CALL TO ORDER:
Deb Schutte called the meeting to order at 1:00 p.m. and presided over the meeting. Introductions were made.

NEW MEMBERS
Deb announced State Representative and parent advocate, Lisa Heddens, as the newest member to the committee. Lisa will be attending the April meeting.

MEMBERS PRESENT:

MEMBERS ABSENT:
James Matsuda, Neil Mandsager, Robert A. Lee, and Representative Lisa Heddens

OTHER ATTENDEES:
Judy Miller, Catherine Evers, Pam DeBoer, Tonya Diehn, and Sherry Smith.

APPROVAL OF MINUTES:
The minutes for the October 10, 2003 were reviewed. Christina Trout and Catherine Evers made corrections.

Motion made by Nancylee to approve the October minutes with the changes suggested by Christina Trout and Catherine Evers.
Seconded by Diana Cates.

I. ANNOUNCEMENTS:
Carol announced that they have two candidates for the metabolic geneticist position. They are both very highly qualified. They will be coming for interviews in February and March. Carol will keep everyone posted.

BDAC Meeting Schedule
Tonya inquired if committee members would be able to attend the meetings on a different Friday of the month. Tonya also asked if they would prefer holding the meetings via ICN or the University Hygienic Laboratory’s teleconference system. The entire group voted to move the April BDAC meeting to April 2. The meeting will be held over the University Hygienic Laboratory’s teleconference system. Stan made the arrangements. The sites will be Iowa City and Des Moines. The July meeting will be held on July 9 and will be held in Grinnell. Upon Nancylee’s suggestion, the group agreed to hold two face-to-face meetings per year.
II COORDINATOR REPORT Tonya Diehn

Subcommittees
The Cystic Fibrosis Subcommittee is considering new information and is reconvening to determine if a proposal for cystic fibrosis and newborn screening should be written. Tonya inquired if the subcommittee should decide to make the recommendation, would the committee members want to vote on the recommendation via email or at the April meeting. Since the recommendation will have to be approved through the Iowa Department of Public Health, the members did not feel a vote from the BDAC was necessary. Members felt if the health department approved the recommendation, that the proposal should be written and then brought to the BDAC for review and potential approval.

Genetic Implementation Grant Update
The grant will end on May 31, 2004. Some of the activities involved with the grant include the Newborn Screening Newsletter and the Iowa Birth Defects Registry Parent Notification Project. The Center for Genetics is looking at different possibilities for funding each project.

Legislative Session
Birth Defects Institute Code Revisions: The Iowa Department of Public Health and the Assistant Attorney General, Heather Adams reviewed the revisions. Heather ruled that the term genomics reflected research, was an unknown term and was open to misinterpretation and misunderstanding by citizens and legislators. She recommended the inclusion of several items to help with the statutory authority of the programs and that a different name be selected for the program. Tonya provided everyone with Heather’s final revision of the code. The name that was selected to replace the “Birth Defects Institute” and “The Center for Genomics” is “Center for Congenital and Inherited Disorders.” This was chosen from a list of suggestions made by the BDAC members and others involved in the genetic programs.

Representative Petersen will be introducing a bill that will establish a work group to develop a stillbirth protocol through the health department and require the Iowa Birth Defects Registry to perform stillbirth surveillance as an additional responsibility. Her initial draft of the bill established the workgroup and surveillance under the Birth Defects Institute chapter and recommended a name change to Childbirth Research Institute. Tonya, the IDPH legislative liaison, Paul Romitti, and others met with Representatives Petersen and Heddens about this draft. They discussed Representative Heddens’ bill last legislative session to change the name of the Institute and the Birth Defects Advisory Committee’s work. Representative Peterson agreed to incorporate the Birth Defects Institute code revisions into her stillbirth legislation. The code revisions were submitted to the bill drafter of Representative Petersen’s bill this morning.

Tonya cannot take comments from the advisory committee and provide them to the bill drafter; however, if the bill is introduced, Tonya will be able to take comments at that time. The new bill will have a directive that the name of the Iowa Birth Defects Registry will be changed. The name will not be listed in the Iowa Code but will be in the administrative rules.

III Iowa Birth Defects Registry Appropriations Update

Representatives Murphy and Heddens have introduced in the house a bill to appropriate the birth certificate funds that are currently being held in the general fund.
to the Iowa Birth Defects Registry. Representative Heddens is redrafting the bill to include language that is similar to the Senate bill. The Senate version is currently in the Senate Appropriation Committee. The House bill will be more of a supplemental bill rather than an annual appropriation bill. If anyone has questions, this bill can be found in the Legislative website under House File 2003.

IV Newborn Dried Blood Spot Retention Policy Subcommittee

Summary of Recommendations Tonya Diehn
The Newborn Dried Blood Spot Retention Policy Subcommittee met. The members of the subcommittee were from the Medical Examiners office, Iowa Birth Defects Registry, and Newborn Metabolic Screening Program along with a representative from the Public Health Department as well. The handout provided prior to the meeting contained background information, a summary, and proposal.

Recommendation 1: The newborn dried blood spot cards should be retained at a temperature of –70°C for one year. (The 1st recommendation of the proposal has been modified, the original storage temperature recommendation was –20 °C. The modification occurred as the result of Dr. William Rhead discussing with the Medical Examiner’s office that the cards need to be stored at -70°C for enzyme studies.) Recommendation 2: Following the first year of storage at –70 °C, the dried blood spot cards should be stored at room temperature for another four years. Recommendation 3: Increase newborn metabolic screening fee by $ .50 to cover the storage, inventory, and monetary cost estimates, effective FY 2005. Recommendation 4: Permit use of identifiable newborn dried blood spot cards for research projects with secured human subject review committee, Iowa Department of Public Health approval, and parental consent.

Subcommittee Proposal

Stan has contacted hygienic labs from other states to inquire about their policies for long-term storage of newborn blood spot cards. The subcommittee reviewed several of these policies. The subcommittee proposal was guided by the New England policy. Paul discussed opportunities with long-term storage including how it could benefit the Medical Examiner’s office, its potential use for research and DNA screening studies.

Storage Needs and Retention Periods

Stan discussed the document, “Upon receipt, specimens will be logged-in and testing begun.” The document outlines the flow within the laboratory and the recognition that the specimens will be maintained in a secure manner. The specimens would be stored in a coded fashion with no immediate identifiable information associated with the specimen when put in storage. The code would be maintained at the laboratory with specific identifiers. It would not be traceable or accessible to anyone other than members of the lab.

Judy Miller asked how the subcommittee came up with 1 and 4 year retention periods. Is that standard with what other states are doing? Some states maintain the specimens until the infant is an adult. Stan explained the one-year retention period and the –70 °C storage condition was determined by the needs of the Medical Examiner’s office. Most SIDS deaths occur between 6-8 months of age. All of these cases have a metabolic workup and the ME’s office may request a newborn dried blood spot specimen for additional studies. It could possibly up to a year before a specimen for
metabolic and enzyme studies would be requested. The primary purpose of retaining
the specimens is for program purposes, to improve the Newborn Screening Program.
Without the availability of specimens, Stan discussed, there is no opportunity for the
INMSP to examine if there was a missed case to improve procedures in the
laboratory. The purposes of the laboratory and the Medical Examiner’s office for
retaining the specimens would be resolved in one year.

There is no justification to maintain storage conditions at –70 °C beyond a year
because of the cost associated with retaining the specimens. Therefore, after one
year, the specimens would be moved to room temperature. It’s appropriate to store
them for longer. The retention period selected is a starting point that will require
further study and review by the program. Paul mentioned the language in the
proposals was to store for a minimum of four years. Paul and Stan discussed room
temperature storage versus 4 °C. The primary value for the storing the specimens at
this longer retention period would be for DNA studies. Stan mentioned that with
adequate room control for temperature and humidity, the gain for maintaining the
specimens at 4 °C would not be much different than at room temperature. Paul
mentioned long-term storage would justify the initial monetary cost for the first 12
months of storage.

Discussion

Stan provided the attendees with cost estimates. The first year costs are estimated to
be $21,945. Costs include –70°C freezer, storage system, quality control, storage
supplies (such as bags), desiccant, and labor. Subsequent years are estimated to be
$13,520.00/yr. Cost includes freezer replacement cost recovery, quality control,
storage supplies and labor.

Deb Schutte asked if the proposed fee increase to cover storage and monitoring costs
would also include retrieval of the specimens. Stan mentioned the Medical
Examiner’s office had provided an approximate number of specimens they may want
to retrieve within a year’s period. Stan had included that amount in the storage cost.
However, with research applications, the retrieval process may be quite involved. For
research requests, there would be a retrieval charge.

Judy inquired about the current retention time for specimens. Stan answered they are
being saved for 30 days at room temperature at the newborn screening laboratory in a
secure locker. Judy asked who approves the use of retained specimens. The proposed
policy recommends for:

**Research use:** human subjects review committee, BDAC, IDPH and Board of Health
approval along with parental consent.

**Medical Examiner:** program on demonstration of parental consent

**Diagnostic/clinical use:** program on demonstration of parental consent

**Anonymized specimens:** human subjects review committee, BDAC, IDPH and Board
of Health.

Judy inquired the outcome if the researchers want samples within the five year period
and we have told the public we are retaining specimens for five years. Stan discussed
that if a researcher requests a specimen, they will receive a paper punch from one of
the dried blood spots. The entire card would not be provided.

Tonya discussed that the proposed policy is specific to the health department and
would be an overriding policy. The newborn screening laboratory will have their own policy that will detail the storage, retention, and use of specimens including research. Stan clarified the proposed policy and recommendations are for residual blood spot specimen storage. Residual means the portion of specimen that is remaining after the designated needs of the newborn screening program have been met. The retention of blood spot specimens should never compromise the function and quality of the screening program. There will be cases with no residual specimen available and the laboratory would document this.

Christina discussed the diagnostic/clinical purposes section. It can be a slippery slope when trying to differentiate between what is research and what is clinically diagnostic. Some research leads to a clinical diagnosis. There was discussion about how to clarify the language to permit research to determine an individual’s clinical diagnosis versus allowing a parent to request a specimen for a research project. Christina suggested replacing the word clinical with diagnostic before laboratory. The intent of the use of the specimen should be clarified for the research, diagnostic, and medical examiner’s sections.

Another issue discussed was the ownership of the specimen: the lab, state, or parent? Parental rights were discussed. Stan discussed that the INMSP brochure indicates that the specimens are the property of the state. However, the administrative rules do not indicate ownership. Tonya will seek guidance from the assistant attorney general about who is the owner of the specimen and how who is identified affects the use and release of specimens.

The notice section of the proposed policy is hard to understand. Parents need to know clearly if they do not want their child’s specimen to be involved in research, they have the option to request their child’s specimen not be stored. The storage issue itself will be challenging to explain to parents. Education about storage and potential uses of the residual specimen needs to be provided to parents. They need to be aware and this needs to done without potentially scaring them from having the screen itself. The language currently on the brochure should be reviewed to determine if it is appropriate to include in the notice section. Michelle recommended softening the wording and make sure contact information is available.

Judy discussed that it would be important to include patient’s address and phone number on the collection form for follow-up and retrieval purposes.

Greg Garvin asked how many research and Medical Examiners requests for dried blood spot specimens have been received by the INMSP. Tonya discussed that during the last several years, there has been two requests for research. There has been Medical Examiners requests, but the specimens have already been destroyed.

**Motions**

Motion to accept recommendation 1, to retain the newborn dried blood spots at −70 °C for one year, was made by Jerry Wickersham. Motion was seconded by Nancylee Ziese.

Members voted unanimously to accept the recommendation.

Motion to accept recommendation 2, following the first year of storage at −70 °C, the dried blood spot cards should be retained at room temperature for another four years,
was made by Greg Garvin. Motion was seconded by Jerry Wickersham.

Members voted unanimously to accept recommendation 2.

Motion to accept recommendation 3, to increase newborn metabolic screening fee by $.50 to cover the storage, inventory, and monitoring costs effective FY 2005 was made by Roger Williamson. Motion was seconded by Nancylee Ziese.

Members voted unanimously to accept recommendation 3 under number three. Diana Cates asked if consent for clinical or diagnostic testing is implied by an absence of a refusal which is invited by the document given to the parents. If I as a parent read the document and thought that only research that would potentially benefit my child would be permitted by my failure to refuse, I would wonder how that researcher got my name when they contacted me later about a project. It was discussed that the Iowa Neonatal Metabolic Screening Program would not release names to a researcher. The researcher may obtain names through public records or may have a health care provider, clinical program or registry contact families first to see if they are interested in the study. Research studies with identifiers and the requirement for parental consent raises issues for noticing parents and the need to be clear in our parental information on how the blood spots would be stored and removed.

Motion to accept the recommendation under number four, permission for the use of identifiable newborn dried blood spot cards for research projects with secured human subject review committee, Iowa Department of Public Health approval, and parental consent, was made by Linda Brown. Motion was seconded by Jerry Wickersham.

Members voted unanimously to accept the recommendation under number four.

Christina Trout motioned that the subcommittee made the changes recommended by the BDAC and clarify in the proposal the issues of legal access and ownership, parental notification, and clinical versus diagnostic purposes. Jerry Wickersham seconded the motion. Discussion included that parental notification should address parental rights to withdraw a specimen at the state level.

Members voted unanimously to accept the motion.

**Pilot program for dried blood spot storage**

Stan discussed as we are looking to change the retention policy, if there is an opportunity for the laboratory to begin managing these specimens to develop procedures and policy. He asked for approval for the laboratory to initiate a pilot to begin retaining these specimens at room temperature and follow the steps outlined in the “upon receipt…” Michelle Hall expressed that she felt a pilot addressing these necessary requirements would be important before implementation of the new policy.

Stan asked if he needed to request developmental funds. He estimated that the cost would be $4800. Stan asked if a proposal for developmental funds could go directly to IDPH or if it would need to come back to the BDAC.

Deb Schutte motioned to recommend that a pilot study be performed and for the BDAC to review a proposal to use developmental funds at the April meeting. Motion was seconded by Michelle Hall. The pilot study will commence when the recommendations are approved. Specimens will be held at room temperature and will
Linda asked what steps would have to occur before implementation of the IDPH policy could take place. Tonya discussed that the proposal and recommendations would need to be reviewed by Heather Adams, the assistant attorney general. After her approval, IDPH would review and approve. Then Stan would write the UHL specific policy. The UHL lawyers would also need to be involved in the process. The goal would be to have this ready for implementation by the time the newborn screening lab moves into its new facility. Stan indicated that would be in December 2004. The group voted unanimously to approve the motion.

Proposal to Establish Laboratory Parameters for First Trimester Maternal Serum Screening Analytes

Roger stated the current standard for screening is the Quad Test, which is alpha-fetoprotein, unconjugated estriol, human chorionic gonadotropin, and inhibin-A. The screening can detect 75% of Down syndrome cases with a false positive rate of 5%. There is now interest in first trimester screening for a number of reasons. It can potentially permit women to undergo diagnostic testing earlier if indicated. The best test, however, is to integrate both 1st trimester and 2nd trimester screening results. He mentioned there have been published retrospective studies finding that first trimester screening can be as effective for Down Syndrome, Trisomy 18, and Trisomy 13 detection as second trimester screening.

Optimal screening parameters are to measure:

PAPP-A (pregnancy associated protein plasma A): A protein that is lower with Down’s syndrome pregnancies during the first 10-14 weeks.

Free Beta subunit (human chorionic gonadotropin) HCG: Elevated in Down’s syndrome pregnancies during the first 10-14 weeks.

Ultrasound measurement of the nuchal translucency: A parameter to measure the fluid under the skin at the back of the neck. The nuchal translucency measurement is difficult to evaluate. Ultrasonographers would need additional training to perform the measurement. Six staff members from Roger’s unit have already attended the Fetal Medicine Foundation in London, England to train for the procedure and have been certified. It is Roger’s understanding that the perinatal offices in Des Moines are having some of their ultrasonographers trained.

First trimester screening options could include:
1. Maternal age only in which the woman would be offered chorionic villus sampling
2. Blood screening for PAPP-A and HCG no ultrasound parameter
3. Complete blood screen in which maternal age, PAPP-A, HCG and nuchal translucency are evaluated.

What they’ve been waiting for, in terms of the first trimester screening, has been the results of two large collaborative studies, one for the United Kingdom entitled SURUSS (serum, urine, ultrasound screening study). This study involved approximately 47,000 women from 25 units in the UK. They have published their results, which suggests that first trimester screening has the same efficacy as 2nd trimester screening. The best screening for women who do not want the more invasive screenings (i.e. chorionic sampling or amniocentesis) would be to combine the results of the 1st and 2nd trimester screenings into an integrated result. This modestly increases the detection rate, but greatly lowers the rate of false-positive rate.
down to 1.2%. The screening costs are more, but that's more than made up for by the decrease in the number of diagnostic procedures performed.

Another study which was performed in the United States, is titled the FASTER Trial (First and Second Trimester Evaluation of Risk). The results for this study came out last week and only in abstract form. This study basically replicated the findings of the SURUSS study (London). This study also suggested 1st trimester screening is efficacious and that the best test would be to combine the results of the 1st and 2nd trimester screenings.

Since the results of both trials have been published, Roger thinks there will be more interest in first trimester screening. They have received a number of queries from patients and physicians. He also thinks it is timely to consider establishing laboratory parameters for first trimester analytes for PAPP-A and HCG. There are some patent issues and to get around this with beta-HCG, one may have to use inhibin-A in the first trimester, but this not at all clear at this point.

Roger is seeking approval to establish medians for these first trimester analytes. They still need to determine a mechanism to obtain the specimens for each gestational week from 10 to 14 weeks. They need to work on a budget to do so but Stan has brought a preliminary budget. They need to come with how education to physicians would occur and they have had some discussion about this. What they really want to do at this stage is to lay the foundation of why first trimester screening is going to be more sought after by patients and to establish the rationale for beginning to set up the program.

**Discussion**

Tonya asked for clarification. Does Roger want the committee to approve that they can begin establishing the medians? And if approved, then you would determine the mechanism and the budget, write a proposal and come back to the committee? Roger wants approval to begin the process and what that would involve would be to decide how they are going to collect the blood specimens.

Stan then discussed that a minimum of 300 specimens would be needed to establish medians for PAPP-A and free beta HCG. Stan provided the following information pertaining to the estimated costs for the testing of 300 specimens.

<table>
<thead>
<tr>
<th>Test</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAPP-A (Plasma Associated Plasma Protein A)</td>
<td>$5.00/ specimen</td>
</tr>
<tr>
<td>Free Beta HCG</td>
<td>$2.00/ specimen</td>
</tr>
</tbody>
</table>

Stan also mentioned there are patent issues related to the use of the Free Beta HCG for this application. There are royalties and a licensure fee required to be able to perform the Free Beta HCG test. It would cost approximately $100,000 to begin the process. Stan mentioned that since the University of Iowa Hygienic Lab is a state agency, there might be a possibility to be exempt from the royalty and licensure fees of performing the Free Beta HCG tests. Stan doesn’t know this for sure yet but will check further into the issue. If it were not possible to be exempt from the fees, an alternative marker would be Inhibin A. However, there is controversy about the accuracy of the Inhibin A testing. Hopefully, the study being conducted in England will prove that Inhibin A is an accurate marker for first trimester screening.

If Inhibin A were included, the cost would be $5.00 a specimen. The total cost to establish the medians of 300 specimens will be $2,100 for Free Beta HCG and PAPP-
A or $3,000 for Inhibin A and PAPP-A.

Tonya asked if Stan knew for sure which markers would be used to establish medians. Stan answered that for sure PAPP-A would be used; however, he will not know about the Free Beta HCG until he receives information pertaining to the royalty and licensure fees. If the royalty and licensure fees are waived, PAPP-A and Free Beta HCG medians will be established. Otherwise, medians for Inhibin-A will be established.

Tonya asked for clarification, is the program just establishing medians but not determining if the program would be doing first screening and/or integrated screening? Roger discussed that once they establish the first trimester medians, they would determine the options. Tonya asked if Roger was seeking approval for median establishment to establish first trimester screening through the Expanded Maternal Serum Alpha Fetoprotein Screening Program. Roger said yes. Tonya asked Roger if he thinks a statewide program should perform 1st trimester screening. Roger’s program thinks yes but it is open to discussion. Linda asked why Tonya was questioning this.

Tonya expressed her concern about the inclusion of the nuchal translucency ultrasound measurement in the screening. Tonya inquired how it would be possible to incorporate this into a statewide screening program when the measurement requires certification to include it. Roger mentioned that the ultrasound is not absolutely necessary; however, it would be optimal to have the ultrasound measurement. Without the ultrasound, the risk assessment could be calculated based on the PAPP-A and Free Beta HCG markers only. Stan indicated that the program currently incorporates ultrasound information on gestational age into the second trimester screening algorithm. The difference for first trimester screening is that ultrasound measurement is equivalent to a biochemical marker. Stan briefly discussed the benefits and detection rates of 3 marker first trimester screening, 5 marker integrated screening, and 6 marker integrated screening.

Dr. Neil Mandsager was not able to attend the meeting; however he had asked Tonya to voice his questions and concerns regarding the 1st trimester screening to the BDAC members. Tonya read his questions and comments. Neil inquired how the ultrasound component would be incorporated into the expanded MSAFP screening program? Would the ultrasound results, i.e. nuchal measurement simply be sent to the lab to be incorporated with the lab results? Who will be doing the ultrasounds? What is the quality control for the ultrasounds? Will the state require ultrasound certification for first trimester screening in the same way the national companies are doing? After all, ultrasound is a critical component to the screening quality control, it’s just as important for this component as the laboratory component. Would one ever consider utilizing a laboratory screening program that does not have a built-in quality control program? As Neil understands first trimester screening, he can’t see how a statewide program can function without well-defined quality control for all aspects, including ultrasound. He is interested in hearing from those proposing the project.

In another email, Neil asked if there would be discussion with insurance companies to determine what they would cover. If insurance pays for 12 week U/S and labs, will they still pay for a comprehensive U/S at 20 weeks? He continues that he doesn’t doubt that someone will begin to provide 1st trimester screening in Iowa. His office is preparing for it, but hasn’t decided if and when to proceed yet. He has concerns about how to maintain quality control for the ultrasound component if offered as a state
program. Roger stated that they would only include the nuchal ultrasound measurement if someone certified completed it. Tonya asked if the different levels of sensitivity would be recorded on the report.

Stan discussed that with the availability of first trimester screening, there is no longer one best maternal screening option but a complexity and a multitude of options. We can’t have a single testing algorithm that will work for all women. As a state program, shouldn’t we offer all maternal serum screening options?

Roger is assuming that the integrated test will become “standard of care.” Tonya feels it would be best to involve the medical community outside of this program, and the insurance companies in the development of the first trimester screening program. Garvin mentioned that if the integrated testing became “standard of care” it would be difficult for insurance companies not to pay the claims.

Roger feels that if the program does not take care of the testing, the specimens will be sent to Mayo, or other commercial laboratories instead of staying in Iowa. Once that happens, it will be difficult for practitioners to switch back to the Iowa labs.

There was a discussion about the timeframe for establishing medians, difficulties with obtaining specimens, and what funds would be used to develop the medians.

Roger suggested that he and his staff should develop a more formal and informative proposal and would like to bring it in front of the committee during the April meeting.

Linda motioned that the 1st trimester screening proposal be moved to the April meeting. Jerry Wickersham seconded the motion.

V. WRAP-UP

The next meeting will be in April 2, 2004 at 1:00 PM. The meeting will be held via ICN.

ADJOURNMENT

The meeting was adjourned at 4:20 p.m.

Minutes respectively submitted by Sherry Smith.