Illinois Department of Public Health (IDPH)
Genetic and Metabolic Diseases Advisory Committee
Newborn Screening Laboratory Subcommittee
Minutes – August 27, 2008
2121 W. Taylor St., Rm. 139E
Chicago, Illinois

Subcommittee Members in Attendance
Dr. George Hoganson (Subcommittee Chair), University of Illinois at Chicago
Audio Conference Attendance
Kristin Culp-Clementz, Children's Memorial Hospital
Sunetra Reddy, University of Chicago
Dr. Gopal Srinivasan, Mt. Sinai Neonatology
Dr. Patrick Zeller, Pediatric Endocrinologist

IDPH Staff
Dr. David Jinks, Newborn Screening Laboratory
Tom Johnson, IDPH Office of Health Protection
Mike Petros, Newborn Screening Laboratory
Barbara DeLuka, Genetics/Newborn Screening Program
IDPH Audio Conference Attendance
Heather Gardner, Genetics/Newborn Screening Program
Claudia Nash, Genetics/Newborn Screening Program
Kate Seymore, Genetics/Newborn Screening Program
Danielle Harold, Graduate Student Intern University of Illinois at Springfield

Call to order by Dr. Hoganson at 1:10 PM
Introductions
Minutes of May 21, 2008 meeting were reviewed and approved.

IDPH Laboratory Report and Discussion
Dr. Jinks presented an analysis of confirmed disorders for the period July 2002 through July 2008. During this period 1,127,435 specimens were tested with a combined incidence of 1 disorder for every 650 specimens. The confirmed disorder total currently includes galactosemia carriers. This policy was questioned, although no decision to revise this practice was made. The number of confirmed cases appears typical for the number of babies screened.

Mike Petros reported on the results of cystic fibrosis screening, and during the period March through July 2008, the lab reported 320 presumptive positive abnormals, see attachments 1, 2 and 3. Twenty-two babies were subsequently diagnosed with CF.*

*Subsequently, one baby and the parents had DNA analysis that indicated the baby was heterozygous for DF508 with no second mutation was detected; see attachment 4 for updated information.

Four of these babies had newborn screens that indicated heterozygous status for CF. Dr. Hoganson stated that Division of Specialized Care would provide gene sequencing as follow-up testing for abnormal CF screens, and asked if gene sequencing was performed on these children to identify the second CF mutation. Follow-up staff will check with the CF specialists for gene sequencing results.* Claudia Nash stated that in one of these cases, mutation analysis of the mother's blood sample detected a mutation not present in the Tepnel © CF newborn screening test panel. It was mentioned that DSCC most likely would only cover expenses when diagnostic sweat testing was not an option due to the infant's low birth weight or medical complications. A conference call for the CF specialists and CF Center staff is planned for later this year to discuss CF screening results and issues.

Mike Petros stated the laboratory is now reporting positive screens for alpha thalassemia, and that of 17,375 specimens screened for alpha thalassemia, eight positive screens were reported. Kristin Culp-Clementz stated that one infant referred to the Children's Memorial hematology clinic with a positive screen was diagnosed with alpha thalassemia, hemoglobin H disease, by DNA analysis performed in Oakland, CA. Kristin asked about two cases in which NICU infants had positive screens for alpha thalassemia; in both cases the positive screen samples were delayed for over two weeks in transit to the lab. Because these two babies had other newborn screening samples that tested normal, the babies' pediatricians were not recommending electophoresis, isoelectric focusing or other diagnostic testing to rule out alpha thalassemia, but would monitor the babies. There was discussion about the limitations of the currently employed ~~testing~~ ~~kits~~ HPLC system with regards to Bart's hemoglobin. ~~and that~~ Screening reliability will improve greatly with the ~~arrival~~ availability of ~~newly~~ improved HPLC equipment ~~and kits~~. Alpha thalassemia confirmed cases will be reported as a sub-set of hemoglobinopathies and included long term follow-up.

There was discussion among members about the screening of samples from older infants, particularly adoptions of foreign born infants and toddlers. Laboratory reports provide disclaimers regarding the possible effects of age at time of specimen collection and that cut-off values are validated for newborns. Hemoglobin types and immunoreactive trypsinogen (IRT) levels are most affected by age at time of specimen collection. While testing of older children may detect some disorders, detectability of other analytes is dependant upon patient age- ~~will change with age~~.

Increased incidence of congenital hypothyroidism cases was again discussed. Dr. Zeller indicated a world-wide increased incidence has been associated with higher prevalence among some races and ethnic groups, and birth increases within these populations, however this theory has not been proven. There have been increases in the number of newborns with early TSH elevations necessitating treatment. In some of these cases treatment may be discontinued after three years of age when normal thyroid function is determined by ultra sound and/or technetium thyroid scanning, indicating a transient rather than primary congenital hypothyroidism. After discussion of the need for review of long-term follow-up data on congenital hypothyroidism cases, Dr. Zeller

offered to review reports used to obtain diagnostic information and to encourage better reporting of follow-up data at the Midwest Pediatric Endocrine Society

Dr. Hoganson opened discussion regarding developments in testing for severe combined immune deficiency disorders (SCID). No guidance from Legal Services was available at this time. The possibility of internal laboratory testing using identified and de-identified samples was discussed. The need for objective assessment of potential benefit versus harm for testing identified samples with unproven methodologies was discussed. In conclusion, there was agreement that approval by both the Department's institutional review board (IRB) and the IRB of any participating hospitals would be necessary, along with memorandums of agreement between the agents would certainly precede any movement toward the use of residual newborn screening blood samples.

Next topic was preparations towards lysosomal storage disease (LSD) screening. There will be a conference call September 9, 2008 to discuss necessary Administrative Rule changes, and the proposed changes must be approved by IDPH Legal Services. The proposed Rule should be filed in the Illinois Register in January 2009. There was discussion about the laboratory methods required for LSD screening and whether DNA sequencing in addition to tandem mass spectrometry was necessary. The New York Newborn Screening Program utilizes DNA analysis to reduce false positive screens for Krabbe disease. It was suggested that the proposed Rule change should include a general statement about the use of DNA testing, as the development of molecular screening will continue to improve testing methods for newborn screening disorders in the future. Dr. Hoganson pointed out that molecular screening for galacotsemia would greatly improve sensitivity over current methods and reduce the relatively high false positive rate of current screening. The consensus was the proposed Administrative Rule change should include a fee increase based on calculations of expenses necessary to develop the actual testing for LSD screening, and that appropriate allowances for inclusion of molecular DNA testing were also necessary.

There was discussion of the time frame for LSD testing development which is dependent upon the availability of funding for equipment, laboratory renovations, personnel hiring and intensive training which requires travel to CDC for in-house training.

Claudia Nash mentioned a new Fragile X research study in which Rush University Medical Center, Chicago is participating. She also discussed the recent audio conference presented by the Secretary's Committee on Heritable Diseases regarding the addition of new disorders to the American College of Medical Genetics uniform list of newborn screening disorders to be included in all state screening programs. Dr. Hoganson recommended that IDPH develop a formal process for evaluation of new disorders to be added to the newborn screening test panel, and it was suggested that this issue be addressed by the full Advisory Committee.

Claudia Nash also indicated changes to the current specimen collection form were being evaluated, and these included a tear off portion for the baby's parents to improve parent awareness of newborn screening and as an educational resource. Additional costs would most likely be covered by the Newborn Screening Program, rather than the Laboratory. Samples will be shared with the Sub-Committee members.

The next meeting was originally scheduled for October 29; however, this meeting will be rescheduled to November 5 from 9-11 AM. Announcements will be sent to members along with the meeting minutes.

The meeting was adjourned at 11:00 AM.

Minutes prepared by Barbara DeLuka 9/11/08