Illinois Department of Public Health (IDPH)
Genetic and Metabolic Diseases Advisory Committee (GMDAC)
Newborn Screening Laboratory Subcommittee
Minutes – January 6, 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
Dr. Gopal Srinivasan, Mt. Sinai Hospital
Kristin Culp, Children's Memorial Hospital
Sunetra Reddy, University of Chicago

IDPH Staff
Dr. David Jinks, Newborn Screening Laboratory
Mike Petros, Newborn Screening Laboratory
William Calvert, Newborn Screening Laboratory
Dr. John Nawrocki, IDPH Molecular 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

Call to order by Dr. Hoganson at 1:07 PM
Introductions
Minutes of August 29, 2009 meeting were approved.

IDPH Report and Discussion
Confirmed Cases
Dr. Jinks presented the list of diagnosed cases (see attachment 1), and there was discussion about the diagnosis of two cases of carbamoylphosphate synthetase deficiency (CPS)*. Low levels of citrulline which may indicate CPS or OTC (ornithine transcarbamylase deficiency) are now reported to physicians when detected. When a low citrulline level is detected, second tier testing of the glutamine level is also now performed. The use of several ratios in relation to CPS/OTC screening was discussed, including: phenylalanine/citrulline, glutamine/citrulline, valine/citrulline and alanine/citrulline ratios. The value of these ratios in detecting CPS/OTC has been reviewed, and at this time, it is not clear how informative these ratios will be. Glycine levels are not informative for these disorders.

* The first CPS case was initially reported as having a borderline elevated glycine level in a NICU newborn. The baby was transferred for tertiary care, and clinically diagnosed with CPS. No repeat newborn screen was obtained. The second CPS case was reported as a borderline low citrulline level on the initial newborn screen; the retest specimen also had a low citrulline level, with an elevated glutamine level, which Dr. Jinks indicated may be more indicative of true OTC/CPS cases. Following clinical diagnosis, a third CPS case was detected retrospectively with low citrulline with elevated ratios and glutamine. A clinically diagnosed female infant with

OTC was not detectable using low citrulline, and the above mentioned ratios on the first specimen. These two cases are not included in the attached confirmed case totals.

There was further discussion about the need to differentiate clinically diagnosed cases from those detected primarily through initial abnormal newborn screens, as well as cases diagnosed following normal newborn screens. While these cases are reported in annual process data reports supplied to members of the Advisory Committee, long-term tracking of all confirmed cases will be improved with implementation of the new data system.

Newborn Screening Data System

The laboratory will soon begin beta testing of the new data system, and follow-up program staff will begin on site training on the new system later this month. Key concerns remain the server reaction time and the possibility of moving a server to Chicago to increase processing speed. The initial implementation of the new system will cover laboratory and short-term follow-up requirements. Other system developments will enable Web based hospital data entry of patient demographic information and/or HL7 data transfers of demographics and test results. It is anticipated that authorized physicians and clinical specialists will have direct access to look up newborn screening test results. Later developments may enable clinical specialists to enter patient information directly into the data system for long-term follow-up of diagnosed cases.

IDPH Staffing and LSD Phase-in Pilot

The newborn screening fee increase became effective January 1, 2010. Two laboratory staff positions have been filled, one in MS/MS lab and one for the LSD phase-in pilot. Laboratory data entry staff shortages have been addressed within the Division of Laboratories, and any previous data entry delays have been alleviated. One follow-up staff position that has been vacant for approximately one year will be filled in February 2010. Two additional follow-up positions remain vacant at the present time.

LSD phase-in pilot will begin with processing blind samples utilizing the Advanced Liquid Logic Inc. microfluidic assays. Currently, chips for Pompe, Fabry, Hunter's and Hurler's diseases are being developed, and additional disorders are expected to be added: Krabbe, Gaucher and Niemann Pick diseases. Further discussion within the Division of Laboratories, and planning for implementation of the phase-in pilot is ongoing. Dr. Jinks has been in contact with Dr. Bob Vogt at the Centers for Disease Control and Prevention regarding the progress of test development for LSD and severe combined immune deficiency (SCID), which was recently implemented in Wisconsin. Grants for SCID test development may still be available from Modell Foundation and Baxter Healthcare Corporation.

Cystic Fibrosis Screening

Dr. Nawrocki discussed the purchase and utilization of new test kits for cystic fibrosis (CF) screening, and in compliance with state procurement and bidding process requirements, a new manufacturer was awarded the contract for supplying CF test kits. There are slight variances between the old and new test kits in the number and type of CFTR mutations included. There may be slightly fewer of the very rare CFTR mutations with higher representation among Hispanic or other minority groups included in the new kits. The kits in current use were produced by Tepnel, which was bought out by GenProbe in early 2009. GenProbe decided not to continue the CF test product, which necessitated this change. The CF Centers and specialists have been provided information about the new test kits, and use of the new kits is expected to begin in late February, or early March 2010.

Congenital Adrenal Hyperplasia, Alpha Thalassemia and Galactosemia Screening
Data regarding the number and type of abnormal screens for congenital adrenal hyperplasia (CAH) was provided (see attachment 2). Although the number of presumptive positive (high level) abnormal results has remained constant, the total number of lower level positive screens has decreased dramatically with use of the new CAH test kits. These CAH test kits were put into use beginning in mid August. The new kits utilize a more specific antibody for detection of possible CAH cases.

The number of positive screens for alpha thalassemia has stabilized, and more primary care physicians are referring positive alpha thalassemia screen newborns for specialized diagnostic testing.

There was discussion about lowering reportable total galactose cut-off values in an effort to better detect galactokinase deficient (GALK) galactosemia. The group acknowledged that lowering cut-offs would potentially increase the number of cases requiring follow-up services, repeat NBS samples and/or diagnostic testing. Other state newborn screening programs have similar, or higher total galactose cut-off values than IDPH, and most do not focus attention on detection of GALK or epimerase deficiency (GALE). GALK and GALE cases are usually detected as a by-product of IDPH primary screening for classical galactosemia due to galactose-1-phosphate uridyltransferase deficiency (GALT). Most states, including Illinois, list these disorders as reportable when detected at the National Newborn Screening and Genetics Resource Center Web site (NNSGRC), www.genes-r-us.uthscsa.edu. Further discussion at the next GMDAC Advisory Committee meeting was suggested to address this issue.

Other Discussion
Subcommittee meetings for 2010 will be scheduled approximately every four months on Wednesdays, alternating between morning and afternoon. A list of proposed dates will be sent to members, along with the minutes. Proposed meeting dates will be coordinated in conjunction with the April and September Advisory Committee meetings. The meeting was adjourned at 2:45.

Minutes respectfully submitted by Barbara DeLuka – 1/22/10