Considerations and Recommendations for a National Policy Regarding the Retention and Use of Dried Blood Spot Specimens after Newborn Screening

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ACHDNC Work Group –

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Executive Summary

Considerations and Recommendations for a National Policy Regarding the Retention and Use of Dried Blood Spot Specimens after Newborn Screening

Newborn screening is a highly successful public health program that identifies rare genetic, congenital and functional disorders and assures early management and follow-up for those affected. Newborn screening is regulated and implemented by states, and each state has laws that either require or allow newborn screening. Newborn screening policies are usually implemented with input from multi-disciplinary advisory committees that include consumers, health care and public health professionals and others. While state responsibility allows for local control and accountability, it also gives rise to wide variation in practices across the country.

All US newborn screening programs obtain dried blood specimens on a special filter paper for laboratory test used in newborn screening. Portions of these specimens (residual specimens) are generally retained for some period of time after testing is complete. The primary justification for retained residual specimens is to benefit the child and family by documenting that a specimen was collected, received, and properly analyzed. Residual specimens may also be used for result verification, and quality assurance activities for the laboratory and program (including new test validation). A collection of stored specimens is often referred to as a “biobank.”

Newborn screening specimens are unique. They are usually the first blood specimen in a baby’s life and they are collected on essentially all newborns. They provide critical information about risk for certain inherited conditions. They also have the potential to generate population-based knowledge that can improve the health of children, support families, and provide information critical to understanding the antecedents of adult diseases.

Residual specimen storage must assure that the confidentiality and privacy of families is respected and that the specimens are protected. Policies are needed in each state to promote public trust, emphasize transparency of administrative practices, and create supporting information that encourages informed public participation.

This is a guidance document for use by the U.S. Secretary of Health and Human Services’ Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC; roster of members available at http://www.hrsa.gov/heritabledisorderscommittee/governance/roster.htm) in their deliberations toward development of a national policy statement. It is designed to review the issues facing newborn screening programs and to develop a national guidance policy for programs that retain and use dried blood specimens after newborn screening is completed.

CONCLUSION/RECOMMENDATIONS

Since the initial guidance for retention, storage of use of residual dried blood spots in 19961, there have been noticeable improvements in policy development. In state newborn screening programs, there are currently two distinct philosophies regarding the storage and use of residual dried blood spots: 1) short-term storage (<3 years), presumably for program quality assurance and test improvement; and 2) long-term storage (> 18 years), presumably for public health research. There is heightened awareness in the research and consumer communities concerning both the potential value of specimens and the potential privacy issues. Privacy issues are compounded by the lack of standardized consent policies across state
programs, the lack of a universal legal definition of specimen ownership once the screening process is complete, and the lack of public awareness of newborn screening.

Because newborn screening is the only medical screening program that reaches the entire population of newborns, it is unique and the processes surrounding it must be carefully and thoughtfully approached. Residual blood specimens provide an excellent opportunity for storage and use in a biobank after screening is complete and the results have been validated. However, at the present time, this is a secondary purpose that may not have been adequately addressed in state law or policy. Therefore, residual specimen use must be carefully considered anticipating both the potential benefits and risks. To assist in this process, the ACHDNC should consider the following recommendations:

1) **All state newborn screening programs should have a legally reviewed and accepted policy addressing the disposition of dried blood specimens remaining after newborn screening testing is complete and the screening results have been validated.** Multidisciplinary input, including consumers, should be solicited and thoughtfully considered in developing such a policy. This specimen disposition policy should include the length of time for which specimens will be stored and storage conditions. Compliance with storage processes included in NCCLS/CLSI Standard LA4-A5 or its current edition is recommended. Any data linkages should be carefully addressed and privacy and confidentiality assured.

2) **All state newborn screening programs should have a legally reviewed and accepted policy that specifies who may access and use dried blood specimens once they arrive at the state-designated newborn screening laboratory, including further access after newborn screening tests are completed.** Multidisciplinary input, including consumers, should be solicited and thoughtfully considered in developing such a policy. This specimen access policy should include any uses prior to and after the newborn screening laboratory testing and validation process. If uses of dried blood spot specimens outside of newborn screening are allowed, then handling and disposition of the specimen should be addressed and privacy and confidentiality of any associated patient information assured.

3) **As part of the educational process of the newborn screening system, all state newborn screening programs should maintain and distribute educationally and culturally appropriate information that includes basic information about the use or potential use of the dried blood specimens.** Where long-term storage policies or other options exist relative to storage of residual dried blood spots, such information should be included in prenatal education materials.

4) **All state newborn screening programs should work proactively to ensure that all families receiving prenatal care are educated about newborn screening.** This activity should include appropriate steps to inform and train prenatal care providers regarding their educational responsibilities within the newborn screening system. Processes should be in place to evaluate the extent, timing and understanding of prenatal education with an eye towards educational program improvement.

5) **If residual blood specimens are to be available for any process outside of the legally required newborn screening process for which they were obtained, an indication of the parents’ awareness and willingness to participate should exist in compliance with federal research requirements.**

A consent (opt in) or a dissent (opt out) process may meet this requirement depending on purposes for which specimens will be used. The use of residual specimens for program evaluation (e.g. repeat testing as a quality check) or process improvement (e.g. non-commercial, internal program
new test development) are valid components of the newborn screening system and, therefore, should not require additional consent.

6) **Newborn screening programs should assess the utility of any additional consent/dissent process implemented in order to better address issues of storage and use of residual dried blood specimens.** The federal government is encouraged to consider this as a priority and to provide funding for utility assessment projects over the next 5 years.

7) **The federal government is encouraged to provide administrative support and funding to develop:**

- Model consent/dissent processes for the use of residual newborn screening specimens;
- Model educational programs for the general public on the importance of newborn screening and the potential uses of residual specimens to generate population-based knowledge about health and disease;
- National data on the utility of any additional consent/dissent processes implemented relative to potential research uses of residual newborn screening specimens;
- Educational materials with facts about potential uses of residual newborn screening specimens for both consumers and prenatal healthcare providers.

**Note:** During the vetting process (webinars) to the stakeholder community, questions and discussions led to development of the following proposed (optional) recommendation. Since this proposed recommendation was not shared with the stakeholders in the webinars and not unanimously embraced by all members of the ACHDNC Work Group, it is listed here separately for your consideration and discussion.

**Optional Recommendation**

*Where state newborn screening programs elect to maintain a long-term newborn screening biobank of residual newborn screening specimens, a secure third party key holder system (“honest broker”), with appropriate consent, should be used to allow for emergency linkages in de-identified specimen studies.* The key holder would have the ability to reveal critical health information to a study subject should such information be discovered during the course of the research, and the ability to obtain and reveal personal information from a subject to a researcher, if such information were deemed to be of critical importance. In either case, consent from the study participant or appropriate parent or guardian would be required.

INTRODUCTION

Newborn screening (NBS) is a system characterized by highly successful public health programs that provide early identification of rare genetic, congenital and functional disorders, and assure early management and follow-up care for those affected. In the U.S., NBS programs are regulated and implemented by the states and each state has a law that either requires or allows NBS. NBS policies are usually implemented with input from multi-disciplinary advisory committees that include consumers, healthcare and public health professionals, and others. While this approach allows for local control and accountability, it also leads to variation in practices across the country.

All US NBS programs obtain and use blood specimens dried onto special filter paper for laboratory screening tests. Unused portions of these specimens (residual specimens) are generally retained for some period of time after testing is complete. The primary justification for retaining residual specimens is to benefit the child and family by documenting that a specimen was collected, received, and properly analyzed by the screening program. Residual specimens may also be used for result verification and quality assurance activities for the program and laboratory (including new test validation). This collection of stored specimens is often referred to as a ‘biobank.’

NBS specimens are unique and valuable resources. They are usually the first blood specimen in a baby’s life and they are collected on essentially all newborns. They provide critical information about risk for certain congenital conditions. They also have the potential to generate population-based knowledge that can improve the health of children, support families, and provide information critical to understanding the antecedents of adult diseases. Therefore, residual specimen storage must assure that the confidentiality and privacy of families are respected and that the specimens are protected. Policies are needed in each state to promote public trust, emphasize transparency of administrative practices, and create supporting information that encourages informed public participation.

This is a guidance document for use by the U.S. Secretary of Health and Human Services’ Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC; roster of members available at http://www.hrsa.gov/heritabledisorderscommittee/governance/roster.htm) in deliberating development of a national policy recommendation. It is designed to review issues facing NBS programs and serve as a guide policy development for retaining and using residual NBS specimens. The document content and suggested recommendations were developed by a Work Group that included representation from public health, academia, and parent advocacy institutions/organizations, and was vetted to a wide audience of consumers, healthcare specialists, and public health policy makers by a series of webinars prior to its presentation to the ACHDNC. Preliminary work included an extensive review of the literature on storage and use of material remaining after newborn screening. Both technical and non-technical issues were studied with the intent to develop reasonable and appropriate draft recommendations for blood spot storage and use at the state level that might also benefit the nation in a broader context. Experiences of others who have already dealt with these issues at a national level were explored in order to profit from lessons learned. Particular attention was paid to experiences from the Danish newborn screening program and the work of their ‘biobank’ task group in establishing criteria for access to human biological materials and to the work currently ongoing to develop a “BioTrust” in the State of Michigan.
POLICY, ETHICAL AND LEGAL ISSUES

There is a heightened awareness of the research value of residual NBS specimens as a result of the success of the human genome initiative. DNA and RNA can be extracted from the dried blood specimens used for NBS, and there is increasing bioinformatics capability allowing the linking of DNA information with clinical data. International guidelines have been suggested as a means of emphasizing the importance of preserving newborn blood specimens in repositories for the benefit of future generations but none currently exist. The issues and possibilities surrounding national, regional or state repositories of residual NBS specimens have been discussed in at least two national meetings with no clear resolution. Appropriate stewardship and public trust have been repeatedly identified as essential elements of a successful repository, but no consensus model repository has emerged.

All states require that any baby born within the state’s jurisdiction be screened for certain congenital conditions that can result in catastrophic consequences if left undetected and unmanaged. As part of the screening process, a blood specimen is collected, usually by a heel stick, and the blood is absorbed onto a special blood collection device, air dried and submitted to the state’s designated newborn screening laboratory. Most (but not all) states provide a mechanism for opting out of the screening process, but consent for screening is almost universally not required. In some programs, the associated rules accompanying the NBS statute define ownership of the specimen, once collected and submitted, as residing with the State, and there is at least one supporting legal decision that might apply (see Ownership below). Nonetheless, a clear definition of specimen ownership is not generally recognized, and ethical questions exist about specimen use following screening. Despite awareness of the issues and previously published guidance encouraging state policy development, clear policies regarding retention time, storage conditions and possible uses of the blood specimen remaining after screening do not exist for all programs. Where they exist, there is considerable variation in content between programs.

There are important NBS program uses for residual specimens that may remain after screening per se is complete. These include program quality assurance and test validation, parental requests for other testing (particularly in cases where an infant has died without an obvious cause and when future pregnancies may be contemplated), and court ordered forensic uses. NBS programs have reported numerous additional requests for specimen usage over the years including public health projects. As one example, the CDC-sponsored HIV Seroprevalence Survey among Childbearing Women utilized fully anonymized residual NBS specimens to evaluate the extent of HIV infections in child-bearing women nationally as an aid to better targeting public health educational and other resources. Residual NBS specimens are valuable evidence that appropriate testing has occurred. The existence of a residual specimen proves that the screening laboratory received it and assumed the responsibility for analyzing it correctly. Additionally, should the child develop inexplicable symptoms or neurodevelopmental delay later in life, the residual specimen could be reanalyzed or other tests applied to determine whether the condition was congenital or acquired (perhaps through environmental interactions). "Case control studies" are also possible using residual specimens to determine concentrations of biomarkers in children who develop certain disorders in comparison with similar markers in healthy children (controls). Such studies have the potential to provide insight into the mechanisms behind the origin of diseases and their potential screening biomarkers.

Increased public awareness of stored residual NBS specimens has raised concerns about the privacy of the medical information they might reveal (such as disease susceptibility) through current and future technological advances. In addition to the federal privacy laws that exist, and state laws specifically pertaining to NBS, additional state privacy laws may impact specimen storage/use [two recent reviews discuss this subject]. Most of the legal and ethical questions surrounding retention of residual NBS specimens have been reviewed in depth elsewhere and will not be revisited here. It suffices to say that the
potential research value of residual NBS specimens has increased the need for national harmonization of specimen storage and accession policies for both ethical and legal reasons. While a recent Institute of Medicine report took the position that NBS banked specimens should be available for research “only if identifiers have been removed,” many questions remain unanswered.

Because of the increasing number of requests for residual dried blood spots (DBSs), the procedures and regulations regarding their release and use should be formalized. A 2002 study of the storage and usage practices in U.S. NBS programs revealed that almost all programs stored their residual specimens with identifiers present. Only 2 of the 36 programs that reported their short-term storage practices kept specimens completely deidentified. Three programs reported using a coding system that kept information private unless decoded. One-third of the reporting programs stored residual specimens for no officially stated reason; the remainder reported storage for specific purposes including future testing (13 of 36), special testing at the request of the family after the death of the child (7 of 36), quality control to check errors in testing (8 of 36), and research (5 of 36). The mechanisms for using aggregate data obtained from NBS were also reported to vary. In some cases researchers were required to have IRB approval at their own institution, while some required IRB approval at the state health department. In some cases, individual requests were required to be submitted to the NBS program director and in a few cases, requests were individually reviewed by senior NBS staff members. A slightly later study showed that 74% of states used residual specimens for NBS test evaluation and 28% used them for epidemiological and pathophysiological research studies. Only 57% reported having internal written policies for specimen usage.

In order to determine current storage practices, we reviewed online data reported by the states to the National Newborn Screening and Genetics Resource Center (NNSGRC; available at: http://www2.uthscsa.edu/nnsis) and validated these data through email contacts (100% compliance). Currently, 67% (34 of 51) state programs (including D.C.) retain residual blood specimens for less than 3 years accounting for approximately 46% of all U.S. newborns (see Figure 1). The remaining 33% save their residual blood spots for eighteen or more years (~54% of births) with at least 6 saving them indefinitely (others indicating 18-21 yr. storage may eventually save them indefinitely, but currently they are extending their policy on a year-by-year basis). Despite the recommendations of a national standard suggesting that short-term specimen storage occur at +4 °C and long-term storage at -20 °C, with desiccant in both cases, storage conditions vary from ambient to ~20 °C with variable uses of desiccant (Note: Desiccant is not necessary if the humidity of the storage facility is <30%).

![Figure 1. Reported Residual Bloodspot Storage (9/2009) (Ascending Order)](image)
Ownership
Two of the more important legal and ethical questions that arise concern ownership of the blood specimen and ownership of the information gathered, produced or potentially revealed as part of NBS or related processes. The President’s Council on Bioethics\textsuperscript{16} has framed a number of associated questions:

“To whom does this information properly belong? Does it belong to the child alone, to use or to disregard as he or she sees fit once he or she becomes an adult? Or do parents (as some of them seem to believe) have an unlimited right to know the genetic abnormalities of their children? Do physicians have a claim on such information once it exists? Should the state in which the child is born, in the interest of building ever more useful genomic databases, have a presumptive right to “biobank” the child’s genotypic data? If newborn screening detected a range of unfavorable predispositions in the child’s genome, would they amount to “pre-existing conditions” that insurers or even potential employers would be entitled to consult before offering the patient health insurance or employment?”\textsuperscript{16}

State laws and regulations pertaining to NBS specimen/information storage vary and their impact or potential impact on specimen use was extensively reviewed in 2006.\textsuperscript{17} At that time only 9 states had specific statutory or regulatory requirements for retaining NBS information and specimens. Prescribed retention periods varied from 1 month to indefinitely (then as now). In some state/territorial jurisdictions, parents may choose the return or destruction of their newborn’s specimen after a specified time period (e.g., 2 years in South Carolina, 60 days in Minnesota and 45 days in Texas). or they may allow it to be stored and used for research. The 2006 report noted that retention requirements did not specify whether NBS specimens themselves were a record in Florida, Idaho, and Ohio, but in California, Maine, Michigan, and Washington, newborn screening specimens were declared to be the property of the state (in Maine a parent may object to state ownership in writing).\textsuperscript{17} Utah has since identified specimens as property of the state (with defined considerations about education and specimen use) [Utah R398-1-15/ http://www.rules.utah.gov/publicat/code/r398/r398-001.htm#T15].

The legal question of specimen ownership may have been answered already. In a 1990 decision, the Supreme Court of the State of California held, in Moore v. Regents of the University of California (51 Cal. 3d 120; 271 Cal. Rptr. 146; 793 P.2d 479), that there were no property rights in one’s own body parts after medical removal. Since all states require NBS, with an opportunity for refusal (opt out) in most cases, the state would appear to have ownership of the screening specimens for purposes of NBS and related uses. Even so, legal and ethical obligations differ and clarifications on a program by program basis will likely be required. This is especially true where the research use is not the original intended use and where no consent for research was obtained.

Stewardship
State public health departments have an ethical and legal obligation to exercise the highest care in receiving, storing and protecting newborn DBSs from unauthorized use. The public has a right to expect that NBS specimens are cared for in a manner that protects personal information and eliminates misuse and mistrust. Previous U.S. guidelines noted that, “Whenever a sample is retrieved, documentation should be kept indicating: (1) who had access to the specimen; (2) the purpose for which the specimen was accessed; (3) the authorizing authority; (4) the chain-of-custody from retrieval to analysis; (5) the amount of specimen released; (6) the results of any analysis of the sample; and (7) changes to any demographic or descriptive data. Appropriate and secured records should be maintained in a manner similar to that required for maintaining legal evidence in forensic laboratories.”\textsuperscript{18}

Despite a reluctance of many in the screening field to label NBS specimen storage facilities as biobanks, the public and the media routinely use this terminology. As a result, comparisons with other biobanks are
often made. Since there is little experience with formalized long-term storage of residual NBS specimens in the U.S., lessons learned from others with more experience may be informative. As a prime example, the Danish government initiated a national NBS biobank in 1993 (see operational details in Appendix). This biobank was established for 3 stated purposes: (1) diagnosis and treatment of PKU and CH (including repeat testing, quality assurance and group statistics); (2) diagnostic use later in infancy (requiring informed consent from the parents); and (3) research (requiring approval of the scientific ethics committee system). The Executive Order that initiated the Danish biobank was replaced in 2004 by detailed operational guidelines that required strict compliance with laws on processing personal data (assigning management responsibility), patient’s rights (allowing opt out including destruction/retrieval), scientific ethics, and confidential health information. Additionally a complaint procedure was prescribed. These strict regulations were considered to be necessary tools to ensure appropriate accountability and to gain public trust. To date, there have been no reported misuses of the Danish NBS-Biobank or its associated Register and public acceptance is high.

In the U.S., recent attention has turned to the ‘Michigan Neonatal BioTrust,’ a developing long-term NBS specimen repository for expanded research use. In Michigan, residual NBS specimens are stored for 21.5 years and are accessible for approved uses on a case by case basis. In the beginning of the development of the repository project, a bioethicist was recruited to advise the Michigan Department of Community Health on ways to make the archived specimens more accessible to researchers while considering and addressing the many ethical issues. The result was creation of a detailed business plan for a phased-in, research accessible biobank (see more details in the Appendix) that, within a framework of patient information privacy and public health research promotion, would address specimen storage, increased health research, linkages to related public health data, greater accessibility of research results, and be self sustaining after 5 years. The ‘BioTrust’ will house specimens in an appropriately controlled environment with privacy safeguards and will control specimen access through an ‘honest broker’ (third party key holder) system. In this model, the ‘honest broker’ will have access to specimens and their linked information and will facilitate research requests in a manner that assures only limited and necessary information accessibility to researchers and privacy/confidentiality to patients. This linkage system will allow anonymous research while providing the possibility of access to additional information for the researcher if critical findings require such, or the transmittal of critical information to the patient. In either case, consent for information sharing would be required.

While national or regional biobanks such as that in Denmark or Michigan provide useful models, they also represent a possible first step to a global consortium of such biobanks. These consortia would exist for two primary reasons. First, joint analyses of important, but uncommon, gene variants could generate more definitive results than could be generated from individual (and likely underpowered) studies. Second, reasonable expectations from funders and beneficiaries could perhaps result in more efficient and effective collaborations similar to the Human Genome Project and the Global HIV Vaccine Enterprise. In turn, this could lead to accessible and affordable studies in diverse populations that allow imaginative search for common and rare genetic and other biological correlates of global diseases. Indeed, the recent Translational Research Network proposed by the National Institutes of Health provides the impetus for a U.S. national biobank based on similar hypotheses. A few research biobanks have already been established in some developing countries. The Chinese Kadoorie study and the Mexican biobank were both designed primarily to discover correlates of non-communicable diseases in adults, and a smaller national DNA bank exists in Gambia.

In at least 4 states, laws exist that define the details of procedures and processes for storage of and access to residual NBS specimens (see Appendix: Michigan, Minnesota, South Carolina, Texas,). In each of these, parents are to be given the opportunity to allow long-term storage of the residual NBS specimen through an informed process that allows refusal. While the exact processes vary somewhat, the intended
consequences are the same – utilization of residual NBS specimens only with the agreement of the parents or guardian of the newborn. Other models of storage and access exist (e.g., Maryland, in which a research review committee examines and recommends which projects requesting the use of residual NBS specimens should proceed to IRB approval). There is increased attention paid to opt out information through pamphlets and websites (e.g. Michigan, available at http://www.mnbb.org/).

- Privacy protections
The issue of privacy and the use of residual blood spots are closely linked to parental education and informed decision-making (discussed later under Consent Issues). There continues to be public mistrust about the possible uses of NBS specimens. Concerns focus on possible discrimination, psychological harm, identification of paternity, and social injustices; however, there are no documented cases of harm resulting from either concern relative to use of NBS specimens. While some state statutes specifically address newborn screening privacy, there are additional broader health laws, regulations and medical standards of practice that may also affect NBS. Five states (Alaska, Colorado, Florida, Georgia, and Louisiana) have defined genetic information explicitly as personal property, and Alaska has extended this property right to DNA. Eight of 30 states/territories with genetic privacy laws were reported to have laws that might extend to NBS. However, depending on the definition of genetic information or genetic testing in a particular statute, technologies used in NBS may not be covered. Privacy laws in the other 22 states either did not specifically name NBS as a covered entity or exempted it as a public health program.

Federal privacy regulations (the ‘Privacy Rule’) have been in place since April 2003 (45 CFR Parts 160 and 164). These regulations provide specific exemptions and allowances for public health activities and to those providing services associated with those activities. NBS, as an exempted public health program, may use and disclose information for treatment, payment, or health care operations without the individual’s consent or authorization. ‘Operations’ include most routine program activities except for research. Research conducted by state or federal programs as mandated by relevant law is permitted as a public health activity. For research by private researchers or research not mandated by law (e.g., a prevalence study using identifiable names), both the privacy and the research rules apply. Research with human subjects conducted with federal funding (or involving researchers otherwise covered by federal law) is regulated by 45 CFR Part 46 (the ‘Common Rule’). Because research is not considered by the federal privacy rule to be part of treatment, payment, or operations, a researcher wishing to access identifiable personal health information (also called Protected Health Information – PHI) must either:

“(1) de-identify the health information so that the patient cannot be determined. De-identification occurs once the following items are redacted from the data to be used by the researcher: names; all geographic subdivisions smaller than a state, including address, except for the initial 3 digits of a zip code (there are special rules for zip codes containing 20,000 or fewer people; all dates, except the year including birth date; telephone number; fax number; electronic mail address; Social Security number; medical record number; health plan beneficiary number; account numbers; certificate/license numbers; vehicle identification and serial numbers; device identifiers and serial numbers; URLs; IP address numbers; biometric identifiers; full-face photos or comparable images; and any other unique identifying number, characteristic or code; or

(2) have the patient authorize access to the PHI, unless a Privacy Board or an IRB waives the need for authorization in accordance with specific requirements designed to protect privacy. Those requirements include a finding that the research could not practicably be conducted without the waiver, that data will not be reused or disclosed to a third party, and that there is an adequate plan to protect privacy (164.512(i)); or
(3) construct a Limited Data Set, where the data are provided to a researcher who has signed a Data Use Agreement. A Limited Data Set can include dates and geographic information, but not street addresses or other direct identifiers listed above. A Data Use Agreement establishes the permitted uses of the limited data set and says the researcher will not further use or disclose the information, will protect it, and will not identify or contact the individuals whose data are in the set. For research using DNA derived from dried blood spots: a. there must be de-identification, which can most easily be accomplished by simply snipping off a piece of the specimen and providing no other information; or b. there must be parental or legal guardian written authorization on a Privacy Rule compliant form; or c. there must be a waiver of the need for authorization properly granted by a Privacy Board or IRB; or d. there must be a Limited Data Set containing only general geographic information and relevant dates, coupled with a data use agreement signed by the researcher (see privacyrulesandresearch.nih.gov).” 29

In addition to the privacy considerations above, NBS laboratories are also governed by the Clinical Laboratory Amendments of 1988 (CLIA), which require confidentiality of patient information throughout all phases of the testing process under laboratory control (42 CFR §493.1231).30 Additional state licensure or contract requirements may also exist. The CDC has recommended that laboratories performing molecular genetic testing (which may include both NBS laboratories, diagnostic laboratories working in collaboration with the NBS program, and research laboratories) should establish and follow procedures and protocols that include defined responsibilities of all employees to ensure appropriate access, documentation, storage, release, and transfer of confidential information and prohibit unauthorized or unnecessary access or disclosure.31

- Awareness and Education

In 2000, the AAP Newborn Screening Task Force recommended developing educational materials for parents that include information about the storage and use of residual samples.31 A recent study by Goldenberg32 has determined that only 12 states currently include mention of specimen storage in their NBS educational pamphlet. Regardless of the content, studies have shown that there is little effort currently ongoing to involve prenatal care providers in the newborn screening system.34 The American College of Obstetricians and Gynecologists (ACOG) has published a position paper (ACOG Committee on Genetics Opinion 88) that encourages its members to become aware and involved in state newborn screening efforts.

A recent study of the attitudes of women towards a hypothetical pediatric biobank showed that Caucasians were the most willing to enroll their children, while non-Black minorities were the most uncertain about what they would do. Women with only one previous child were the most willing to enroll their child, while women with no previous children were the most uncertain. When women were asked why they would or would not enroll their child into a biobank, 26% of the 207 responders did not feel that they had enough information, 10% were concerned about risks, and 8% were concerned about privacy. Consent issues were a concern in 8% of cases including a desire to have the father included or to have the child consented at a later age. Of 90 women explaining why they would enroll their child, 53% expressed altruistic reasons to benefit society and 20% described the potential to benefit their own child or family. This study found a general understanding of research but there were significant misperceptions about what participation in a biobank entailed. These misperceptions confirmed a need for increased public education about research participants’ general rights to privacy in research, and what enrollment in a biobank entails. In particular, there was a need to more clearly explain what information researchers or others might access.35

Information sharing has been shown to positively correlate with participation in research. A 1998 study of 93 subjects showed a high percentage of willingness to participate in hypothetical biobank research.
studies with only 13% placing some restrictions on the type of research to be done. Similarly, analysis of 1670 consent forms from clinical research participants at the National Institutes of Health showed 87% agreement to authorize research on any medical condition. A 2008 hypothetical biobank study also found potential participants would place restrictions on the type of research to be performed with over 90% supporting all conditions proposed. In addition to their willingness to enroll, potential participants were also optimistic that the research would achieve significant clinical results in the near future. Trust and belief that the research would be integrated fairly into clinical care were also found to correlate with enrollment.

Community engagement to help relevant programs understand public privacy concerns has been identified as a useful step in helping recruit and retain biobank participants. It has also been suggested that researchers should translate community knowledge and concerns about children into responsive and realistic study protocols. A longitudinal study of children (who eventually transition to adulthood) should retain some degree of flexibility to account for differing rights as children transition to adults. Clear communication at the outset about consent, dissent and re-consent, as well as the scope, risks and benefits of studies are considered to be essential.

Consent/Dissent Issues
The feature that makes blood spot repositories so potent -- mandatory screening means that they capture entire populations - also makes them ethically and legally complex. In the U.S., parents of newborns are rarely informed that specimens will be stored and could be available for research and some have argued that, while consent may be a good idea, in practice it could be alarming to families. On the other hand, biobanks (including the collection and storage of residual NBS specimens) for public health and related research require clear regulation with a meaningful consent/dissent process in order to maintain public trust.

Most often, consent for research is for a single project, and researchers must re-consent individuals if they wish to undertake another project. Occasionally, consent is broader and open-ended, in which case study participants agree to specimen storage and use for future unspecified purposes. This broad or ‘blanket’ consent is not as common and is problematic under the federal privacy regulations which call for specific consent for specific research projects (see federal privacy rule 08-14-02 preamble 53231); therefore, institutional review boards are reticent to approve such consent processes. Since the retention and use of DBSs cannot anticipate all future purposes, blanket consent for future research is likely to be a consideration. While broad consent maximizes possible specimen uses, it also creates the potential for uses that some consenters might find objectionable and it must take into account HIPAA consent and privacy requirements; therefore, blanket consent must be approached carefully. Of interest is a 2004 German National Ethics Council opinion that different options do not need to be offered in the informed consent process for samples obtained during medical care. Additionally, informed consent may be waived when samples and data are completely anonymous, unless a prior contrary wish has been expressed. “Donors should be able to give generalized consent to the use of their samples and data for the purposes of medical - including genetic – research.” Length of storage and use of data were regarded similarly with neither limited in advance. The German approach exemplifies a gradual move towards allowing biobanks to obtain a broad consent for future secondary research. To minimize privacy concerns,
anonymized or double coded specimens/data [with a third party key holder (see Appendix for discussion of Michigan ‘honest broker’) controlling release and use of information] are sometimes used. Further, there are a number of systems in development that would allow individuals to determine consent in a more dynamic manner (e.g. PatientsLikeMe, Private Access). In this way, consenting individuals participate for the public good, while maintaining personal values and autonomy and may ultimately enhance research activities and outcomes.\textsuperscript{45}

Residual DBSs can be stored unidentified (anonymized), linked, or with identifiers. The use of residual NBS specimens represents perhaps the most currently visible example of the need for consensus on the ethical rules governing the use of bodily tissues.\textsuperscript{43} Potential research use also raises the question of ‘meaningful’ consent. Some form of consent or formal IRB waiver of consent appears to be necessary if NBS specimens are to be placed into a repository for research purposes since creation of a research repository is, in and of itself, research. (See: OHRP Nov. 7, 1997, Issues to Consider in the Research Use of Stored Data or Tissues, http://www.hhs.gov/ohrp/humansubjects/guidance/reposit.htm and the OHRP Guidance on Research Involving Coded Private Information or Biological Specimens, http://www.hhs.gov/ohrp/humansubjects/guidance/cdebiol.htm). In the case of linked or identified specimens, the American Academy of Pediatrics (AAP) has noted that parents should be informed of the specimen retention policy and asked for consent for storage of residual blood spots.\textsuperscript{33} While consent (opt in) is often used to indicate approval of the individual for storage and use of their specimen, successful models for opting out (dissent) also exist, as for example with the Danish newborn screening biobank (see Appendix).

While medical privacy advocates and ethicists argue that parents must be asked for consent before residual NBS specimens are kept,\textsuperscript{46} others argue that meaningful consent is impossible since parents cannot be adequately educated about all potential uses and outcomes.\textsuperscript{18} Prudent advice seems to exist in previously published guidance from our Canadian colleagues:\textsuperscript{14}

\begin{quote}
"Well informed parents are best placed to consider their child's health and should be aware that they or their child might or might not be contacted or affected by future studies or policies....Although length and purpose of storage might not represent major concerns for new parents, ideally, written information about sample collection, storage and future uses must be given to all parents as part of the newborn screening program. It is advisable that this information be relayed to parents by health professionals, such as gynecologists, obstetricians or nurses, during prenatal visits, to ensure that parents have fully understood the information that has been provided and to give them the opportunity to ask questions. Information pamphlets should describe the reasons for storage, specifying whether dried blood spot (DBSs) will be used for diagnostic testing and treatment, for control and documentation of previously performed analyses should suspicion of diseases arise later in life, quality assurance of screening programs, for the development of new and better assays, in epidemiological studies, for specific disease testing if unexpected events occur during the newborn's first year of life or after, or for research projects.\textsuperscript{47} In addition, information should be given on methods of storage (anonymized, coded, or identifiable). Parents should be told about the security measures that have been implemented to protect the confidentiality of medical and genetic information found on the DBS cards. Furthermore, parents should receive information regarding those who will have access to the stored DBSs and whether permission will be sought from them or from an Ethical review board should any third parties wish to have access to the samples for research use."
\end{quote}

The way in which NBS specimens and related (genetic) information are stored is particularly important in considering whether consent is necessary for secondary uses. The AAP Newborn Screening Task Force recommended that archived dried blood specimens should be made available for research only if
identifiers are removed. Anonymization of data is generally thought to set aside the requirement to obtain explicit consent. If specimens are not identifiable then they are not considered "personal" and data-subjects are at very low risk of being harmed. While consent is waived when archived specimens are anonymized, to anonymize NBS specimens without obtaining consent at the time of collection for anticipated, anonymized research, is considered by some as questionable and a threat to public trust in research endeavors with such specimens. When investigators need access to linked or coded specimens, renewed consent from the parents (or from the subject, if the latter has reached the legal age to consent) is often required. In rare circumstances and when specific criteria are met, ethical review boards have authority to waive consent requirements. This generally happens when research is of minimal risk, when it will not adversely affect the subject's rights and welfare, when it is impracticable to obtain consent and whenever appropriate, subjects will be provided with pertinent information after participation. Subject to ethical review board approval and parental consent has been obtained, the use of identified or coded specimens has also been deemed acceptable if researchers can demonstrate that NBS specimens are the best specimens available and that similar data could not be obtained from adults. If the research study does not require that donators be re-contacted or identified, some have suggested that existing medical records and stored specimens that contain identifying information can be made available for research without explicit individual consent or ethical review board approval.

**Legal Back-up**

Legal challenges to newborn screening issues, while often involving individual physicians and hospitals, can do involve state health departments. Typically, litigation of NBS cases in which the state is named as a defendant will be handled by the State Attorney General’s Office of the State Health Department’s Office of General Counsel. In such cases, expertise in health care law is a necessity. Lawsuits filed over the use of NBS data or specimens invariably involve the state health department as the custodian of these items. As example, citizens groups in Minnesota and Texas have recently filed lawsuits over residual NBS specimen storage and usage issues. With the increasing attention surrounding residual specimen storage and use, it is imperative that state health department legal offices be aware of legalities and points of legal exposure within the NBS system. Issues regarding storage and use of stored specimens considered ‘historical archives’ for which consent/dissent for storage and/or use was not previously obtained may also exist and may constitute additional legal issues. State NBS and privacy laws, federal privacy issues, research requirements, and product liability issues (testing kits, new products, etc.) also represent possible legal concerns.

**Position Statements – Professional Groups**

**ACMG** - In a previous position statement for clinical genetic laboratories, the American College of Medical Genetics (ACMG) took the position that testing facilities should establish laboratory policies regarding specimen retention and appropriate storage conditions. A more recent ACMG position statement on newborn screening noted that: 1) residual NBS specimens are a valuable national resource that can contribute significantly to the health of our children; 2) newborn screening blood spots are stored with rigorous control and respect for privacy and confidentiality to protect the public; and 3) if a state decides that newborn screening blood spots should not be retained or used for anything more than the screening test, it is critical that individuals have the option of having their children’s dried blood spots deposited in a national repository which will allow for necessary studies under appropriate privacy and confidentiality protections. ACMG Standards and Guidelines state that the retention of a patient's DNA should be in compliance with state and federal laws. Re-use of patient DNA specimens, i.e., subsequent use and retention is as allowed by the patient.

**APHL** - The Association of Public Health Laboratories (APHL) has a position policy that supports the development of national consensus policies, procedures, and standards for retaining residual DBS specimens following NBS analysis. These policies and procedures must recognize existing federal
regulations for clinical testing, state laws, professional guidelines, and ethical and legal precedents. The policies should allow for introduction of new analytes and techniques into the NBS arena. To meet recognized laboratory quality assurance practices, DBS specimens must be retained for a time period and under conditions that permit analytical validation. There may be other reasons other reasons to save DBS specimens, including test development, research, and forensic identification. To retain residual for such purpose requires clear guidelines that are incorporated into national consensus policies that state public health departments can follow in carrying out their authorized NBS programs.54

CLSI - The Clinical and Laboratory Standards Institute (CLSI) guideline55 states that, “Beyond the usual medico-legal considerations that determine advisable durations for retention of all clinico-pathologic specimens, molecular genetic specimens – particularly the DNA contained therein – have potential importance for family studies and distance descendants long after the present patient is deceased. The patient’s DNA could prove essential for either linkage studies or direct mutation identification, perhaps involving tests not yet developed. A primary issue regarding specimen retention involves ethical and legal considerations, such as specimen ownership, confidentiality, and informed consent. Until universal recommendations are adopted or until regulations are implemented, each laboratory should establish its own policy regarding specimen retention and the use of archived specimens or stored DNA. A laboratory specimen retention policy should consider the following factors: 1) type of specimens retained (e.g., dried blood on filter paper), 2) analytes tested (e.g., DNA, RNA, or both), 3) test results or the genotypes detected. (If only abnormal specimens are retained, identifying false-negative results at a later date will be difficult. This practice also might introduce bias if a preponderance of specimens with abnormal test results is used to verify or establish performance specifications for future testing.), 4) test volume, and 5) new technologies that might not produce residual specimens.55

AAP - The AAP Newborn Screening Task Force published its final report in 2000.33 In addition to proposing a national newborn screening plan (blueprint) for the future, this Task Force also made recommendations concerning residual NBS specimen storage and use. Their recommendations included the following:

“1) Using national recommendations, each State program should develop and implement policies and procedures for retention of residual NBS blood samples that articulate the rationale and objectives for storage, the intended duration of storage, whether storage is with or without identifiers, and guidelines for use of identifiable and unlinked samples; 2) Develop educational materials for parents that include information regarding the storage and uses of residual specimens; 3) Develop model consent forms and informational materials for parental permission for retention and use of newborn screening specimens (to date these models have not been developed for NBS program use); 4) Develop policies and procedures for unlinked/linked residual specimens in research/surveillance; and 5) Organize collaborative efforts to develop minimum standards for storage and database technology to facilitate appropriate storage of residual newborn screening blood specimens at the state level and consider creating a national or multi-state population-based specimen source for research in which consent is obtained from the individuals from whom the tissue (blood) is obtained.”33

TECHNICAL CONSIDERATIONS

● Specimen Quality
The national standard for blood collection on filter paper56 currently in use defines the characteristics of DBSs required for analysis. Because the collection cards constitute federally approved specimen collection devices, careful handling to prevent contamination is essential, particularly from extraneous DNA which may be transmitted by touching. Lightly abrasive contact between specimens on filter paper has been shown to result in DNA cross-contamination; however, where contamination was detected,
levels were insufficient to affect most routine molecular genetic NBS assays.\textsuperscript{57} Since cross-contamination by contact (leaching) is possible, specimen-to-specimen contact should be avoided. It is standard practice to submit NBS specimens in transport envelopes rotated 180° from each other to avoid specimen contact unless physical barriers are presents (e.g. fold-over flaps or non-absorbent paper).\textsuperscript{56} Should punching and cutting tools be used for DNA specimen procurement, they must be cleaned before each use to avoid carry-over contamination between specimens.\textsuperscript{58}

Since the amount of residual specimen material that remains after NBS tests are completed is limited, if used for other purposes, its use should be of significant impact, especially if a relatively large amount of specimen is required. Previous U.S. guidance suggested that policies should prioritize the possible uses of residual specimens and should ensure that at least one blood spot is retained for possible use for the specific benefit of the patient.\textsuperscript{18} Personal data on the information portion of collection cards should be kept separate from stored blood specimens, with secure access restricted to authorized personnel.\textsuperscript{2}

\textbf{Analyte Stability}

Assorted stability studies have demonstrated the extractability and stability over time of DNA in DBSs on filter paper. While genomic DNA was shown to be stable under tropical conditions for at least 11 years at ambient temperature, the DNA quality for amplification of larger DNA fragments decreased when specimens were stored for longer than 10 years.\textsuperscript{59} Studies in Washington State showed that storage for 25 years, at times without air conditioning, yielded successful genotyping results. However, the investigators noted that the climate in Washington is moderate, and study assays primarily used short amplicons - genotype might not be determinable for all subjects for assays requiring long amplicons.\textsuperscript{60} A study of 70 well-DBSs stored for 19 months at ambient temperature gave adequate forensically useful DNA.\textsuperscript{61} Likewise, whole genomic amplified DNA from DBS specimens archived for 15 to 25 years was used for reliable genome–wide scans and was found to be a cost effective alternative to collecting new specimens.\textsuperscript{62} The quantitative RNA stability in DBS has also been demonstrated for specimens\textsuperscript{63, 64} stored at 4 °C with controlled relative humidity maintained at 30% for up to 20 years.\textsuperscript{65}

Stability of non-DNA biomarkers commonly used in NBS has been shown to vary across analytes, with many showing degradation within a few months.\textsuperscript{18} No significant loss of phenylalanine, leucine, tyrosine, methionine and valine was observed in analyte-enriched blood spots during 1 year of storage at -20 °C, whereas all amino acids showed degradation at 37 °C within 30 days. Methionine was the least stable of the amino acids tested.\textsuperscript{56} While acylcarnitines have shown stability for at least 330 days at -18 °C, at room temperature; they are readily hydrolyzed to free carnitine (with its level increasing during storage) and the corresponding fatty acids. The velocity of decay is logarithmic and depends on the chain length of the acylcarnitines.\textsuperscript{67} Studies have shown that stored blood spots should only be used for retrospective quantitation of acylcarnitines if appropriate correction for sample decay during storage is applied.\textsuperscript{67} A tandem mass spectrometry evaluation of the long-term stability of acylcarnitines and amino acids in dried-blood stored for 15 years at ambient conditions showed that, with the exception of free carnitine and valine, all metabolite concentrations decreased.\textsuperscript{68} Free carnitine increased during the first 5 years with the largest increase in the first year during which it rose 40%. Phenylalanine, alanine, arginine and leucine decreased exponentially. Citrulline, glycine and ornithine decreased markedly during the first 5 years. Methionine was the least stable of the amino acids. Many of the acylcarnitines decrease significantly during the first 5 years and more gradually thereafter. Tyrosine was relatively stable compared to most other amino acids in that it decreased more gradually during the first 5 years. Valine was considered stable since no significant change was found during the 15 years. Medium and long-chain acylcarnitines could not be analyzed because of low physiological concentrations.\textsuperscript{68}
● Storage Conditions
Optimal operation of a DBS storage facility requires that storage be carefully planned and that storage conditions be specified and monitored. If the purpose for saving DBS specimens involves future analysis, screening programs should investigate data that address the stability of various analytes when making decisions about storage conditions. The defined purpose of storing samples should dictate the environmental parameters for storage. Ideally, residual DBSs should be stored frozen (preferably at -20°C) in sealed bags of low gas permeability containing a desiccant and a humidity indicator. Specimens retained only for DNA testing may be stored at ambient conditions (preferably refrigerated at 4°C) in sealed bags of low gas permeability and containing a desiccant for humidity control. In all storage situations, precautions should be taken to ensure that possible contamination from specimen-to-specimen contact is not a problem. Several publications have demonstrated the recovery of quality DNA from DBS stored at ambient conditions. During storage, a humidity indicator should be periodically monitored and appropriate action taken to reactivate the desiccant when humidity exceeds 30% or some other designated level of action. Every DBS should be properly identified. An index or catalog should be maintained so that any individual sample can be easily located. A quality assurance system is necessary for documenting the integrity of the stored DBS.

● Retention Conditions
Laboratory genetic testing guidelines exist and appear to be applicable to NBS testing. Additionally CLIA requires laboratories to establish and follow written policies and procedure that assure positive identification and optimum integrity of a patient’s specimen from time of collection through completion of testing and reporting of results. ACMG Standards and Guidelines state that the laboratory should retain the original patient sample until all testing is completed and the report has been completed. Depending on specimen stability, technology, space, and cost, tested specimens for molecular genetic tests for heritable conditions should be retained as long as possible after the completion of testing and reporting of results. It has been recommended that at a minimum, stabile tested patient specimens should be retained after testing until the next proficiency testing or the next alternative performance assessment to allow for identification of problems in patient testing and for corrective action to be taken.

Specimen retention times vary widely among state newborn screening programs as demonstrated in Figure 1. At least 10 programs have indicated their intention to maintain archives of specimens indefinitely. Because of the cost and complexity of specimen storage, only a few programs are known to store their residual NBS specimens frozen (-20°C) in sealed bags containing a desiccant. Notwithstanding storage challenges, some states have retained large numbers of residual specimens, often exceeding 1 million. Where specimen storage exists, a quality assurance system should ensure validity of stored samples for their intended purpose. Where a defined purpose exists such that a control specimen can be stored, the control should be stored under identical conditions. In order to prevent location bias, control samples should be randomized in the storage system. Specimens that may be analytically unacceptable for NBS analysis may still contain usable analytes, including DNA, and should be stored under similar conditions to specimens that were analytically acceptable.

Specimen storage must be carefully planned such that specimens are kept readily accessible, secure, and environmentally sound. A storage policy should exist with input from others with experience and NBS stakeholders, including researchers and the public. The long-term cost and technical logistics of maintaining a specimen bank should be anticipated. Systems for easy access and retrieval should be carefully designed, and storage conditions should be maintained with careful documentation. Flow charting the specimen retrieval process and electronic specimen identification should be a part of the cataloging process. Safe disposal of samples no longer required for examination should be accomplished in accordance with local regulations regarding waste disposal. Care should be taken to dissociate patient identifiers from the blood spots. If samples must be transported off site for incineration
or destruction, precautions should be taken to assure that confidentiality of samples during transportation and destruction is maintained and that appropriate disposal of samples is achieved (i.e., no identifying information should be attached). The program’s specified length of retention for DBSs should be consistently met, and all disposal activities should be documented.

- **Transport to/from Researchers**

Handling and transport of residual NBS specimens should conform to the established processes for transport of specimens to the screening laboratory in accordance with OSHA guidelines and with the understanding that any human tissue and fluids may harbor infectious agents. DBS specimens can be shipped or transported by mail or other carrier with no reasonable expectations of occupational exposure to blood or other potentially infectious material. “Standard precautions” and compliance with local regulations and institutional policies are required in preparing NBS specimens for shipment. The identified packaging system must meet the basic triple packaging system, i.e., blood absorbed into paper, an inner envelope or other protective cover, and an outer envelope of high quality paper. U.S. transport standards are harmonized with the World Health Organization’s Guidance on Regulations for the Transport of Infectious Substances and the International Civil Aviation Organization’s Technical Instructions for Safe Transport of Dangerous Goods by Air.

DBS specimens must not be packaged in airtight, leak-proof sealed containers (e.g., plastic or foil bags) because the lack of air exchange in the inner environment of a sealed container causes heat buildup and moisture accumulation. Heat, direct sunlight, humidity, and moisture are detrimental to stability of DBS specimens and analyte recovery. The inclusion of desiccant packs will aid in preventing moisture accumulation, but shipping conditions are uncontrolled, and desiccant has limited effectiveness. Local postal, courier, and other transport regulations must be followed. If local regulations require enclosure in airtight, leak-proof sealed containers (plastic or foil bags) for transportation, then sufficient numbers of desiccant packages must be included to ensure minimal exposure of specimens to excessive moisture. Indicator cards may be used to monitor humidity. Specimens known to contain an infectious agent should be transported with special precautions according to local regulations (e.g., required packaging and outside warning label).

**FINANCIAL CONSIDERATIONS**

“Policymakers have an ethical obligation of stewardship to weigh the benefits against the costs when directing resources to newborn screening systems and their components.” The sources of funding for newborn screening vary across states depending on local infrastructure resources available, monies from external sources that can be used for newborn screening, and the definition of system components that require financial support. A recent review of NBS financing reported that 90% of all NBS programs have a fee paid by parents or a third party payer, 61% utilize some funding from the Maternal and Child Health Services Title V block grant, 33% receive some funding from state general revenue/general public health appropriations, and 24% obtain direct reimbursement from Medicaid (without passing through a third party). While this report noted that 64% of NBS programs received budget increases between 2002 and 2005 (72% from fees and to a lesser extent from Medicaid, the Title V block grant, and state general revenues), the exact impact of recent national financial difficulties on NBS programs is not accurately known. The financial impact of a specimen storage program requires that the components of such a program must be carefully and comprehensively defined in order to determine their expense. As a minimum there will be costs associated with the storage and retrieval process, professional and consumer education, and other issues such as consent/dissent forms and processes, researcher costs, etc. Because many NBS programs see a national position that encourages better education, control and facilitation of residual NBS specimens as an unfunded mandate, consideration of federal financial support is needed.
**Storage and Retrieval**

All NBS programs retain residual NBS specimens for some period of time, usually with at least one identification number. Linkage to demographic information usually exists until such time as deidentification may be initiated for privacy protection for some research uses. The national blood spot collection standard recommends that specimens should be refrigerated (for up to 6 months) until they are either destroyed or stored frozen for a longer-term. Desiccation is also recommended to prevent adverse effects of moisture.\(^{56}\) The majority of programs currently maintain specimen storage under standard laboratory conditions – room temperature without desiccant. Thus, additional expenses will exist for most programs if residual NBS specimens are properly stored. Additionally, expenses are anticipated for computerized specimen, data, and permission tracking.

Greater costs are anticipated when residual specimens are maintained long-term. Published reports of storage and related costs are rare, so anecdotal costing reports must be assessed to formulate estimates of costs. Proper long-term storage requires the desiccant to be monitored and replaced periodically to maintain ‘dry’ storage. Specimen access may be either through a manual or automated filing system. Automated systems will identify exact storage location instantaneously, while a manual system may take longer depending on the volume of stored cards. The level of sophistication of storage affects pricing, which may include bar coding and the additional expense of bar code reading. Specimen volume dictates storage capacity and security, which may vary from a small walk-in freezer to a small warehouse. Storage capacity impacts electrical cost and security costs, which may include costs for security personnel.

As one cost example, the South Carolina public health screening laboratory uses a dedicated walk-in freezer to store residual specimens (~55,000/year) for up to 3 years (depending on the disbursement option chosen by the guardian at the time of collection). Retrieval costs include a database that provides physical location information to facilitate a manual searching process. The retrieval process cannot be realistically separated into component parts, and has been estimated on the basis of employee time. Approximately 0.67 FTE is required for an annual cost of $40,500 (salary + fringe + indirect + health services support). Primary laboratory non-personnel expenses include the cost of freezing and storage. Annual freezing costs include: freezer rental at $6,000/yr (200 sq. ft. at $30 sq. ft.); maintenance at $500 (assuming no equipment failures), and; electricity at $6,850 (3 hp compressor = 3450 watts/yr; electric rate = .09355/KW/hr). Packaging/storage supplies add approximately $850 to the overall cost for a total of approximately $14,000 for laboratory non-personnel storage costs. Thus, the annual cost for specimen storage and retrieval in South Carolina is approximately $54,500 for storage of ~165,000 specimens with minimal retrieval.\(^{78}\)

The much larger California program (~560,000/year) currently maintains the largest NBS storage facility with a total of approximately 15 million residual specimens kept frozen and desiccated. Regulations specify the process for specimen retrieval and usage requests. Specimens are stored in a rental facility at a cost of approximately $150,000/yr through a contract that provides for backup contingencies and security. There are additional charges for forklift operations when a pallet of specimen storage boxes must be moved but this cost is insignificant compared to the total contract. Retrieval costs have been calculated to be approximately $30/specimen based on the personnel time required for accessing, labeling, and shipping. Accessing involves cutting out an already punched circle and asking the user to return the remainder following their project use.\(^{79}\)

SeraCare is a commercial storage company dealing in individual specimen storage. DBSs are currently stored in freezer boxes with 25 cards to a box. Each specimen is stored in a separate storage bag with
desiccant. Specimens are typically stored at -20°C or -80°C. Current charges include: ambient, $0.03; +4°C or -20°C, $0.35; -80°C, $0.57; and liquid nitrogen, $0.32 per specimen per year.  

For the Danish Healthcare Biobank, residual specimen retention uses a government owned storage facility and contains about 2 million specimen cards. The freezer (-20 °C) contains space for ~ 3 million collection cards. Specimens are kept in small boxes containing 400 cards each and these small boxes are located in larger boxes for more efficient retrieval. No desiccant is required since the humidity is very low and specimens are not kept in plastic bags. No contamination has been noted in large studies using specimens maintained by this storage procedure. A contingency freezer is available. Specimen retrieval is manual and a database maintains permission records that allows for easy specimen identification and location using the personal identity number of the mother or child. Automated retrieval is considered excessively expensive and unnecessary. Only authorized personal have access to the locked freezer. A central unit at the institution monitors the freezer operation constantly. There is a specimen retrieval charge of approximately $20 per specimen to recover storage and operating cost of $20,000 per year. Storage costs are considered to be low and specimens are efficiently stored and retrieved. 

- Education
The role of the obstetrician as an educator in the newborn screening process has been defined. Unfortunately, most still do not function in this role. A 2005 questionnaire study of Hawaii obstetricians showed that less than 15% could correctly answer knowledge questions about newborn screening. Fewer than 20% reported discussing NBS with patients, and of those, only one-quarter correctly answered the NBS questions. The need for provider education was confirmed by a California study that found most prenatal care providers believed that newborn screening participation was important; however, 25% reported not discussing it with any of their patients and most who did discuss it, did not discuss it with all patients. Prenatal care providers seemed to believe hospital staff or pediatricians would discuss NBS with their patients. Nearly 1/3 of patients never received NBS educational materials from their prenatal care provider, even though prenatal care providers in California are legally required to provide them. 

While these studies validate the need for better physician education to meet the educational needs of the screening program, studies have also shown that the responsibility for informing parents about the screening process has not been clearly defined in many programs. A 2005 survey about educational responsibility indicated that only 25% of programs encouraged prenatal care providers to educate parents about NBS and less than 50% felt that primary care providers had some educational responsibility for informing parents about newborn screening. A recently published Canadian study reported that virtually all midwives and almost half of the nurses reported discussing NBS with parents whereas less than one sixth of the physicians did so. Providers who perceive a responsibility to inform parents were 3 times more likely to report discussing NBS with parents. Those who lacked confidence to inform parents were 70% less likely to discuss NBS. Research has also shown that the educational materials developed for parents often do not meet the standard recommended by the AAP, and there are important variations between programs in the information provided to parents. The most common educational mechanism remains a brochure provided in the hospital package of informational materials for the mother. Focus groups of parents have shown that written information should be presented in a user-friendly and easy-to-read format, and parents are most interested in information that they deem relevant and practical and that emphasizes what they need to know and do. 

Typically a NBS educational program will need to: (1) inform prenatal and other healthcare providers and policy makers about the issues related to residual NBS specimen storage, and; (2) inform parents about the issues related to NBS specimen storage and potential use, and their options. While models of informational brochures for NBS programs exist, they do not generally address residual specimen storage issues. The degree to which individual program education currently addresses newborn screening issues
coupled with the comprehensiveness of education that may be needed to address specimen storage issues will have a significant cost, at least at start-up. Additionally, there will be costs at the point-of-care to provide the additional information, a California pilot program for MS/MS found that the labor cost required to have each parent sign an informed consent form at the specimen collection resulted in many parents never being approached or having their decision documented.86

- **Associated Costs**

In order to supply information about specimen use and to obtain proof of understanding and acceptance by parents, blood spot collection kit modifications may be necessary. In some programs, specific wording requirements already exist and specific forms and wording must be used (see NBS statues for TX [Texas Health and Safety Code, Title 2 Ch 33 Sec 011-012.]; MN [Minnesota Statutes, Ch 144 Sec 125]; SC [South Carolina Code of Laws, Title 44 Ch 37 Sec 30.]; MO [Missouri Revised Statutes, Ch 191 Sec 331.]; MI [Michigan Compiled Laws, Public Health Code Act 368 of 1978 Ch 333 Sec 5430]. South Carolina modified their blood collection card to have the specimen retention information and consent form as multi-layer tear-off forms attached to the reverse side of the blood collection card—the addition of this form added an approximate cost of $5 per 100 collection cards. A legislative requirement in Texas has resulted in the need to add an additional page to the collection card. In addition to costs associated with changes to the blood collection card, other printed materials may be required as part of the consent/dissent process. Residual NBS specimens must be placed in storage and then retrieved and shipped if research uses are approved. Costs for these activities will vary depending on local salary schedules, the manner of specimen storage, the location of the storage facility, the number of specimens required for a project, the de-identification or other specimen preparative processes, method of transport to and from the research facility, and method of specimen destruction. Environmental control and possible chain of custody requirements for specimens in transit may add expenses. While individually these costs may be small, collectively they may be substantial and therefore should not be dismissed without consideration.

**CONCLUSION**

Since the initial guidance for retention, storage of use of residual DBSs in 199618, there have been noticeable improvements in policy development among state NBS programs. Nevertheless, there remain two distinct philosophies regarding the storage and use of residual DBSs: 1) short-term storage (<3 years), presumably for program quality assurance and test improvement; and 2) long-term storage (> 18 years), presumably for public health research. While two-thirds of state programs maintain the philosophy that specimens should not be stored long-term for research, the number of newborns affected are less than 50% of the newborn population.87

There is heightened awareness in the research and consumer communities concerning both the potential value of specimens and the potential privacy issues. Privacy issues are compounded by the lack of standardized consent policies across state programs, the lack of a universal legal definition of specimen ownership once the screening process is complete, and the lack of public awareness of newborn screening. In light of growing use of residual NBS specimens and their potential secondary applications, proactive solutions should be envisaged to ensure proper public education, protection of parental choice, an informed process for consent/dissent, and stricter enforcement of genetic privacy and confidentiality.14 Public trust and transparency of operations should be the goal of all programs seeking to store residual NBS specimens. Open and informed dialogue between public health organizations and the public they serve should be improved and expanded as part of the screening process.

Because newborn screening is the only medical screening program that reaches the entire population of newborns, it is unique and the processes surrounding it must be carefully and thoughtfully approached.
Residual blood specimens provide an excellent opportunity for storage and use in a biobank after screening is complete and the results have been validated. However, at the present time, this is a secondary purpose that may not have been adequately addressed in state law or policy. Therefore, residual specimen use must be carefully considered anticipating both the potential benefits and risks.

RECOMMENDATIONS

To assist in harmonizing the storage and use of residual NBS specimens, the ACHDNC should consider the following recommendations:

1) **All state newborn screening programs should have a legally reviewed and accepted policy addressing the disposition of dried blood specimens remaining after newborn screening testing is complete and the screening results have been validated.** Multidisciplinary input, including consumers, should be solicited and thoughtfully considered in developing such a policy. This specimen disposition policy should include the length of time for which specimens will be stored and storage conditions. Compliance with storage processes included in NCCLS/CLSI Standard LA4-A5 or its current edition is recommended. Any data linkages should be carefully addressed and confidentiality assured. Appropriate measures should be in place for confidentiality.

2) **All state newborn screening programs should have a legally reviewed and accepted policy that specifies who may access and use dried blood specimens once they arrive at the state-designated newborn screening laboratory, including further access after newborn screening tests are completed.** Multidisciplinary input, including consumers, should be solicited and thoughtfully considered in developing such a policy. This specimen access policy should include any uses prior to and after the newborn screening laboratory testing and validation process. If uses of dried blood spot specimens outside of newborn screening are allowed, then handling and disposition of the specimen should be addressed along with confidentiality of any associated patient information.

3) **As part of the educational process of the newborn screening system, all state newborn screening programs should maintain and distribute educationally and culturally appropriate information that includes basic information about the use or potential use of the dried blood specimens.** Where long-term storage policies or other options exist relative to storage of residual dried blood spots, such information should be included in prenatal education materials.

4) **All state newborn screening programs should work proactively to ensure that all families receiving prenatal care are educated about newborn screening.** This activity should include appropriate steps to inform and train prenatal care providers regarding their educational responsibilities within the newborn screening system. Processes should be in place to evaluate the extent, timing and understanding of prenatal education with an eye towards educational program improvement.

5) **If residual blood specimens are to be available for any process outside of the legally required newborn screening process for which they were obtained, an indication of the parents’ awareness and willingness to participate should exist in compliance with federal research requirements (45CFR46 [http://ohsr.od.nih.gov/guidelines/45cfr46.html]).** A consent (opt in) or a dissent (opt out) process may meet this requirement depending on purposes for which specimens will be used. The use of residual specimens for program evaluation (e.g. repeat testing as a quality check) or process improvement (e.g. non-commercial, internal program new test development) are valid components of the newborn screening system and, therefore, should not require additional consent.
6) **Newborn screening programs should evaluate the utility of any additional consent/dissent process implemented in order to better address issues of storage and use of residual dried blood specimens.** In this respect, the federal government is encouraged to provide funding for NBS programs to evaluate the utility of any new consent/dissent processes implemented relative to specimen storage as a means of improving their systems.

7) **The federal government is encouraged to provide administrative support and funding to develop:**

- Model consent/dissent processes for the use of residual newborn screening specimens;
- Model educational programs for the general public on the importance of newborn screening and the potential uses of residual specimens to generate population-based knowledge about health and disease;
- National data on the utility of any additional consent/dissent processes implemented relative to potential research uses of residual newborn screening specimens; and
- Educational materials with facts about potential uses of residual newborn screening specimens for both consumers and prenatal healthcare providers.

**Note:** During the vetting process (webinars) to the stakeholder community, questions and discussions led to development of the following proposed (optional) recommendation. Since this proposed recommendation was not shared with the stakeholders in the webinars and not unanimously embraced by all members of the ACHDNC Work Group, it is listed here separately for your consideration and discussion.

**Optional Recommendation**

*Where state newborn screening programs elect to maintain a long-term newborn screening biobank of residual newborn screening specimens, a secure third party key holder system (“honest broker”), with appropriate consent, should be used to allow for emergency linkages in de-identified specimen studies.* The key holder would have the ability to reveal critical health information to a study subject should such information be discovered during the course of the research, and the ability to obtain and reveal personal information from a subject to a researcher, if such information were deemed to be of critical importance. In either case, consent from the study participant or appropriate parent or guardian would be required.

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APPENDIX 1. Examples of Residual Dried Blood Spot Biobanks

1. Danish NBS Healthcare Biobank (homepage: [http://www.ssi.dk](http://www.ssi.dk))

For more than 25 years, residual dried-blood spot specimens (DBSs) from the Danish NBS program have been stored in a healthcare biobank. The storage has taken place according to regulations from the Danish Ministry of Health (1993) and recently according to new guidelines for the establishment and operation of biobanks in general (2004). After routine newborn screening (NBS), residual DBSs are stored at -20 °C in a secure cold room inside a secure building. The Danish Biobank and Register contains residual NBS specimens from virtually all newborns in Denmark since 1982 - about 1.8 million specimen cards. The stated purpose of the storage is: (1) diagnosis and treatment of congenital disorders including documentation, repeat testing, quality assurance, statistics and improvement of screening methods; (2) diagnostic use later in infancy after informed consent; (3) legal use after court order; and (4) the possibility of research projects after approval by the Danish Scientific Ethical Committee System, The Danish Data Protection Agency and the NBS-Biobank Steering Committee.

The operation and use of the NBS Biobank was regulated by an executive order from the Danish Ministry of Health from 1993 until 2004. The Ethical Council, the Central Scientific Ethical Committee and the National Board of Health were also involved in the regulations. These regulations have now been replaced by detailed General Operational Guidelines for Biobanks in Denmark in compliance with Acts on Processing of Personal Data, Patient’s Rights, Health 546/2005 and the Biomedical Research Ethics Committee System. No specific Act on biobanks per se has been made in Denmark, but the 2004 regulations and guidelines make the operations of the Danish NBS-Biobank more secure. The Danish NBS-Biobank has been used in several research projects for etiological studies of a number of disorders, recently employing new sensitive multiplex technologies and genetic analyses utilizing whole-genome amplified DNA.62

Prior to collecting the NBS screening specimen, parents are informed about NBS and residual DBS storage by local health professionals using program-prepared educational pamphlets ([www.ssi.dk/nyfoedte](http://www.ssi.dk/nyfoedte)) and through information available on the homepage of the Staten Serum Institute (SSI) ([http://www.ssi.dk](http://www.ssi.dk)). Information about storage of residual NBS specimens focuses on possible uses for: 1) documentation, retesting and diagnosis later in infancy; 2) quality assurance and assay improvement; and 3) research. The parents may opt-out of biobank storage at the time of blood sampling by marking the data portion of the specimen collection card or any time later either by a written letter to the SSI or by registering in the central Use of Tissue Registry. Several safety procedures also exist for both the data registry and the biobank. The residual specimens are stored in a separate freezer facility (-20 °C) and they are linked to the individual data forms only by a unique specimen number. The database archive is located in another building and access to both facilities is restricted to authorized health personal only. The NBS-Biobank has been included in the ISO 17025 accreditation of the screening laboratory since 1998. Yearly inspections by DANAK (Danish Accreditation Authority) ensure that the biobank adheres to this certification concerning trace-ability, documentation, and quality assurance.3

2. Michigan Newborn Screening Program and Michigan BioTrust for Health


The NBS laboratory routinely saves all NBS specimens after testing is complete unless otherwise directed by a parent or guardian. The NBS program’s brochure and website provides information
about retention of NBS specimens. In accordance with state law, some leftover de-identified specimens may be used for medical research after all directly identifying information (name, address, etc) has been removed. However, the NBS laboratory always retains one full circle of the blood specimen in case it is ever needed for the child or family. Parents, who wish to have their newborn’s leftover specimen stored by the laboratory, but not made available for possible medical research, may complete the Directive to Remove NBS Specimen from Research, and mail or fax the completed/signed form to the laboratory. Parents who wish to have their newborn’s screening specimen destroyed after completion of the screening tests may fill out the Directive to Destroy NBS Specimen and mail or fax the completed/signed form to the laboratory. The directives to save or to destroy specimens require signatures of the requestor and the ‘to destroy’ form requires authenticated identity (driver’s license, passport, etc) of the requestor. Once the individual from whom the specimen was collected reaches 18 years of age, they may make the request themselves. The MDCH owns the residual 3.5 million specimens collected over many years and has recently changed storage conditions and retention period from ambient storage for 21.5 years to indefinitely at –20°C. Specimens tested after September 2008 requires informed consent for use of residual specimens in research studies. MDCH’s residual specimens that have authorized permission for research use are currently being moved to the Michigan Neonatal BioTrust (below).


A draft business plan (2008) for the Michigan residual NBS specimen repository was produced at the request of the MDCH. “The objectives were: (1) to identify alternative storage conditions and space for their archive of dried blood spots that creates more opportunities for health research; (2) to provide linkages between the specimens and other public health data sources; (3) to make the results of research available to the broad research community; and (4) to accomplish these within a framework that protects the identity and ethical treatment of participants, and promotes a public health research agenda.”

A not-for-profit organization, the Michigan Neonatal BioTrust, is being created to implement the business plan and to prepare and make available the archived specimens for research. The BioTrust will provide stewardship of residual NBS specimens, but the MDCH will retain ownership of the specimens and oversee the research use of the specimens. Full implementation of the Michigan Neonatal BioTrust is expected to require $3.9 million in funding over a five year period. From year six onward the BioTrust is expected to be self-sustaining. Self sustainability will be obtained with support from Michigan’s three major research universities: Wayne State University, Michigan State University (MSU), and the University of Michigan. Wayne State University’s TechTown - a growing center of excellence in biobanking - will maintain the storage facility, with expertise in archiving, retrieving, shipping and handling biological specimens for research, and will provide the capability to amplify DNA as needed to ensure that this resource is available and sustainable. MSU provides extensive experience and expertise in assembling de-identified data from other Michigan data warehouses and linkage to the National Children’s Study and its related data. MSU medical ethics researchers have already initiated projects to determine public acceptance of research uses for archived specimens. The University of Michigan’s School of Public Health has extensive experience in community engagement and public education concerning the use of residual NBS specimens for research and in studying the ethical, legal and social implications of genetics research and practice. Each of these universities is expected to contribute substantially to a unified and effectively operated specimen repository. The BioTrust management is exploring also the possibility of a fee structure system to recover storage and linkage costs.
A multi-phased approach will be implemented for the Michigan Neonatal BioTrust as follows:

(Phase 1) The Van Andel Research Institute in Michigan has considerable experience with evaluating and identifying ideal storage conditions for biospecimens, and they will be responsible for identifying optimal specimen storage conditions and assisting with implementation. Residual NBS specimens currently stored will be identified with bar code labels, repackaged and moved to a secure location in TechTown;

(Phase 2) As part of the repository design to be self-sustaining, the BioTrust will increase the research value of the residual NBS specimens by first linking to the test results from the MDCH’s Newborn Screening Laboratory and later to different registries and databases that detail disorders, diseases, treatments and outcomes. The data currently associated with NBS specimens will be developed into a searchable database. Linking information from other databases is important to increase the value of the specimens for epidemiologic and genetic research; therefore, the BioTrust will establish business use agreements with other programs whenever possible in order to access their data; and (Phase 3) An “Honest Broker” function will be introduced to enhance and pilot the merging and de-identification of data from multiple sources. The “honest broker” acts as the intermediary between the specimen source (biobank) and the research investigator. The “honest broker” assigns each specimen and corresponding information a unique code and maintains the linkage to individual identities. The specimens are stored and distributed with this unique code. In this way only coded specimens and information can be used anonymously for research, but mechanisms still exist for additional information to be relayed in both directions (e.g., medical record information to broker to researcher; researcher to broker to medical record information). The link should not be accessible to research investigators unless a) the source has explicitly consented to having their directly-identifiable specimen and data used by researchers; and b) the research cannot practicably be carried out with coded specimens. The intermediary is the gatekeeper who ensures that the scope and preferences of the informed consent are honored. In this model the researcher cannot serve as his/her “honest broker.” This model allows for secondary and future users to proceed with a minimum of regulatory burden.


South Carolina law requires the Department Health and Environmental Control to store the child’s residual NBS blood specimen in a specified manner. After NBS tests are completed, the residual NBS specimens are stored with no humidity control in a freezer (-20 °C) at the state laboratory. The storage is highly protected and each specimen is held under strict confidentiality. A child’s DBS can only be released for approved research, without any identifying information, to learn new information about diseases. The law allows the parent or guardian to choose one of three options, if they do not want the specimen handled in this way; however, they are not required to select an option. The options are: 1) specimen stored by state but not used for research, 2) specimen destroyed two years after testing, and 3) specimen returned to parents two years after the testing date, if requested in writing. There is a box to be checked and a consent form to be signed on the reverse side of blood collection card. If no boxes are checked and/or the form is not signed, then specimen is retained at -20 °C for up to 3 years (typically 2 and a half years — space/staff dependent) and may be released only for anonymous confidential studies. Specimens may also be released with parent’s consent or with a court order/subpoena.

4. Texas NBS Program (homepage: http://www.dshs.state.tx.us/lab/nbsBloodspots.shtm)

Beginning with specimens stored since 2002, the state will store the residual specimens from all newborns for 25 years. Before 2002, specimens were discarded after 6 months. Once the NBS test is complete, the specimen card is securely stored for public health uses, e.g., on-going quality assurance/quality control and research that seeks more effective ways to test, treat and cure serious childhood diseases [see Health & Safety Code Sec. 33.017(b)-(c)]. For any use outside of the Department of State Health Services (DSHS), identifying information must be removed from the blood spot card so
that it cannot be connected to the identity of the child. Identifying information linking a child to a blood spot card is not allowed outside of DSHS without advance consent of the child’s parent, managing conservator or legal guardian unless otherwise provided by law. The residual specimens are stored in the DSHS Laboratory for one year at ambient temperature in containers with no humidity control. After one year the residual blood spot portion of the collection cards with a unique identifier are transported to a facility for storage off-site at the Texas A&M University where they are stored in boxes at ambient temperature with no humidity control. Over 5.4 million residual specimens are in storage.

Physicians, nurses, and other medical professionals must disclose to parents or guardians that blood taken from their newborn to screen for various disorders will be stored by the state and could be used for beneficial public health uses such as quality control or research. If the child’s parent (legal guardian or managing conservator) decides that they do not want the child’s blood spot card to be used for any other purpose after the NBS test results have been determined, Texas state law (changed earlier in 2009) allows parents to instruct DSHS to destroy their child’s NBS blood spot specimen after the NBS testing is complete. The law also requires a disclosure (information) form discussing allowable post-test uses of the blood spots, so that the parents can make an informed decision on the matter. DSHS has placed the disclosure information at the top of the destruction request form (provided at birth and available on the DSHS website), as directed by the new law. If the parent wishes to take advantage of this option, they completely fill out and submit the form, “Directive to Destroy” the blood spot card after testing. Upon receipt of a completed “Directive to Destroy” form, the department will destroy the blood spot within 60 days. Some health care providers initially implementing the new requirements have mistakenly labored under the impression that each parent must sign the destruction request form, with the result that many forms are being returned ultimately targeting the NBS specimen card for destruction when this may not be the intent of the parent. A study to determine the exact impact of this process and a method of improving it must be completed by December 2010.

The law requires providers to give the disclosure/destruction request form to the parents at the birth and at any subsequent newborn screen specimen collection (two specimens are currently required in Texas), but there is no legal obligation for healthcare providers to have the parents sign the form, or for the providers to return signed forms to DSHS. The decision to sign the form is entirely up to the parent, after they read the disclosure statement, and it is up to the parent to return a signed form to DSHS if they decide they do want to request destruction of their blood spot card. The law requires that DSHS develop a mechanism for the providers to verify that they have provided the disclosure information to the parent. This was accomplished in the interim by adding a label to the cards that has a check box that the healthcare provider would mark indicating that the disclosure information was provided to the parent. In the future, this will become a permanent feature of the NBS specimen collection kit.

5. Minnesota NBS Program

(Homepage: http://health.state.mn.us/newbornscreening/research.html)

Parents have the option to not receive NBS by signing a ‘Refusal of Newborn Screening’ form. Following NBS, the Minnesota Department of Health (MDH) securely stores leftover blood specimen and NBS results. The MDH has securely stored residual NBS specimens since July 1, 1997. By August 1, 2008, approximately 792,000 newborn screening specimens were in storage. Specimens received between July 1, 1997 and September 7, 2005 are securely stored in an offsite protected record center. MDH employees do not have direct access to these specimens. Requests for specimens housed at the offsite record center go through both a trained Records Coordinator and the outside record management and document storage facility. Residual specimens retained before 2005 are stored at ambient temperature; however, residual specimens obtained after 2005 are stored at -20 °C with desiccant. Educational information about retention of residual specimens is available on the MDH Newborn Screening Information brochure and at the MDH website.
The parent or guardian may choose to have the screening results and the blood specimen destroyed. This request can be made at birth or at any future time. In the case of the ‘Directive to Destroy Form’ neither a permanent record of the test nor the leftover blood are kept by MDH. When a request to destroy is received, the blood specimen is destroyed within 45 days and results are destroyed 24 months after the initial screen took place. The ‘Directive to Destroy Form’ and examples of past uses of residual blood spots in research efforts are provided on the MDH website – “How Minnesota babies benefit from dried blood spot use.”

Specimens received by MDH beginning September 8, 2005 are stored onsite in a locked storage room. Only MDH employees who have received extensive data privacy training are allowed access to this area. MDH stores these specimens securely and in accordance with strict data and genetic privacy standards. The following reasons for storage are paraphrased from the website: 1) results or specimens may be requested by the family or the baby's healthcare team; 2) tests can be repeated if needed without getting another blood specimen; 3) for other health-related testing (at parent request); 4) to help identify a missing or deceased child (parent’s request); and 5) provides a permanent record that MDH completed the screening. In other cases, with all identifying information removed, specimens may be used to: 1) to ensure high quality testing (quality control); 2) develop new tests for more disorders; and 3) to contribute to public health studies and research for a better understanding of diseases to benefit the general public.