all positive screen samples for alpha thalassemia directly from the IDPH lab to the Children's Hospital Oakland Research Institute (CHORI) for reflex molecular diagnostic testing. Although this testing is provided free of charge, in many cases primary care physicians do not refer newborns with positive screens for alpha thalassemia to the Chicago Comprehensive Thalassemia Center as recommended, nor do they send blood samples to CHORI for the necessary specialized diagnostic testing as is suggested by IDPH. IDPH submission of all positive samples to CHORI would assure the proper follow-up diagnostic testing is performed. The laboratory standard operating procedure (SOP) could be written to include send-out of newborn screening samples for reflex testing for alpha thalassemia, much like the proposed SOP for implementing reflex molecular testing for lysosomal storage disease screening for Krabbe later this year. This policy is currently in effect in Iowa. Kristin Culp-Clemenz will discuss this proposal with Dr. Alexis Thompson, the director of the Chicago Comprehensive Thalassemia Center and will provide contact information for the CHORI Center.

Newborn Screening Data System

Beginning July 1, the laboratory will begin reporting NBS results using the new data system. Until the follow-up portion is ready and validated, the laboratory will enter data into both new and old systems so as not to negatively impact follow-up staff. IDPH laboratory newborn screening reports will be updated and sample copies will be faxed to all members. Hospitals will also receive copies of the new report. There was discussion about CLIA reporting requirements for both IDPH and hospital laboratories, and the electronic data entry options and e-reports that will become available to all hospitals in the future.

Follow-up program is planning the move to a new location, 535 W. Jefferson, Springfield, at the end of June, and work on the follow-up side of the new data system has been delayed. Use of the new system by follow-up staff is expected to begin around August 1. Laboratory staff will continue entering all abnormal case information into the existing mainframe data system until the new Follow-up data system piece is fully implemented.

IDPH LSD Phase-in Pilot and Staffing

Dr. Jinks reported that the Department is preparing a Memorandum of Agreement document with Advanced Liquid Logic Inc. and Duke University for development of LSD assays, and a business case proposal. These should be secured in July, and will allow options for bidding for equipment and supplies to enable the LSD phase-in pilot for all babies born at University of Chicago and Northwestern Memorial, Prentice Women's Hospital.

While laboratory positions have been filled, two follow-up staff vacancies have continued for over thirteen months. In addition, two new positions will be necessary for LSD follow-up, and as a further complication, two more key staff vacancies will occur later this year due to retirements. Members questioned the need for closer staff coordination between the newborn screening laboratory and follow-up programs and the possibility of including both programs in the same IDPH Office, rather than splitting the two programs between Office of Health Protection and Office of Health Promotion. The Subcommittee members agreed to this suggestion and proposed writing a recommendation to the IDPH Director, Assistant Director, or Chief of Staff.

There was mention of the Secretary's Committee on Heritable Diseases recommendation to add severe combined immune deficiency (SCID) to the American College of Medical Genetics (ACMG) uniform core panel of newborn screening disorders, increasing the core from 29 disorders, all of which Illinois currently includes in screening, to 30 disorders. Currently, Wisconsin has mandated screening for SCID, and Massachusetts universally provides SCID screening. The Newborn Screening Program was recently contacted by the parent of a child with SCID who is interested in promoting SCID screening in Illinois.

Galactosemia Testing

When the equipment becomes available, possibly after August 1, the laboratory will begin using a revised test algorithm for galactosemia screening. All samples will be tested for both GALT enzyme activity and total galactose (galactose and galactose-1-phosphate) level. This new methodology should reduce current delays in second tier GALT testing for newborns on soy or NPO, as waiting for demographic data entry will no longer be necessary. There was discussion about possible increases in false positive screens due to heat exposure causing enzyme degradation, especially during the summer months.

Confirmed Case Data Collection

The need for improved collection of confirmed case data was discussed. One suggestion mentioned was that specialists could provide IDPH with a copy of the final consultant's report to the primary care provider for each diagnosed newborn screening case. Although this may make data entry more challenging for follow-up staff, it would simplify the work of the speciality centers in completing follow-up reports and might help increase the response of specialists.

There was discussion concerning recent publications in the journal *Pediatrics* regarding congenital hypothyroidism and transient hypothyroidism. Dr. Zeller offered to contact his fellow pediatric endocrinologists to discuss the importance of providing IDPH with additional case information for presumptively diagnosed cases of hypothyroidism and congenital adrenal hyperplasia. Follow-up staff will obtain e-mail addresses for the IDPH designated pediatric endocrinologists.

CLSI Guidelines for Newborn Screening in the NICU

Information on the current IDPH guidelines and those of the Clinical Laboratory Standards Institute (CLSI) were provided (see attachments). The major differences center on time of collection of the initial sample and the routine repeat sample, as well as the indicator for the NICU protocol (admission to special care or actual birth weight). The benefit gained from testing prior to 24 hours unless the baby is transfused seems questionable, and the IDPH protocol addresses early collection prior to transfusion. It was suggested that the IDPH NICU protocol for the routine repeat specimen collection could be changed from "day 14 or prior to discharge whichever is first", to day 30 of life or prior to discharge

whichever is first. This would assure most very low birth weight babies (less than 1500 grams) are retested at a point more likely to detect later onset hypothyroidism, and avoid false positives for babies still on TPN at day 14. There is to be further discussion with the Perinatal Network Administrators and interested neonatologists on this topic.

Ad Hoc Subcommittee for Newborn Screening Expansion Protocol
The GMDAC Advisory Committee recommended creation of an ad hoc subcommittee to develop a protocol for addressing future expansion of the Illinois newborn screening test panel at the April 29th meeting. Laboratory Subcommittee members and other parties interested in joining this ad hoc committee were invited to contact Claudia Nash or Dr. Hoganson. Meetings will be by phone conference and may begin in July. Invitations will be sent to all GMDAC Advisory Committee members, Illinois Chapter of American Academy of Pediatrics (ICAAP), IDPH Perinatal Network Administrators, Illinois Hospital Association, and University of Illinois Division of Specialized Care for Children (DSCC). The parent of a child with an inherited metabolic disorder has also indicated interest in joining the proposed ad hoc committee.

Other Discussion
Claudia Nash suggested that providing speakers on the use of residual dried blood spots might be an appropriate topic for the fall meeting of the GMDAC. The next meeting is scheduled for September 1, 2010 from 1-3 PM. The meeting was adjourned at 10:50.

Minutes respectfully submitted by Barbara DeLuka – 6/16/10