Advisory Committee on Heritable Disorders in Newborns and Children

Summary of Third Meeting
November 3, 2015

Please note: These minutes are pending formal approval by the Committee. Corrections or notations will be incorporated in the final minutes.

The Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC) was convened for its second meeting at 10:09 a.m. EST on Tuesday, November 3, 2015, and adjourned at 4:00 p.m. In accordance with the provisions of Public Law 92-463, the meeting was open for public comment.

COMMITTEE MEMBERS

Don Bailey, Ph.D., M.Ed.
Distinguished Fellow
Early Childhood Development
RTI International

Joseph A. Bocchini, Jr., M.D.
(Committee Chairperson)
Professor and Chairman
Department of Pediatrics
Louisiana State University

Jeffrey Botkin, M.D., M.P.H.
Professor of Pediatrics and Medical Ethics
Associate Vice President for Research
University of Utah

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California Department of Public Health

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Medical Genetics and Pediatrics
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Children's Memorial Hospital

Catherine A. L. Wicklund, M.S., C.G.C.
Feinberg School of Medicine
Center for Genetic Medicine
Northwestern University

EX-OFFICIO MEMBERS

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Kamila Mistry, Ph.D., M.P.H.
Senior Advisor
Child Health and Quality Improvement

Centers for Disease Control and Prevention
Coleen A. Boyle, Ph.D., M.S.
Director
National Center on Birth Defects and
Developmental Disabilities

Food and Drug Administration
Kellie B. Kelm, Ph.D.
Chief, Cardio-Renal Diagnostic Devices Branch
Division of Chemistry and
Toxicology Devices
Office of In Vitro Diagnostic Devices
Evaluation and Safety

Health Resources and Services Administration
Michael Lu, M.D., M.P.H.
Associate Administrator
Maternal and Child Health Bureau

National Institutes of Health
Catherine Y. Spong, M.D.
Acting Director
Eunice Kennedy Shriver National Institute of
Child Health and Human Development

DESIGNATED FEDERAL OFFICIAL
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Health Resources and Services Administration
Genetic Services Branch
Maternal and Child Health Bureau

LIAISONS AND ORGANIZATIONAL REPRESENTATIVES

American Academy of Family Physicians
Robert Ostrander, M.D.
Valley View Family Practice

American Academy of Pediatrics
Beth Tarini, M.D., M.S., F.A.A.P.
University of Michigan Health System

American College of Medical Genetics and Genomics
Michael S. Watson, Ph.D., F.A.C.M.G.
Executive Director

American College of Obstetricians and Gynecologists
Joseph R. Biggio, Jr., M.D.
Professor and Vice-Chair
Director, Division of Maternal Fetal Medicine
Medical Director, Obstetric Services
University of Alabama at Birmingham

Association of Maternal and Child Health Programs
Debbie Badawi, M.D.
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Maryland Department of Health and Mental Hygiene

Association of Public Health Laboratories
Susan M. Tanksley, Ph.D.
Manager, Laboratory Operations Unit
Texas Department of State Health Services

Association of State and Territorial Health Officials
Christopher Kus, M.D., M.P.H.
Associate Medical Director
Division of Family Health
New York State Department of Health

Department of Defense
Adam B. Kanis, M.D.
Department of Pediatrics
MCHK-PE Tripler Army Medical Center

Genetic Alliance
Natasha F. Bonhomme
Vice President of Strategic Development

March of Dimes
Edward R. McCabe, M.D., Ph.D.
Senior Vice President and Medical Director

National Society of Genetic Counselors
Cate Walsh Vockley, M.S., C.G.C.S.
Senior Genetic Counselor
Division of Medical Genetics
Children's Hospital of Pittsburgh

Society for Inherited Metabolic Disorders
Carol Greene, M.D.
University of Maryland Medical System
Pediatric Genetics

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I. Administrative Business

Joseph A. Bocchini, Jr. M.D.
Committee Chair
Professor and Chairman
Department of Pediatrics
Louisiana State University

A. Welcome and Roll Call

Dr. Joseph Bocchini welcomed the Committee members and other participants to the third meeting of the Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC) and took roll. Voting members present were:

- Dr. Don Bailey
- Dr. Bocchini
- Dr. Jeffrey Botkin
- Dr. Fred Lorey
- Dr. Dietrich Matern
- Dr. Stephen McDonough
- Ms. Catherine Wicklund

Ex Officio members present were:

- Agency for Healthcare Research and Quality: Dr. Kamila Mistry
- Centers for Disease Control and Prevention: Dr. Colleen Boyle
- Food and Drug Administration: Dr. Kellie Kelm
- Health Resources and Services Administration (HRSA): Ms. Joan Scott (for Dr. Michael Lu)
- National Institutes of Health: Dr. Melissa Parisi (for Dr. Catherine Spong)

Organizational representatives present were:

- American Academy of Family Physicians (AAFP): Dr. Robert Ostrander
- American College of Medical Genetics (ACMG): Dr. Michael Watson
- Association of Maternal and Child Health: Dr. Debbie Badawi
- Association of Public Health Laboratories (APHL): Dr. Susan Tanksley
- Association of State and Territorial Health Officials: Dr. Christopher Kus
- Genetic Alliance: Ms. Natasha Bonhomme
- March of Dimes: Dr. Edward McCabe
- National Society of Genetic Counselors: Ms. Cate Walsh Vockley
- Society for Inherited Metabolic Disorders: Dr. Carole Greene

B. Approval of August Meeting Minutes

Committee members offered no comments or recommended changes to the meeting minutes for the August 2015 ACHDNC meeting. Dr. McDonough made a motion to approve the minutes, which was seconded by Dr. Boyle. Dr. Bocchini took a roll call vote for the approval of the minutes. The Committee members present approved the minutes unanimously.

C. **Secretarial Correspondence**

Dr. Bocchini reported that Secretary of Health and Human Services (HHS) Sylvia Mathews Burwell replied to the Committee's recommendation concerning the inclusion of Mucopolysaccharidosis 1 on the Recommended Uniform Screening Panel (RUSP). The Secretary requested that the recommendation be reviewed by the Interagency Coordinating Committee (ICC). Additionally, the Committee's recommendations to the Secretary concerning newborn screening (NBS) informed consent are under review, as is the Committee's recommendation concerning Adrenoleukodystrophy.

D. **ACHDNC Bylaws Changes and Vote**

Dr. Bocchini explained that the Committee's bylaws were updated to reflect the new legislative authority. The changes include an increase in the number of organizational representatives, up to a total of 15. The increase provides an opportunity for organizations that are interested in becoming involved with the Committee in a formal manner to do so. The 12 organizations currently represented will continue to be part of the group. All organizational representatives will have wide-ranging interests in NBS and heritable disorders, and their work will help to inform the activities of the Committee. Organizational representative membership will be reassessed every three years to ensure that the organizations' interests, expertise, missions, and relevancy continue to benefit the Committee in its implementation of its objectives, activities, and duties. Additionally, organizations will be asked to reaffirm their commitment to serve every three years. Organizations that are interested in serving must submit an application to the HRSA Designated Federal Official; selection will be based on organizations' interest, expertise, mission, relevancy, and benefit to the Committee. Organizations will be able to continue to serve as organizational representatives indefinitely provided their missions and activities continue to align with the priorities of the Committee. More information on the application and selection process will be available on the Committee's website in the near future.

Dr. McDonough asked whether there had been any communication with the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) or the hospital association concerning the possibility of service on the Committee. Dr. Bocchini replied affirmatively. The Committee has been corresponding with JCAHO concerning working with the Committee on timeliness issues. The initial response from JCAHO was positive, but there have been some difficulties identifying a representative. Ms. Debi Sarkar indicated that there will be a follow-up meeting with JCAHO during which she anticipated discussing the appointment of a representative who could serve on the Timeliness Workgroup. Dr. McCabe reported that the March of Dimes (MoD) has not yet been able to engage JCAHO on NBS issues.
Dr. McDonough made a motion to accept the changes in the bylaws, as presented in the briefing book. Dr. Botkin seconded the motion. Dr. Bocchini took a roll call vote, and the Committee members present approved the updated bylaws unanimously.

E. **Other Business**

Ms. Sarkar reviewed the ethics and conflict of interest recusal requirements for voting members and outlined the process for participating in the webinar for Committee members, organizational representatives, and the public. She also reviewed key portions of the Federal Advisory Committee Act that guides the operation of the Committee, including the role of public comment and participation by non-Committee members.

II. Overview of the Implications of the Federal Policy for the Protection of Human Subjects Notice of Proposed Rulemaking for Newborn Screening

Michelle Huckaby Lewis, M.D., J.D.
Research Scholar
Berman Institute of Bioethics
Johns Hopkins University

Dr. Michelle Huckaby Lewis' presentation provided background information on the Common Rule and her interpretation of the Notice of Proposed Rule Making (NPRM) concerning human subjects research.

She provided an overview of the significant changes proposed :

- Improving informed consent (increased transparency) and implementing new requirements about the information that must be given to prospective subjects.
- Requiring informed consent for secondary research use of stored biospecimens.
- Excluding certain categories of research from the Common Rule.
- Adding new categories of exempt research.
- Changing systems rules concerning the requirements for waiver of consent (Dr. Lewis did not anticipate that waivers would be used often in NBS-related research).
- Requiring the use of a single institutional review board (IRB) for cooperative research.
- Eliminating the need for continuing review requirements for studies that undergo expedited review.
- Extending the scope of the policy to cover all clinical trials, regardless of funding source.

Dr. Lewis focused her presentation on the potential implications of the proposed new rules on NBS, NBS laboratories, and NBS research. The NPRM treats each of three types of research related to NBS – de-identified data (not covered by the Common Rule), identifiable private information, and biospecimens – differently. Currently, the governing authority in this area is Amendment 12 of the Newborn Screening Save Lives Reauthorization Act of 2014.

Aspects of the NPRM that pertain to NBS include changes in definitions (specifically those concerning human subjects research); in exclusions and exemptions and the effects of these changes on secondary research uses of identifiable private information and dried blood spots (DBS); in requirements related to privacy safeguards; and in requirements concerning informed consent and broad consent. The NPRM includes both exclusions (activities for which the Common Rule does not apply) and exemptions (activities for which certain parts of the Common Rule apply).

Dr. Lewis concluded her remarks by reviewing several of the questions identified in the NPRM for public comment..

Committee Discussion:

- In response to a question from a Committee member concerning the exclusion of de-identified specimens, Dr. Lewis indicated that they are potentially excluded for certain activities. There are some circumstances in which de-identified DBS could be used.
- A Committee member pointed out that individual institutions often want to use their own IRBs rather than a single IRB. Dr. Lewis stated that the proposed rule would require the use of a single IRB.
- Concerning the use of samples for program development (e.g., adding a new test or disorder to a screening panel), Dr. Lewis indicated that there would need to be a determination concerning whether the activity was or was not research. OHRP is working on clarifying these sorts of issues from a laboratory perspective, but has not yet completed its work. There is an exclusion for implementation of a practice that has already been accepted. In cases where an NBS laboratory is bringing on a new test for a condition for which it is already testing, a different exclusion could

potentially apply; using samples from people with a known disorder to test a new method is excluded because there is no new information being generated.

- Dr. Bocchini responded to a Committee member's question about the ACHDNC's response to the proposed rule by indicating that he hoped the PSW would have recommendations that the group could consider for submission during the comment period. Otherwise, the Committee would work by email to reach consensus on a response to the NPRM.
- Dr. Botkin reported that the PSW did not reach any firm conclusions concerning specific comments that should be made and welcomed any comments from the full Committee.
- A Committee member recommended pulling together a list of completed projects that used NBS specimens that would not be feasible under the proposed rule. Dr. Matern reported that his program has tried multiple times to use a consent process in its work testing protocols, but had extreme difficulty in implementing consent processes that are efficient and not overly expensive.
- An organizational representative expressed his concern that the proposed rule would present a significant barrier to frontline research and asked how other countries handle this issue. Dr. Matern indicated that the regulations vary greatly in other countries. His program works with other countries with less restrictive policies. He did not think it would be fair to use other populations when programs cannot access those in their own countries.
- Dr. Lewis responded to a question concerning various timelines associated with the proposed rule by stating that there is still much uncertainty with regard to when the template would be presented to the public. OHRP has previously indicated that the various parts of the proposed rule stand alone (i.e., the template is not necessary to determine whether the rules are goods ones). She did not know the timelines for creating and presenting the template. She acknowledged that this could create procedural issues for the NBS community (e.g., how to fit the information into the existing documentation associated with screening).
- With regard to state-funded research and the new IRB requirements, Dr. Lewis indicated that the proposed rule applies to federally-funded research, with the exception of clinical trials, which would be subject to the rule regardless of the source of funding.
- Dr. Botkin indicated that the Secretary's Advisory Committee on Human Research Protections (SACHRP) is likely to recommend that the new regulations be implemented three years after the templates are finished because limiting the implementation period to three years overall could leave the regulated community very little time to implement the rule if it takes a couple of years to develop the template.
- An organizational representative asked if investigators using the broad consent template could avoid having to go through IRB review and those using an investigator-developed consent form would have to undergo limited IRB review. Dr. Lewis replied affirmatively.
- An organizational representative pointed out the difficulties that NBS programs that wish to retain specimens for future studies will encounter when they try to develop consent procedures that the practitioners must follow given that the NBS program staff do not actually see patients and cannot regulate the way such procedures are followed. Dr. Lewis indicated that this is one of the process issues that should be pointed out to OHRP.
- In response to a question concerning the 10-year limit for consent as it pertains to the collection or use of specimens, Dr. Lewis explained that the provision does not apply in the NBS context, except with the possible situation of obtaining consent in the prenatal period. The provision applies to other clinical settings. The informed consent document must include the amount of time that the samples can continue to be used for research; indefinitely is one of the possible options.
- With regard to the issue of the level of literacy of potential subjects and the consent form, Dr. Lewis indicated that the NPRM does not address literacy levels for the consent form. It specifies that the form include information that a reasonable person would want to know. There is no requirement to assess the level of understanding of the person.
- An organizational representative recommended comparing the work done in the NBS context (both work that is and is not considered research) to the NPRM to determine how NBS activities fall out under the proposed rule.

III. Public Comments

Mr. Dean Suhr, MLD Foundation: Mr. Suhr reported that the MLD Foundation planned to release a draft paper on the RUSP roundtable meeting held in August. Based on feedback received after the meeting, the Foundation will continue the work of the roundtable through two meetings in 2016. Additionally, a working group for advocacy groups is being formed based on work being done by the EveryLife Foundation's Community Congress, which organizes advocacy groups in a collaborative way to work toward common goals. The Community Congress will take place on November 4. He anticipated that the Congress' 2016 project would be the development of a state toolkit focused on improving the understanding of state public health programs and legislation concerning NBS in order to better support advocacy efforts.

Mr. William Morris: Mr. Morris spoke as the parent of four children. Two children have heritable disorders (one with PKU & one with Krabbe). The child who had Krabbe died due to lack of diagnosis. He advocated for more and better education for providers and parents concerning the importance of NBS, specifically the development of prenatal education guidelines for NBS. The growing number of conditions on the RUSP compounds the problems resulting from a lack of education. Prenatal education would help parents understand the critical nature of confirmation testing and diagnosis.

IV. Transition Models from Pediatric to Adult Health Care: Innovative Strategies

Patience White, M.D., M.A.
Co-Project Director
Got Transition/Center for Health Care Transition

Dr. Patience White's presentation provided an overview of strategies and challenges to transition emerging young adults from pediatric to adult health care.

Dr. White put the transition issue in the context of several national initiatives. The Affordable Care Act provides insurance expansions for young adults and includes transition as an essential health home service. The National Committee for Quality Assurance developed medical home standards on transition. Transitions are part of the Healthy People 2020 goals. The new Title V Transition Performance Measure looks at the percentage of children with and without special needs who receive services necessary to transition to adult health care. Finally, the Centers for Medicare & Medicaid Services and its Center for Medicare and Medicaid Innovation are focusing on transition issues, with an emphasis on the transition from hospital to home. She indicated that the health care community is just beginning to think about the transition from pediatric to adult health care.

The American Academy of Pediatrics, American Academy of Family Physicians, and the American College of Physicians published a joint report on health care transitions in 2011. The report provides an algorithm for progressing through transitions. It includes a pathway for youth with special health care needs. The algorithm can be used in a variety of health settings, systems, and environments. The transition process begins at age 12, and the target for completion of the transition is between ages 18-22.

The Bureau of Maternal and Child Health funds a national center, Got Transition, which set up learning collaboratives with primary and specialty care practices in Washington, D.C.; Boston, Mass.; Denver, Colo.; New Hampshire; Minnesota; and Wisconsin. Collaborative activities took place from 2010 through 2012 and used well-tested learning methodologies. They demonstrated that the six core elements and tools developed for the collaboratives were feasible for use in clinical settings and resulted in quality improvements in the transition process. Findings from the collaboratives were published in the *Journal of Adolescent Health* in 2014.

Elements of Transition
Dr. White described the Six Core Elements of Transition:

Element	Action	Age
Transition Policy	Discuss transition policy	12-14
Transition Tracking & Monitoring	Track Progress	14-18
Transition Readiness	Assess skills	14-18
Transition Planning	Develop transition plan	14-18
Transfer of Care	Transfer documents	18-21
Transition Complete	Confirm completion	3-6 months after transfer

The Got Transition project took the six elements and developed three packages designed for use by for pediatric, family medicine, and meds-peds providers that focus on transitioning youth to adult care providers, on transitioning to an adult approach to care without changing providers (for family medicine and meds-peds providers), and on integrating young adults into adult health care. Dr. White focused her remarks on the transition from pediatric to adult providers.

Committee Discussion:

- In response to a question from a Committee member concerning the inclusion of a genetics subspecialty in the group of 11 societies customizing the templates, Dr. White promised to send the list of participating societies to the Committee.
- A Committee member noted that ACMG developed several factsheets for the transition from pediatrics to adult care for some of the inborn errors of metabolism. Dr. White added that some of the specialty societies have their own transition tools, some of which are being adapted for other specialties. Got Transition hopes that the process will also be adapted along with the tools.
- An organizational representative stated that the New York Mid-Atlantic Consortium conducted a project on transitions that concluded that training programs are the best way to disseminate information on transitions. The ACMG fact sheets provide basic background information for receiving providers as well as information on topics such as sexuality and reproduction that are of concern to youth and their families. Dr. White indicated that med-peds has developed objectives and a plan for training. Some residency programs hold joint training sessions with pediatric and medical residents that focus on specific, unusual diseases, including related transition issues. Some schools are looking at linking colleges and medical schools to provide opportunities for both adult and pediatric providers to become more comfortable working with college-aged adults.

V. Raising Awareness in Newborn Screening: Strategies and Updates

Natasha Bonhomme
Vice President of Strategic Partnership
Genetic Alliance

Ms. Bonhomme described the challenges to communicating about NBS, including the introduction of new technologies, a lack of basic information about NBS, the focus on giving birth and recovery, and a lack of best practices for educating people about NBS at different points in time and provided an overview of current strategies underway to address these challenges. Ms. Bonhomme stressed the importance of re-establishing the value of NBS, providing consistent messages in multiple places through multiple sources, embedding messages in established communications channels (especially by driving information to target audiences), and determining whether there are common messages around NBS or its various components.

Sample Strategies for NBS Education
Immune Deficiency Foundation
The Immune Deficiency Foundation developed a video that traces a family's experience with severe combined immunodeficiency. By using a family experience, it helps connect the message to the listener

through the shared experience of being pregnant and giving birth. Associated brochures and handouts emphasize the interpersonal connection. Ms. Bonhomme shared several examples of messaging on social media that discuss NBS in the context of what is going to happen in the first few days of a newborn's life; incorporating these messages in places that people are already looking at makes it more likely that they will find messages about NBS topics.

NBS educational efforts in Minnesota and Texas.
Minnesota created an infographic explaining what happens after NBS with regard to the options for the storage and use of DBS. Changes in the policy concerning obtaining consent for the storage and use of NBS bloodspots formed the impetus for the development of the infographic. The information is targeted toward parents and helps them navigate through the available options. The state has also used billboards in its outreach effort. She indicated that it will be interesting to learn how successful the billboards were in effectively communicating with the target audiences.

Texas includes a fair amount of information on the NBS collection form. The state also has a lot of information on its public health webpage. While individual parents might not visit the site, it serves as a resource for those individuals who teach others in settings such as prenatal classes, new moms groups, and classes for new parents.

Newborn Screening Clearinghouse Update
The NBS clearinghouse, Baby's First Test, informs and empowers families and health care professionals throughout the NBS process (prenatal education through diagnosis). The clearinghouse has more than 10,000 pages of content covering general NBS topics, information on what to expect during NBS, tips for living with detected conditions, blogs, conditions for which each state screens, and resources for each condition.

Traffic to the website has increased significantly, especially within the last 18 months. Ms. Bonhomme attributed the increase in visits to long-term efforts to spread the word about the clearinghouse and to working with groups that are traditional NBS stakeholders but are heavily involved in the maternal and child health arena. The clearinghouse anticipates that it will have more than 1 million users by the end of the year. Most visitors only come to the site once because they find the information that they need. The most popular content relates to conditions screened by state, screening procedures, phenylketonuria, and condition-specific pages. The number of organic searches (i.e., general searches for NBS using keywords) has increased significantly from 2014 to 2015.

Use of mobile devices continues to grow. People are moving away from their desktops and using their mobile devices more and more to access a wide variety of information. Earlier in the year, Baby's First Test exceeded the 50 percent mark in users accessing the site through mobile devices, with such mobile users more than doubling each year. In response to the increase in the use of mobile devices, the clearinghouse developed a mobile application. The app makes it easy to navigate to state or condition information. Beta testing is wrapping up, and the app should be ready for launch by the end of the month.

Additionally, the clearinghouse refreshed its website design. The new design allows users to search for state-specific and condition-specific information from the homepage. The site is also available in Spanish. A professional translator translated all 10,000 pages of content; the goal of the translation was to ensure that the site was not just correct but that it was properly adapted for the Spanish-speaking community. The Spanish version of the website is currently undergoing a final review by an individual with extensive experience in developing public health communications concerning maternal and child health messaging to the Spanish-speaking population in the United States.

Upcoming Initiatives
The clearinghouse is in the process of conceptualizing a new engagement tool, the WikiNewborn Screening Forum/Public Square. The platform will create a virtual public square in which the NBS community can convene to discuss issues and current topics in real time. The public (i.e., parents, those whose lives or work are touched by NBS issues) does not have access to some of the meetings and other opportunities

available to NBS professionals to discuss important issues; this consumer-led, consumer-centric initiative will provide opportunities to discuss issues of concern to them. The goal is to have three virtual town hall meetings on different topics each year. The forum will also host a variety of webinars on NBS topics. The forum will be incorporated into the www.BabysFirstTest.org site.

The clearinghouse just launched a user survey on the webpage designed to learn more about who visits the site and whether they find the information for which they are looking. The clearinghouse is also working with www.NewbornScreeningEducation.org, the Virginia Department of Health, and the University of Virginia to incorporate continuing education modules and links to modules into its website. Additionally, there is an ongoing effort to add new content to the website. Ms. Bonhomme stressed that the key audiences of the website, including the general public, parents, providers, and policymakers, generally have a low understanding of genetics and screening. The clearinghouse strives to meet their information needs.

Committee Discussion:

- A Committee member asked about the idea of using search engines to bring the clearinghouse information to people who are conducting searches for prenatal information. Ms. Bonhomme explained that getting information to rank higher on search results often requires payment of a fee to a search engine. In the past year, Google recognized the Baby's First Test website as a top site (this recognizes that the site is mobile friendly and optimizes for any device), which means that the site is ranked higher in search results. Additionally, Genetic Alliance has a Google advertising grant; it gives part of the grant to the project to create ads for the website. Finally, the project is working with Test for Baby to send out to three different NBS messages to Test for Baby users.
- In response to a question concerning the interests of visitors to the website, Ms. Bonhomme indicated that the survey that was recently launched will help illuminate whether people are visiting because of a positive screening result or because they are looking for general information and whether they are seeking information before or after a test. Approximately 70 percent of visitors look for information on the conditions for which their respective states screen.
- An organizational representative asked about the website's ability to track users' activity once they enter the site. Ms. Bonhomme replied that the survey should help the clearinghouse determine whether it should implement such a capacity.
- Ms. Bonhomme responded to a question concerning other apps for NBS information by stating that there are many pregnancy-related apps, many of which deal with fertility issues and fetal developmental stages. The clearinghouse has reached out to many of these groups to get more information. These groups are interested in the number of visits to a website. Now that the number of visits to the Baby's First Test site are up, it will be easier to form partnerships with other groups. Some sites view linking the clearinghouse website or posting its content as advertising, while the clearinghouse views it as getting important public health information out to as many people as possible. As a result, the clearing house is working on bringing together federal agencies and professional societies to disseminate NBS information to the general public.

Workgroup Updates

The Committee created three workgroups to address issues related to pilot studies, cost analysis, and timeliness. These groups are working on identifying the essential elements needed to move the nomination of a condition through the evidence review process and allow the Committee to make a decision concerning recommendation for the RUSP within the nine-month timeframe mandated by the legislation.

VI. Workgroup Update – Pilot Study Workgroup

Jeffrey Botkin, M.D., M.P.H.
Committee Member

Dr. Botkin explained that the PSW is charged with recognizing existing efforts, identifying other resources, and identifying information required to move a condition forward. He anticipated presenting a report at the Committee's face-to-face meeting in February 2016, which will complete the group's work.

The PSW met the previous day and focused its discussion on the NPRM on human subjects research. There is broad support, both nationally and among the PSW members, for many of the elements in the NPRM. The NPRM shows that there was an effort to simplify some issues, reduce IRB workloads, and clarify some issues that had been confusing in the past. The final regulations may be somewhat different than those proposed in the NPRM, and it might take several years to fully implement them. In the meantime, the NBS community will be guided by Section 12 of the Newborn Screening Saves Lives Reauthorization Act of 2014 and any related guidance provided by OHRP.

NPRM Issues

Ongoing testing to assess or maintain quality with laboratories is a focus of the NPRM, which attempts to separate QA activities from research activities. Additionally, steps necessary to implement screening for a condition with known analytic and clinical validity are likely to fall outside of the research domain; states should have no problems implementing screenings for conditions on the RUSP if they use established laboratory methods and approaches. Finally, activities related to emergency preparedness and continuity of operations would not be considered research.

Activities that could be considered research under the proposed rules would include method development studies that include evaluations designed to establish analytic performance of a method and demonstrate clinical validity. The definition of research has not changed. This means that studies designed to contribute to generalizable knowledge fall under the research umbrella. Examples of activities that could be considered research include studies that make significant changes to an existing method and go beyond the scope of the original method and studies involving the re-testing of stored material that are designed to contribute to generalizable knowledge.

Early adopting states might consider one of two options for implementing their programs in light of the proposed new rules. First, they could avoid using federal funds for new test development and rely solely on state funds for these activities. By using state funds, they would avoid falling under the Common Rule. This assumes that IRBs do not determine that the new rules represent a change in ethical standards that should be applied to all research regardless of funding sources. A second option would be to obtain consent to conduct research using residual DBS. Compliance with the Secretary's template would be very important in this instance. Michigan and Massachusetts use an approach similar to this option, with the former reporting that between 60 percent and 70 percent of parents consent and the latter reporting a slightly higher rate of consent. Dr. Botkin anticipated that use of the second option would significantly reduce the number of samples available. Because of the administrative complexities and the risks of running afoul of the new rules, states may choose to not be early adopters.

The PSW also had concerns about the uncertainty regarding the timeline for making the template available. It is not clear whether the wording used for the template will fit on NBS collection devices. Additionally, having the template available before it is implemented would allow programs to develop new materials prior to the implementation of the new rules. There were also some concerns about whether hospitals and birthing centers will be considered to be engaging in research because they are seeking informed consent for NBS research and how the new rules will affect the ability of researchers to work with states with large numbers of birthing facilities.

The PSW was concerned that template would require the redesign of existing NBS collection cards to accommodate it. Other concerns related to the storage of samples, especially in cases where parents did not consent but later wanted testing of the sample for other clinical purposes.

Dr. Botkin identified several issues that the Workgroup believed should be taken under consideration by the full Committee:

- Parental consent will be required for research use of DBS (waivers will be rare and will be made only where there is compelling scientific justification and consented samples are not available).

- Specimens collected before the new regulation become effective must have individually identifiable information removed. This would create three categories – specimens collected before the Reauthorization Act, under the Reauthorization Act, and after the new rules – that will have different implications for research projects.
- The new regulations will supersede the law in Section 12 of the Reauthorization Act (the proposed regulations have more extensive consent requirements and limited circumstances for waivers).

Dr. Botkin stated that the new regulations will promote transparency and trust within the general public. They will require the creation of new forms and processes for retaining samples for research purposes. The length and complexity of the new consent information poses challenges for clinicians in all contexts, especially when the consent is not relevant to the treatment needs of the patient; this creates extra, tangential work that might not be feasible in many settings. Additionally, he did not believe that it would be possible to include all of necessary information required by the proposed regulation on the back of a Guthrie card in a readable font size. The PSW also had concerns about whether the complex consent form and process would actually support informed decision making.

Dr. Botkin reported that SACHRP has been discussing issues related to the NPRM and will meet in December to draft final recommendations in response to the NPRM. He anticipated that SACHRP would not be supportive of the proposed changes in the biospecimen rule because there is already an excellent record of safety and there has been a significant underestimation of the complexity and burden of obtaining informed consent from people flowing through clinical services. The proposed regulations run the risk of making the consent perfunctory, thus limiting the intended value of the process. The proposed regulations are likely to result in a loss of access to valuable specimens and the possibility of conducting population-level research. Finally, the proposed rule does not prevent potentially controversial uses because there are few restrictions on the use of samples once consent has been obtained. SACHRP is likely to recommend a process of notice with an explicit opportunity for people to opt out of retention and use.

The PSW considered some recommendations concerning the NPRM, but did not reach a consensus because it did not have time to craft the appropriate language. The Committee needs to determine whether it wants to develop a response to the proposed rules and how to do so in the time available. One possible recommendation could be to encourage HHS to adequately support OHRP in its efforts to develop guidance and templates in support of the new rules.

Committee Discussion:

- A Committee member asked whether SACHRP planned to comment on either or both of the two alternate proposals for biospecimens. Dr. Botkin indicated that SACHRP had not spent much time considering the alternate approaches. He believed, personally, that the public is more concerned about sequencing of biosamples than about other forms of testing. The sequencing proposal could address those concerns without otherwise burdening traditional uses of biospecimens, such as those used for NBS purposes.
- Dr. Bocchini suggested that the Committee develop a list of issues and barriers to NBS that would likely result from implementation of the proposed regulations and submit it with any comments that the members could pull together rather than develop a formal set of recommendations.
- A Committee member asked whether there is a requirement that consent must occur in the birth hospital. Dr. Botkin indicated place of consent is not specified. There has been some discussion of implementing prenatal consent; this might be hampered by regulatory and information technology complexities. The Committee member pointed out that some hospitals would refuse to implement the consent process if it is too burdensome. Dr. Botkin indicated that such decisions would be made at the institutional level. It might still be possible to save specimens for non-research purposes (e.g., QA and QI) without consent.
- A Committee member supported the idea of submitting a list of issues or questions for clarification concerning how the guidance would apply in the context of NBS.
- A Committee member stressed the importance of the Committee, as an advisory body, raising concerns over how the proposed regulations could affect public health activities.

- A Committee member noted that the proposed regulations attempt to design a consent process that will be uniform across the full spectrum of clinical contexts. Having a uniform approach would prevent the tailoring of consent to the specific needs and concerns of various groups.

Dr. Bocchini indicated that the Committee would develop a list of key concerns, in the form of questions, about how the proposed regulations would affect NBS programs and about the consent form and process in response to the NPRM.

VII. Workgroup Update – Cost Analysis Workgroup

Alex Kemper, M.D., M.P.H., M.S.
Condition Review Workgroup

Dr. Kemper summarized the discussion from the previous day's meeting of the Cost Analysis Workgroup (CAW), which is charged with considering methods to assess the cost of NBS expansion as required by the Reauthorization Act. The CAW will submit a report to the Committee on how to incorporate cost assessment into the decision making process. Dr. Kemper focused his remarks on the cost analysis method, the required data, and the way in which findings could be used.

The main constraint on the cost analysis is the nine-month review process mandated by the Reauthorization Act. The lack of data on the relevant screening test and diagnostic evaluation/outcomes is another constraining factor. The complexity in the process will also play a role in the Committee's ability to conduct the assessment in a meaningful way.

The CAW designed a tailored budget impact analysis to respond to the requirements in the Reauthorization Act. The analysis will primarily take the perspective of the state or budget holder and assess the costs of implementing NBS for the condition under consideration. Of secondary concern will be the societal perspective (i.e., the costs faced by families, health care providers, and public and private payers). Dr. Kemper indicated that the time constraints would prevent a full evaluation of the societal perspective. The analysis will consider the costs to a state if it implements a screening over a two-year period. All costs related to screening through those related to short-term follow-up will be considered. Costs related to treatment and long-term outcomes are beyond the scope of the analysis.

Laboratory costs include equipment and reagents, installation of equipment, laboratory space and utilities, staffing, and laboratory information systems. Laboratory equipment and reagent costs should factor in the cost to purchase kits or develop a test, unit pricing versus bundled pricing, and purchase versus leasing costs.

Costs related to care delivery include educational outreach, reporting (including recalls), and short-term follow-up with diagnostic confirmation. Although some of the clinical costs for short-term follow-up could be paid by private insurance, the CAW counted these costs as ones born by the state.

Costs in the secondary category are those that are important but for which the ability to collect data might be limited. Costs in this category include costs to families, costs to payers other than the state, and, possibly, long-term costs. Each cost analysis report should include an explanation concerning the degree to which data on these costs is available and the extent to which they were used in the analysis.

States vary greatly in areas that could affect the cost analysis. Some of these areas of variability are birth rate, geographic location, existing laboratory facilities and personnel, laboratory information systems, use of outside laboratories, resources shared with other states, availability of and contracts with specialty centers for short-term follow-up, service contract specifics, and NBS funding structure. The CAW would like to develop a way to show how factors such as these come into play and where the cost for specific factors may vary by state.

Dr. Kemper indicated that some of the data needed for the cost analysis could come from the surveys done by the Condition Review Workgroup (CRW). Most of the information will be obtained through detailed interviews with key informants in the NBS field and from the limited number of vendors that support each test. Finally, the analysis effort could draw on existing data held by APHL or the NewSteps360 program.

The findings from the cost analysis will be helpful not only for assessing whether a condition should be added to the RUSP but also for states as they move forward with adoption.

Remaining activities for the CAW include developing a complete list of data elements, reviewing the cost analysis methods in the context of other CRW activities, drafting the methods, and pre-testing the methods. An initial draft report should be ready by December 15, and the final presentation of the CAW's efforts will be given during the February 2016 meeting.

Committee Discussion:

- An organizational representative noted the importance of understanding and explaining that there is little to no cost savings in short-term follow-up. Costs averted, such as institutionalization or other costs to society, are realized over the long term. Dr. Kemper pointed out the analysis in not one of cost effectiveness. The CAW would like to be able to get to the long-term analysis if time allows.

VIII. Workgroup Update – Timeliness 2.0 Workgroup

Kellie Kelm, Ph.D.
Ex-Officio Member

Catherine A. L. Wicklund, M.S., C.G.C.
Committee Member

Ms. Wicklund stated that the Timeliness 2.0 Workgroup (T2W) was charged with optimizing strategies to address NBS specimen collection and transport; collecting and disseminating timeliness-specific practices from state NBS programs, including those that have implemented efficiencies in collection, transport, screening, and follow-up; and investigating strategies for improved standardization of communication of NBS results to providers and families.

During the August meeting, the T2W discussed hospital processes related to specimen collections and identified areas in which the group could make contributions. The T2W also identified potential partners for addressing timeliness in the hospital setting. During the previous day's meeting, the Workgroup heard presentations from groups in Iowa and Michigan that have been working on timeliness issues.

Iowa CoIIN for Timeliness in NBS
Ms. Wicklund reminded the participants that Iowa was one of seven states that participated in the Collaborative Improvement and Innovation Network (CoIIN). The Iowa CoIIN project began in January and is ongoing. The project team members represent major components of the NBS process. The project has provided educational programs to five birthing centers and intends to provide educational programs to another eight birthing centers. The program resulted in three of the first five birthing centers starting their own CoIIN teams. The project is providing feedback to the state on timeliness and comparing the birthing centers with each other, which has fostered competition among the hospitals to get higher numbers of their samples to the laboratory within a certain amount of time.

Michigan Use of Hospital-Specific Cutoffs to Evaluate NBS Specimen Transit Time
Dr. Kelm reported on a Michigan project that focused on one change that the state made in an effort to improve transit time of NBS specimens. The original measure was the percent of specimens received at the laboratory within 72 hours of collection. Although it was easy to understand and calculate, it did not identify hospitals that could improve their timeliness nor could it adjust for weekends or varying pick-up times. As a result, the project implemented hospital-specific cutoffs to account for specimen collection time, collection day, and pickup time. The project provided hospitals with tables that indicated when specimens should arrive at the laboratory based on the courier pick-up time. Over the five quarters that the

study has been active, the number of samples arriving within the target timeframe has increased at a fairly steady rate.

A common theme that emerged from the two presentations was the importance of education about the NBS process, including the critical, time-sensitive nature of the test. Identifying key people who could influence hospital staff was also important. Other factors that proved to be important to efforts to improve timeliness were partnering with other state organizations, monitoring courier utilizations, identifying the key outcomes to measure, and identifying incentives to encourage change.

Moving forward, the T2W plans to request more presentations from states to identify lessons learned, reaching out to new partners and sharing lessons learned to help states improve their timeliness, exploring the possibility of using implementation science to improve timeliness, and applying the same process being used for timeliness of arrival at the laboratory to the timely reporting of results to providers and families. Dr. Kelm added that the Workgroup plans to reach out to states to determine which states are focusing on timeliness in the hospital setting.

IX. Future Meetings & Topics

In 2016, the Committee will hold four meetings:

- February 11-12
- May 9-10
- July 25-26,
- November 3-4

Dr. Bocchini indicated that the standing subcommittees would resume their work beginning with the February 2016 meeting, and he anticipated that they would begin to work on some of the topics identified during the Committee's August meeting. Potential topics to be taken up by the subcommittees include: making recommendations for upgrading or downgrading conditions on the RUSP (or removing them), addressing the issues related to Gaucher disease, delving into the ethics of multiplex screening platforms, consideration of heritable disorders that are not on the RUSP, consideration of prenatal aspects of heritable disorders including non-invasive prenatal testing, and studying outcomes issues with an emphasis on public health benefits of screening in the newborn period.

X. Adjournment

Dr. Bocchini thanked the Committee members for their contributions and adjourned the meeting at 4:00 p.m.