Illinois Department of Public Health (IDPH)
Genetic and Metabolic Diseases Advisory Committee (GMDAC)
Newborn Screening Laboratory Subcommittee
Minutes – July 29, 2009
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
Dr. Joel Charrow (GMDAC Chair), Children's Memorial Hospital
Attendance by Audio Conference
Kristin Culp, Children's Memorial Hospital
Sunetra Reddy, University of Chicago
Dr. Gopal Srinivasan, Mt. Sinai Neonatology

IDPH Staff
Dr. David Jinks, Newborn Screening Laboratory
Tom Johnson, Division Chief
Mike Petros, Newborn Screening Laboratory
Representing IDPH Molecular Laboratory:
Dr. Jennifer Crew, Dr. John Nawrocki, Joel Price

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

Call to order by Dr. Hoganson at 9:10 AM
Introductions
Minutes of April 1, 2009 meeting were approved.

Molecular Laboratory Testing
IDPH Molecular Laboratory staff discussed the process for DNA mutation analysis component of cystic fibrosis (CF) screening and the challenges encountered since implementation of CF screening began March 2008. Each day samples with immunotrypsinogen (IRT) levels within the top 4% are tested for 44 CFTR mutations and three polymorphisms. This includes around 200 newborn screening (NBS) samples per week. DNA analysis is performed four days per week by IDPH Molecular Lab staff. The manufacturer of the test kits, Tepnel has been responsive to concerns about several alleles and software problems encountered with these kits. The contract will be reviewed and open bidding for the next three year contract is required. Overall the implementation has been successful with few problems encountered. Dr. Nawrocki indicated he is reviewing microarray assay options for CF, which may be considered in the future.

There was discussion about the IDPH Molecular lab's capacity to implement additional DNA testing necessary when IDPH implements testing for lysosomal storage diseases (LSD). The need for either an IDPH genetics molecular section with dedicated staff or outsourcing of LSD molecular testing was

recognized. Second tier DNA testing for legacy NBS disorders, including galactosemia to increase screening reliability was also mentioned. Although this second tier DNA testing would not be as complex as LSD molecular testing, any additional molecular testing will require Clinical Laboratory Standards Institute validation, training of staff and increases in the budget. Current budget constraints may preclude any second tier DNA testing during the next two years, although the development of new disease specific microarrays and the potential of these tests to improve newborn screening were acknowledged.

IDPH Laboratory Report and Discussion

Dr. Jinks discussed laboratory results and confirmed cases for the period July 2002 through June 2009*. During this period 1,297,405 specimens were tested. It was acknowledged that the diagnosed case report originally distributed to members included cases with presumptive diagnoses, and that in some cases, additional information collected from the sub-specialists later lead to more accurate definitive diagnoses. Follow-up Program staff will provide a clarified report of cases with definitive diagnoses to all members. The availability of more accurate disease registry reports should improve as the new NBS data system is fully implemented. There was discussion about abnormal MS/MS results suggestive of carbamoylphosphate synthetase (CPS) and ornithine transcarbamylase (OTC) deficiencies, and one case of CPS deficiency was recently identified by elevated glycine and low citrulline levels detected on NBS samples.

*See attached report "Confirmed Case Summary".

Dr. Jinks reported that the laboratory portion of the new NBS database is near completion. There have been some data transfer delays related to the connections required to connect the laboratory to IDPH servers based in Springfield, but these are being addressed. The new Follow-up Program data system was delayed due to problems with the sub-contractor. These have been addressed by the primary contractor, Perkin Elmer, and hands-on testing of the Follow-up system is scheduled to begin later this year. Development of the system to accommodate metabolic formula distribution is also being addressed. Utilization of the current mainframe NBS laboratory system will be necessary for the interim.

Funding for LSD screening development was discussed. IDPH applied for a CDC grant to enable the IDPH Newborn Screening Laboratory to work with Advanced Liquid Logic Inc. in development of more efficient, less expensive micro-fluidic fluorometric assays for LSD screening, but an announcement has not been made regarding the grant award. In addition to the existing Advanced Liquid Logic assays for Fabry, Gaucher and Pompe, new assays for Krabbe and Niemann-Pick are being developed. Dr. Jinks will remain in contact with CDC researchers, Bob Vogt and Victor DeJesus. Funding for equipment and laboratory staff should be available for LSD screening, and the Administrative Rule changes proposing the screening fee increase to $78 per specimen could be authorized by December 2009. Unless funds are diverted from the dedicated metabolic screening fund, this increase should provide sufficient funding for the laboratory equipment for LSD pilot testing. Personnel concerns were discussed; the NBS Laboratory plans to fill four to five positions. Follow-up program currently has three vacant positions, with requests to fill these vacancies in progress.

Dr. Jinks informed members there have been no new developments with regard to NBS for severe combined immune deficiency (SCID). Currently, only Wisconsin is screening for SCID, and this screening was implemented in response to a legislative directive. It was acknowledged that currently there are no pediatric immunologist members of the GMDAC, or any the Sub-committees.

Subcommittee members discussed drafting a recommendation to implement SCID screening with funding provided by a fee increase. It was noted that Illinois newborn screening fees are currently lower than those of many other states. Members acknowledged that past disorder additions, including CF, were based on the recommendation of the GMDAC, and if the Committee members drafted a white paper about the SCID disorder, and testing and treatment options, IDPH could provide cost estimates for implementation. This process was used to add CF.

Claudia Nash informed the members that the Illinois Hospital Association comments to the currently proposed Rule change suggested defining the rationale for adding new disorders based on the recommendation of the GMDAC to the Director of the IDPH. Clarification of this process could be incorporated into the Metabolic Screening and Treatment Code, and although separate legislative initiatives would not be barred, a defined process might encourage better oversight of the process. The GMDAC could appoint a task force to address addition of new disorders based on recommendations from American College of Medical Genetics, CDC and other national organizations.

Testing and reporting of results for congenital adrenal hyperplasia (CAH), alpha thalassemia, and galactosemia were discussed. Mike Petros reported that IDPH is part of a multi-state evaluation for a new CAH screening kit, and that preliminary results show these kits to be more specific, which should decrease CAH false positive rates. Dr. Jinks indicated new high performance liquid chromatography equipment with reflex testing for hemoglobinopathies, including alpha thalassemia, is available, and bidding by the manufacturer is underway. This new equipment includes improved software and mechanics, and may be available by year end. There was discussion about galactosemia screening. IDPH screens primarily for galactose-1-phosphate uridyltransferase (GALT) deficiency, or classical galactosemia, but will report abnormal results suggestive of epimerase and galactokinase deficiencies. There was discussion about revision of total galactose cut-off values and the resulting increase in abnormal screenings requiring additional NBS samples and diagnostic testing. Galactosemia screening data and information about galactosemia protocols utilized by other states will be provided to the members.

Other Discussion

The next Subcommittee meeting was originally scheduled for November 4, 2009; however, a new date will be suggested to facilitate a meeting prior to the Advisory Committee meeting scheduled for October 29, 2009. The meeting was adjourned at 11:20 AM.

Minutes respectfully submitted by Barbara DeLuka - 8/10/09