

Newborn Screening In America: Problems and Policies



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INTRODUCTION

BEFORE THEY ARE even a week old, ninety-eight percent of the 4.3 million babies born annually in the United States have a small sample of blood taken from their heels.¹ These newborn bloodspots (NBS) are then screened for a variety of inherited conditions and may later be stored in state-operated databases. Patient advocacy groups and public health officials have described these residual sample “biobanks” using phrases like “invaluable resource”² or “superb database.”³ Although there are concrete benefits of newborn testing, there are also troubling consent and privacy issues raised by the screening, storage, and use of the samples.

In recent years, the number of conditions for which newborns are screened has expanded rapidly, raising several questions. In its proposal for a “uniform screening panel,” a battery of newborn screening tests to be adopted by all U.S. jurisdictions, the American College of Medical Genetics departed from the traditional screening criteria laid out by Wilson and Jungner, which limit screening to well-understood, treatable conditions for which screening generates a direct benefit to the infant. Though all of the recommended core conditions conform to these requirements, some of the secondary conditions do not, effectively relaxing the requirements for including a condition in the newborn screening panel. As a result of loosening these terms, some states are beginning to add conditions that are not as well understood to their screening panels, like Krabbe, with questionable benefit to diagnosed infants. Additionally, newborn screening is often conducted in a manner that raises questions about the associated consent procedures. Many states do not give parents the ability to

decline screening, and parents are often unaware about these screening programs and their consent options.

With respect to sample storage and use, there is also little transparency regarding storage procedures or the use of the samples after they have been screened. Even though parents want informed consent to store and use the samples, many states do not have clearly articulated policies about consent for the storage and use of samples or may not effectively communicate these policies to parents. The absence of clearly articulated and communicated consent policies is particularly problematic because of the mismatch between the promise of maintaining residual sample databases and the actual benefits generated by such storage. As mentioned above, public health officials and patient groups often emphasize the value that these databases represent for public health research, but the actual benefits generated may be less dramatic than their statements would suggest.

This paper examines the questions raised above in greater detail. Part I provides a brief overview of the history of NBS screening in the United States. Part II compares the promise of newborn screening with the actual benefits generated by the storage and use of the residual samples. Part III discusses the parental consent problems raised by the screening, storage, and use of residual samples in research. Part IV examines the recent lawsuits about sample storage and use that were brought by parents in Minnesota and Texas. Finally, Part V discusses potential policy solutions to the previously identified problems related to the screening, storage, and use of NBS samples.

PART I: A BRIEF HISTORY OF NEWBORN SCREENING

NEWBORN SCREENING in the United States began with genetic testing for phenylketonuria (PKU) in the 1960s.⁴ PKU is a rare genetic condition in which an individual is unable to break down the amino acid phenylalanine.⁵ If left untreated, the accumulation of phenylalanine in the blood can cause mental retardation; however, if it is diagnosed early, the affected child can be put on a low-phenylalanine diet, promoting normal brain development.⁶ In 1961, Robert Guthrie developed a simple way to test for PKU in infants: doctors would collect and store a small sample of blood on filter paper (known as a Guthrie card), and a bacterial inhibition assay would then be performed on this sample to test for PKU.⁷ His discovery made wide-scale PKU screening possible.⁸

At the same time Guthrie was developing his PKU assay, several social and political forces were mobilizing to make use of this test. In 1963, President Kennedy signed Public Law 88-164 and Public Law 88-156, which authorized the federal government to provide grants to states to create comprehensive plans to address mental retardation.⁹ In this same period, the National Association for Retarded Citizens (NARC) also increased its advocacy efforts aimed at securing more federal government funding for intellectual disabilities. These forces coalesced in 1962, when Robert MacCready, the chair of NARC's Public Health Services Committee and the state laboratory director for Massachusetts, began a pilot screening program that tested all infants born in Massachusetts for PKU.¹⁰

The Massachusetts screening program was part of a twenty-nine state study funded by the Children's Bureau,

but it was the first program that screened infants in every hospital in a given state.¹¹ As a result of this near-universal screening, the Massachusetts study alone accounted for ten of the thirty-nine total PKU cases identified by the multi-state Children's Bureau study.¹² The success of Massachusetts' PKU screening program prompted MacCready to lobby for mandatory PKU screening legislation in the state.¹³ MacCready also persuaded NARC to support the passage of similar legislation in other states, and by 1968, forty-three states had passed PKU screening legislation modeled after the Massachusetts law.¹⁴ Today, every state has laws mandating newborn screening for PKU.¹⁵

It is worth noting that unlike many medical tests, information from newborn screening tests are obtained and maintained by the state. After they are born, infants and children are taken to pediatricians for routine testing every few months.¹⁶ Doctors screen children for a variety of conditions, including anemia, hearing, vision, and developmental milestones,¹⁷ and this information is maintained by the physician and becomes part of the child's medical record. In the case of newborn screening, however, the test results are maintained by the state conducting the screening. To date, studies have not offered an explanation accounting for this difference, but perhaps one can look to the history of newborn screening for an answer. As discussed in the previous paragraph, newborn screening began with testing for PKU. Because these tests were originally conducted at the state level, beginning with MacCready's seminal Massachusetts study, it is possible

that modern NBS screening occurs at the state level purely through happenstance. As support for this theory, researcher Erin Rothwell once stated, “I don’t know any program that started out 20, 30 years ago that said ‘let’s start newborn screening so we could have samples to store’ . . . [T]his kind of happened unexpectedly and it is a great resource.”¹⁸

Whatever the reason for the current practice of having states maintain newborn screening results, since the 1960s, screening has expanded beyond testing for PKU to include many other conditions. However, because states developed

their screening panels independently of one another, the number and type of conditions screened would vary greatly from one state to another. This observed variance in state newborn screening panels prompted the American College of Medical Genetics (ACMG) to propose a uniform newborn screening panel, and in 2005, the ACMG issued a report recommending that all states screen twenty-nine core conditions as part of a core panel, with twenty-five additional conditions as part of a secondary panel.¹⁹ These conditions are listed in Table 1 below.²⁰

TABLE 1: ACMG RECOMMENDED UNIFORM SCREENING PANEL

CORE PANEL

1. Propionic academia
2. Methylmalonic acidemia (methylmalonyl-CoA mutase)
3. Methylmalonic acidemia (cobalamin disorders)
4. Isovaleric acidemia
5. 3-Methylcrotonyl-CoA carboxylase deficiency
6. 3-Hydroxy-3-methylglutaric aciduria
7. Holocarboxylase synthase deficiency
8. β -Ketothiolase deficiency
9. Glutaric acidemia type I
10. Carnitine uptake defect/carnitine transport defect
11. Medium-chain acyl-CoA dehydrogenase deficiency
12. Very long-chain acyl-CoA dehydrogenase deficiency
13. Long-chain L-3 hydroxyacyl-CoA dehydrogenase deficiency
14. Trifunctional protein deficiency
15. Argininosuccinic aciduria
16. Citrullinemia, type I
17. Maple syrup urine disease
18. Homocystinuria
19. Classic phenylketonuria
20. Tyrosinemia, type I
21. Primary congenital hypothyroidism
22. Congenital adrenal hyperplasia
23. S, S disease (Sickle cell anemia)
24. S, β -thalassemia
25. S, C disease
26. Biotinidase deficiency
27. Cystic fibrosis
28. Classic galactosemia
29. Hearing

SECONDARY PANEL

1. Methylmalonic acidemia with homocystinuria
2. Malonic acidemia
3. Isobutyrylglycinuria
4. 2-Methylbutyrylglycinuria
5. 3-Methylglutaconic aciduria
6. 2-Methyl-3-hydroxybutyric aciduria
7. Short-chain acyl-CoA dehydrogenase deficiency
8. Medium/short-chain L-3-hydroxyacyl-CoA dehydrogenase deficiency
9. Glutaric acidemia type II
10. Medium-chain ketoacyl-CoA thiolase deficiency
11. 2,4 Dienoyl-CoA reductase deficiency
12. Carnitine palmitoyltransferase type I deficiency
13. Carnitine palmitoyltransferase type II deficiency
14. Carnitine acylcarnitine translocase deficiency
15. Argininemia
16. Citrullinemia, type II
17. Hypermethioninemia
18. Benign hyperphenylalaninemia
19. Biopterin defect in cofactor biosynthesis
20. Biopterin defect in cofactor regeneration
21. Tyrosinemia, type II
22. Tyrosinemia, type III
23. Various other hemoglobinopathies
24. Galactosepimerase deficiency
25. Galactokinase deficiency

While the push for uniformity seems relatively benign, there are several problems with the methodology employed by ACMG to generate its uniform panel. The ACMG abandoned the traditional criteria for determining the appropriateness of screening for a particular condition, as laid out by James Wilson and Gunnar Jungner and adopted by the World Health Organization in 1968.²¹ Although these ten criteria were not specifically developed for newborn screening, they are still widely cited in articles about newborn screening, even today.²² These ten criteria are listed in Table 2 below.²³

TABLE 2: WILSON AND JUNGNER’S 10 CRITERIA FOR SCREENING

1. The condition sought should be an important health problem.
2. There should be an accepted treatment for patients with recognized disease.
3. Facilities for diagnosis and treatment should be available.
4. There should be a recognizable latent or early symptomatic stage.
5. There should be a suitable test or examination.
6. The test should be acceptable to the population.
7. The natural history of the condition, including development from latent to declared disease, should be adequately understood.
8. There should be an agreed policy on whom to treat as patients.
9. The cost of case-finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole.
10. Case-finding should be a continuing process and not a “once and for all” project .

Although the ACMG listed the Wilson and Jungner criteria in its paper detailing its uniform panel, it did not explicitly apply them because “many of [these] criteria are subjective and therefore less amenable to the application of a metric and therefore quantification.”²⁴ Instead, the ACMG ultimately determined that its core panel of twenty-nine

conditions all conformed to the following three, self-generated criteria: all had 1) “[s]pecific and sensitive screening tests,” 2) “[s]ufficiently well understood natural histories,” and 3) “[a]vailable and efficacious treatments.”²⁵ These principles, despite representing a departure from the classical test for screening, do appear to conform to the principles laid out by Wilson and Jungner. In particular, the inclusion of the “available and efficacious treatment” requirement echoes Wilson and Junger’s statement that “[o]f all the criteria that a screening test should fulfill, the ability to treat the condition adequately, when discovered, is perhaps the most important.”²⁶

Although the ACMG did require its core panel of twenty-nine conditions to satisfy each of the three criteria laid out above, it dispensed with these requirements for the twenty-five conditions in the secondary panel. More specifically, the ACMG waived the second and third criteria: it stated that some conditions were placed in the secondary panel despite “the lack of proven efficacious treatment,” whereas others were placed in this panel even though their “natural histor[ies] were not sufficiently well understood.”²⁷ This explains how a condition like dienyoyl-CoA reductase deficiency was included in the secondary panel. Only one case of this condition has ever been reported, so its mode of inheritance is not well understood, nor is there a known treatment²⁸; however, because it is possible to test for the condition, the ACMG determined that it was appropriate to include it in the secondary panel.²⁹ Thus, with respect to the secondary panel, the ACMG seemed to reject the Wilson and Jungner criteria entirely, considering screening for the secondary conditions to be appropriate as long as there was a “specific and sensitive screening test” for that condition.

However, it is unclear whether the screening test employed by the ACMG satisfies even this first screening requirement. The ACMG identified the secondary conditions to be included in the panel using multiplex platforms, like tandem mass spectrometry, which allows for testing of multiple conditions using a single sample.³⁰ Because these tests are not condition-specific, they call into question whether multiplex tests satisfy the “specific and sensitive” criterion articulated by the ACMG. An additional source of uncertainty arises from the mode in which the multiplex tests are conducted. Multiplex tests can be done in two modes: “selective monitoring” screens “only for those conditions that have been deemed appropriate for screening,” whereas a “full profile” screen tests for all conditions that can possibly be tested for, “without regard to the distinction

between appropriate and inappropriate target conditions.”³¹ Because the ACMG advocates use of the second, “full profile” mode, the multiplex testing is even less specific than it would otherwise be. The ACMG justifies its position on the grounds of “the inherent value of multiplex technology to public health”³² and because the tests enable “the maximal use of technology.”³³

In 2008, the President’s Council on Bioethics published a report about newborn screening scrutinizing the ACMG’s recommended uniform screening panel. While the Council did not explicitly criticize the expansion of screening, it did express some doubt about the ACMG’s methods for doing so. The Council noted that the ACMG’s loosened screening criteria for the secondary panel effectively expanded the number of conditions that could be included in the newborn screening panel in the future.³⁴ As discussed above, rather than limiting screening to conditions that were treatable, as Wilson and Jungner recommended, the ACMG instead expanded screening to include conditions that simply could be tested for using multiplex platforms. If states adopt the ACMG’s proposal and mandate screening for conditions on both the core and secondary panels, any positive result on either panel would be reported to families, despite the fact that different criteria were used to determine the conditions included in each panel.³⁵ Despite these concerns, however, the Secretary’s Advisory Committee on Heritable Disorders in Newborns and Children expressed approval of the ACMG’s proposal and recommended that all states adopt the panel.³⁶ As of August 2012, all states have adopted the core panel, and many appear to be in the process of adopting conditions on the secondary panel.³⁷

Since the ACMG issued its report, the number of conditions on states’ newborn screening panels has expanded greatly and today the number of conditions tested for ranges from thirty in Arkansas to fifty-eight in Massachusetts and Mississippi.³⁸ Some states have even gone beyond the ACMG’s core and secondary panels to include other conditions. For example, New York screens for Krabbe, and both Illinois and Missouri are in the process of adding this condition to their screening panels.³⁹ Krabbe is a condition that illustrates the problems raised by loosening the screening criteria, as the ACMG did in its report. Ariel Bleicher points out that “researchers do not understand late-onset Krabbe well enough to know when, if ever, any of these children will develop symptoms.”⁴⁰ In fact, Bleicher notes that “only four of those children [in New York who tested

positive for the genetic marker for Krabbe] have developed Krabbe symptoms, whereas the other 20 continue to appear healthy.”⁴¹ Had the ACMG not relaxed its requirements for the conditions on the secondary panel, conditions like Krabbe would likely not have been included on newborn screening panels.

The expansion of state screening panels can be attributed, at least in part, to the efforts by patient groups. Echoing the success of NARC in the 1960s, in recent years patient advocacy groups have lobbied states to expand the number of conditions on state screening panels.⁴² As a result of these advocacy efforts, New York, Missouri, New Mexico, and Illinois have mandated the inclusion of additional conditions, like certain lysosomal storage disorders (LSDs), into their newborn screening panels.⁴³ Parents of affected children often lead these campaigns, and their successes can be partly attributed to the emotional and impassioned appeals these parents present.⁴⁴ It is easy to understand why these parents are so passionate about expanding screening, given that many of them have either lost children to the conditions they argue should be included in the screening panels, or they have affected children whose lives were saved by newborn screening for their conditions. These tragedies and triumphs should not be trivialized, and the motivations of these parents are admirable, but their lobbying does raise a few questions.

One source of concern is the fact that parent-led advocacy groups often have the support of pharmaceutical companies and manufacturers of tandem mass spectrometry technology, both of which have “a vested interest in the promotion of treatments for the disorder the group represents.”⁴⁵ Pharmaceutical companies stand to benefit from expanded newborn screening because an increase in the number of individuals diagnosed with particular inherited conditions will increase the demand for treatments for these conditions. Likewise, companies manufacturing and marketing tandem mass spectrometry technology also stand to benefit from expanded screening because the inclusion of more conditions on screening panels will create a greater demand for the testing technology. This is exactly why some have expressed apprehension about the joint lobbying of these tandem mass spectrometry companies and patient groups.⁴⁶ Thus, the close relationship between patient advocacy groups and pharmaceutical companies and tandem mass spectrometry manufacturers may complicate the answer to the question of who really benefits from expanded screening panels.

Another source of concern is that parents affiliated with patient groups may not adequately represent the interests of all parents. For example, the parents of affected children may not represent the interests of the vast majority of parents whose children do not have any of the conditions screened for in these panels. Parents of unaffected children may feel strongly about refusing screening because of their religious or personal beliefs, the financial costs associated with screening, or the emotional costs of knowing that their child has a certain genetic condition. However, the voices of these parents are often not heard in the discussion about newborn screening.

Another parent group noticeably absent from this discussion are those parents who have received false positive results.⁴⁷ These parents often experience great emotional distress after receiving the initial screening results, and just as the benefits of true positive results should not be diminished, the distress of a false positive result should not be trivialized. One mother whose son initially tested positive for cystic fibrosis recalled that her husband cried when she revealed the first test's results to him.⁴⁸ This anxiety also does not necessarily end even after receiving notification of a false positive. "Some parents continue to wonder why the initial markers showed any problem, and secretly worry that disease will emerge, after all. Some become wildly overprotective or find that stress infuses their family dynamics."⁴⁹

As the President's Council on Bioethics noted, the ACMG seemed to justify its expansion of the newborn screening panel by broadening the traditional conception of benefit. Recall that Wilson and Jungner placed a premium on the requirement that the condition was treatable. As applied to newborn screening, this translates into a requirement that there be an identifiable benefit to the newborn. However, instead of considering whether screening for a condition benefits the newborn, the ACMG shifted attention to the newborn's family, stating that screening allows parents to determine whether there is a "genetic risk"⁵⁰ to others in the family. But assessing this "genetic risk" may not be so straightforward. It is important to note that when screening

for a particular condition, the test result is not a simple positive or negative. Instead, the test calculates a metabolic value that falls somewhere on a spectrum of values, and the clinical salience of small deviations from the normal range is unclear.

The ACMG also shifted the focus away from the newborn by repeatedly citing the potential societal benefits of newborn screening. In addition to the "inherent value . . . to public health" noted earlier in this section, the ACMG also stated that newborn screening affords society the opportunity to "better [understand] disease history and characteristics" and provides hope for "earlier medical interventions" to be developed in the future.⁵¹ Thus, the ACMG effectively determined that the potential individual benefits to the newborn are superseded by benefits to entire families or to society as a whole. Noticeably absent are the opinions of the parties providing these samples: the parents of the babies being screened for various conditions.

The ACMG's choice to shift the discussion about screening benefits exemplifies a kind of medical paternalism. Bioethicists have previously disapproved of medical researchers "judging individuals incapable of managing important health information" and withholding this information, thereby "violating [these individuals'] autonomous right to knowledge about their own person."⁵² However, some bioethicists have since expanded this conception of paternalism to also include "a right to ignorance based on an interest in not knowing medical information," or a right not to know.⁵³ Fiona Alice Miller writes that when the preferences of the individual undergoing screening are unknown, as in the case of newborn screening, authorities must identify "a compelling reason" to override this right and disclose test results to families.⁵⁴ Miller offers "avoidance of harm or service of a legitimate public interest" as examples of appropriate justifications.⁵⁵ Although the ACMG report does mention some potential public health benefits of screening, these benefits are described in vague and abstract terms, as shown by the text quoted above. The next section of this paper compares these promises to the actual benefits generated by newborn screening, storage, and use of residual bloodspots in research.

PART II: THE BENEFITS OF NEWBORN SCREENING: PROMISE VS. REALITY

SINCE THE INCEPTION of newborn screening in the 1960s, this procedure has undoubtedly saved thousands of lives and improved the quality of life for thousands more. It is estimated that “[e]very year, between 4,000 and 5,000 infants are correctly identified as having serious genetic disorders, including some that would result in disability or death if they weren’t flagged so treatment could begin.”⁵⁶ A quick Google search for “newborn screening benefits” turns up numerous personal stories from parents whose children are able to lead normal, healthy lives because of early screening and treatment of various genetic conditions. One parent shared the following story:

At eleven days old, Seth was diagnosed with Classical PKU . . . The miracle that I took completely for granted was the fact that PKU can be screened for, detected prior to damage, and treated. As my family and I settled into adjusting to the requirements of caring for a child with a genetic disorder, I failed to realize how truly blessed and fortunate I was. My child was healthy and would remain so because of successful treatment and control of his disorder.⁵⁷

Another parent explained that in addition to experiencing the “fear” and “anger” associated with receiving a hearing impairment diagnosis, she also felt “[h]appiness . . . that we finally knew Wyatt’s true identity” and “[r]elief . . . that we conclusively knew the levels that he was hearing at and could begin our journey of raising a hearing impaired child.”⁵⁸ One cannot diminish the value of saving or im-

proving so many lives, and that is not what this report seeks to do. However, it is possible that the benefits of screening have been somewhat overstated.

The benefits of screening have been overstated, in part, because the rarity of these conditions is often underemphasized. George Annas has noted that “[a]t the observed rate [of screening], it would take 500 years before one case [of PKU] was missed because of parental refusal” and predicted that the same would be true of other conditions added to the newborn screening panel.⁵⁹ It is also important to note that many initial positive results are actually false positives. Dr. Philip M. Farrell, a professor of pediatrics at the University of Wisconsin, estimated that on the expanded newborn screening panel, only about “one in fifty of every ‘positive’ newborn screening test detects actual disease,” the rest being false positives.⁶⁰ He noted that the average rate of false positives “can vary widely” between the conditions tested, from one in ten positive tests for cystic fibrosis being a true positive result to one in 100 or one in 200 positive tests for congenital adrenal hyperplasia being a true positive result.⁶¹

As an additional complication, Dr. Piero Rinaldo, a professor of laboratory medicine at the Mayo Clinic, noted that due to state-to-state differences in skill and resource availability, “parents in one state might find that false positive rates are as low as 0.01 percent of all newborn tests, while parents a few states over may find as many as 1.52 percent of those tests are false alarms.”⁶² He also noted that the positive predictive value (PPV), which is the “probability that a patient with a positive test result actually has the disorder in question,” can also vary wildly from one state to another.

Some states have a PPV of nearly 3 percent, which means that only 3 percent of the people who test positive for the disease actually have it, and 97 percent are false positives. In other states, the PPV is much better, above 50 percent. So far, only 28 states have been willing to report their results and then only anonymously.⁶³

Even more troubling, a 2000 study found that despite advances in technology, “there has been little change in the PPVs associated with newborn screening results,” indicating “that there has been no improvement in the number of false-positive test results in newborn screening programs.”⁶⁴

An additional reason why the benefits of screening may be overstated is that the “public health benefits” cited by the ACMG and echoed by public health officials and patients’ groups may not live up to their promise. Recall that the ACMG stated that newborn screening offers the opportunity to “better [understand] disease history and characteristics” and provides hope for “earlier medical interventions” to be developed in the future. After speaking with public health officials from New York, Massachusetts, and North Carolina, however, it is not clear that these promises about “public health benefits” have, as yet, been fulfilled.⁶⁵ Officials in these states explained how they used residual bloodspots collected from screening to conduct quality control tests for existing tests for screening panel conditions. A Massachusetts official also described how the state had used these samples to formulate its own test for severe combined immunodeficiency (SCID) because no commercial test was available. When questioned about the representativeness of these uses of residual bloodspots, all the public health officials surveyed expressed the opinion that their states’ uses were likely representative of most states. However, while formulating screening tests and ensuring that existing tests meet certain quality standards are certainly beneficial applications of newborn screening, they seem to fall short of the stated promises of elucidating disease characteristics and generating earlier interventions.

Given these arguably less grand benefits of screening, it is also not clear why state health departments are mostly conducting this research. The public health officials surveyed stated that state health departments were the primary enti-

ties conducting quality assurance studies on existing newborn screening tests and formulating new tests. This practice stands in sharp contrast to the way research projects are usually conducted, in which private commercial entities, independent researchers, and university researchers are all working on similar research projects. The reason for the noticeable absence of other research entities is simple: unlike state health departments, which in many cases do not need parental consent to conduct such research,⁶⁶ other research entities would have to obtain parental consent before using residual samples for any research. Although the waiver of the parental consent requirement undoubtedly makes the research process less complicated, requesting parental consent has several important benefits. First, requiring consent would arguably be less privacy invasive than conducting research without the parents’ knowledge. Additionally, imposing a parental consent requirement would likely entail obtaining and maintaining fewer samples, which could decrease research costs because fewer resources are expended. Thus, if the samples are mostly being used for research related to testing, it is not clear why states should be conducting this research, rather than other entities.

When asked about other applications of newborn screening, none of the public health officials consulted for this paper could offer examples of research projects that had yielded results aligned with the promises stated in the ACMG paper. Further investigation unearthed one Minnesota study that had used residual bloodspot samples to study mercury exposure levels in the Lake Superior Basin,⁶⁷ as well as several articles from the 1990s that used residual samples to examine the prevalence of HIV in newborns to formulate recommendations about screening pregnant women for HIV.⁶⁸ While these studies undoubtedly have public health applications, they are not the kind of benefits promised by the ACMG. Given the apparent mismatch between the scale of the screening benefits described by the ACMG and the magnitude of the actual benefits described by public health officials and demonstrated in medical literature, it is clear that the benefits of newborn screening do not justify failing to address the concerns identified above. As the next section discusses, the cost-benefit analysis is further complicated when one considers the consent issues raised by screening, storage, and use of the samples in research.

PART III: CONSENT ISSUES RAISED BY THE SCREENING, STORAGE, AND USE OF RESIDUAL BLOODSPOTS IN RESEARCH

A. CONSENT ISSUES RELATED TO SCREENING

The Nuremberg Code lays out ten ethical principles for human research and was written in response to the experiments carried out by Nazi doctors during World War II.⁶⁹ According to the first of these principles,

The voluntary consent of the human subject is absolutely essential. This means that the person involved should have the legal capacity to give consent; should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, overreaching or other form of constraint or coercion; and should have sufficient knowledge and comprehension as to enable him to make an understanding and enlightened decision.⁷⁰

From this excerpt, three precepts underpinning informed consent emerge: 1) consent must be voluntary, 2) there must be freedom of choice, and 3) the participant must have sufficient understanding of the subject matter.⁷¹ However, in the case of NBS screening, it is not clear that all three of these principles are always satisfied.

In 2007, President Bush signed the Newborn Screening Saves Lives Act, which provides grants to entities administering newborn screening programs.⁷² These grants are given to provide screening and health services to newborns, training to healthcare professionals, education to parents, and “to establish, maintain, and operate a system to assess and coordinate treatment relating to congenital,

genetic, and metabolic disorders.”⁷³ If one examines the revision dates of states’ newborn screening statutes, it appears that many states made changes to their screening programs after 2007.⁷⁴ Given that “funding and priority setting for specimen preservation”⁷⁵ can vary from jurisdiction to jurisdiction, perhaps these changes can be attributed to the passage of the Act.

By encouraging states to expand their existing screening program, the Act effectively offers federal approval of the newborn screening status quo in which states conduct the tests and maintain the results. It is also worth noting that the Act is silent on the subject of informed consent, and because of this omission, the fifty-one jurisdictions (the fifty states plus the District of Columbia) were left to decide the consent procedures that would apply within their jurisdictions. Many jurisdictions do not offer parents a meaningful choice to refuse screening. Thirty-three jurisdictions allow parents to abstain on religious grounds, and in only two of those jurisdictions is abstention explicitly allowed on other grounds.⁷⁶ Three states (Nebraska, South Dakota, and West Virginia) prohibit refusal on any grounds.⁷⁷

In many jurisdictions that do allow parents to refuse testing, “no communication with parents about NBS is required prior to screening.”⁷⁸ Erin Rothwell suggests that the justification for this waiver of informed consent is that the benefits of screening are “sufficiently great that parental permission need not be sought.”⁷⁹ However, as discussed in the previous section, this justification may be overstated. Recall that voluntary screening for rare conditions may only minimally decrease the risk of missing an affected in-

fant because an initial positive result is far more likely to be a false positive than a true positive result.

Given the higher prevalence of false positive results, George Annas suggested that the debate surrounding consent should not be framed in terms of whether “parents have the right to consign their child to . . . irreversible mental retardation” (in the case of PKU) but instead whether mandatory screening represents “a legitimate exercise of the state’s public health powers.”⁸⁰ However, in the hospitals where screening is conducted, the debate about screening does appear to center around the potential harm of refusing screening. Doctors may pressure new parents into screening their infants by overemphasizing the dangers of refusing screening. For example, one woman observed a pediatrician telling her daughter, a new mother, “that her baby could die if she did not have them do this test,” apparently without explaining to the mother that there was a much greater chance of generating a false positive result.⁸¹

Such statements may place enormous pressure on vulnerable new parents, even if these parents have serious objections to screening. The grandmother quoted in the previous paragraph reported that the hospital staff’s treatment made her daughter feel “guilty” for refusing NBS screening.⁸² Another woman described her daughter receiving similar treatment from a hospital nurse: “My daughter signed a paper stating she did not want the PKU test done . . . [and t]he nurse huffed out of the room saying that [refusal of screening] doesn’t happen.”⁸³ Because this type of treatment pressures parents into consenting to screening, it cuts against both voluntary consent and freedom of choice.

Additionally, the notion that parental consent is unnecessary runs counter to the wishes of many parents, as demonstrated by a study conducted by Jeffrey Botkin and colleagues. This 2012 survey showed that when asked whether it was “alright” to conduct newborn screening without parental permission, participants were almost equally split, with 25.5 percent responding “definitely alright,” 24% responding “probably alright,” 18% responding “probably not alright,” and 32% responding “definitely not alright.”⁸⁴ Stanford Law School professor and bioethicist Henry Greely assessed a twelve percent refusal rate as “not trivial”;⁸⁵ applying this standard, Botkin’s results suggest that parents have a strong desire for informed consent. Given that approximately four million children are born annually in the United States, Botkin’s study suggests that about two million parents each year would object to the absence of informed consent, which represents a significant demand for

the implementation of informed consent procedures.

Recall that the third principle of informed consent articulated by the Nuremberg Code requires participants to have sufficient knowledge of the subject matter. In his study, Botkin noted that the participants’ knowledge of NBS was “limited,” as demonstrated by their responses in the focus group discussions.⁸⁶ This observation suggests that the third Nuremberg Code requirement for informed consent may not be fulfilled, even in jurisdictions where parents may refuse newborn screening. Although all states provide parents with NBS brochures or information sheets after the baby is born, “these materials often are intermingled with other educational materials and samples of infant care items so there is little insistence that parents attend to this information.”⁸⁷ Additionally, “many brochures do not conform with professional recommendations for content and quality such as clear explanations of the benefits and risk of screening.”⁸⁸

A study by L. McKechnie & A. B. Gill also noted that the timing of such information is often less than ideal, stating that new parents are often “emotionally overwhelmed, preoccupied with their baby, or unwell” after the birth of child.⁸⁹ These parents may not be prepared to provide informed consent under the circumstances, as anecdotal evidence suggests. One parent described the sensory overload after the birth of a child, stating,

The 48 hours in the hospital setting for a birth is a zoo. Everyone’s coming in at all hours. My wife was hardly left alone. In fact, for our fourth child, my wife says it was such a blur that she can hardly remember choosing our son’s name.⁹⁰

It is not surprising, then, that McKechnie and Gill’s study found that almost twenty percent of parents surveyed either expressed doubt about having actually consented to the screening or could not remember whether they had given consent.⁹¹

Another possible reason that many parents have limited knowledge about newborn screening is that physicians may not be effectively communicating information to parents. Lainie Friedman Ross writes that because screening is often mandatory, and because this process is coordinated by state health departments rather than hospitals, “pediatricians know very little about what conditions are included in NBS panels and the methodologies used to detect them.”⁹² As a result, these physicians “are ill-prepared to explain the like-

likelihood of disease after a patient receives a positive result, and they often know little about the condition for which the patient needs to undergo further work-up.”⁹³ Doctors with years of medical education and experience are “ill-prepared” to explain the procedures and implications of newborn screening to parents. It is not surprising then that many parents demonstrate limited knowledge of NBS screening practices, challenging efforts to bolster parental informed consent.

Even if parents are informed about newborn screening, hospital staff may not be informed about the procedures that must be followed if parents wish to refuse screening. This creates difficulties for parents who want to decline testing because they often find it difficult to complete the necessary paperwork to opt out of NBS screening. One parent stated, “Our nurses didn’t even know we could opt out. . . . We kept being redirected as to who to go to to get the right paperwork. Postpartum nurses, nursery nurses, HUCs, no one knew where to find it.”⁹⁴ Another mother described the resulting frustration:

We knew we could decline [screening,] but when we got to the hospital[, the medical professionals had] never heard of such a thing. Once they figured out that we could [refuse,] they didn’t have the forms. We were on our way out of the hospital, and the whole thing was frustrating.⁹⁵

Thus, even in states where it is possible to refuse newborn screening, exercising such an option may be extremely difficult.

The absence or inadequate implementation of informed consent procedures will become increasingly problematic as more and more conditions are added to the NBS screening panel. Lainie Friedman Ross explains that the justification for informed parental consent “may become even stronger as newborn screening moves [toward] screening for conditions that are less serious, lack effective treatments, or present later in childhood.”⁹⁶ Although most of the ACMG uniform panel consists of conditions that do have effective early treatment options, the loosening of the traditional screening requirements discussed in Part I, exemplified by the inclusion of conditions like dienyol-CoA reductase deficiency or Krabbe in some states’ screening panels, suggests that there is a move in the direction feared by Ross. If, as she predicts, newborn screening continues to expand, then the arguments against obtaining informed

consent from parents begin to weaken because the implications of screening become less clear. It makes sense in these circumstances to provide parents with more information about the potential risks and benefits of testing for these conditions so that they can make the best possible decision as proxy consenters for their children. It is not clear, however, whether such a move toward greater parental control over screening is actually taking place.

B. CONSENT ISSUES RELATED TO STORAGE OF NBS SAMPLES

As the previous subsection discussed, there are several problems arising from the current practices for newborn screening: despite strong parental demands for informed consent, few U.S. jurisdictions allow parents to refuse screening. Additionally, across all jurisdictions, there appears to be inadequate communication of NBS information to parents, which can be attributed to unclear NBS informational materials, poor timing of communication, and medical staff either pressuring parents to screen their children or being uninformed about procedures for refusing screening. This subsection discusses how similar problems are also present in the procedures related to storage of residual bloodspots after screening has been completed.

One problem regarding the storage of residual samples is confusion over ownership of the samples. In addition to providing grants supporting the expansion of newborn screening programs, as discussed in the previous subsection, the Newborn Screening Saves Lives Act also supports the creation of “regional centers” to conduct research about treatment of the screened-for disorders,⁹⁷ as well as the creation of a national “Hunter Kelly Newborn Screening Research Program,” which is responsible for “carrying out, coordinating, and expanding research in newborn screening.”⁹⁸ Such textual references to cooperative screening efforts might suggest that the federal government may claim ownership of the residual bloodspots, although to date, there have not been any recorded incidences of the federal government exerting these property rights.

Instead, it appears that much of the debate about the storage of residual bloodspots centers on disputes between states and individuals – particularly parents – regarding ownership of the samples. Beth A. Tarini et al. summarized the problem:

[A]lthough storage of NBS samples is a routine practice in many states, the majority of states do not

actively obtain parent permission to store blood samples. In some states, parents who do not want their children's samples used for research have the right to contact the state and request that their children's samples be destroyed. In general though, most state programs do not actively provide parents with information regarding policies for storage and use of NBS samples, and it is unclear how many parents are aware of these storage and use policies.⁹⁹

Tarini et al. found that 77.9 percent of the parents surveyed would allow storage of the NBS sample for some length of time, but only 38.5 percent would actually allow indefinite storage of samples.¹⁰⁰

Erin Rothwell's study also examined parental attitudes regarding storage of residual bloodspots. She and her colleagues found that most survey participants felt that residual bloodspot samples should be destroyed after the screening process was complete.¹⁰¹ Rothwell's finding is consistent with data from a 2010 Cogent Research study, which found that fifty-seven percent of participants wanted to destroy their DNA samples after testing on the sample had been completed.¹⁰² Rothwell's study also found that participants believed they owned the sample. One participant stated, "This is the property of the state, but the state is like a non-entity and the people make up the states so we all own it." In fact, the study found that most participants felt that parents either owned or should own their children's residual bloodspot samples.¹⁰³ Despite this expressed desire for ownership, however, four states (California, Maine, Utah, and Washington) have regulations explicitly stating that, once collected, residual bloodspots become the property of the state.¹⁰⁴

Rothwell also found that participants expressed a desire for informed consent for the storage of the samples.¹⁰⁵ She and her colleagues attributed this desire for informed consent to parents wanting to feel involved in the screening process.¹⁰⁶ In fact, parents have articulated exactly this desire. One father stated,

I would remember if a 4-page document had been placed in front of us explaining why the [state department of health] was going to store my son's DNA for its own purposes following the PKU testing. No such information was provided, not even a paragraph. Indeed, I didn't learn about [this] practice until . . . 6 months after my son's birth.¹⁰⁷

Another mother described a similar experience: "I was NEVER show[n] any information [about the storage of NBS samples]. There was no paper . . . that explained what was going to happen with this blood sample[,] and there was no paper . . . saying I could opt out."¹⁰⁸ However, despite parental desire for informed consent, only twelve U.S. jurisdictions currently have legislation or regulations related to parental consent for storage.¹⁰⁹

Unlike newborn screening legislation and regulation, which is mostly consistent between the fifty-one jurisdictions examined, a survey of their respective storage practices reveals a great deal of inconsistency. As mentioned previously, jurisdictions vary widely in how they view ownership of the residual bloodspots and their policies regarding consent to storage. Additionally, the fifty-one jurisdictions exhibit great variance in the amount of time they store the bloodspots, with some states only storing these samples for a month and others storing them indefinitely.¹¹⁰ One possible explanation for this inconsistency is that some jurisdictions, for example Kentucky, do not have a bloodspot retention period specified in their laws or regulations. Thus, the newborn screening programs in these jurisdictions may have the discretion to determine their own retention periods, and may be able to change at will the length of time their residual samples are stored.

As discussed above, the Newborn Screening Saves Lives Act may be responsible for the post-2007 revisions seen in many states' laws and regulations. With the influx of newborn screening resources, one might expect states to begin storing samples for longer periods of time. Indeed, between 2008 and 2011, Samuel W. Anderson observed that seven states had increased their retention period.¹¹¹ However, in this same period, he also observed that five states had decreased their retention times.¹¹² These decreases may be attributable to the 2009 Texas and Minnesota lawsuits in which parents objected to these states' non-consensual storage of residual bloodspots. These cases will be discussed in greater detail in the next section, but perhaps certain jurisdictions were afraid of generating similar negative publicity and therefore decreased their sample retention times.

The methods state laboratories use to store the bloodspots represent an additional source of variance in the jurisdictions' storage policies. As Anderson noted, these storage mechanisms can vary greatly.

Iowa stores samples for one year at -80 degrees

Celsius, then four years at room temperature; Utah keeps the samples at room temperature for a week before cooling them to -20 degrees Celsius. Mississippi keeps the blood spots in Ziploc bags in a freezer. Louisiana's samples spend 30 days refrigerated in "gas permeable bags."¹¹³

Anderson's report noted that six states did not even have a written policy regarding the storage and disposal on NBS samples.¹¹⁴ When a state lacks a clearly articulated policy governing sample storage, it is hard to imagine that such a state would have clearly articulated policies to prevent privacy breaches. This is because the act of storage itself may embody the risk of a privacy breach.

The Electronic Privacy Information Center noted that, given the sensitivity of the information they store,

DNA databanks require appropriate safeguards for storage of physical samples, database security for DNA profile databases, and security mechanisms to protect the links between the two. This creates several potential points at which individual privacy can be violated and requires complex and multi-layered security arrangements, as well as appropriate audit and accountability measures.¹¹⁵

The problem of privacy breaches is not just a hypothetical problem, as indicated by recent breaches of several high-profile biobanks. In 2006, Trey Sutherland, an Alzheimer's researcher with the NIH, was found to have given pharmaceutical giant Pfizer 3000 spinal fluid samples from 538 research participants in exchange for \$600,000 in consulting and lecture fees.¹¹⁶ Even more recently, in December 2010, a laptop was stolen from the Cord Blood Registry,¹¹⁷ the largest stem cell bank in the world.¹¹⁸

These high-profile biobank breaches demonstrate a need for stringent security measures for newborn bloodspot databases. To date there have been no documented security breaches of NBS databases, but the security procedures implemented in some states may indicate potential vulnerability to such breaches. Although both New York and Massachusetts have restricted access to the buildings in which the samples are stored, statements made by newborn screening officials in those states suggest that access to the databases themselves may not be so secure. In New York, for example, the freezer containing the samples is not locked, and in Massachusetts, one of the two freezers in

which samples are kept has no lock on it. While public health officials explain that a lock on the freezer would make it more difficult for scientists working with the samples to access the bloodspots, it is undeniable that the absence of such a lock also increases the possibility of a security breach. Given past breaches at the Cord Blood Registry and NIH, fears of similar breaches of newborn residual bloodspot databases may not be unfounded.

Even in states with written storage policies and locked freezers, there is still no guarantee that individuals' genetic information is secure. Some states like New York keep paper cards with identifying information in their storage facilities, which presents a serious data security issue in the event of a security breach. Additionally, although many states require that the samples' identifying information be kept confidential by "anonymizing" or "de-identifying" the bloodspots, even so-called anonymized blood samples may be traced back to the sample donor. With an anonymized sample, the subject's identity has been "irreversibly severed to prevent any future re-identification."¹¹⁹ "[D]ata can be considered anonymized if it cannot be linked back to the subject in any way."¹²⁰ To anonymize data, "it is insufficient to simply scramble a subject identifier"; instead, one "must scramble the subject identifier and then discard the key that links the new subject identifier with the original subject identifier."¹²¹

There is a subtle distinction between anonymization and "de-identification." De-identification merely "involves the removal of personally identifying information in order to protect personal privacy," and as such, "de-identified data may not necessarily be anonymized data."¹²² Whereas an anonymized sample has the donor's identifying information permanently destroyed, with a de-identified sample, "the personally identifying information may be able to be re-associated with the data at a later time," and "[i]n such cases, anonymized data is a particularized subset of de-identified data."¹²³ However, it is important to note that the distinctions between anonymization and deidentification are largely semantic, and because researchers often interchange these words, they will henceforth be used interchangeably in this report.

Although anonymization or de-identification of NBS samples may appear at first blush to eliminate the risk of potential privacy violations, such protections may be illusory. In 2008, a study conducted by Nils Homer and colleagues demonstrated that researchers "could easily identify individuals within pooled, anonymized data sets if they

had a small amount of identified genetic information for reference.”¹²⁴ Homer stated that the study’s findings “show a clear path for identifying whether specific individuals are within a [particular medical] study” and acknowledged that “anonymization” of genetic information “does not completely mask identity.”¹²⁵ Stephanie Fullerton et al. stated that as a result of studies like Homer’s, “[i]t is no longer clear that we can promise anonymity to participants.”¹²⁶ Although most newborn screening programs do not require consent and therefore do not promise anonymity, Fullerton’s observation is still salient for those parents concerned about violations of genetic privacy.

C. CONSENT ISSUES RELATED TO USE OF NBS SAMPLES FOR RESEARCH

Similar to the consent issues related to screening and storage of NBS samples, the issues surrounding the use of residual bloodspots for research also involves a debate regarding ownership, privacy, access, and consent. This is unsurprising, since initial screening and storage are prerequisites for subsequent research on the collected samples. As a brief explanatory note, “research,” as it is used in this section, refers to any study that makes use of NBS samples after screening, whether that is for quality assurance purposes or for broader “public health” purposes.

Recall that Jeffrey Botkin’s study showed that about half the parents surveyed wanted informed consent for NBS screening, and Erin Rothwell’s study demonstrated that most parents would prefer that consent was required for sample storage. Echoing parental desire for consent to screening and storage, the survey by Beth A. Tarini and colleagues revealed that many parents also believe that research on residual samples should not be conducted without parental consent. They found that

[i]f parental permission was obtained, most parents reported that they would either be ‘very willing’ (38%) or ‘somewhat willing’ (37.4%) to permit use of their children’s newborn screening samples for future research studies . . . If parental permission was not obtained, substantially fewer parents reported that they would either be ‘very willing’ (11.3%) or ‘somewhat willing’ (16.9%) to permit use of the NBS sample for research. Moreover, over half of parents (55.7%) would be very unwilling’ to permit the use of their child’s newborn screening sample for research purposes.¹²⁷

The Tarini study also noted that “[t]here was no significant association between parent gender, race/ethnicity, education, household income, number of children, age of [first] child, or age of [second] child” correlated with parents’ responses.¹²⁸ From this evidence, one may conclude that there is broad demand from many parents – regardless of their background – to be involved in the decision-making process regarding the use of their children’s newborn bloodspot samples. In Erin Rothwell’s study, parents were able to articulate the potential benefits of having greater control over this process. Rothwell found that “[p]articipants felt that informed consent would . . . establish more communication over the type of studies conducted on the samples . . . [and] would also involve state health departments that would help develop and define a process for involving the parents.”¹²⁹ However, an examination of federal and state laws and regulations reveals that parents are often completely cut out of the decision-making process altogether.

A federal regulation (45 CFR 46) exists that governs the use of human subjects in research. This regulation, often referred to as the “Common Rule,” includes provisions about obtaining parental consent and lists the requirements for informed consent. However, section 46.101(b)(4) of the Common Rule states that any “[r]esearch involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens” is exempt from informed consent and parental consent requirements “if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.”¹³⁰ Thus, federal regulations explicitly allow NBS samples to be used in research without informed parental consent if the samples are anonymized.¹³¹ However, as discussed in the previous section, such de-identification may only provide illusory privacy protection.

The problems associated with data anonymization are particularly troubling, given that many parents may be concerned about violations of genetic privacy. The Cogent Research study found that “the proportion of Americans who are concerned about how their genetic information would be stored and who would have access to that information, has climbed from 65% in 2006 to an all-time high of 71% in 2010.”¹³² It is important to note that those surveyed expressed concern about privacy breaches themselves, rather than discrimination that could potentially occur after privacy has been breached. In other words, individuals viewed the violation of their privacy as an intrinsic

sic harm separate from discrimination. This finding suggests that parents may also be concerned about the violation of their genetic privacy as separate from future discrimination. Additionally, the Cogent study found that while “close to half (47%) of all Americans say they would be interested in using their genetic information for the purpose of understanding and optimizing their health,” “two thirds (63%) say they would be more interested in doing so if they were assured that, by law, no one could access their DNA information without their consent.”¹³³ This finding suggests that privacy and consent are likely intertwined in many parents’ minds and that these parents would prefer that consent be obtained prior to research being conducted on their children’s residual bloodspots.

Rothwell’s study supports this idea. Participants “repeatedly” expressed fear that the discovery of a predisposition to a condition would lead to future discrimination on this basis.¹³⁴ The participants were particularly concerned that such diagnoses would compromise an individual’s ability to get a job or could lead to discrimination by insurance companies.¹³⁵ This is not a trivial concern; in 2010, a woman sued her former employer after the employer found out that she carried a gene predisposing her to breast cancer and subsequently fired her.¹³⁶ It is important to note that although this dispute would be resolved under the Genetic Information Nondiscrimination Act of 2008 (GINA), the protections afforded by GINA are limited to health insurance providers and employers. GINA does not cover life, disability, and long-term care insurance, which are just some of the other ways an individual may be discriminated against. Many of the participants in Rothwell’s study pointed to the uncertainty of “future genetic and technological advancements” as the cause of their fears.¹³⁷ Interestingly, members of state NBS advisory committees have also echoed these fears.¹³⁸

The Rothwell study also provided evidence that parents

doubted the benefits of anonymized data. Recall that data “anonymization” is a somewhat deceptive term, since there is evidence that an individual’s genetic information, even if initially stripped of its identifying information, may still be traced back to that individual. Thus, parental distrust of de-identification is understandable. Rothwell found that “[p]articipants questioned the benefit of anonymized research if [researchers] could not communicate the results back to the person.”¹³⁹ This finding seems to suggest that for many parents, the limited individual benefits to infants, coupled with the risk of privacy breaches, outweigh the benefits of using NBS samples in research. However, many medical professionals appear to feel differently. Rothwell’s survey included a group consisting of pediatricians and nurse practitioners. This group expressed the opinion that there was value in building a large database of residual bloodspots, which could later be used in epidemiological studies.¹⁴⁰ Interestingly, Rothwell noted that these answers changed when the respondents considered the same question, but this time from the point of view of a parent rather than a medical professional. One respondent’s statement neatly captured this tension: “As a parent I’d want that information back if my child’s blood tested positive for something. As a physician I still think all the [epidemiological data] are valuable regardless of whether or not parents get any feedback.”¹⁴¹

These survey results echo the ACMG report, which, as discussed earlier, shifted the benefit discussion from focusing on direct medical benefit to the infant to instead emphasizing potential public health benefits. Whereas the parents surveyed seemed more concerned about the benefits to their children, the participating researchers seemed more concerned with the research value that the NBS samples represented. A recent Texas lawsuit, *Beleno v. Texas Department of State Health Services*, illustrates the danger of having a sharp disconnect between researchers’ desires and parental desires. The next section discusses the details of this case.

PART IV: NBS STORAGE AND USE CASE STUDIES: TEXAS AND MINNESOTA

CASE 1: TEXAS

Like many states, the Texas Department of State Health Services (DSHS) has been collecting residual NBS samples since the introduction of mandatory PKU testing in the 1960s.¹⁴² Until 2002, these samples were “thrown out after a short storage period,”¹⁴³ but beginning in 2002, DSHS began to store these samples indefinitely, with the stated purpose of conducting “research into causes of selected diseases.”¹⁴⁴ Presumably, the state encountered difficulties in storing and maintaining a database of bloodspots that was growing at a rate of 800,000 samples per year,¹⁴⁵ and in 2006, DSHS began an agreement with Texas A&M University to have the university store the samples.¹⁴⁶ Although Texas A&M wanted to notify the public about this change by issuing a press release, DSHS ultimately overruled this plan.¹⁴⁷ From subsequently released DSHS emails, it appears that the agency was aware of potential privacy issues. For example, one email from a DSHS employee stated, “This [press release] makes me nervous. Genetic privacy is a big ethical issue . . . a press release would most likely only generate negative publicity.”¹⁴⁸ Thus, DSHS officials ultimately instituted this significant policy change without even notifying parents, much less obtaining their consent.

Researchers subsequently requested access to the Texas database “to study the gene involved in club foot, to inspect the DNA of infants who develop childhood cancer, [and] to examine prenatal lead exposure.”¹⁴⁹ DSHS was not secretive about the use of NBS samples in these research projects, but the agency did attempt to hide that it gave residual bloodspots to the United States Armed Forces DNA Identifi-

fication Laboratory (AFDIL).¹⁵⁰ Between 2003 and 2007, DSHS provided 800 de-identified NBS samples to AFDIL “to help create a national mtDNA database.”¹⁵¹ Mitochondrial DNA (abbreviated mtDNA) is “a naturally abundant DNA molecule” that since the 1990s has been used in forensic DNA identification.¹⁵² However, mtDNA is “only as valuable as its sample size”¹⁵³ because its use as an identification tool is dependent upon having a complete enough mtDNA database to compare a sample against.

AFDIL has been using mtDNA since 1993 to identify the skeletal remains of military personnel and return these remains to their families.¹⁵⁴ As part of George W. Bush’s DNA Initiative, in 2003, AFDIL approached DSHS about acquiring access to the state’s NBS samples for the purpose of expanding AFDIL’s mtDNA database.¹⁵⁵ In particular, AFDIL “researchers wanted ‘anonymous and maternally unrelated’ blood samples from Texas Caucasians, African-Americans and Asians — and from Hispanics and Native Americans in particular — to round out their genetic record.”¹⁵⁶ According to AFDIL research proposals, “federal officials [eventually] hoped to be able to share this data worldwide, ‘for international law enforcement and investigation in the context of homeland security and anti-terrorism efforts.’”¹⁵⁷ DSHS did not publicize its collaboration with AFDIL, nor did it accept money for AFDIL’s use of the Texas bloodspots.¹⁵⁸

According to the released DSHS emails, when the agency began providing NBS samples to researchers, it was actually aware of the potential parental consent issues.¹⁵⁹ One researcher wrote that he would prefer not to go through the

process of obtaining consent.¹⁶⁰ Another stated that although parental consent for the use of the samples was not sought by the agency, he believed DSHS “already use[d] (de-identified?) blood spots for some research, so [it] may not be a big deal.”¹⁶¹ Despite this apparent unease, the agency did not implement any procedures to obtain informed consent from parents.

This practice might have continued for much longer than it did, but on February 22, 2009, Mary Ann Roser, a medical reporter at the Austin American-Statesman, issued a report publicizing Texas’ storage of newborn bloodspots.¹⁶² The article caught the attention of a Texas mother, Andrea Beleno, and her father-in-law Jim Harrington, a civil rights attorney and the founder and director of the Texas Civil Rights Project (TCRP).¹⁶³ In March 2009, TRCP filed suit in the Western District of Texas against DSHS and Texas A&M on behalf of five families, with Beleno designated as the lead plaintiff in the case.¹⁶⁴ Four of the five families had children whose samples were stored by the state after 2002; the fifth plaintiff was pregnant at the time the suit was filed and gave birth in August of 2009. The suit alleged that the defendants had violated the children’s Fourth Amendment rights by conducting an unlawful search and seizure and that they had violated the children’s privacy rights under the Fourteenth Amendment “by collecting and indefinitely storing the cards without consent.”¹⁶⁵

On May 27, 2009, after the suit was filed but before the court had issued its ruling, the Texas legislature passed a bill amending the state’s laws about newborn screening. The bill gave parents the ability to opt out of the post-screening sample storage process,¹⁶⁶ ensured the de-identification of samples that were stored,¹⁶⁷ and required oversight of state newborn screening and storage practices by an institutional review board.¹⁶⁸ After the bill was passed, DSHS and Texas A&M attempted to use this legislative change to their advantage, arguing that the bill’s amendments effectively rendered the plaintiffs’ suit moot. However, the court determined that the new bill did not retroactively apply to the residual bloodspots that had already been collected, which included samples collected from the four plaintiffs whose children were already born at the time the suit was filed.¹⁶⁹ Because the fifth plaintiff did not give birth until after the bill was passed, the court determined that her suit was moot.¹⁷⁰

The court also considered the issue of standing, focusing on whether the plaintiffs had sustained injuries that the court could remedy. The defendants alleged that the plain-

tiffs had suffered no real injuries because there was only the “potential” for misuse of the NBS samples in question.¹⁷¹ Interestingly, the court rejected this argument, stating, “[T] here is a reasonable fear of the potential for misuse because of the continued storage of the samples. Continuous and pervasive acts resulting in reasonable fear is enough for injury-in-fact.”¹⁷² The court’s interpretation of injury is significant. Such a decision means that “a plaintiff suing a laboratory or researcher would not necessarily have to show that his own sample was misused, only that his sample was part of the group of samples subject to misuse.”¹⁷³ Legal commentator Adam Doerr wrote that in the case of newborn screening, “this requirement will be easy to meet.”¹⁷⁴

The court went on to address the plaintiffs’ claims, beginning with the allegations that DSHS and Texas A&M violated the children’s constitutional rights. The court did not definitively resolve the Fourth Amendment claim, instead simply stating that the claim was “plausible on its face” and dismissing the defendants’ motion to dismiss on these grounds. However, the court did state that plaintiffs did plead sufficient factual content for the court “to draw the reasonable inference that defendants [were] liable” for violating the plaintiffs’ “protected liberty and privacy rights” under the Fourteenth Amendment.¹⁷⁵ The court agreed with the plaintiffs’ claim that the residual bloodspot samples “contain deeply private medical and genetic information, and were expropriated without knowledge or consent,” determining that these storage and use practices involved “bodily integrity.”¹⁷⁶ Thus, the court recognized that non-consensual storage of NBS samples is an inherent violation of individual privacy rights. Doerr noted that the court’s decision about the Fourteenth Amendment issues “could be significant in future cases, possibly providing a form of constitutional protection in situations where the Common Rule may not apply.”¹⁷⁷

Ultimately, the case did not go to trial because DSHS and Texas A&M decided to settle. The settlement agreement did not award the plaintiffs any money, but it did require the defendants to destroy all samples that were collected without parental consent before May 27, 2009, the date specified in the revised Texas Code.¹⁷⁸ As a result, in February of 2011, 5.3 million residual bloodspots were removed from DSHS and Texas A&M storage facilities and taken to a medical incineration facility to be destroyed.¹⁷⁹ The president of the Texas A&M Health Science Center, Dr. Nancy Dickey, stated that although she was glad to have reached an agreement with the plaintiffs, she was “sad-

dened . . . that a superb database has been lost” because the information could have been used “to shed light on causes of congenital birth defects and potentially led to preventive measures saving thousands of infants and their families the distress these defects cause.”¹⁸⁰

The settlement agreement also stipulated that that DSHS inform the plaintiffs about “how their children’s blood was used and any financial transactions involving the specimens.”¹⁸¹ Additionally, the agency agreed to “post information on its newborn screening Web site [sic], including a list of all research projects for which it has provided newborn-screening blood specimens.”¹⁸² As of August 2012, there were no such projects listed on the DSHS website. Additionally, in May of 2011, the Texas state legislature “voted to change the research portion of its newborn screening [program] from opt-out to opt-in,”¹⁸³ meaning that parents would now have to provide affirmative consent before their children’s residual bloodspots were used in research projects. All in all, then, the Beleno outcome was a significant “victory” for TCRP; as the organization’s website proudly notes, the case also represented the first decision of its kind in the country.¹⁸⁴ It was not the last, however, as the Minnesota Bearder case demonstrates.

CASE 2: MINNESOTA

In 2003, Minnesota privacy activists from the Citizen’s Council for Health Freedom (CCHF) became aware of the state’s storage practices while examining an annual Minnesota appropriations bill.¹⁸⁵ As part of Minnesota’s screening procedures, five bloodspot samples are taken from the newborn, three of which are sent to the Mayo Clinic, while the remaining two are retained by the Minnesota Department of Health (MDH).¹⁸⁶ According to the MDH website,

*the Mayo Clinic is under contract with MDH to perform some of the newborn screening tests . . . Rather than duplicating the work and equipment available at the Mayo Clinic, MDH sends part of each specimen to the Mayo Clinic for testing.*¹⁸⁷

Thus, CCHF activists came to learn that MDH had residual bloodspot samples dating back to 1997.¹⁸⁸

The organization was concerned about the lack of parental knowledge about these storage practices and was “determined to do all that [it] could to stop this practice.”¹⁸⁹ Twila Brase, the president of CCHF, began distributing information wherever she went to raise awareness of these

practices. According to a Nature article, “every time she [flew], she [took] a stack of wallet-sized cards to hand out at the gate” with attention-grabbing messages like “Protect your baby” and “Reclaim their DNA!”¹⁹⁰ As a result of the organization’s efforts, parents began contacting the group to complain about and speak out against the practice.¹⁹¹ Few parents who had contacted MDH on their own and raised objections to the storage of their children’s residual bloodspots actually received responses to these complaints.

In 2009, CCHF began calling Minnesota attorneys to identify families willing to be parties to a lawsuit against MDH. On June 30, 2009, nine families representing twenty-five children filed suit against MDH in the Hennepin County District Court, alleging that the agency had violated “their statutory, common law, and constitutional privacy rights.”¹⁹² In particular, the plaintiffs argued that the storage of the residual bloodspots violated the state law governing the “[t]reatment of genetic information held by government entities and other persons,” Minn. Stat. 13.386. The families sought enforcement of this law, which they argued prohibited “the collection and storage of genetic information . . . without informed written consent.”¹⁹³

Minn. Stat. 13.386, referred to by Minnesota courts as the “Genetic Privacy Act” (“GPA” or “the Act”), was passed in 2006. “The GPA became effective as of August 1, 2006, and applied to genetic information collected on or after that date.”¹⁹⁴ Two sections of the statute were particularly relevant to the Bearder case. The first of these was subdivision 1, which allows for two possible meanings of “genetic information.” Part (a) states that genetic information means

*information about an identifiable individual derived from the presence, absence, alteration, or mutation of a gene, or the presence or absence of a specific DNA or RNA marker, which has been obtained from an analysis of: (1) the individual’s biological information or specimen; or (2) the biological information or specimen of a person to whom the individual is related.*¹⁹⁵

Part (b) provides an alternate definition, stating that genetic information can also refer to “medical or biological information collected from an individual about a particular genetic condition that is or might be used to provide medical care to that individual or the individual’s family members.”¹⁹⁶

The other relevant portion of the GPA was subdivision 3. This section prohibits the collection of genetic informa-

tion by a government agency without written informed consent “unless otherwise expressly provided by law”.¹⁹⁷ Subdivision 3 also states that genetic information “may be used only for purposes to which the individual has given written informed consent” and that it “may be stored only for a period of time to which the individual has given written informed consent.”¹⁹⁸

The Bearder case turned on two questions. The first question was whether NBS samples qualified as “genetic information” under subdivision 1 of the GPA. The second was whether MDH’s newborn screening program violated subdivision 3’s informed consent requirements. This second question, in turn, involved the interplay between the GPA and the Minnesota statutes governing the state’s newborn screening program, Minn. Stat. 144.125 through 144.128. According to these statutes, the newborn screening program requires the state’s commissioner of health

*to prescribe the manner of testing, recording, and reporting of newborn screening results; mandates those who perform screenings to advise parents that the blood specimens and test results may be retained; and permits parents either to decline to have their infants tested or to require destruction of the blood specimens or test results following screening.*¹⁹⁹

The statutes also stipulate that any bloodspots “remaining after a screening test may be stored by the health department,” provided that parents receive information about the screening program and do not submit a written request to destroy the sample.²⁰⁰

The Minnesota District Court found that of the twenty-five children represented in the suit, sixteen were born after the effective date of the GPA, and therefore, these sixteen children had no standing to litigate.²⁰¹ As for the remaining nine children, the court determined that these children’s NBS samples were “biological samples, not genetic information as defined in the GPA.”²⁰² Furthermore, the court determined that even if the residual bloodspots were considered to be genetic material, “[t]he GPA does not supersede specific existing law such as the NBS Program.”²⁰³ For these reasons, on November 24, 2009, the district court granted MDH’s motion to dismiss.²⁰⁴ In response, CCHF issued a press release calling the decision a “faulty ruling” and stating that they “look[ed] forward to the appeal.”²⁰⁵

Unfortunately for CCHF, this first appeal was unsuccess-

ful: the Minnesota Court of Appeals affirmed the district’s court order to dismiss the case in November of the following year.²⁰⁶ The court of appeals stated,

*While the newborn screening statute permits use of newborn screening specimens for purposes related to that program, it does not provide for the specimen remainders to be used for purposes outside the newborn screening program. As such, any use of the specimens for purposes not related to the newborn screening program is subject to the written informed consent requirements of the genetic privacy act.*²⁰⁷

However, because the plaintiffs could not demonstrate that the nine children’s bloodspots had been used “in any public health studies or research,” the court determined that plaintiffs had failed “to offer ‘substantial evidence’ to support their Genetic Privacy Act claim, or their other claims for tort, violation of privacy, or governmental taking.”²⁰⁸

The case was again appealed, this time to the state’s supreme court, which handed down a ruling on November 16, 2011.²⁰⁹ The Minnesota Supreme Court first determined that the residual bloodspots were “genetic information” under the Part (b) definition given in the GPA. The court explained that the Part (b) definition “is broader in scope [than the Part (a) definition] because it encompasses ‘medical or biological information’ about an individual,” which the court interpreted to include blood samples.²¹⁰ The court noted that because residual bloodspots “unquestionably contain genetic information,” “[i]t would be impossible to collect, use, store, or disseminate those samples without also collecting, using, storing, or disseminating the genetic information contained in those samples.”²¹¹ For this reason, the court concluded that the GPA was applicable to NBS samples.²¹²

The Supreme Court then determined that none of the state’s newborn screening statutes created an “express exception” to the GPA’s informed consent requirements for the storage and use of the residual bloodspots.²¹³ Any exceptions existed

only to the extent that the Department is authorized to administer newborn screening by testing the samples for heritable and congenital disorders, recording and reporting those test results, maintaining a registry of positive cases for the purpose of follow-up services, and storing those test results as

*required by federal law. The newborn screening statutes do not expressly authorize the Department to conduct any other use, storage, or dissemination of the blood samples.*²¹⁴

Although MDH justified its non-consensual storage and use of NBS samples on the grounds that doing so would allow it to “improve its screening methods,”²¹⁵ the Supreme Court rejected this explanation, stating that the “[u]se of genetic information for purposes other than the screening of newborn children and for follow-up services requires written informed consent.”²¹⁶ CCHF was “cheered by this good news.”²¹⁷ The organization’s press release about the Minnesota Supreme Court’s decision stated, “We are pleased that these nine families were willing to sue the State of Minnesota . . . Their action and this decision now secures the genetic privacy rights and informed written consent rights of all Minnesota parents and newborn citizens.”²¹⁸

The Minnesota Supreme Court remanded the case back to the district court that had originally heard the case to determine the appropriate remedy.²¹⁹ On January 31, 2012, MDH issued a press release stating that after a hearing before the district court on January 26, the agency had

*been given permission by Hennepin County District Court Judge Mel Dickstein to begin destroying the blood spot collection cards . . . in order to comply with [the] Minnesota Supreme Court decision. The destruction will include all those specimens received on or after Nov[ember] 16, 2011, the date of the Supreme Court decision.*²²⁰

The press release explained that the samples would be destroyed after the seventy-one day retention period required to confirm a positive diagnosis from the newborn screening panel.²²¹ Minnesota Health Commissioner Dr. Edward Ehlinger lamented the destruction of the bloodspots, which he described as “a valuable public health resource,” but stated that “it [was] necessary to take this step in order to comply with the Supreme Court’s decision in the Bearder case.”²²² Thus, beginning on January 30, “the state began autoclaving and then shredding blood spots collected since the decision.”²²³ Additionally, the Minnesota legislature has since passed modifications to its newborn screening statutes requiring informed parental consent for the storage of the samples.²²⁴

PART V: BEGINNING THE POLICY DEBATE

THE CASES DESCRIBED in the previous section demonstrate the real negative consequences that are possible in the absence of informed consent procedures for newborn screening, storage, and use of samples in research. There are, however several possible ways to remedy the informed consent problems identified in Part III. Lainie Freidman Ross proposed a tiered model for consent requiring separate consent procedures for screening and storage of the samples.²²⁵ Requiring separate consent forms for each of these processes, rather than bundling them into a single consent process, has the advantage of clarity. There would be no question of whether a parent had consented to just screening or both screening and storage if there were two separate steps. Adopting a bifurcated approach to consent also would allow parents to tailor the procedures to suit their desires. If, for example, a parent wanted his or her child to go through the screening program but objected to the subsequent storage of the child's residual bloodspot, that parent could consent to the initial screening step but express refusal at the second storage step. The Task Force on Genetic Screening, the Newborn Screening Task Force, and the President's Council on Bioethics have all expressed approval of a two-tiered model of consent.²²⁶

Ross believes that the initial screening step should involve an "opt-in" model of consent.²²⁷ In the opt-in model, parents must express affirmative consent in order to become part of the newborn screening program, and in the absence of affirmative consent, screening will not be conducted. Ross writes that such a model "shows respect for parental decision-making authority."²²⁸ The opt-in model

differs from the "opt-out" model that some states have, in which newborns undergo screening by default, unless the child's parents explicitly refuse screening. It is important to note that the opt-out model is not a true model of consent because it does not require any form of consent; instead, the opt-out model functions as a substitute for consent. As of August 2012, all of the forty-eight states that permit refusal (however limited the opportunity to refuse may be) employ the opt-out model.²²⁹

One problem of the opt-out model is the ambiguity posed by silence. As applied to the case of newborn screening, a parent who does not voice objection to the screening program may still approve of the program and consent to screening even if s/he does not express affirmative consent. On the other hand, that same parent may disapprove of newborn screening and want to opt out of the program, but s/he is either uninformed about or unaware of the program and therefore does not express explicit refusal. In both cases, however, the outcome is the same: the infant will undergo screening. Thus, the opt-out model for screening depends upon parents being well informed about the screening programs and their consent options. The reality, however, is that many parents are not well informed about screening programs or consent, due to inopportune methods and timing of information dissemination and the lack of adequate training for medical professionals responsible for communicating the information.²³⁰ Thus, the only way to be sure that someone is truly consenting to screening is to obtain his or her affirmative consent, as required by the opt-in model.

Like the opt-out model, the opt-in model also benefits from having parents who are well informed about the risks and benefits of screening. Three studies have offered various solutions to remedy the informational asymmetries that disadvantage parents. First, L. McKechnie and A.B. Gill's study advocates "antenatal consent," essentially requiring medical professionals to secure parental consent to newborn screening before the baby was born.²³¹ They write that given the stress surrounding the labor process, the "[v]alidity of consent obtained during labor might be questionable. Equally, obtaining consent from high risk pregnancies may put undue stress on parents."²³² Second, Jeffrey Botkin's study suggests that showing parents a movie to educate them about newborn screening was far more effective than distributing brochures. Botkin and his colleagues found that "[a]cceptability by the public of sample retention and use was enhanced by providing substantive information about the pros and cons of this practice through an educational movie."²³³ In fact, "the single most consistent variable associated with support for [bloodspot] use was viewing the educational movie."²³⁴ It is also worth noting that the costs of producing a video may actually be lower than designing and printing brochures. Finally, Hasegawa's study suggests bolstering NBS training for medical professionals by "clearly delineating [obstetricians'] responsibilities in counseling families about NBS," making educational resources for newborn screening available to obstetricians, and crafting a coherent national policy about NBS education.²³⁵ Implementing all three of these suggestions would likely go a long way in educating parents about the benefits and risks newborn screening.

As mentioned before, the Task Force on Genetic Screening, the Newborn Screening Task Force, and the President's Council on Bioethics all advocate a two-tiered model of consent. All three organizations propose that the second tier, which deals with the storage of residual bloodspots, should also implement an opt-in model of consent.²³⁶ As with opt-in screening, requiring parents to express affirmative consent for storage promotes clarity: if state agencies were required to provide parents with information about the storage of the residual samples and obtain affirmative consent for this type of storage, there would be no question about whether a particular parent had actually approved this procedure.

An additional benefit of implementing opt-in storage is that it aligns with many parents' desire to be involved in these decision-making processes. Recall that some participants in the Rothwell study felt that the residual samples

remained the property of the family, rather than the state, and that many of the participants expressed a desire for informed consent for storage. The Texas and Minnesota lawsuits further emphasize the parental desire for informed consent to storage, as well as the danger of failing to acknowledge this desire. The plaintiff parents in both cases seemed to be most upset about the storage of the newborn samples without their knowledge, and the courts in both cases concluded that such storage should require affirmative, opt-in consent.

Another rationale for adopting an opt-in model of consent for storage of residual bloodspots is that such a model acknowledges the risk of security breaches of storage facilities. As discussed in Part III, several high-profile biobanks have been breached in the past. Although there is no indication that any NBS databases have suffered similar breaches, several states' storage practices suggests that they may be vulnerable to such breaches. Requiring parents to affirmatively consent to storage of their children's residual bloodspots makes parents aware of this risk, which may in turn prompt states to implement greater security measures.

A final reason to require affirmative consent for storage is that it promotes greater governmental transparency. Such transparency is especially important because of how newborn screening and storage are treated in state laws. A study by the Genetics and Public Policy Center identified twelve states that had carved out exceptions for newborn screening from their genetic privacy laws,²³⁷ meaning that information obtained from newborn screening did not enjoy the same privacy protections as other type of genetic information. A possible rationale for creating this exception is that it facilitates medical research. As Samuel W. Anderson noted, "[r]esearchers and administrators working with these samples know very well how alarming newborn blood spot biobanking can sound to the layperson," which explains why many of these "clinicians, researchers and state labs would prefer these projects to keep a low profile."²³⁸ Indeed, the released emails from the Texas Department of State Health Services demonstrate exactly this concern. However, public health officials' desire to avoid controversy must be balanced against parental interest in being informed about the storage and use of their children's bloodspots. It is also important to balance the officials' stated research purposes, which include elucidating disease mechanisms and devising new treatments, against the actual benefits conferred, which appear to be mostly related to testing. Given many parents' desire for informed con-

sent, the overstated benefits of screening and storage, and the outcomes of the Beleno and Bearder lawsuits, states would be well advised to begin requiring informed parental consent for sample storage.

To be fair, the two-tiered opt-in model is not without its flaws. For example, one potential problem with this proposal is that “families will conflate newborn screening itself with breach of their privacy and will opt out of the screening.”²³⁹ There is, in fact, some empirical evidence to support this claim.

Data provided to [CCHF] by the MDH indicate that parental concern about the genetic privacy of their newborns is on the rise. In 2003, two families asked

the state to destroy their infant’s blood sample, the written results of the baby’s screening, or both. By 2010, that number had grown to 712 . . . Over the same period, the number of families opting out of newborn screening altogether grew from 2 to 156.²⁴⁰

Although, as George Annas pointed out, there is only a slim chance that parental refusal would lead to an undiagnosed inherited metabolic condition, there is still a possibility that such events could occur. Additionally, implementing this model of consent could possibly increase the total cost of screening, as well as place greater responsibility (and therefore liability) on the medical professionals charged with obtaining informed consent.

CONCLUSION

WHEN ANALYZING NEWBORN screening programs, it is important to critically consider all of the potential benefits, as well as any associated disadvantages. The current systems for newborn screening, as well as those for the storage and use of residual samples, appear to have evolved purely through happenstance, instead of developing through critical, strategic planning. As a result, the disadvantages of the current screening system are often overlooked or dismissed. For this reason, it is important to stimulate a national discussion about newborn screening that involves multiple perspectives, so that the full complexity of the issue is represented and considered.

The need for greater discussion about newborn screening is made even more urgent by the host of new technologies related to prenatal genetic screening. Non-invasive prenatal genetic diagnosis (NIPD) now makes it possible to test for harmful genetic conditions as early as seven weeks into pregnancy, without posing any discernible risk to the mother or fetus.²⁴¹ If NIPD becomes widely available, it could conceivably be used in place of NBS screening because it would allow physicians to do in utero what they now do after a baby is born. The widespread adoption of NIPD also has the potential to change the characteristics of the human population, as women may choose to terminate pregnancies in which they received a positive result for a certain condition. Thus, there is an urgent need to understand and discuss newborn screening and storage practices, as these new technologies present the opportunity to reconsider the current screening system.

Reconsidering the current system begins with understanding how the status quo developed. Newborn screening

has a long history, beginning with mandatory screening for PKU in the 1960s. In recent years, states have rapidly expanded their screening panels, spurred in part by the ACMG's 2005 recommendation for a uniform screening panel, and all evidence points to a continued increase in the number of tested conditions. However, this report has also shown that these changes have all taken place without much involvement from the general public. Instead, these policy changes are largely the product of joint efforts between patients' groups, public health professionals, and researchers.

Although expanded screening is justified on the basis of saving lives, certain conditions on the ACMG panel do not meet the Wilson and Jungner criteria, nor do they meet the ACMG's own criteria for screening. Loosening the criteria for appropriate screening may have dubious benefits, as demonstrated by the screening for Krabbe, and ignores the real harm caused by false positive test results. Additionally, prolonged storage of samples is justified by arguing that it will help elucidate disease mechanisms and yield new treatment options. However, the apparent dearth of published scientific studies making use of NBS databases to generate these promised findings calls into question these groups' assertions. Focusing on the promised benefits of sample storage also obscures privacy violations resulting from non-consensual storage and use of these samples. Given parental desire for informed consent and the outcomes of the Beleno and Bearder cases, states should consider adopting a two-tiered model of consent with separate opt-in informed consent procedures for both screening and storage of newborn bloodspot samples.

Newborn screening is one of the few forms of genetic testing to which almost everyone is exposed. Yet, as Jeffrey Botkin's study noted, parental knowledge of newborn screening and storage practices were "limited." For this reason, the absence of informed consent procedures in many states is troubling, especially given the newborn screening exceptions to many states' genetic privacy laws. To ensure

that parental desire for informed consent is balanced against facilitation of beneficial scientific research, there must be greater discussion and debate about newborn screening, storage, and use practices that involves all segments of the public. Because newborn screening is so ubiquitous, this discussion cannot happen quickly enough.

APPENDIX A: STATE-BY-STATE SURVEY OF NBS LEGISLATION AND REGULATION

Jurisdiction	Adopted ACMG Panel? ²⁴²	Number of Conditions Tested ²⁴²	Consent Procedures for Newborn Screening ²⁴³	Consent Procedures for Storage and Use of Residual	Bloodspots ²⁴³ Samples Retention Time ²⁴⁴
ALABAMA ALA. CODE §22-20-3 (1991)	Full core, partial secondary	44	Parents allowed to refuse on religious grounds only	Not stated in state legislation or regulation	3 months
ALASKA ALASKA STAT. ANN. §18.15.210 (West 006)	Full core, partial secondary	51	Parents allowed to refuse on religious grounds only	Not stated in state legislation or regulation or regulation	3 years
ARIZONA ARIZ. REV. STAT. ANN. § 36-694 (2008)	Full core, partial secondary	42	Parents allowed to refuse if they submit a written waiver form after hearing about the benefits of newborn screening and the risks associated with refusing	Information may be disclosed for purposes such as medical research with written parental consent; Specific consent for storage not required	90 days
ARKANSAS ARK. STAT. ANN. § 20-15-302 (West 2005)	Full core, partial secondary	30	Parents allowed to refuse on medical, religious, or philosophical grounds	Samples cannot be released to outside groups or individuals without express written parental consent; Specific consent for storage not required	3-6 months
CALIFORNIA CAL. HEALTH & SAFETY CODE § 125001 (West 2012)	Full core, partial secondary	53	Parents allowed to refuse on religious grounds only and must submit written refusal	At any time, parents can submit written refusal to have samples stored or used in research;	Indefinitely (no length of time specified)
COLORADO COLO. REV. STAT. ANN. § 25-4-1001 (West 1981)	Full core, partial secondary	46	Parents allowed to refuse on religious or personal grounds	Identifiable genetic information linked to an individual cannot be released without consent of patient or guardian; Specific consent for storage not required	6 months
CONNECTICUT CONN. GEN. STAT. ANN. § 19a-55 (West 2011)	Full core, partial secondary	56	Parents allowed to refuse on religious grounds only and must submit written refusal	Not stated in state legislation or regulation	6 months

Jurisdiction	Adopted ACMG Panel? ²⁴²	Number of Conditions Tested ²⁴²	Consent Procedures for Newborn Screening ²⁴³	Consent Procedures for Storage and Use of Residual	Bloodspot ²⁴³ Samples Retention Time ²⁴⁴
DELAWARE DEL. CODE ANN. tit. 16, §§ 1220-1227 (1998)	Full core, partial secondary	51	Parents allowed to refuse on religious grounds only Samples cannot be used for research without written parental consent;	Specific consent for storage not required	3 years
DISTRICT OF COLUMBIA D.C. CODE § 7-832 (2001)	Full core and secondary	55	Parents allowed to refuse for any reason after being informed about purpose of screening	Not stated in state legislation or regulation	1 year
FLORIDA FLA. STAT. ANN. § 383.14 (West 2011)	Full core, partial secondary	46	Parents allowed to refuse for any reason if they submit written refusal	Not stated in state legislation or regulation	6 months
GEORGIA Ga. CodeAnn. § 31-12-7 (West 2007)	Full core, partial secondary	51	Parents allowed to refuse on religious grounds only	Not stated in state legislation or regulation	12 weeks
HAWAII HAW. REV. STAT. § 321-291 (West 199)	Full core, partial secondary	50	Parents allowed to refuse on religious grounds only and must submit written refusal	All information must be kept confidential and may only be used for designated purposes (medical intervention, counseling, scientific research, reporting); Specific consent for storage not required	1 year
IDAHO IDAHO CODE ANN. § 39-909 (West 1974)	Full core, partial secondary	50	Parents allowed to refuse on religious grounds only and must submit written refusal	Without written parental consent, samples cannot be used for anything but retesting, diagnosis, or quality assurance; Specific consent for storage not required	1 year
ILLINOIS 410 ILL. COMP. STAT. ANN. 240 (West 1983)	Full core, partial secondary	57	Parents allowed to refuse on religious grounds only and must submit written refusal	Not stated in state legislation or regulation	If sample tests positive, 5 years; otherwise, 2-4 months

Jurisdiction	Adopted ACMG Panel? ²⁴²	Number of Conditions Tested ²⁴²	Consent Procedures for Newborn Screening ²⁴³	Consent Procedures for Storage and Use of Residual	Bloodspot ^s ²⁴³ Samples Retention Time ²⁴⁴
INDIANA IND. CODE ANN. §§ 16-41-17-1 to 16-14-17-11 (West 2011)	Full core, partial secondary	53	Parents allowed to refuse on religious grounds only and must submit written refusal	Parents may ask the state's newborn screening program to not to use or share information collected from the sample, but the program may not be able to comply with the request; Specific consent for storage not required	23 years
IOWA IOWA CODE ANN. § 136A.5 (West 2004)	Full core, partial secondary	51	Parents may refuse screening	Samples may be used in research if the identifying information is removed or if written parental consent is obtained; Specific consent for storage not required	5 years
KANSAS KAN. STAT. ANN. §65-180 (West 2007)	Full core, partial secondary	30	Parents allowed to refuse on religious grounds only	Samples may be used in quality assurance tests or validation of new tests, and may be shared with other laboratories but only if de-identified; Specific consent for storage not required	1 month
KENTUCKY KY. REV. STAT. ANN. § 214.155 (West 2006)	Full core, partial secondary	49	Parents allowed to refuse on religious grounds only and must submit written refusal	Samples may be used for quality assurance and validation studies; Samples are not released for research purposes; Specific consent for storage not required	1 month
LOUISIANA LA. REV. STAT. ANN. § 1299:1 (2007)	Full core, partial secondary	31	Parents may refuse screening	Samples may be used by the state's public health laboratory to conduct experiments, projects, and develop tests; Samples may be exchanged between states (AL, GA, LA, FL, MS, NC, SC, TN); Specific consent for storage not required	1 month

Jurisdiction	Adopted ACMG Panel? ²⁴²	Number of Conditions Tested ²⁴²	Consent Procedures for Newborn Screening ²⁴³	Consent Procedures for Storage and Use of Residual	Bloodspot ²⁴³ Samples Retention Time ²⁴⁴
MAINE ME. REV. STAT. ANN. tit. 22, § 1533 (2009)	Full core, partial secondary	49	Parents allowed to refuse on religious grounds	Samples may be destroyed at the parents' request	Indefinitely
MARYLAND MD. CODE. ANN., HEALTH-GEN. §13-111 (West 2011)	Full core and secondary	55	Parents allowed to refuse for any reason if they submit written refusal	Samples may only be used for initial screening or supplemental testing while in storage; Samples cannot be used for research without approval of the Newborn Screening Program and an IRB; Specific consent for storage not required	25 years
MASSACHUSETTS MASS. GEN. LAWS ANN. ch. 111, §110A (West 1986)	Full core and secondary	58	Parents allowed to refuse on religious grounds only and must submit written refusal	Parents may refuse to allow their children's samples to be included in pilot studies for new screening tests; Specific consent for storage not required	21.5 to 22 years
MICHIGAN MICH. COMP. LAWS ANN. § 333.5431 (West 2003)	Full core, partial secondary	53	Parents may refuse screening	All samples stored as part of the Michigan BioTrust, which makes NBS samples available for research; However, parents may request that their children's samples be destroyed or that they not be used in research	Indefinitely
MINNESOTA MINN. STAT. ANN. § 144.125 (West 2012)	Full core and secondary	55	Parents allowed to refuse for any reason if they submit written refusal	During the standard retention period, samples may only be used for routine operations; If parents would like the sample to be held longer than the standard retention period, they must complete and submit a written form requesting a longer retention period	If sample yields an abnormal result, 24 months; otherwise, 71 days

NEWBORN SCREENING IN AMERICA: PROBLEMS AND POLICIES

Jurisdiction	Adopted ACMG Panel? ²⁴²	Number of Conditions Tested ²⁴²	Consent Procedures for Newborn Screening ²⁴³	Consent Procedures for Storage and Use of Residual	Bloodspot ^s Retention Time ²⁴⁴
MISSISSIPPI MISS. CODE ANN. § 41-21-201 (West 2002)	Full core and secondary	58	Parents allowed to refuse on religious grounds only Samples may not be used for research purposes;	Specific consent for storage not required	1 year
MISSOURI MO. ANN. STAT. § 191.331 (West 2007)	Full core, partial secondary	57	Parents allowed to refuse on religious grounds only and must submit written refusal	Samples may be used for research purposes if approved by the state's Department of Health and Senior services and if the sample is stripped of identifying information; Parents may request that samples be returned to them, destroyed, or stored but not used in research	5 years
MONTANA MONT. CODE ANN. § 50-19-203 (West 2007)	Full core, partial secondary	49	Parents allowed to refuse if they submit a written waiver form after hearing about the benefits of newborn screening and the risks associated with refusing	Samples may be stored and used for re-testing or validation and comparison studies for the development of new tests; Specific consent for storage not required	1 year
NEBRASKA NEB. REV. STAT. ANN. §§ 71-519 to 71-524 (West 2007)	Full core and secondary	57	Parents are not allowed to refuse screening for any reason	Samples stored for up to 90 days may only be used for quality assurance purposes and to ensure accuracy of the test result; After 90 days, samples may be used for research, but only with written consent from parents, regardless of whether the samples are anonymous or not; Specific consent for storage not required	90 – 120 days
NEVADA NEV. ADMIN. CODE § 442.020 to 442.090 (2012)	Full core, partial secondary	50	Parents allowed to refuse on religious grounds only and must submit written refusal	Not stated in state legislation or regulation	1 year

Jurisdiction	Adopted ACMG Panel? ²⁴²	Number of Conditions Tested ²⁴²	Consent Procedures for Newborn Screening ²⁴³	Consent Procedures for Storage and Use of Residual	Bloodspot ²⁴³ Samples Retention Time ²⁴⁴
NEW HAMPSHIRE N.H. REV STAT. ANN. § 132:10-a (2012)	Full core, partial secondary	47	Parents allowed to refuse if they submit a written waiver form after hearing about the benefits of newborn screening and the risks associated with refusing	Samples are not permitted to be used for any purpose besides screening without written parental consent; Specific consent for storage not required	6 months
NEW JERSEY N.J. STAT. ANN. § 26:2-110 (West 1988)	Full core and secondary	55	Parents allowed to refuse on religious grounds only and must submit written refusal	Samples are not permitted to be used for any purpose besides screening without written parental consent or a court order; Specific consent for storage not required	23 years
NEW MEXICO N.M. STAT. ANN. § 24-1-6 (West 2010)	Full core, partial secondary	51	Parents allowed to refuse if they submit a written waiver form after hearing about the benefits of newborn screening and the risks associated with refusing	Not stated in state legislation or regulation	1 year
NEW YORK N.Y. PUB. HEALTH LAW § 2500-a (McKinney 1986)	Full core, partial secondary	54	Parents allowed to refuse on religious grounds only and must submit a written waiver form after hearing about the benefits of newborn screening and the risks associated with refusing	Parents may request samples be destroyed or not be used in research	27 years
NORTH CAROLINA N.C. GEN. STAT. ANN. § 130A-125 (West 2008)	Full core, partial secondary	44	Parents allowed to refuse for any reason if they submit written refusal	Not stated in state legislation or regulation	5 years

NEWBORN SCREENING IN AMERICA: PROBLEMS AND POLICIES

Jurisdiction	Adopted ACMG Panel? ²⁴²	Number of Conditions Tested ²⁴²	Consent Procedures for Newborn Screening ²⁴³	Consent Procedures for Storage and Use of Residual	Bloodspot ^s Retention Time ²⁴⁴
NORTH DAKOTA N.D. CENT. CODE ANN. § 23-01-03.1 (West 2011)	Full core, partial secondary	53	Parents allowed to refuse if they submit written refusal	Samples may be used for medical, psychological, or sociological research provided that confidentiality is maintained and the project is sponsored by a college or university, government entity, nonprofit medical association, or pharmaceutical company; The state may charge for access to specimens; Specific consent for storage not required	Indefinitely
OHIO OHIO REV. CODE ANN. § 3701.501 (West 2003)	Full core, partial secondary	44	Parents allowed to refuse on religious grounds only and must submit written refusal	Not stated in state legislation or regulation	2 years
OKLAHOMA OKLA. STAT. ANN. tit. 63, § 1-533 (West 2005)	Full core, partial secondary	50	Parents allowed to refuse on religious grounds only and must submit written refusal	Samples may only be stored and used for research or other purposes if the state obtains written parental consent first	42 days
OREGON OR. REV. STAT. ANN. § 433.285 (West 2009)	Full core, partial secondary	51	Parents allowed to refuse on religious grounds only and must submit written refusal	Parents may request in writing that a sample be destroyed or returned to them	1 year
PENNSYLVANIA tit. 35 PA. CONS. STAT. ANN. §§ 621-625 (West 1992)	Full core, partial secondary	58	Parents allowed to refuse on religious grounds only and must submit written refusal	Samples may not be used for research; Specific consent for storage not required	8 months
RHODE ISLAND R.I. GEN. LAWS ANN. § 23-13-14 (West 2011)	Full core, partial secondary	35	Parents allowed to refuse on religious grounds only	Not stated in state legislation or regulation	23 years

Jurisdiction	Adopted ACMG Panel? ²⁴²	Number of Conditions Tested ²⁴²	Consent Procedures for Newborn Screening ²⁴³	Consent Procedures for Storage and Use of Residual	Bloodspot ²⁴³ Samples Retention Time ²⁴⁴
SOUTH CAROLINA S.C. CODE ANN. § 44-37-30 (2002)	Full core, partial secondary	53	Parents allowed to refuse on religious grounds only and must submit written refusal	After sample testing is complete, the specimen is destroyed; samples may not be used for research or purposes other than screening; Parents may request that samples be returned to them or destroyed after the retention period is over; Samples may be exchanged between states (AL, GA, LA, FL, MS, NC, SC, TN)	2 years
SOUTH DAKOTA S.D. CODIFIED LAWS §§ 34-24-17 to 34-24-25 (1990)	Full core, partial secondary	51	Parents are not allowed to refuse screening for any reason	Not stated in state legislation or regulation	1 month
TENNESSEE TENN. CODE ANN. §§ 68-5-401 to 68-5-507 (West 2011)	Full core, partial secondary	56	Parents allowed to refuse on religious grounds only and must submit written refusal	Not stated in state legislation or regulation	Confirmed tests are held indefinitely; negative tests are held for 12 months
TEXAS TEX. HEALTH & SAFETY CODE ANN. § 33 (West 2011)	Full core, partial secondary	53	Parents allowed to refuse on religious grounds only and must submit written refusal	Samples are destroyed after the retention period ends, unless parents submit a written request to retain the samples longer; Parents may request that the sample be destroyed before the retention period is over	2 years
UTAH UTAH CODE ANN. § 26-10-6 (West 2011)	Full core, partial secondary	50	Parents allowed to refuse on religious grounds only and must submit written refusal	Parents may request in writing that a sample be destroyed; Samples may be used for quality assurance or research purposes	At least 90 days

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Jurisdiction	Adopted ACMG Panel? ²⁴²	Number of Conditions Tested ²⁴²	Consent Procedures for Newborn Screening ²⁴³	Consent Procedures for Storage and Use of Residual	Bloodspot ²⁴³ Samples Retention Time ²⁴⁴
VERMONT tit. 12 ch. 5 VT. CODE R. § 1:2 (2012)	Full core, partial secondary	45	Parents allowed to refuse after hearing about the benefits of newborn screening and the risks associated with refusing	Samples may not be used for purposes related to the state's DNA database; Specific consent for storage not required	Indefinitely
VIRGINIA VA. CODE ANN. § 32.1-65 (West 2012)	Full core, partial secondary	48	Parents allowed to refuse on religious grounds only and must submit written refusal	Samples may not be used for purposes other than newborn screening and are never released without written and notarized parental consent; Specific consent for storage not required	If sample yields an abnormal result, 10 years; otherwise, 6 months
WASHINGTON WASH. REV. CODE ANN. § 70.83.020 (West 2010)	Full core, partial secondary	44	Parents allowed to refuse on religious grounds only and must sign a waiver	Parents may request in writing that a sample be destroyed after screening has been completed	21 years
WEST VIRGINIA W. VA. CODE ANN. § 16-23-3 (West 2008)	Full core and secondary	56	Parents are not allowed to refuse screening for any reason	Information about samples may not be disclosed, with the exception of anonymous statistical research; Specific consent for storage not required	3 months
WISCONSIN WIS. STAT. ANN. § 253.13 (West 2012)	Full core, partial secondary	50	Parents allowed to refuse on religious grounds only and must be informed about the benefits of newborn screening and the risks associated with refusing	Information about samples may not be disclosed, with the exception of anonymous statistical research or as permitted under the state's public health records laws; Specific consent for storage not required	1 year
WYOMING WYO. STAT. ANN. § 35-4-801 (West 2009)	Full core, partial secondary	45	Parents allowed to refuse if they submit a waiver form	Samples are stored by the Oregon State Public Health Laboratory (OSPHL); Samples may not be used for research or made available to anyone outside OSPHL without written parental consent; Specific consent for storage not required	1 year

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