



Public Health Laboratory, Newborn Screening Program

601 Robert Street North

St. Paul, MN 55155-2531

651-201-5466

www.health.state.mn.us/newbornscreening

Newborn Screening Program Study

On Comprehensive and Sustainable Long-Term Storage and Use

Minnesota Department of Health
Report to the Minnesota Legislature 2014

February 1, 2014

Newborn Screening Program Study

February 1, 2014

For more information, contact:

Public Health Laboratory/Newborn Screening Program

Minnesota Department of Health

601 Robert Street North

Saint Paul, MN, 55155

Phone: 651-201-5466

Fax: 651-215-6285

TTY: 651-201-5797

As requested by Minnesota Statute 3.197: This report cost approximately \$6,200 to prepare, including staff time, printing and mailing expenses.

Upon request, this material will be made available in an alternative format such as large print, Braille or audio recording.

Printed on recycled paper

Newborn Screening Program Study

Table of Contents

	Page
Executive Summary	1
Introduction and Background	6
<i>What is Newborn Screening?</i>	6
<i>Blood Spot Screening</i>	8
<i>Hearing Screening</i>	10
<i>Pulse Oximetry Screening for Critical Congenital Heart Disease</i>	10
<i>After Newborn Screening: Storage and Use</i>	11
Review of Current Law	13
<i>Historical Background of Current Law</i>	14
<i>Current Law</i>	15
Adequacy of Current Law and Issues Encountered	15
<i>Performing Quality Assurance and Quality Improvement (QA/QI)</i>	15
<i>Obtaining Written Informed Consent for Extended Storage and Use</i>	18
<i>Providing Long Term Follow-up for Disorders on the Newborn Screening Panel</i>	19
<i>Affecting Minnesota Families</i>	22
<i>Conducting Public Health Research</i>	25
Storage and Use Models	25
Education Strategies and Addressing Privacy Concerns	29
Access Plans and Protocols	31
Conclusion	32
Glossary	33
Literature and Resources Cited	35
Appendices	
<i>Appendix A: Text of Newborn Screening Statutes</i>	
<i>Appendix B: List of Consultants</i>	
<i>Appendix C: Consultant Interview Questions</i>	
<i>Appendix D: 2014 Newborn Screening Panel</i>	
<i>Appendix E: Newborn Screening Parent Fact Sheet</i>	
<i>Appendix F: State Retention Periods for Blood Spots and Test Results</i>	
<i>Appendix G: Fiscal Assumptions</i>	

Executive Summary

The Commissioner of Health has been directed to review and evaluate the current newborn screening law and storage and use retention times by consulting with medical, research, and data privacy experts. The commissioner has considered the following:

- (1) peer-reviewed medical research into the diagnosis and treatment of heritable and congenital disease;
- (2) strategies for education of parents and families about the utility of advancing new knowledge through research on blood spots and test data made possible by long-term storage and use;
- (3) plans and protocols for clinical and research access to test result data;
- (4) minimizing the administrative burden on hospitals and health care providers in the operation of the newborn screening program;
- (5) the adequacy of current law on the standard retention period for test results under Minnesota Statutes, section 144.125, subdivision 6; and
- (6) privacy concerns associated with parental consent options and long-term storage and use of blood samples and test data.

Newborn screening, mandated under Minnesota Statutes, sections 144.125 to 144.128 and Minnesota Statutes 144.966, is a critical public health program that protects the health of infants born with rare, but treatable, disorders. With a simple blood test collected by the hospital and analysis done by the Minnesota Public Health Laboratory, doctors can tell whether newborns have certain life-threatening conditions and, if necessary, treat them right away to prevent later health problems and possible death. Currently, the Minnesota Newborn Screening Program screens more than 68,000 Minnesota newborns annually for more than 50 serious but treatable disorders, including congenital hearing loss and critical congenital heart disease (CCHD). Out of the 68,000 babies screened each year, approximately 140 infants are found to have a serious, life-threatening disorder, approximately 250 infants are identified with hearing loss, and 125 are expected to be diagnosed with a CCHD.

In 2012, the Minnesota legislature made changes to the newborn screening law. Specifically, the new law directed the commissioner of health to destroy all blood spots with negative test results 71 days after collection; destroy blood spots with positive test results at 24 months; and destroy test results 24 months after the results are reported. The legislation also listed acceptable uses for the blood spots and test results. Due to some

concerns on whether the new retention period was adequate to run the program and protect the health of babies, the 2013 legislature directed the commissioner of health to review the newborn screening program and evaluate the scientific and medical validity of a comprehensive and sustainable long-term storage and use plan for the test results and submit a report to the legislature. This report summarizes the work conducted to fulfill this charge. In summary, our review of the literature and discussion with experts suggests that current law does not meet the needs of the program or expectations of Minnesota families, and thus, different models are described. A review of the scientific literature and interviews with numerous experts suggest there are several areas where current law is inadequate: quality assurance/quality improvement; long term follow-up for affected children and their families; allowing for further health testing for families who request it; and public health research.

Quality Assurance and Quality Improvement

The Association of Public Health Laboratories asserts that there is no margin for error in newborn screening; precise analysis and complete follow-up are required to protect the health of children (3). To this end, the current law has presented several challenges to the MDH Newborn Screening Program's Quality Assurance and Quality Improvement efforts that are required to maintain and enhance the quality of testing and preserve accountability if errors occur. Some of the concerns around QA/QI include, but are not limited to: the reduction of false positive and false negative results, the refinement of cut-off values, the application of second tier-testing, and the ability to effectively meet federal Clinical Laboratory Improvement Amendments requirements.

Long Term Follow-Up

According to the Clinical and Laboratory Standards Institute, an effective and complete newborn screening system is comprised of six segments: testing, follow-up, diagnosis, treatment and/or management, evaluation, and education. Newborn screening follow-up can be further divided into two broad categories: short-term follow-up and long-term follow-up. The primary aim of newborn screening is to provide intervention to affected newborns; long term follow-up is the means by which the effectiveness of interventions and the accountability of newborn screening programs can be ensured. Such follow-up determines if newborn screening programs are achieving their main aims of preventing mortality and mitigating morbidity.

Providing families with long term follow-up services involves the assurance and provision of quality disease management, disorder-specific treatment, and age-appropriate preventive care. Activities that help ensure appropriate follow-up include: engaging affected individuals and their families as partners in care management, performing continuous quality improvement, gaining knowledge into pathophysiology and treatment options, and evaluating data related to care and outcomes. Such follow-up is vital to the evaluation of newborn screening

benefits throughout the life of an individual, as well as to the family and society (10). The suggested timeframe for providing follow-up services in the United States is through the age of 21(11).

Minnesota's current law does not allow access to information beyond two years from date of results reporting without written informed consent, even for LTFU purposes. This impairs the ability of Minnesota's long term follow-up program to assist families of a child with a confirmed diagnosis in coordinating medical care, connecting affected individuals to effective treatment options, reducing health disparities, and meeting their public health mission.

Negative Impacts on Families

The short retention periods for both blood spots and test results required by current state law has negatively impacted several Minnesota families due to the program's inability to retrieve vital information. Parents have previously asked to use saved blood spots and test results to help diagnose a disease in their child, for research, or to find reasons for their child's untimely death. Clinicians interviewed for this report also noted that they have used samples and test results many times prior to the current statute to help understand a child's illness, often when a child was many years old. Under current law, if clinicians request this information after a child is two years old, the information will likely have been destroyed and will no longer be available for this purpose.

Public Health Research

Under the current statute, written informed consent is required for developing new newborn screening tests or for public health research. Without consented blood spots and test results from enough individuals to represent the state's population, further understanding of diseases, potential treatments, and new test development may not occur. For example, implementing screening for severe combined immune deficiency (SCID) in Minnesota was delayed over a year because consented blood spots were not available to help develop the screen.

Obtaining written informed consent from an individual is more than just a signature on a form. The informed consent process involves three key components: 1) providing enough information so the individual can make an informed decision, 2) facilitating understanding by the individual, and 3) promoting a voluntary decision (6). Experts consulted for this legislative report consistently agree that implementing a true informed consent process would present a large administrative burden on Minnesota birth facilities. On average, the expert consultants estimated that each consent discussion would take 15-30 minutes to complete, which would result in an additional cost of about \$300 per infant.

Numerous experts interviewed for this report indicated that destroying blood spots and test results will have a significantly negative impact on research and patient care. Opportunities for clinicians and researchers to learn

more about pediatric illness will be lost, finding effective treatments may be delayed, and Minnesota will become less competitive when it comes to getting grant money for research.

Storage and use models

Interviews with a variety of medical research experts and with parents and agency staff revealed various models for a comprehensive and sustainable storage and use plan for newborn screening blood spots and test results. Based on these interviews and the information gathered, three possible models were developed.

Option One: Current Law

No changes are made to the current law in Minnesota Statutes, section 144.125. Under this model, the standard retention period for dried blood spots is 71 days if the results are all negative and two years if the results are positive. All test results, regardless of outcome, are destroyed at two years. During these periods, dried blood spots and test results without patient consent can only be used for program operations as currently defined in Minnesota statute. As mentioned in the 'Adequacy of Current Law and Issues Encountered' section of this report on pages 15-25, this model has resulted in serious concerns from both a program and citizen perspective. Written informed consent from the family is required for any extended storage beyond the current retention periods or for use outside of testing and program operations.

MDH and the majority of those interviewed believe that maintaining current law will be detrimental to the program and will result in harm to Minnesota children and their families. Several interviewees noted that current law has weakened the program, made the state and healthcare providers less accountable, and has resulted in negative consequences for families.

Option Two: Complete Opt-Out

Minnesota Statutes, section 144.125, is amended to be an opt-out program for long-term storage, for certain newborn screening uses, and for other public health uses with de-identified dried blood spots and test results. Under this model, the standard retention period for dried blood spots and test results, regardless of result, would be 18 years. During this period of time, families would have the option to opt out of storage and use of their child's blood spots and/or test results. If a family did not exercise their option to opt out, the de-identified blood spots and/or test results could be used for program operations as currently defined in Minnesota statute, as well as new test development and public health research. Written informed consent would still be required for public health studies involving identifiable information. While some of the medical, research and data privacy experts interviewed suggested that this model still protects privacy and alleviates issues arising with the current law, a

few felt that written informed consent should still be part of this process for any research use. Those who felt written informed consent should be required for all public health research felt that consent for research use is a standard of practice in most medical settings, and that newborn screening programs should follow suit.

Option Three: Research Opt-In

Minnesota Statutes, section 144.125, is amended to extend standard retention periods for both dried blood spots and test results to 18 years. During this time, specimens and test results can only be used without consent for program operations as defined in section 144.125, subdivision 5. Written informed consent would be necessary for any further use. This model allows for samples and test results to be available to families should they unexpectedly need them, but maintains a consent process for the development of new tests and public health research uses. This is similar to the model currently employed by the state of Michigan; however, new test development is not considered research under their policy, so consent is not needed for the purpose of developing new tests in Michigan.

Introduction

During the 2013 legislative session, the legislature directed the Minnesota Department of Health (MDH) to review the Newborn Screening Program and evaluate the scientific and medical validity of a comprehensive and sustainable long-term storage and use plan for dried blood spots and test results under Minnesota Statutes, section 144.125 (See Minnesota Laws 2013, chapter 82, section 39. Refer to Appendix A for the complete text of the legislation). The legislation also required MDH to submit a report to the legislature by February 1, 2014, on the scientific and medical validity of a comprehensive and sustainable long-term storage and use plan for newborn screening blood spots and test results.

As part of the evaluation, MDH was directed to “consult with medical research and data privacy experts, including, but not limited to, specialists in metabolic care, immunology, pediatrics, epidemiology, nutrition, pulmonology, cardiology, endocrinology, hematology, hearing care, and medical genetics, as well as patient advocacy and data privacy groups.”

Thus, between September and November of 2013, MDH conducted 25 interviews with individuals who have a variety of expertise (refer to Appendices B and C for a complete list of individuals consulted and consultant interview questions).

The following report presents information on the history of newborn screening and its importance to the state of Minnesota, a review of the current newborn screening law, models for long-term storage and use of blood spots and test results, and strategies to educate the public.

Background

What is Newborn Screening?

Newborn screening began in the United States more than 50 years ago when Dr. Robert Guthrie developed a screening test for a rare disorder called phenylketonuria (PKU) using a small amount of newborn blood dried on filter paper. Since the early 1960s, newborn screening has become a critical state-based public health program that protects the health of infants born with rare, but treatable, disorders.

As the concept of newborn screening grew nationwide, each state developed its own newborn screening program. Over time, however, numerous state-to-state discrepancies arose, including the number of disorders on each state’s screening panel, the way that programs followed up on positive results, and the educational materials available to parents and providers. With so many discrepancies, it became clear that greater

uniformity among states would benefit families, healthcare providers, and newborn screening programs. Therefore, in 2002, the United States Department of Health and Human Services commissioned the American College of Medical Genetics to convene a group of experts to analyze scientific literature, gather expert opinion, and assess newborn screening systems nationwide in order to recommend a uniform screening panel of conditions for all states. This expert group developed and recommended a panel of 31 primary and 26 secondary conditions that all state newborn screening programs would mandate as part of routine screening. Many factors influenced the decision to include a disorder on the uniform screening panel, including the severity of the condition, the availability of an effective treatment, the time it takes for symptoms to develop, and the availability and cost of the screening test.

In 2003, the United States Department of Health and Human Services established the Secretary's Advisory Committee on Heritable Disorders in Newborns and Children to provide long-term expertise and recommendations for uniform screening. The advisory committee reviews and makes final decisions on conditions nominated for inclusion on the recommended uniform screening panel. Each state uses this committee's guidance to determine which disorders to screen for and how its program will function.

In Minnesota, newborn screening is legislatively mandated under Minnesota Statutes, sections 144.125 to 144.128, and Minnesota Statutes, section 144.966 (Refer to Appendix A). A current list of tests included in Minnesota's newborn screening panel is in Appendix D.

The Minnesota Newborn Screening Program screens more than 68,000 Minnesota newborns annually for more than 50 serious but treatable disorders, including congenital hearing loss and critical congenital heart disease (CCHD). Out of the 68,000 babies screened each year, approximately 140 infants are found to have a serious, life-threatening disorder and approximately 250 infants are identified with hearing loss. Although pulse oximetry screening for CCHD continues to be implemented statewide at this time, it is estimated that this screening test will detect approximately 125 infants born with a critical heart defect in Minnesota each year.

It is vital that all children with disorders detected by newborn screening be immediately connected to primary and specialty care before developing symptoms. Early detection and treatment minimizes the negative impact (such as developmental disability or death) of these disorders. Newborn screening protects the child's health and provides an opportunity for that child to grow up and become a fully contributing citizen of Minnesota.

The newborn screening process includes a number of components. These components include: educating parents and providers about screening, collecting blood spots, testing the blood spots, connecting families with medical specialists, and providing specialized resources and treatment for affected children. To accomplish these activities, the MDH Newborn Screening Program works in partnership with families, healthcare providers, patient advocacy organizations, and other stakeholders who play a role in improving the health of Minnesota children.

The following is a brief overview of the newborn screening process, which includes screening for heritable and congenital disorders using dried blood spots, as well as screening for hearing loss and critical congenital heart disease (CCHD).

Blood Spot Screening

Newborn screening blood specimens are collected 24 to 48 hours after birth on special filter paper (commonly referred to as a “screening card”). Hospitals and other birth attendants, such as midwives, purchase the screening cards from MDH for the statutorily set price of \$150 each. The newborn screening card sales fund Minnesota’s program, including the cost of parental and provider education, the testing itself, and follow-up for families with positive screening results. As required by Minnesota law, the department provides educational materials to birth facilities and midwives. The healthcare provider must then provide parents with these materials, discuss the information with them, and answer any questions the family may have before an infant is screened. The Newborn Screening Program has created a parent fact sheet (Refer to Appendix E) that provides parents with information about newborn screening, possible uses of blood spots and test results after screening, proven risks and benefits of screening and the storage and use of blood spots and test results, and their right to refuse screening. Individuals collecting blood spots are required to record in the infant’s medical record that the family received this information and were given the opportunity to ask questions. This education and documentation must occur prior to all three screens: blood spot, hearing, and pulse oximetry for CCHD.

After educating parents about newborn screening, a physician, nurse, midwife, or other trained healthcare provider will collect a few drops of blood from the infant’s heel and place them onto the filter paper. Along with the drops of blood, demographic information about the newborn is documented on the screening card. This information includes the baby’s name, date of birth, weight, mother’s name, and name of the infant’s primary care provider. After the sample dries, it is sent to MDH to be tested for the conditions included in Minnesota’s newborn screening panel. The MDH Newborn Screening Laboratory screens approximately 200 blood spots received each day. Since 2004, the MDH Newborn Screening Program has contracted with a private laboratory

to perform some of the testing for newborn screening. High standards of quality are maintained and all results are reviewed for accuracy before they are released by MDH. All program staff members undergo rigorous training, including data privacy training. Complete results from newborn screening blood spot testing are usually available to the infant's primary care provider 3 to 5 days from the infant's date of birth, so that affected children may begin receiving necessary treatment before they are a week old

Healthcare provider education about newborn screening results is crucial since these disorders are rare and most providers have not seen, diagnosed, or treated them. Therefore, if a screening result is positive and indicates a need for further medical attention and follow-up, certified genetic counselors at MDH immediately call the infant's primary care provider. MDH genetic counselors give primary care providers a copy of the infant's newborn screening report, education about the disorder for which the infant is at risk, and contact information for specialists who can provide consultation on follow-up.

Reports sent out to providers only contain an interpretation of the results (i.e., negative or positive), and do not usually contain the actual test values and cut-off values. Actual test values and cut-off values are available on reports with positive results, but only for the test with the positive result. For most results, the exact test values are only available through the Newborn Screening Program. Specialists or healthcare providers looking for this level of detail on their patients must contact the Newborn Screening Program for this information because it is not kept anywhere else and cut-off values change over time.

Although most infants with these disorders seem healthy and have no outward signs or symptoms at birth, they are already being affected by the disorder. Early diagnosis and treatment before symptoms begin are critical to the child's health and development. Without screening, these disorders are usually not recognized until the infant is sick and already suffering the effects of the disorder.

Testing performed by the Newborn Screening Program is not diagnostic, and positive screening tests must be confirmed through additional testing. After confirmation of a diagnosis by a specialist, the child's case is transferred to the MDH Newborn and Child Follow-Up unit, which is charged with connecting the family to financial, medical, and support services specific to their disorder. Follow-up for affected children found by newborn screening is available until the child reaches adulthood in order to ensure ongoing care coordination and to help improve medical, educational, and social outcomes for the child and family.

Hearing Screening

Speech and language begin to develop at birth. If infants have problems with hearing and do not receive the appropriate intervention services, they will have trouble with speech and language throughout their lives. Diagnosing infants with hearing loss by three months of age and beginning intervention at no later than six months of age, gives infants the best chance to reach their full potential in communication, language, and social skills. The earlier they are connected with services, the better.

Newborn hearing screening takes place in the hospital before the family is discharged or by the family's midwife shortly after birth. Two types of hearing screening tests may be used. Both tests are safe and comfortable and measure the newborn's internal response to sounds. The test takes between five and ten minutes and is usually done while the infant is asleep. If the infant does not pass the first hearing test, another hearing test will be done either at the infant's clinic or by an audiologist when the infant is about two weeks old. A diagnosis of hearing loss should be made as soon as possible, but no later than three months of age. After a child is diagnosed with a hearing loss, intervention services can begin with help from MDH's Newborn and Child Follow-Up unit. The primary focus of intervention is to assist the family and includes referrals to Help Me Grow and parent-to-parent support. The goal of these services is to ensure that infants with hearing loss develop age-appropriate language, social, and cognitive skills.

In 2007, the Minnesota Legislature mandated newborn hearing screening and reporting of results to the MDH Newborn Screening Program. This legislation has allowed many more children to get the services they need by creating a comprehensive system of hearing screening and follow-up for all infants.

MDH Newborn Screening Program staff work to ensure that all infants are screened and that test results are promptly reported to the program. If the program receives a report that a child did not pass his or her hearing screen, staff confirm that the child is referred to an audiologist or other professional for diagnostic evaluations.

In 2013, the Minnesota Legislature approved a retention period of 18 years for hearing screening results and follow-up information for all children who are screened (See Minnesota Laws 2013, chapter 82, section 15).

Pulse Oximetry Screening for Critical Congenital Heart Disease

Congenital heart defects are the most common and the most lethal birth defects, accounting for nearly 30 percent of all infant deaths due to birth defects (1). The incidence of congenital heart defects is one in every 100 infants, with approximately 25 percent of these children having critical congenital heart disease (CCHD).

CCHD is defined as heart disease that requires surgery or intervention within the first year of life. Infants with CCHD are at significant risk for death or disability if their condition is not diagnosed soon after birth. In Minnesota, about 125 (or 18 per 10,000) newborns will have CCHD every year.

In 2013, pulse oximetry screening for CCHD in Minnesota became legislatively mandated. Before that time, screening for CCHD in well-baby nurseries was not done in most Minnesota birth facilities. By the end of 2014, all Minnesota birth facilities will be expected to have a CCHD screening program in place.

Before universal pulse oximetry screening, the only way to pick up CCHD after birth was through a physical examination. During this exam, if the healthcare provider heard a murmur or noticed other subtle signs of CCHD, the infant may have been referred for more testing. However, infants with CCHD do not always have these symptoms; therefore, about one-third of them were sent home undiagnosed. At home and without treatment, these infants can develop serious complications or die within the first days or weeks of life.

Newborn screening using pulse oximetry can identify infants with CCHD before they develop symptoms. Pulse oximetry is a non-invasive test that uses a sensor on the hand and foot to determine the infant's pulse rate and amount of oxygen in the blood. Low levels of oxygen in the blood can be a sign of CCHD. Once identified, infants with CCHD can be evaluated by pediatric cardiologists and receive care and treatment. Pre-symptomatic detection and treatment of CCHD can prevent death and disability, as well as reduce long-term healthcare costs.

After Newborn Screening: Storage and Use of Dried Blood Spots and Test Results in the United States

After blood spot screening is complete, a small amount of dried blood remains on the newborn screening card. The amount of blood left on the card after screening may vary depending on quality and quantity of the blood spots and the need for follow-up testing. The total amount of dried blood left on the filter paper is approximately 0.2 milliliters, which is equal to about 4 drops or 1/25 of a teaspoon

State newborn screening labs throughout the country keep and store the test results as well as the dried blood spots because of their continued value to the family, laboratory, and public health. The following is a description of the different uses:

For families, dried blood spots and test results may be used for further health-related tests for their children. For example, dried blood spots may be used to help determine the cause of disease in a child of their siblings or to help explain why a child died unexpectedly. Often, the unique nature of the newborn's dried blood spots allows

for information not otherwise available using later blood draws from the child. The dried blood spots may also be used in the case of a missing or deceased child, to help confirm the identity of the child.

Newborn screening programs most often use test results and dried blood spots for quality assurance and quality improvement within the laboratory. Quality assurance and quality improvement help newborn screening programs ensure that testing accurately detects the disorders, diagnoses are not delayed, and an overall high level of performance and program accountability is maintained. When blood spots are used for quality assurance and quality improvement, all private information, including demographic information, is removed, so laboratory staff cannot identify the infant. When performing quality assurance in the laboratory, it is necessary to use blood spots from a newborn. Adult blood samples cannot be used for this purpose. Analytes (the elements detected by the screening tests) found in newborn blood often differ from analytes found in adult blood. For example, newborn screening for the condition cystic fibrosis (CF) first looks at an enzyme called immunoreactive trypsinogen (IRT), which is usually elevated in children with CF. Since IRT disappears as a child matures and is usually not found in the body after two months of age, adult blood samples cannot be used by the Newborn Screening Program to perform the quality assurance needed for CF screening (2).

Newborn screening is not a diagnostic test. A diagnostic test is performed to determine the presence or absence of a disease when an individual shows signs or symptoms of the disease or after an abnormal screening test. A screening test, like newborn screening, on the other hand, is used to help identify individuals who do not have any symptoms and determine if they are at risk of having the disease. Screening tests are designed to be very sensitive; however, on rare occasions, the screening test fails to detect the disorder in an affected child. This is referred to as a ‘false negative’ result.

When the Newborn Screening Program receives a report from a healthcare provider that a child is affected with a disorder that should have been detected by newborn screening, laboratory staff members retest the infant’s dried blood spot to determine why the disorder was not identified properly. Retesting the dried blood spot and looking back at the child’s test results help to improve the Newborn Screening Program by providing valuable information for improving the test and/or the test cut-off values. This ongoing assessment makes screening better for future Minnesota infants and holds the laboratory accountable. False negatives can occur at any time, and in some cases, are not reported to the Newborn Screening Program until years after the child was born.

Preserving test results is another important part of program quality assurance and improvement. Examining test results over time helps the laboratory make changes that better serve all Minnesota newborns and families. Only

by examining many years' worth of information can the Newborn Screening Program truly function in a public health capacity. Looking at disorder trends improves the program, which ultimately helps save, improve, and extend the lives of Minnesota's youngest citizens.

Dried blood spots and test results are often used to develop new newborn screening tests that can help improve the health of even more children. Newborn screening has expanded from screening for just one condition (PKU) to including over 50 different serious and life-threatening conditions. The success of this expansion has come largely as a result of utilizing dried blood spots and test results to add testing for new disorders, which in turn, has increased the value of newborn screening to the nation's health. The addition of new disorders and the research involved to develop new tests is often driven by families of affected children who wish to contribute to helping save more infants.

Finally, dried blood spots and test results have the potential to be used for important public health research. Examples of research done on dried blood spots include looking at possible causes of childhood cancer as well as examining how exposure to toxic metals like mercury in the prenatal period may affect brain development. All requests to use specimens or information must be reviewed and approved by the Newborn Screening Program. If a request is for research or for any use other than program operations (as defined in Minnesota Statutes, section 144.125), an institutional review board or ethics committee must also review and approve prior to release of consented blood spots or test results.

As in all states, Minnesota's primary concern for dried blood spot and test result storage and use is maintaining security and protection of privacy while helping foster the attainment of valuable medical knowledge. Privacy protections and patient confidentiality laws ensure that blood spots and test results cannot be misused. Protecting the interests of the infants from whom the dried blood spots and test results are obtained is of the utmost importance. The Minnesota Newborn Screening Program adheres to the federal policy for human-subject research in the United States. This policy is in the Department of Health and Human Services regulations, 45 C.F.R. pt. 46, and is also known as the Common Rule. The Common Rule outlines the basic provisions for institutional review boards (IRBs), informed consent, and assurances of compliance.

Review of Current Law

The Minnesota Newborn Screening Program was established 49 years ago and is legislatively mandated under Minnesota Statutes, sections 144.125 to 144.128, and Minnesota Statutes, section 144.966. The law requires that all infants be tested for heritable and congenital disorders, including hearing loss and critical congenital

heart disease, unless the parent or guardian chooses to opt out of screening altogether. It also requires that birth providers educate parents of newborns about the benefits of newborn screening, the newborn screening process, retention practices, and parental options.

Historical Background of Current Law

Before 2006, blood spots and test results were stored indefinitely, however parents could elect to have their child's blood spots and/or test results destroyed after screening was complete. During this time, if any public health research or development of new tests for newborn screening was done, only de-identified or anonymized dried blood spots and test results were used.

In 2006, Minnesota Statutes, section 13.386 (the Genetic Privacy Act), was enacted. In a 2006-2007 rulemaking proceeding, an Administrative Law Judge raised questions about the application of section 13.386 to newborn screening. MDH subsequently sought clarification from the Legislature on this issue. MDH's 2008 legislative proposal clarified that the Newborn Screening Program could continue to do program operations for quality assurance and quality improvement and allowed some public health research. MDH's proposal was originally approved by Governor Pawlenty and passed by the Legislature. In the end, however, Governor Pawlenty vetoed the bill because of concerns about distinguishing between program operations and research, and specifically, what uses should be permitted without parental consent.

In March 2009, MDH was sued in state court by nine families, alleging violations of section 13.386 and violations of the state and U.S. constitutions. The lawsuit was dismissed by the District Court on November 24, 2009. On August 24, 2010, the Court of Appeals upheld the District Court ruling. The Minnesota Supreme Court overturned the District Court and Court of Appeals decisions with its November 16, 2011 ruling. The Supreme Court remanded the case back to the District Court to determine if there should be any remedies. While considering this case, the District Court ordered that all blood spots and test results received prior to the Minnesota Supreme Court ruling be preserved.

In January 2014, MDH reached a settlement with the families who had filed suit against the Newborn Screening Program. Under the terms of the agreement, MDH has returned the minor plaintiffs' blood spots and, within 120 days of the effective date of the settlement, will destroy the minor plaintiffs' test results.

MDH also agreed to pay a portion of the plaintiffs' attorneys' fees. The court made no determinations or awards, and has dismissed the case. As a result of the settlement, the District Court order to preserve the blood

spots and test results was lifted, and MDH destroyed approximately 1.1 million archived blood spots and is in the process of destroying over 2 million test results. These blood spots and test results were all collected prior to the November 16, 2011, Supreme Court decision and had been held in storage under court order since that time.

Current Law

In response to the Supreme Court ruling, the 2012 Legislature amended Minnesota Statutes, section 144.125, to create a retention period of 71 days from receipt of the sample for all blood spots with negative test results. Blood spots with positive test results have a retention period of 24 months from receipt of the sample. The legislation also created a retention period for test results (the information from the screening) of 24 months after reporting of the results. Blood spots must be destroyed within one week of the end of their retention period. Test results must be destroyed within one month of the end of their retention period. Within these given retention periods, the law dictates under what circumstances the blood spots or test results can be used, and limits the uses to those necessary for program operations only.

While the federal Common Rule permits research on anonymized specimens without informed consent, it does require consent should the study use any specimens that have associated identifying information. Minnesota law now requires written informed consent for all research and development of new screening tests, regardless of whether the dried blood spots or test results have been de-identified/anonymized or not.

Finally, the new legislation requires a parent or legal guardian's written informed consent for storage and use of blood spots and/or test results beyond the current retention periods. Written informed consent allows for storage and use until the child turns 18 or a revocation of consent is received by MDH. The consent form specifically states the purposes for which MDH may use the blood spots and test results, as described in statute. A review of current retention periods for both dried blood spots and test results throughout the United States can be found in Appendix F.

Adequacy of Current Law and Issues Encountered

Performing Quality Assurance and Quality Improvement (QA/QI)

The Association of Public Health Laboratories (APHL) asserts that there is no margin for error in newborn screening; precise analysis and complete follow-up are required to protect the health of children (3). To this end, the current law has presented several challenges to the MDH Newborn Screening Program's Quality Assurance (QA) and Quality Improvement (QI) efforts that are required to maintain and enhance the quality of testing and preserve program accountability. Some of the concerns around QA/QI include, but are not limited

to: the reduction of false positive and false negative results, the refinement of cut-off values, the application of second tier-testing, and the ability to effectively meet federal Clinical Laboratory Improvement Amendments requirements.

False Positives and False Negatives

A critical part of QA/QI in newborn screening focuses on those infants that test positive for a disorder, but are later found to not have it. These are called ‘false positives.’ Ongoing efforts to reduce false positive cases within the laboratory require continuous analysis of both negative and positive test results over time.

By looking at the typical test results for unaffected and affected infants, the laboratory can adjust the test’s cut-off values to better identify only those children who are truly affected, so-called ‘true positives’. Laboratories need to use their own methodologies, performance, and population to refine test cut-off values. Because many of the disorders on the newborn screening panel are rare, with only one or two affected children identified annually, two years does not produce enough information from which to make these decisions. Under current law, the Newborn Screening Program is losing this information, which is profoundly limiting to the Program and represents a loss of important and fundamental information that would benefit all Minnesota infants.

Without the ability to perform this type of quality assurance, the number of false positives in Minnesota is expected to rise. This increase in false positives harms both individual families and the medical system as a whole. Studies have shown that some parents whose children have a false positive result experience distress and are not reassured by normal follow-up testing. Additionally, studies examining health care utilization after a false positive newborn screening result illustrate an increase in outpatient visits (4). Other impacts of false positive results include, but are not limited to: increased parental anxiety; increased costs to parents; increased costs to society; increased burden on the medical system; decreased credibility of the Newborn Screening Program; and decreased trust of healthcare providers. When there are too many false positives, healthcare providers often make assumptions that a positive result is likely to be false, which also delays follow-up.

Another vital part of QA/QI in newborn screening examines those infants that screen negative for a disorder, but are later found to actually be affected. These are called ‘false negatives.’ The Newborn Screening Program’s goal is to identify every child affected with a disorder on the screening panel, so any missed cases are taken very seriously. When the Newborn Screening Program receives a report from a healthcare provider that a child is affected with a disorder that should have been detected by newborn screening, laboratory staff members retest the infant’s blood spot and look back at the test results to determine why the disorder was not identified

properly (see Background section). However, most false negative cases do not get reported to the Newborn Screening Program until well after the blood spot has been destroyed at 71 days, as is required under current law. This results in decreased program accountability and an inability to refine the testing process to prevent false negative results in the future. An example of the impact of the program's inability to investigate false-negative test results is included below in the section on 'Affecting Minnesota Families.'

Second-tier Testing

For some disorders on the Minnesota newborn screening panel, two separate tests may be performed before a result is considered abnormal. The first test is performed on all newborns, whereas the second test is only done if the initial test is abnormal. These second tests are known as 'second-tier tests,' and are performed using the original blood spot so that another sample does not have to be needlessly collected from the newborn.

Second-tier tests are more complex and look at additional elements in the blood that can help support or refute the initial test results. Second-tier tests are not typically used for primary screening because of cost and complexity. However, utilizing this two-tiered testing approach before reporting results helps confirm abnormal results, reduces reporting of false positive results, and improves the newborn screening experience for families. Because second-tier testing increases the cost of testing, it is important that appropriate cut-off values be set in order to reduce false positive results from the initial test. As mentioned above, test results collected over a long period of time are used to adjust cut-off values and two years does not provide enough information to do make these needed adjustments.

Federal Clinical Laboratory Improvement Amendments (CLIA) Requirements

The Federal Clinical Laboratory Improvement Amendments (CLIA) of 1988 regulate all laboratory testing conducted on human samples in the United States and cover approximately 239,000 laboratories throughout the country. The objective of CLIA is to ensure quality laboratory testing. All newborn screening laboratories must achieve and maintain CLIA certification in order to perform newborn screening (3).

Laboratories with CLIA certification must demonstrate that each test is accurate, precise, and able to distinguish between negative and positive results. The Minnesota Newborn Screening Program uses ten different types of tests, all of which must undergo internal validation checks. Each test must also have associated documentation, including records from the validation checks, to ensure the test is working properly and that the laboratory can provide the highest quality testing for all infants. These validations are a critical component of quality assurance. According to CLIA, the documentation and the records generated from checking the tests must be kept for as long as the laboratory instrument used to perform the test is used by the laboratory, which is often more than two years (5). In order to comply with the current state law, Newborn Screening Program Laboratory

staff must sort through all documentation and redact by hand identifying information so that the necessary equipment documentation can be retained in accordance with federal law, but in a form where individuals cannot be identified, which is required by state law. Ensuring compliance of both state and federal law in this way is adding significant time and costs to the basic operations of the program.

Obtaining Written Informed Consent for Extended Storage and Use

Under the current statute, written informed consent is required for developing new newborn screening tests or for public health research. Without consented blood spots and test results from enough individuals to represent the state's population, further understanding of diseases, potential treatments, and new test development may not occur. For example, implementing screening for severe combined immune deficiency (SCID) in Minnesota was delayed over a year because consented blood spots were not available to help develop the screen.

Obtaining written informed consent from an individual is more than just a signature on a form. The informed consent process involves three key components: 1) providing enough information so the individual can make an informed decision, 2) facilitating understanding by the individual, and 3) promoting a voluntary decision (6). Experts consulted for this legislative report consistently agree that implementing a true informed consent process would present a large administrative burden on Minnesota birth facilities. On average, the expert consultants estimated that each consent discussion would take 15-30 minutes to complete, which would result in an additional cost of about \$300 per infant.

There are currently two state newborn screening programs, Michigan and Texas, who have implemented policies requiring written informed consent to use the dried blood spots for research purposes. In these states, new test development is not considered research use. In Michigan, all dried blood spots and test results are stored for over 20 years and used for program operations, including test development, without consent. Consent is obtained from parents only for research use outside of newborn screening as part of Michigan's BioTrust for Health (7). The BioTrust is the product of a multi-year initiative to improve preservation and utility of dried blood spots from newborn screening. Recent data from Michigan shows that 59.2 percent of parents have consented to participate in the BioTrust, with decreased participation from the homebirth community and the neonatal intensive care units. Additionally, reports from consultants working with the Michigan program indicate that there are high levels of ethnic disparities in consent rates, an observation they will publish soon.

In Texas, blood spots are kept for two years, unless parents consent to longer storage and use. All test results are kept for 21 years regardless of consent. Consent is obtained from parents only for storage of blood spots past two years and for use in public health research. Recent data from Texas shows that about only 50% of consent

forms given to parents are returned. Of those that are returned, 74% of parents consent to the research use of their child's blood spots. Texas is still working on their educational efforts around long-term storage and use and hope to increase the low return rate of consent forms with increased education and training.

Consultants across the country have indicated that implementing consent for storage and use of blood spots and test results is not a race-neutral policy. Disparities in consent exist for a variety of reasons, including: mistrust of the healthcare system, stereotypes on the parts of the provider and patient, access to care, and communication barriers (8). Because of these issues, non-English speaking families may not reap the benefits of subsequent research since they will not be represented in the samples or test results, resulting in increased health disparities in the state.

Providing Long Term Follow-up for Disorders on the Newborn Screening Panel

According to the Clinical and Laboratory Standards Institute, an effective and complete newborn screening system is comprised of six segments: testing, follow-up, diagnosis, treatment and/or management, evaluation, and education. Newborn screening follow-up can be further divided into two broad categories: short-term follow-up and long-term follow-up (LTFU). The primary aim of newborn screening is to provide early treatment and intervention to affected newborns; LTFU is the means by which the effectiveness of interventions and the accountability of newborn screening programs can be ensured. LTFU helps determine if newborn screening programs are sustaining their main aims of preventing mortality and mitigating morbidity.

LTFU involves the assurance and provision of quality disease management, disorder-specific treatment, and age-appropriate preventive care. Activities that help ensure appropriate LTFU include: engaging affected individuals and their families as partners in care management, performing continuous quality improvement, gaining knowledge into pathophysiology and treatment options, and evaluating information related to care and outcomes. Such follow-up is vital to the evaluation of newborn screening benefits throughout the life of an individual, as well as to the family and society (9). The suggested timeframe for providing LTFU in the United States is through the age of 21(10).

Minnesota's current law does not allow access to information beyond two years from the date the results were reported, even for LTFU purposes. This impairs the ability of Minnesota's LTFU program to assist families of a child with a confirmed diagnosis in coordinating medical care, connecting affected individuals to effective treatment options, reducing health disparities, and meeting their public health mission. The LTFU program has looked at consent options for this population and addresses this below.

Care Coordination through a Medical Home

All individuals with a disorder diagnosed by newborn screening should have their care managed through a medical home because of the complex, multi-care specialist involvement that is often required. A medical home is vital for helping families navigate the medical system and coordinate all of their health care visits. According to the Health Resources and Services Administration, access to a medical home improves health outcomes, reduces emergency room visits, and allows for better communication between families and pediatric health professionals (11). The goal of a LTFU program is to ensure that each affected individual has a medical home so that care can be effectively managed.

Without access to information about children who have been diagnosed with one of the disorders on the newborn screening panel beyond two years, the LTFU program cannot ensure that each child has a medical home and receives effective and coordinated care. It is crucial that all children, no matter their race or income, receive the highest quality of integrated care.

LTFU programs also ensure that families receive the services – financial, social, and family support – that they may be eligible for and/or desire. Research shows that children with special health needs (which include children with a condition diagnosed through newborn screening) have a higher degree of unmet clinical needs than the general population, and have a higher need for services (12). These services, such as medical assistance, transportation, and family support groups, have been shown to improve access to medical care for children with special health needs (13; 14). Minnesota’s LTFU program offers connection for families to family support groups, and in cases where no support group otherwise exists, LTFU program staff have created disorder-specific family support groups. The LTFU program is in a unique position to be knowledgeable about all of the financial, social, and family support services that are available nationally, statewide, and locally, so families do not have to figure this out on their own. Without access to follow-up information beyond two years, it is impossible to offer these services to families as their needs change, which will result in additional and unnecessary burdens for the family.

QA/QI and Reducing Health Disparities

LTFU programs provide QA/QI to the newborn screening process by identifying gaps in clinical care and services. Through consultation with providers, LTFU helps to improve care delivery for children diagnosed with one of the disorders on the newborn screening panel.

The LTFU program has also identified health inequities in care and services through their ongoing contacts with families and providers. The program found significant health inequities, particularly among recent immigrant groups (Hmong), African Americans, and Native Americans. These groups have poorer access to services and worse health outcomes than Whites. The LTFU program is addressing these health inequities by examining access to services and health outcomes across geographic areas and socioeconomic status. Without access to LTFU information throughout the childhood period, it is not possible to continue to identify and address health inequities in clinical care and service provision to children with a newborn screening disorder and their families.

Written Informed Consent for LTFU

In an attempt to maintain their quality of service to Minnesota families while complying with current state law, the LTFU program has developed a consent policy for opting-in to long term follow-up information storage and use beyond two years of age. This LTFU consent is separate from the consent required for storage and use of the newborn screening blood spots and test results. The policy has been in effect since late October 2013. Based on feedback received from specialists and the limited consent uptake seen thus far (less than 20 percent), a consent policy is not an effective solution nor does it allow for staff to adequately perform long-term follow-up as defined by the US Secretary of Health and Human Services' Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children (10).

The LTFU program has worked with specialty clinicians to ask for their assistance in asking families with affected children for consent to long-term follow-up information storage. Clinicians informed the LTFU program that the process of obtaining proper informed consent would take approximately 15-30 minutes per family. Clinicians further felt that they did not have the time needed within the allotted clinical visit to approach families for consent as doing so would take away from discussing medical issues. As a result, most indicated that it would not be possible for them to help the LTFU program obtain consent from families. The LTFU program has asked families for consent via post mail and email; preliminary results indicate that the response rate using these methods is low. Seeking consent in person by program staff is not possible because program staff do not meet with the majority of families. Because of the rarity of the disorders on the newborn screening panel, lacking sufficient records can skew the data and result in incorrect conclusions, and thus misguided programmatic decisions. Furthermore, insufficient records may lead to health inequities if the data disproportionately represents one socio/economic/geographic group. Many families can take a few years to develop a complete understanding of the disorder affecting their son or daughter, which, in turn, may delay their acknowledgement of the need for LTFU. These families that later would like to receive direct LTFU benefits,

such as connection to LTFU-led parent support groups or clinical trials that may benefit their child, would not have the mechanism by which to do so because contact between LTFU and the family would have been lost.

The LTFU program does not have an avenue or the resources with which to seek consent in person from all families who have a child diagnosed with a disorder on the newborn screening panel. Nor does the LTFU program have the ability to obtain consent from families with affected children that are older than two years old, so the LTFU program will lose all information on those children.

Affecting Minnesota Families

The shorter retention periods for both blood spots and test results required by current state law have already negatively impacted several Minnesota families due to the program's inability to retrieve vital information. Parents have previously asked to use saved blood spots and test results to help diagnose a disease in their child, for research, or to find reasons for their child's untimely death. Clinicians interviewed for this report also noted that they have used samples and test results many times prior to the current law to help understand a child's illness, often when a child was many years old. A few examples of these familial uses are presented below:

A False Negative

In July 2013, the Newborn Screening Program was notified of a one-year-old infant who had recently been admitted to the emergency room. The Program was told by the infant's medical specialist that the child had symptoms of a serious metabolic disorder that can be found by newborn screening. The child's newborn screening result was pulled and it was confirmed that all screening results had been normal.

A couple months later, Newborn Screening Program staff received word that the child had indeed been diagnosed with the disorder and that the family wished to have their child's blood spot pulled for reanalysis. A consent form was signed and sent to MDH in September of 2013. However, since the child's newborn screening result had been normal, the blood spots had already been destroyed and were no longer available. Had the blood spots been available, they could have been used to help improve the testing for this disorder and give the family answers as to why their child was not identified by newborn screening.

Seeking an Answer

A family with a child diagnosed with hearing loss faces many uncertainties, such as how best to help their child communicate and what intervention will work best for their family. Following a diagnosis, it is not uncommon for a family to search for the cause of their child's hearing loss. Congenital hearing loss has several possible

causes – genetics, trauma, environment, or a prenatal infection. If the first three causes of hearing loss are ruled out, the last option is to try to determine whether an infection was present at birth. The most common infection in newborns that causes hearing loss is cytomegalovirus (CMV). Newborns exposed to CMV before birth (congenital CMV) are at risk for multiple health problems, including hearing loss. Infants and children infected with CMV after birth rarely have any of these health problems. Unfortunately, symptoms of congenital CMV do not appear until two or more years after birth, making it very difficult to determine whether the infection was congenital or occurred later after birth. Currently, the only way to determine if the infection was present before birth is to use newborn screening dried blood spots. Blood spots have proven to be valuable and effective in diagnosing congenital CMV, which benefits families by providing effective treatment options and answers to their child's hearing loss.

Given that symptoms of congenital CMV do not appear until two or more years after birth, under current law, a child's blood spots will have already been destroyed. This not only restricts advances in understanding this infection for all Minnesota newborns, but it also prevents the child's family from obtaining an answer they desperately wish to know.

A Lost Child:

The day after the destruction of the 1.1 million archived blood spots, Newborn Screening Program staff received a call from Stacy Nugent, who then shared the following story via email:

Paige was our only child. She was born healthy. At around the age of 10 months, she had a seizure. I believe she had one or two more in the next month or two. Her doctor told us not to worry and that it was normal, that she'd outgrow it. We went to a neurologist as well just to be sure. He reassured me of the same thing.

Paige was smart and articulate.

At 8:00 am on March 10, 2010, I received a call from my husband while I was settling in at work that will forever haunt me. He was yelling that Paige wasn't breathing. He was going to drive her to the hospital. When I made it there, they informed me that she was gone. That she had been gone, probably passing sometime around 3-4:00 am. The police questioned us. Our medical examiner was so kind and promised me she'd find out what happened. None of it made sense. Kids do not just die. Paige was 2 years, 1 month and 5 days old. SIDS was supposed to stop at 1 year old. None of it made sense.

Our medical examiner had just heard of Sudden Unexplained Death in Childhood (SUDC) a couple of weeks beforehand. She was familiar with what she needed to do from a pathology perspective. It was a couple of days later that she told us that she thought Paige had died of SUDC. The problem is that SUDC isn't a true cause of death. She told us that it simply meant they didn't know. She said that many kids with a SUDC diagnosis have seizures or heart issues, but the research was still so new that it was difficult to make any conclusions at this time. My husband and I submitted our blood samples to the SUDC research program to try to get answers. Those results were negative.

Our subsequent daughter, Presley, was born in 2011 - 14 months after Paige died. I was a wreck from the moment she was born because I still didn't know why Paige had died, and thus, I really didn't have a way to prevent the same thing from happening to Presley. We did pursue genetic testing for Presley in regards to heart issues, and my husband and I also decided to have ourselves tested, but everything came back negative. We asked if they could test Paige's newborn screening blood spots, but at that time, the technology wasn't quite there yet. They told us to hang tight, because they didn't want to waste her blood spots until the science was further along. Unfortunately, this technology is now available, but Paige's blood spots are not.

It is difficult to be good parents to Presley when you feel like the grim reaper is around every corner. I just wish that I had some answers. After almost four years, I've come to a point where I can accept that I may never know what happened to Paige. We're good parents; actually, we're exceptional parents. Both of my daughters were planned; therefore, I did everything that I could to ensure the best prenatal care. I am an educated professional with a master's degree who researches everything so that I can be an active advocate for my children's health. Unfortunately, I still feel helpless. I wish we knew then what we know now. This is the type of situation where you never know what you may need (blood spots, samples, etc.) until you have just experienced the worst thing imaginable. I hope that other parents won't have to deal with this, but unfortunately, too many will; they just don't know it yet.

Conducting Public Health Research

While dried blood spots and test results are most often used for quality assurance and improvement and for the benefit of individual families, they can also be used for medical and public health research to better understand the causes of disease, impacts on health care costs, and possible factors that contribute to the health of the state's residents. This information allows states to better address public health issues, reduce health care costs associated with screening and follow-up, or find treatments for disease.

Dried blood spots and test results from newborn screening programs provide states with an unbiased, complete sample that is necessary to perform population-based research. The most informative and accurate research studies are the result of very large, unbiased sampling. Finding such a broad, unbiased representation of the population is virtually impossible to achieve outside of newborn screening dried blood spots and test results.

Historically, when blood spots and/or test results have been used for research, the following criteria must have been met:

- The study must help to better understand diseases or improve public health
- The study must be approved by an Institutional Review Board (IRB)
- The blood spots and/or test results are de-identified, so the researchers don't know whose information is being used. Researchers are not given information that can point to one person, unless informed consent has been received.

At this time, a blood spot alone cannot be used to identify a person. If science advances to a point where a blood spot alone can identify a person, policies nationally and statewide will change.

Numerous experts interviewed for this report indicated that destroying blood spots and test results will have a significantly negative impact on public health research and patient care. Opportunities for clinicians and researchers to learn more about pediatric illness will be lost, finding effective treatments may be delayed, and Minnesota will become less competitive when it comes to getting grant money for research.

Storage and Use Models

Interviews with a variety of medical research experts and with parents (see Appendix B), and discussions with agency staff, revealed various models for a comprehensive and sustainable storage and use plan for newborn screening blood spots and test results. Based on these interviews and the information gathered, three possible models were developed and are discussed below. These models are also presented in Table 1 on page 28.

Option One: Current Law

No changes are made to the current law in Minnesota Statutes, section 144.125. Under this model, the standard retention period for dried blood spots is 71 days if the results are all negative and two years if the results are positive. All test results, regardless of outcome, are destroyed at two years. During these periods, dried blood spots and test results without patient consent can only be used for program operations as currently defined in Minnesota statute. As mentioned in the ‘Adequacy of Current Law and Issues Encountered’ section of this report on pages 15-25, this model has resulted in serious concerns from both a program and citizen perspective. Written informed consent from the family is required for any extended storage beyond the current retention periods or for use outside of testing and program operations.

MDH and the majority of those interviewed believe that maintaining current law will be detrimental to the program and will result in harm to Minnesota children and their families. Several interviewees noted that current law has weakened the program, made the state and healthcare providers less accountable, and has resulted in negative consequences for families.

Option Two: Complete Opt-Out

Minnesota Statutes, section 144.125, is amended to be an opt-out program for long-term storage, for certain newborn screening uses, and for other public health uses with de-identified dried blood spots and test results. Under this model, the standard retention period for dried blood spots and test results, regardless of result, would be 18 years. During this period of time, families would have the option to opt out of storage and use of their child’s blood spots and/or test results. If a family did not exercise their option to opt out, the de-identified blood spots and/or test results could be used for program operations as currently defined in Minnesota statute, as well as new test development and public health research. Written informed consent would still be required for public health studies involving identifiable information. While some of the medical, research and data privacy experts interviewed suggested that this model still protects privacy and alleviates issues arising with the current law, a few felt that written informed consent should still be part of this process for any research use. Those who felt written informed consent should be required for all public health research felt that consent for research use is a standard of practice in most medical settings, and that newborn screening programs should follow suit.

Option Three: Research Opt-In

Minnesota Statutes, section 144.125, is amended to extend standard retention periods for both dried blood spots and test results to 18 years. During this time, specimens and test results can only be used without consent for

program operations as defined in section 144.125, subdivision 5. Written informed consent would be necessary for any further use. This model allows for samples and test results to be available to families should they unexpectedly need them, but maintains a consent process for the development of new tests and public health research uses. This is similar to the model currently employed by the state of Michigan; however, new test development is not considered research under their policy, so consent is not needed for the purpose of developing new tests in Michigan.

Table 1: Three Models for Comprehensive and Sustainable Long-Term Storage and Use of Dried Blood Spots and Test Results

Model	Standard Blood Spot Retention Period	Standard Test Results Retention Period	Permissible Uses without Consent	Consent for Storage	Consent for Further Use	Fiscal Impact
Current Statutory Requirements	71 days for negative results; 2 years for positive results	2 years	Program Operations as defined in 144.125 only	Required past 71 days/2 years	Required past 71 days/2 years	Baseline
Complete Opt-Out	18 years	18 years	Program Operations as defined in 144.125 as well as de-identified Research Use	Not Needed	Only Needed for Research Use with identifiable blood spots or test results	Negligible
Research Opt-In	18 years	18 years	Program Operations as defined in 144.125 only	Not Needed	Required for any use outside of Program Operations as defined in 144.125	Negligible

Education Strategies and Addressing Privacy Concerns

Interviewees offered numerous insights on strategies to inform the public about newborn screening and dried blood spot/test result storage and use. Overall, the general consensus was that education should occur at numerous times, be transparent, and be clear and accessible. Educational efforts that are currently being employed by MDH or will be employed in the near future would include, but are not limited to:

Prenatal Education

Prenatal education is an important avenue for educating parents-to-be about newborn screening. Several recent studies indicate that prenatal education of newborn screening services is very important and yet is inadequately covered. In a study conducted in Wisconsin, only 13 percent of parents recalled receiving information about newborn screening prenatally (15). Many families recommended prenatal education of newborn screening, including both verbal and written information. Specifically, parents wanted to receive education on: what newborn screening is, why it is important, diseases tested for, when parents can expect results, and the meaning of abnormal results. Lastly, that study reported that mothers with “lower income” were 3.7 times less likely to receive prenatal newborn screening education than those with higher income. Another study found that parents wanted information in the third trimester, presented by the primary care provider, and accompanied by a “concise, easy-to-read brochure with contact information” (16). That study also identified language as a major barrier in education.

MDH has already developed specific prenatal education materials aimed at expectant parents, primary care providers, midwives, and obstetricians. These materials include a healthcare provider education folder that explains the risks and benefits of newborn screening and storage and use options. Inside the folder are simple, concise, and easy-to-understand handouts for each expectant parent to take home. The handout has information about newborn screening and contact information for the Newborn Screening Program in case the parents have questions. These materials are being widely used by prenatal healthcare providers and are available on the Newborn Screening Program’s website.

If a new storage and use model is chosen, MDH will develop a simple, concise, easy-to-read brochure that clearly explains newborn screening storage and use practices. The brochure will include the benefits and risks of blood spots and test results storage and use, and a clear and simple table showing the family’s options. The brochure will also include contact information for the program. This brochure will be distributed to primary care providers, midwives, pediatricians, and obstetricians for them to use as a reference, as well as for them to distribute to expectant parents.

Knowledge of newborn screening is particularly low among populations of color and American Indians. MDH is currently working with specific clinics in that serve populations of color and American Indians, and with community group leaders, to develop ways of better educating racial and ethnic groups where language, social customs, or both can serve as an impediment to understanding the benefits, risks, and choices associated with newborn screening.

Public Awareness

MDH is currently exploring different ways of delivering concise and simple messages about newborn screening to the public. Ideas under consideration include billboards, radio public service announcements, public transit venues such as bus stop benches, and spaces inside both buses and light rail. This could be a particularly effective means of educating specific populations that show a low understanding of newborn screening, such as populations of color and American Indians. Public awareness campaigns would be done to ensure that all geographic areas of MN are properly represented, as well as all diverse communities.

Social Media and Videos

Historically, the traditional means of education has been by paper documents – flyers, brochures, etc. Today, there are an increasing number of ways to effectively educate individuals. In particular, many studies have shown that social media can more effectively transmit information than traditional print media. MDH has both Facebook and Twitter accounts, and both are used regularly to educate followers about newborn screening. MDH is also exploring ways of producing short, concise, and easy to understand videos about newborn screening and parental options to be posted on MDH’s YouTube channel. These videos can then easily be used by health care professionals, or accessed directly by the general public.

Training Providers and Submitters

MDH Newborn Screening Program staff members have no direct contact with expectant or new parents. Therefore, the Program relies on healthcare providers and birth center screening staff to deliver information to expectant parents and new parents about newborn screening. This is a challenge because of the diversity of healthcare providers involved – primary care providers, obstetricians, pediatricians, nurses, doulas, midwives, birth educators – and because of the large number of birth centers in MN, resulting in different policies across healthcare provider systems and individual centers.

MDH has also developed several fact sheets about newborn screening, both for providers and for parents. The parent fact sheet provides a broad overview of newborn screening, its benefits and risks, storage and use options, and program contact information. The provider fact sheets go into more detail than the education folder or parent fact sheet, and contain more specific information about the conditions screened for, how the test results are reported, and what the next steps are in the case of a positive screen. The fact sheets also contain contact information for the Newborn Screening Program in case the provider has questions.

The MDH Newborn Screening Program's website contains detailed information about the roles and responsibilities of providers. This section of the Program's website reviews what providers should tell expectant parents about newborn screening, and also contains all the educational materials that providers can access and print for parents.

The MDH Newborn Screening Program will continue to develop education materials for healthcare providers and screening staff. MDH is currently assessing alternative education methods, such as short training videos.

Access Plans and Protocols

As part of this report, the legislature directed the Newborn Screening Program to discuss plans and protocols for clinical and research access to test results and dried blood spots. The following components are keys to this aspect of long-term storage and use:

Institutional Review Board

An Institutional Review Board (IRB) is tasked with reviewing, approving, and monitoring biomedical and behavioral research involving humans. The Food and Drug Administration and the Department of Health and Human Services empower IRBs to approve, require modifications in planned research prior to approval, or disapprove proposed research. The purpose of an IRB review is to ensure that researchers take the appropriate steps to protect the rights and welfare of humans participating in a research study, both prior to research and periodically during research. An IRB proposal review examines the methods and the ethics of the proposed research; ensures fully informed and voluntary participation by the subjects in cases where identifiable information is used, and guarantees that the subjects will be as safe as possible. MDH has an IRB that reviews, approves, and monitors all research studies done at MDH. In addition, all accredited research institutions have and use an IRB to ensure their researchers are conducting ethical and safe research. IRBs are typically composed of at least five individuals: at least one scientist and one non-scientist; at least one "community member" (someone not affiliated with that IRB's institution); and both men and women.

Researchers seeking use of newborn screening test results and/or bloodspots would require approval from the MDH Newborn Screening Program, the MDH IRB, as well as the researcher's IRB. This is true for research using both identifiable and de-identified data.

Community and Scientific Advisory Boards

Access to newborn screening samples and test results for scientific investigation would follow the rigorous IRB process described above. Experts interviewed felt that national and state regulations were already in place to protect individuals participating in research, but that utilizing a community advisory board, as well as a scientific advisory board, would be beneficial and make the process more transparent. A community advisory board would be made up of representatives from different groups and communities who would work with MDH to balance privacy and the public good. The scientific advisory board, on the other hand, would assess the scientific merit of any proposed studies. This board would help ensure that the dried blood spots and/or test results are being used for the benefit of the public and only when there is real scientific value in what is being proposed. This is the model of oversight currently used with the Michigan Biotrust for Health and it has proven successful.

Clinical Access

As is currently the case, families or healthcare providers wishing to utilize a child's dried blood spot or test results for further health-related testing would be able to make this request with consent from the family. Dried blood spots or test result information would not be released for these purposes without the knowledge of the family.

Conclusion

This report and interviews with numerous medical, research, and data privacy experts have identified a number of concerns with the retention periods defined in current law. Therefore, Option One presented on page 26 is not recommended. Options Two and Three (see pages 26-27) are broadly described above. The development and implementation of either of these models could vary considerably in detail. The public's health and privacy concerns must be weighed and balanced. MDH recommends that the Legislature evaluate the options and strike a balance with support from various constituencies that is sufficient to ensure the improvement and maintenance of the Newborn Screening Program for the long term.

Glossary

Abnormal test result: This result means that the baby's screening test showed signs that the baby may be at higher risk of having a condition. The child should have additional testing to confirm or rule out the condition.

Anonymized: The removal of any identification that may link a sample to a specific individual

Congenital disorder: A disorder that is present at birth. The causes of a congenital disorder include infection, injury, genetics, environmental factors, and others.

Cut-off values: The value that marks the difference between a positive and a negative result.

Cystic Fibrosis: An inherited disease characterized by the buildup of thick, sticky mucus that can damage many of the body's organs.

False negative: A result that comes back normal when the disease is in fact present. An example of a false negative would be if a particular test designed to detect PKU returns a negative result but the person actually does have PKU. An example of a false negative from everyday life would be when your household smoke detector does not sound when you have a fire in your home. This would be a serious problem.

False positive: A result that indicates the child may have a condition when, in fact, they do not. An example of a false positive from everyday life would be when your household smoke detector sounds when you burn the toast. This is annoying, but not as serious as a false negative.

Filter paper: A porous paper that is used to collect and store the baby's blood for newborn screening. Blood collected on filter paper is dried before being sent to MDH for testing.

Genetic disorder: An illness caused by one or more abnormalities in genes or chromosomes.

Genetic Counselor: A trained provider who helps families understand and adapt to the medical, psychological, and familial implications of genetic diseases.

Help Me Grow: The Early Intervention program in Minnesota.

Heritable (inherited) disorder: This describes a condition that is caused by an absent or abnormal gene or by a chromosomal defect that is passed from parent(s) to child.

Incidence: The occurrence, rate, or frequency of a disease.

IRB: Institutional Review Board. Committees that review all research projects and make sure that privacy protections are in place and the risks to people are as low as possible.

Medical home: A team-based health care delivery model that provides comprehensive and continuous medical care to patients with the goal of obtaining maximized health outcomes.

Metabolic disorder: A disorder in the way the body breaks down food or other products (metabolism).

MCAD: Medium-chain acyl-CoA dehydrogenase (MCAD) deficiency is a condition that prevents the body from converting certain fats to energy, particularly during periods without food (fasting).

Morbidity: Refers to the disease state of an individual, or the incidence of illness in a population

Mortality: Refers to the state of being mortal, or the incidence of death (number of deaths) in a population.

Negative test results: A negative result means the baby's newborn screen did not show any signs of the conditions included on the newborn screening panel.

Non-invasive test: A medical test or procedure that does not require a doctor to insert any device through the skin or into a body opening.

Parent-to-Parent support: Programs that match parents with similar concerns to provide emotional and informational support.

PKU: Phenylketonuria (commonly known as PKU) is an inherited disorder that increases the levels of a substance called phenylalanine in the blood. Phenylalanine is a building block of proteins (an amino acid) that is obtained through the diet. Babies with PKU cannot metabolize phenylalanine and are slowly poisoned by it, unless they keep to a strict diet low in phenylalanine.

Positive test result: This result means that the baby's screening exam showed signs that the baby may be at higher risk of having one or more of the conditions included on the newborn screening panel. This does not mean that the baby definitely has a medical condition. Follow-up testing must be performed immediately to determine if a condition is actually present.

Pulse Oximetry: A machine that will indicate a child's pulse and oxygen saturation level. It used to screen for Critical Congenital Heart Disease (CCHD).

Quality control: Process to detect, reduce, and correct deficiencies in a laboratory's internal analytical process prior to the release of patient results, in order to ensure the quality of the results reported by the laboratory.

Treatable condition: A condition with a known treatment that can improve the survival and/or quality of life of an individual.

Validation checks: The process to ensure that a test accurately measures what it is supposed to measure.

Literature and Resources Cited

1. Broussard CS, Gilboa SM, Lee KA, Oster M, Petrini JR, Honein MA. Racial/Ethnic Differences in Infant Mortality Attributable to Birth Defects by Gestational Age. *Pediatrics*. 2012; 130:e518-27.
2. Colombo C, et al. Serum levels of immunoreactive trypsin during development: comparison with levels of lipase and amylase. *J Pediatr Gastroenterol Nutr*. 1989; 2:194-9.
3. “Quality Assurance in Newborn Screening.” *Association of Public Health Laboratories*.nd. Web. 2013.
4. Tarini BA, et al. False-positive newborn screening result and future health care use in a state Medicaid cohort. 2011; 128(4): 715-22.
5. Clinical Laboratory Improvement Amendments of 1988. 42CFR§493.1105(a)(3-6).
6. “Informed Consent.” *U.S. Department of Health & Human Services*.nd. Web. 2013
7. Langbo C, Bach J, Kleyn M, Downes FP. From newborn screening to population health research: implementation of the Michigan BioTrust for health. *Public Health Rep*. 2013; 128(5):377-84.
8. Larson EL, Cohn EG, Meyer DD, Boden-Albala B. Consent administrator training to reduce disparities in research participation. *J Nurs Scholarsh*. 2009; 41(1):95-103.
9. Clinical and Laboratory Standards Institute. *Newborn Screening Follow-Up; Approved Guideline – Second Edition*. Published 2013.
10. Kemper A, et al. Long-term follow-up after diagnosis resulting from newborn screening: Statement of the US Secretary of Health and Human Services’ Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children. *Genet Med*. 2008; 10(4): 259-261.
11. Homer C.J., et al. A review of the evidence for the medical home for children with special health care needs. *Pediatrics*. 2008; 122(4) e922-e937.
12. Mayer ML, Cockrell Skinner BS, Slifkin R. Unmet Need for Routine and Specialty Care: Data From the National Survey of Children with Special Health Care Needs. 2004; 113(2): e109-115.
13. Kogan MD, et al. Association Between Underinsurance and Access to Care Among Children With Special Health Care Needs in the United States. *Pediatrics*. 2005; 116(5): 1162-1169.
14. Van Dyck PC, et al. Prevalence and Characteristics of Children With Special Health Care Needs. *Arch Pediatr Adolesc Med*. 2004; 158(9): 884-890.
15. Tluczek A, et al. Newborn screening: an appeal for improved parent education. *J Perinat Neonatal Nurs*. 2009; 23(4): 326-34.
16. Davis TC, et al. Recommendations for Effective Newborn Screening Communication: Results of Focus Groups with Parents, Providers, and Experts. *Pediatrics*. 2006; 117(s3): S326-340.

Appendices

Appendix A

Minnesota Laws 2013, chapter 82, section 39:

Sec. 39. NEWBORN SCREENING PROGRAM STUDY.

(a) The commissioner of health, in consultation with the medical research and advocacy groups identified in paragraph (b), shall review the newborn screening programs in Minnesota Statutes, section 144.125, and evaluate the scientific and medical validity of a comprehensive and sustainable long-term storage and use plan for the test results under Minnesota Statutes, section 144.125. The commissioner shall consider the following:

- (1) peer-reviewed medical research into the diagnosis and treatment of heritable and congenital disease;
- (2) strategies for education of parents and families about the utility of advancing new knowledge through research on blood spots and test data made possible by long-term storage and use;
- (3) plans and protocols for clinical and research access to test result data;
- (4) minimizing the administrative burden on hospitals and health care providers in the operation of the newborn screening program;
- (5) the adequacy of current law on the standard retention period for test results under Minnesota Statutes, section 144.125, subdivision 6; and
- (6) privacy concerns associated with parental consent options and long-term storage and use of blood samples and test data.

(b) As part of the evaluation, the commissioner shall consult with medical research and data privacy experts, including, but not limited to, specialists in metabolic care, immunology, pediatrics, epidemiology, nutrition, pulmonology, cardiology, endocrinology, hematology, hearing care, and medical genetics, as well as patient advocacy and data privacy groups.

(c) By February 1, 2014, the commissioner shall submit a report to the chairs and ranking minority members of the senate and house of representatives committees and divisions with primary jurisdiction on health and human services and data privacy on comprehensive and sustainable long-term storage and usage of the test results.

(d) The commissioner shall conduct the evaluation required under this section within existing appropriations.

144.125 TESTS OF INFANTS FOR HERITABLE AND CONGENITAL DISORDERS.

Subdivision 1. **Duty to perform testing.** (a) It is the duty of (1) the administrative officer or other person in charge of each institution caring for infants 28 days or less of age, (2) the person required in pursuance of the provisions of section 144.215, to register the birth of a child, or (3) the nurse midwife or midwife in attendance at the birth, to arrange to have administered to every infant or child in its care tests for heritable and congenital disorders according to subdivision 2 and rules prescribed by the state commissioner of health.

(b) Testing, recording of test results, reporting of test results, and follow-up of infants with heritable congenital disorders, including hearing loss detected through the early hearing detection and intervention program in section 144.966, shall be performed at the times and in the manner prescribed by the commissioner of health.

(c) The fee to support the newborn screening program, including tests administered under this section and section 144.966, shall be \$135 per specimen. This fee amount shall be deposited in the state treasury and credited to the state government special revenue fund.

(d) The fee to offset the cost of the support services provided under section 144.966, subdivision 3a, shall be \$15 per specimen. This fee shall be deposited in the state treasury and credited to the general fund.

Subd. 2. **Determination of tests to be administered.** The commissioner shall periodically revise the list of tests to be administered for determining the presence of a heritable or congenital disorder. Revisions to the list shall reflect advances in medical science, new and improved testing methods, or other factors that will

improve the public health. In determining whether a test must be administered, the commissioner shall take into consideration the adequacy of analytical methods to detect the heritable or congenital disorder, the ability to treat or prevent medical conditions caused by the heritable or congenital disorder, and the severity of the medical conditions caused by the heritable or congenital disorder. The list of tests to be performed may be revised if the changes are recommended by the advisory committee established under section 144.1255, approved by the commissioner, and published in the State Register. The revision is exempt from the rulemaking requirements in chapter 14, and sections 14.385 and 14.386 do not apply.

Subd. 3. Information provided to parents. (a) The department shall make information and forms available to health care providers who provide prenatal care describing the newborn screening program and the provisions of this section to be used in a discussion with expectant parents and parents of newborns. The department shall make information and forms about newborn screening available to the persons with a duty to perform testing under this section and to expectant parents and parents of newborns using electronic and other means.

(b) Prior to collecting a sample, persons with a duty to perform testing under subdivision 1 must:

(1) provide parents or legal guardians of infants with a document that provides the following information:

(i) the benefits of newborn screening;

(ii) that the blood sample will be used to test for heritable and congenital disorders, as determined under subdivision 2;

(iii) the data that will be collected as part of the testing;

(iv) the standard retention periods for blood samples and test results as provided in subdivision 6;

(v) that blood samples and test results will be used for program operations during the standard retention period in accordance with subdivision 5;

(vi) the Department of Health's Web site address where more information and forms may be obtained; and

(vii) that parents have a right to elect not to have newborn screening performed and a right to secure private testing;

(2) upon request, provide parents or legal guardians of infants with forms necessary to request that the infant not have blood collected for testing; and

(3) record in the infant's medical record that a parent or legal guardian of the infant has received the information provided pursuant to this subdivision and has had an opportunity to ask questions.

(c) Nothing in this section prohibits a parent or legal guardian of an infant from having newborn screening performed by a private entity.

Subd. 4. Parental options. (a) The parent or legal guardian of an infant otherwise subject to testing under this section may elect not to have newborn screening performed.

(b) If a parent or legal guardian elects not to have newborn screening performed, then the election shall be recorded on a form that is signed by the parent or legal guardian. The signed form shall be made part of the infant's medical record and a copy shall be provided to the Department of Health. When a parent or legal guardian elects not to have newborn screening performed, the person with the duty to perform testing under subdivision 1 must follow that election. A written election to decline testing exempts persons with a duty to perform testing and the Department of Health from the requirements of this section and section 144.128.

Subd. 5. Newborn screening program operations. (a) "Newborn screening program operations" means actions, testing, and procedures directly related to the operation of the newborn screening program, limited to the following:

(1) confirmatory testing;

- (2) laboratory quality control assurance and improvement;
- (3) calibration of equipment;
- (4) evaluating and improving the accuracy of newborn screening tests for conditions approved for screening in Minnesota;
- (5) validation of equipment and screening methods; and
- (6) continuity of operations to ensure testing can continue as required by Minnesota law in the event of an emergency.

(b) No research, public health studies, or development of new newborn screening tests shall be conducted under this subdivision.

Subd. 6. Standard retention period for samples and test results. The standard retention period for blood samples with a negative test result is up to 71 days from the date of receipt of the sample. The standard retention period for blood samples with a positive test result is up to 24 months from the date of receipt of the sample. The standard retention period for all test results is up to 24 months from the last date of reporting. Blood samples with a negative test result will be destroyed within one week of the 71-day retention period. Blood samples with a positive test result will be destroyed within one week of the 24-month retention period. All test results will be destroyed within one month of the 24-month retention period. During the standard retention period, the Department of Health may use blood samples and test results for newborn screening program operations in accordance with subdivision 5.

Subd. 7. Parental options for extended storage and use. (a) The parent or legal guardian of an infant otherwise subject to testing under this section may authorize that the infant's blood sample and test results be retained and used by the Department of Health beyond the standard retention periods provided in subdivision 6 for the purposes described in subdivision 9.

(b) The Department of Health must provide a consent form, with an attached Tennessee warning pursuant to section 13.04, subdivision 2. The consent form must provide the following:

- (1) information as to the personal identification and use of samples and test results for studies, including studies used to develop new tests;
- (2) information as to the personal identification and use of samples and test results for public health studies or research not related to newborn screening;
- (3) information that explains that the Department of Health will not store a blood sample or test result for longer than 18 years from an infant's birth date;
- (4) information that explains that, upon approval by the Department of Health's Institutional Review Board, blood samples and test results may be shared with external parties for public health studies or research;
- (5) information that explains that blood samples contain various components, including deoxyribonucleic acid (DNA); and
- (6) the benefits and risks associated with the department's storage of a child's blood sample and test results.

Subd. 8. Extended storage and use of samples and test results. When authorized in writing by a parent or legal guardian under subdivision 7, the Department of Health may store blood samples and test results for a time period not to exceed 18 years from the infant's birth date, and may use the blood samples and test results in accordance with subdivision 9.

Subd. 9. Written, informed consent for other use of samples and test results. With the written, informed consent of a parent or legal guardian, the Department of Health may:

(1) use blood samples and test results for studies related to newborn screening, including studies used to develop new tests; and

(2) use blood samples and test results for public health studies or research not related to newborn screening, and upon approval by the Department of Health's Institutional Review Board, share samples and test results with external parties for public health studies or research.

Subd. 10. Revoking consent for storage and use. A parent or legal guardian may revoke approval for extended storage or use of blood samples or test results at any time by providing a signed and dated form requesting destruction of the blood samples or test results. The Department of Health shall make necessary forms available on the department's Web site. Blood samples must be destroyed within one week of receipt of a request or within one week of the standard retention period for blood samples provided in subdivision 6, whichever is later. Test results must be destroyed within one month of receipt of a request or within one month of the standard retention period for test results provided in subdivision 6, whichever is later.

History: *1965 c 205 s 1; 1977 c 305 s 45; 1Sp1981 c 4 art 1 s 75; 1985 c 248 s 70; 1986 c 444; 1988 c 689 art 2 s 31; 1994 c 636 art 2 s 2; 1997 c 203 art 2 s 11; 1997 c 205 s 19; 1Sp2003 c 14 art 7 s 26; 2007 c 147 art 16 s 7; 2009 c 79 art 10 s 5; 2012 c 292 art 4 s 3-10; 2013 c 108 art 12 s 14; 2013 c 125 art 1 s 30*

Appendix B

Consultant	Position/Representative	Organization/Institution	Date Consulted
Annamarie Saarinen	Co-Founder and Chairman	Newborn Foundation	October 3, 2013
Beth Tarini, M.D., M.S.	Pediatrician/Newborn Screening Education and Ethics Researcher	University of Michigan	September 9, 2013
Candace Lindow-Davies	Family Support Coordinator	Minnesota Hands & Voices, Lifetrack Resources	September 17, 2013
Denise Chrysler, J.D.	Director	Network for Public Health Law, Mid-States Regional Center	October 30, 2013
Ellen Clayton, J.D., M.D.	Professor of Genetics and Health Policy, Pediatrics, and Law	Vanderbilt University, Center for Biomedical Ethics and Society	September 17, 2013
Governor's Council on Developmental Disabilities	Council Members	Multiple	October 2, 2013
Jeff Botkin, M.D., M.P.H.	Chief, Medical Ethics	University of Utah	September 23, 2013
Jill Krueger, J.D.	Senior Attorney	Public Health Law Center at William Mitchell College of Law	October 30, 2013
Julie Jagim, PHN	Chair	Maternal & Child Health Advisory Task Force	October 21, 2013
Kara Hall	Part C Coordinator	Minnesota Department of Education	October 22, 2013
Karen Maschke, Ph.D	Research Scholar; Editor	The Hastings Center; <i>IRB: Ethics & Human Research</i>	September 24, 2013
Lisa Schimmenti, M.D.	Associate Professor/Physician, Division of Genetics and Metabolism	University of Minnesota	October 3, 2013
Logan Spector, Ph.D	Associate Professor, Division of Epidemiology and Clinical Research	University of Minnesota	September 9, 2013
Marilyn Peitso, M.D.	Pediatrician	Minnesota Academy of Family Physicians	September 30, 2013
Mark Schleiss, M.D.	Professor, Division of Pediatric Infectious Disease & Immunology	University of Minnesota	September 17, 2013
Martha Overby, J.D.	State Director of Program Services & Government Affairs	March of Dimes	September 23, 2013
Mary Hartnett	Executive Director	Minnesota Commission for Deaf, Deafblind, and Hard of Hearing Minnesotans	October 21, 2013

Nancy Mendelsohn, M.D.	Medical Director	Children's Hospitals and Clinics of Minnesota, Genetics	October 9, 2013
Natasha Bonhomme	Vice President of Strategic Development/Maternal Child Health	Genetic Alliance	September 30, 2013
Richard Lussky, M.D.	Neonatologist	Hennepin County Medical Center	December 10, 2013
Robert Jacobson, M.D.	Professor of Pediatrics; President	Mayo Clinic; Minnesota Chapter of the American Academy of Pediatrics	September 19, 2013
Sara Chute	International Health Coordinator	MDH Refugee Health Program	October 1, 2013
Stephen Nelson, M.D.	Physician	Children's Hospitals and Clinics of Minnesota, Hematology-Oncology	September 18, 2013
Susan Berry, M.D.	Professor, Director - Division of Genetics and Metabolism	University of Minnesota	September 24, 2013
Twila Brase, PHN	President	Citizen's Council on Health Freedom	Email response received January 17, 2014

Appendix C: Consultant Questions

Current Law

1. Current law requires written informed consent for retention of blood spots beyond 71 days and for test results beyond 2 years for children whose test results are negative. What do you see are the benefits and challenges of this requirement in regards to:
 - a. Birth facility administration/burden
 - b. Privacy concerns for parents
 - c. Education needs
 - d. Ways to obtain written informed consent?

2. Current law requires written informed consent for retention of blood spots beyond 2 years and for test results beyond 2 years for children whose test results are presumptively positive. What do you see are the benefits and challenges of this requirement in regards to:
 - a. Birth facility administration/burden
 - b. Privacy concerns for parents
 - c. Education needs
 - d. Ways to obtain written informed consent?

3. This past legislative session, MN lawmakers approved a retention period of 18 years for Early Hearing Detection and Intervention (EHDI) test results and data for all children who are tested. This retention period is different from other NBS test results and data. What is your reaction to this?

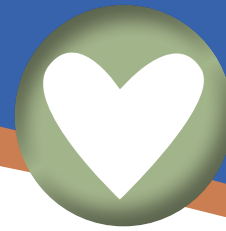
Diagnosis and Treatment of Newborn Screening Disorders

4. Newborn screening requires further diagnostic testing after a presumptive positive result. Please provide your experience with this aspect of the screening process, addressing the following in particular:
 - a. Timeframe for diagnostic testing of different disorders
 - b. Treatment needs in these patients
 - c. Utility, if any, of Newborn Screening results and data for this process
 - d. Utility, if any, of Newborn Screening dried blood spots for this process
 - e. Timeframe for False Negative results to appear

Long Term Storage and Use of Blood Spots and Test Results

5. MDH has been asked to develop a comprehensive and sustainable long-term storage and use plan for blood spots and test results. What are your thoughts on this in regards to:
 - a. Strategies for educating the public about the utility of blood spots and test results for advancing new knowledge?
 - b. Methods for obtaining consent?
 - i. Please describe pros and cons for each method described.
 - c. Location of storage site (i.e., MDH versus third-party)?
 - d. Process to allow clinical and research access to the blood spots and data?
 - e. Ensuring confidentiality and privacy protections?
 - f. Funding mechanisms?

2014 NEWBORN SCREENING PANEL



Amino Acid Disorders

Arginemia (ARG)
 Argininosuccinate acidemia (ASA)
 Biopterin cofactor deficiencies
 Citrullinemia type I (CIT-I)
 Citrullinemia type II (CIT-II)
 Homocystinuria (HCY)
 Hypermethioninemia (MET)
 Hyperphenylalaninemia (H-PHE)
 Maple syrup urine disease (MSUD)
 Phenylketonuria (PKU)
 Tyrosinemia (transient neonatal, type I, type II, type III)

Fatty Acid Oxidation Disorders

Carnitine acylcarnitine translocase deficiency (CACT)
 Carnitine palmitoyltransferase deficiency I (CPT-1)
 Carnitine palmitoyltransferase deficiency II (CPT-II)
 Carnitine uptake deficiency (CUD)
 Dienoyl-CoA reductase deficiency (DE-RED)
 Glutaric acidemia type II (GA-II)
 Long-chain hydroxyacyl-CoA dehydrogenase deficiency (LCHAD)
 Medium-chain acyl-CoA dehydrogenase deficiency (MCAD)
 Medium-chain hydroxy acyl-CoA dehydrogenase deficiency (MCHAD)
 Medium-chain keto acyl-CoA thiolase deficiency (MCKAT)
 Short-chain acyl-CoA dehydrogenase deficiency (SCAD)
 Short chain hydroxy acyl-CoA dehydrogenase deficiency (SCHAD)
 Trifunctional protein deficiency (TFP)
 Very long-chain acyl-CoA dehydrogenase deficiency (VLCAD)

Organic Acid Disorders

2-Methyl-3-hydroxybutyric aciduria (2M3HBA)
 2-Methylbutyryl-CoA dehydrogenase deficiency (2MBG, SBCAD)
 3-Hydroxy-3-methylglutaryl-CoA lyase deficiency (HMG)
 3-Methylcrotonyl-CoA carboxylase deficiency (3-MCC)
 3-Methylglutaconyl-CoA hydratase deficiency (3MGA)
 Beta ketothiolase (BKT)
 Glutaric acidemia type I (GA-1)
 Isobutyryl-CoA dehydrogenase deficiency (IBD)
 Isovaleric acidemia (IVA)
 Malonic acidemia (MAL)
 Methylmalonic acidemia (methylmalonyl-CoA mutase deficiencies)
 Methylmalonic acidemia (some adenosylcobalamin synthesis defects)
 Methylmalonic acidemia (maternal vitamin B12 deficiency)
 Multiple CoA carboxylase deficiency (MCD)
 Propionic acidemia (PA)

Endocrine Disorders

Congenital adrenal hyperplasia (CAH)
 Congenital hypothyroidism (CH)

Hemoglobinopathies

Sickle cell disease (HB S/S)
 Sickle-C disease (HB S/C)
 S-beta thalassemia
 Variant hemoglobinopathies

Others

Biotinidase deficiency (BIO)
 Critical congenital heart disease (CCHD)
 Cystic fibrosis (CF)
 Galactokinase deficiency (GALK)
 Galactose epimerase deficiency (GALE)
 Galactosemia (GALT)
 Hearing loss
 Severe combined immune deficiency (SCID)

Newborn Screening Program

601 Robert Street North
 St. Paul, MN 55155
 Phone: (800) 664-7772
 Fax: (651) 215-6285
newbornscreening@health.state.mn.us
www.health.state.mn.us/newbornscreening

Newborn Screening

FACT SHEET

2014

What is newborn screening?

Newborn screening is a set of tests that check babies for serious disorders that often cannot be seen at birth. These disorders can be found through blood spot, hearing, and pulse oximetry screening. If a disorder is found early through one of these screens, early interventions can help give these babies a healthy start to life.

- 1 When your baby is between 24 and 48 hours old, a few drops of blood will be collected from your baby's heel. These blood spots will be sent to the Minnesota Department of Health newborn screening laboratory to check for over 50 rare but treatable disorders.
- 2 When your baby is around 12 hours old, a hearing screen will be performed to check for hearing loss in the range where speech is heard. A small screening device will play soft sounds and measure your baby's response.
- 3 When your baby is at least 24 hours old, a pulse oximetry screen will be performed to check for critical congenital heart disease (CCHD). This screen measures the amount of oxygen in your baby's blood.

What are the benefits of newborn screening?

Blood spot screening can identify babies with harmful and sometimes fatal disorders. Babies with these disorders often seem healthy at birth but can get sick in just a few days or weeks of life. If these disorders are found early, babies can receive treatment to prevent severe health problems or death.

Hearing screening can identify babies with hearing loss. Hearing loss may affect a child's communication, learning, and development even before it is noticeable to parents or healthcare providers. Early intervention can help children with hearing loss access language and develop on track with their hearing peers.

Pulse oximetry screening can identify babies with serious, life-threatening heart defects. Babies with CCHD often seem healthy at birth but are at risk for disability or death. If CCHD is found early, babies can benefit from surgery or other medical treatments.

What if the results suggest a problem?

A result that suggests a problem does not always mean that your baby has a disorder. Further testing is needed to know what may have caused the result. If your baby's blood spot screen suggests a problem, the Newborn Screening Program will contact your baby's care provider to review the result and discuss what follow-up tests are needed. Your baby's care provider will then contact you to discuss the next steps. If your baby's hearing screen or pulse oximetry screen suggests a problem, a care provider will discuss the next steps with you as soon as screening is complete.

It is important to follow the guidance of your baby's care provider and schedule follow-up appointments as soon as possible.

What will my baby be screened for?

Babies are screened for over 50 disorders that:

- Affect how the body breaks down proteins
- Affect how the body makes energy
- Affect how the body gets nutrients from food
- Affect the immune system
- Affect hearing
- Affect the heart
- Cause hormone problems
- Cause blood problems



What are some of the most common disorders found through screening?

Some of the most common disorders include critical congenital heart disease, hearing loss, sickle cell disease, cystic fibrosis, phenylketonuria (PKU), and congenital hypothyroidism. For a complete list of disorders, visit: www.health.state.mn.us/newbornscreening.

What personal information is written on the newborn screening card?

The newborn screening card contains only the information about mom and baby that will help staff interpret test results and contact your baby's primary care provider if more testing or follow-up is needed. This includes, but is not limited to, baby's name, date of birth, time of birth, mom's name, and the name of baby's primary care provider or clinic.

What happens to the blood spots and test results after screening?

Most of the dried blood is used up during testing. Leftover blood spots are stored for a period of time after screening to allow for follow-up testing, if needed. The blood spots of babies with normal results will be stored for 71 days. The blood spots of babies with positive results will be stored for 24 months. All test results will be kept for 24 months, except for hearing screening results which may be stored for 18 years. After these time periods, blood spots and test results are destroyed. If you do not want your child's blood spots or test results destroyed, you may choose to have them retained by signing a consent form. Please see the Newborn Screening Program website for instructions on how to retain your child's blood spots and test results.

How are the stored blood spots and test results used after screening?

Blood spots may be used to ensure that screening is accurate or to improve test methods. Test results may be used to look at disease trends and improve evaluation of test results. These samples will NOT be used for research, new test development, or public health studies without your written and informed consent.

Can I refuse screening for my baby?

Yes. If you do not want your baby screened, you must complete the Parental Refusal of Newborn Screening form. You can ask your birth provider for a copy of the form or download it from the Newborn Screening Program website. You may also choose to arrange for blood spot screening through a private laboratory.

For more information on newborn screening:

MN Newborn Screening Program

www.health.state.mn.us/newbornscreening

Baby's First Test

www.babysfirsttest.org

Save Babies Through Screening Foundation

www.savebabies.org

MN Early Hearing Detection and Intervention Program

www.improveehdi.org/mn

Appendix F: State Retention Periods*

State	Test Results Retention Time	Dried Blood Spots Retention Time
Alabama	21 years	3 months
Alaska	10+ years	3 years
Arizona	Indefinitely	3 months - specimens of interest or positives kept indefinitely
Arkansas	No Response	3-4 months
California	Indefinitely	Indefinitely
Colorado	6 years	6 months
Connecticut	No Response	6 months
Delaware	Indefinitely	3 years
District of Columbia	No Response	1 year
Florida	7+ years in lab, positives indefinitely	6 months
Georgia	3 years in the lab, follow-up longer	2 months
Hawaii	Indefinitely	1 year
Idaho	10+ years	1 year
Illinois	21 years	2-4 months
Indiana	23 years	23 years
Iowa	Indefinitely	5 years
Kansas	Indefinitely	1 month
Kentucky	Indefinitely	6 months
Louisiana	Indefinitely	1 month
Maine	Indefinitely	Indefinitely
Maryland	Indefinitely	25 years
Massachusetts	No Response	21.5 years
Michigan	Indefinitely	Indefinitely
Minnesota	2 years	71 days if negative, 2 years if positive
Mississippi	Indefinitely	1 year
Missouri	30 years	5 years
Montana	Indefinitely	1 year
Nebraska	29 years	3 months
Nevada	Indefinitely	1 year
New Hampshire	21 years	6 months
New Jersey	23 years	23 years
New Mexico	10+ years	1 year
New York	27 years	27 years
North Carolina	No Response	5 years
North Dakota	Indefinitely	Indefinitely
Ohio	No Response	2 years
Oklahoma	21-23 years	42 days

State	Test Results Retention Time	Dried Blood Spots Retention Time
Oregon	10+ years	1 year
Pennsylvania	21 years	8 months
Rhode Island	23 years	23 years
South Carolina	17+ years	1 year
South Dakota	No Response	1 month
Tennessee	Indefinitely	1 year
Texas	21 years	2 years without consent 25 years with consent
Utah	21 years	Minimum 90 days
Vermont	Indefinitely	Indefinitely
Virginia	23 years	6 months presumptive positives kept 10 years
Washington	21 years	21 years
West Virginia	Indefinitely	3 months
Wisconsin	Indefinitely	1 year
Wyoming	Indefinitely	6 months

* As reported to MDH by the Association of Public Health Laboratories

Appendix G: Fiscal Assumptions

The following assumptions were made when addressing the fiscal impact of the three storage and use models presented in this report:

- 1) The 'Current Statutory Requirements' model represents the Program's fiscal baseline. However, as reported in previous fiscal notes, the following costs were accrued to meet these statutory requirements:
 - a) IT costs for building and testing system to allow for routine destruction of electronic test results;
 - b) Staff time for testing of IT systems and performing routine destruction of blood spots and test results;
 - c) Contract costs, IT costs, and staff time for mass destruction of blood spots and test results.
- 2) The Newborn Screening Program fee increase granted in the 2013-2014 legislative session (Omnibus health and human services finance bill) addresses the above increased costs to the Program, including an increased in education and training, and would allow the Program to absorb the costs of the other models presented. The fiscal impact only remains negligible until there is a significant increase in requests for extended storage of dried blood spots and/or test results.
- 3) Each model would require further costs associated with the research use of the consented blood spots and/or test results (i.e., pulling the information, processing and routing specimens, tracking information). The Program feels that these costs are outside the scope of the current program and would most likely be incurred by a third party.
- 4) With only a high-level fiscal analysis completed, the models presented appear to be fiscally neutral. However, the Program would need additional in-depth analyses at the time of implementation of a chosen model as well as 2-4 years after implementation in order to provide true fiscal impacts.