

# The Untold PKU Testing Story...and Why it Challenges Government-Mandated Newborn (Genetic) Screening

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Newborn screening advocates often refer to the newborn PKU (phenylketonuria) test as evidence of the benefit of screening—and as a rationale for compulsory testing of newborns nationwide.

However, a brief look into the history of PKU testing challenges these assertions. Inaccurate test results, harmed children, untested treatments, and an *increase* in mental retardation mark the untold PKU story.

Now, in the 21<sup>st</sup> century, an attempt to test all newborn babies for a broad range of genetic conditions is emerging—again without scientific evidence of benefit or proper assessment of risk.

Only two states require parent consent.

With children at risk for discrimination and concerns about eugenics arising—and because Congress enacted a 2008 law to nationalize screening—initiatives to protect children, including informed written consent as recommended by the Institute of Medicine should be required for newborn (genetic) screening.

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## Overview

The nearly 50-year old PKU test, performed by taking blood from the baby's heel at birth, is often used as rational to push for compulsory genetic testing of newborn babies today. The test is hailed as having saved countless children from mental retardation.

While the test has been beneficial to many babies, it has also caused devastating

harm to other children, including nutritional deficiencies, death, and an *increase* in the number of children with mental retardation.

History often repeats itself. The failure to properly evaluate the PKU story has led to today's untested expansion of compulsory genetic testing programs for newborns, say experts in research and ethics.

PKU is a rare condition. Approximately, one child out of every 15,000 infants born in the United States is diagnosed with

phenylketonuria (PKU),<sup>1</sup> an enzyme deficiency causing high phenylalanine blood levels that can lead to mental retardation.<sup>2</sup>

Despite protests from physicians and concerned researchers, the PKU test was mandated nationwide in the mid-1960s. After few infants were discovered to have PKU, some state legislators threatened to discontinue the testing program.

In response, advocates of screening children at birth fought to expand the testing program beyond PKU—without proper study of the benefits or risks. In recent years, the testing program for a broader list of genetic conditions became known as “newborn screening.”<sup>3</sup>

Attempts to expand the number of conditions for which all infants are tested continue today with little scientific evidence, or legislative oversight. Like the PKU story, the benefits of genetic testing may be exaggerated and the pitfalls minimized.

Experts in the fields of genetics and bioethics have already expressed concerns about the impact of emerging DNA chip-enhanced testing of infants, including violation of the child’s right “not to know,” potential for future discrimination, use of newborn screening for research purposes, and the possibility of eugenics.

It is time for informed parent consent to be required for all newborn genetic testing. As Dr. Diane Paul, author of “The History of Newborn Phenylketonuria Screening in the U.S.,” a U.S Task Force on Genetic Testing report, says,

*[A] ‘technological imperative’ has combined with unrealistic assumptions about benefits [of screening], and that drives the expansion of screening programs. The lesson that such wholesale expansion is unwarranted has been repeatedly drawn since the early 1960s. Surely it is time to heed it.*<sup>4</sup>

## Exaggerated Claims

In 1960, Dr. Robert Guthrie, who had a mentally retarded son and niece, introduced a blood test for PKU (phenylketonuria, a deficiency in a liver enzyme causing high phenylalanine blood levels that can lead to mental retardation).

Proponents claimed the test would significantly reduce mental retardation by early identification and implementation of a specialized, albeit unpalatable, PKU diet. However, it had long been known that PKU was “the cause of retardation in less than one percent of [the then 5.5 million] institutionalized patients.”<sup>5</sup>

In fact, only 399 children with PKU had been admitted to programs for the mentally retarded over the preceding five years, according to the 1962 Children’s Bureau Census.<sup>6</sup>

Nevertheless, the Bureau adopted a new slogan, “Test Every Newborn For PKU” and President Kennedy, along with the National Association for Retarded Children and the March of Dimes<sup>7</sup>, led the 1961 charge for compulsory screening.<sup>8</sup>

As Dr. Norman Fost, M.D., MPH, testified before The President’s Council on Bioethics in 2002:

*President Kennedy, because of his profound interest in mental retardation, his family’s interest, with Dr. Guthrie formed a so-called PKU lobby and arranged for laws to be passed in all states requiring PKU testing, realizing correctly that doctors in offices would be unlikely to adopt a test for a disease that affected 1 in 10,000 children – something that a pediatrician might never see in his or her entire career. So mandatory newborn screening for PKU became the national policy.*<sup>9</sup>

Scientists were opposed to testing every newborn child. Biochemist Samuel Bessman

argued that many individuals with PKU would be normal without any treatment, and Howard University political scientist Joseph Cooper said the majority of mentally retarded individuals did not suffer from PKU or any genetic defects, and were most in need of social support, not science.<sup>10</sup>

The American Medical Association, the American Academy of Pediatrics and state medical societies also opposed mandatory PKU screening. Articles warning of the danger of “maternal PKU” (see below) were published in the *Journal of Pediatrics* and the *New England Journal of Medicine*, but state legislatures were apparently unaware of these issues.

They began to mandate that all children be tested at birth for PKU. In 1963, Massachusetts became the first state to mandate screening. Today, all 50 states require testing. Only Maryland and Wyoming require the consent of parents.

The American public was unaware of these concerns, and remains so today. People have been led to believe that PKU treatment is as simple as a test and a diet, when the reality is much different.

For example, the child with PKU who has been rescued from mental retardation must eat an expensive, unpalatable diet to maintain his or her IQ—the National Institutes of Health recommends the diet for life<sup>11</sup>—and often has a lifelong struggle with “a host of other cognitive and emotional problems.”<sup>12</sup>

These problems, increasingly visible to professionals today, are mostly invisible to the public.<sup>13</sup>

### **The Trouble with PKU Testing**

Several contemplated dangers of PKU testing did not receive enough public and legislative attention prior to the enactment and implementation of screening mandates. As described below, at least two dangers are now part of the untold PKU story:

- The PKU test was quite inaccurate, causing injury and death in normal children.
- “Maternal PKU” has led to the birth of more mentally retarded children.

#### “Worst Test”

In the early years, the PKU test was extremely inaccurate, and children with and without the disease were injured. The first systematic effort to assess the accuracy of the test did not appear until 1974—*eleven years* after the first state PKU testing mandate.<sup>14</sup>

English biochemist Louis Wolf believed that twice as many patients were being treated for PKU as might be necessary. Yet, in a stunning display of disregard for the children and families who suffered, he considered the financial cost, the unpalatable diet, and dietary deficiencies

*“a small price to pay for preventing the mental deterioration otherwise inevitable in at least half of them.”<sup>15</sup>*

Dr. Diane Paul writes,

*Others thought that unnecessary treatment could itself produce mental retardation. Several reports of deaths and diet-deficiency syndromes suffered by infants on PKU diets led researchers also to fear that some infants with the disease were being harmed by too-drastic treatment or suffering severe malnutrition as the result of diet refusal.<sup>16</sup>*

Dr. Fost echoes Dr. Paul’s statement:

*[T]he PKU test was the worst test in the history of the world...[T]he test had a five percent true positive rate. It had a 95 percent false positive rate. That is, a child with a positive test...had a 20 to 1 chance of being*

*normal. This was not appreciated for many years. So many normal children, we now know, were started on a restricted diet.*

*So many children—we don't know how many—were made retarded by this program. Some were killed. In fact, kwashiorkor [malnutrition found typically in third world countries] developed in America in the PKU program in children who had profound protein malnutrition because of the restricted diet.<sup>17</sup>*

“Major Problem”

The PKU testing program has also led to “maternal PKU” syndrome—mothers diagnosed with PKU as infants growing up and birthing mentally retarded children. Essentially, treated children with PKU become adult females, fail to stay on the PKU diet, develop elevated phenylalanine levels in their blood, and then give birth to mentally retarded infants who do not have PKU:

*[T]he offspring of women with classical PKU who do not maintain good dietary control are at great risk of mental retardation and microencephaly (over 90 percent) and lower risk (12-15 percent) for congenital birth defects and other anomalies.<sup>18</sup>*

While not everyone agrees on the diet required to protect the PKU mother's baby from mental retardation,<sup>19</sup> the policy decision to identify and treat one medical condition—the occurrence of PKU in a small number of infants—led unexpectedly to the development of non-PKU mental retardation and disability in a greater number of infants. According to Diane Paul:

*Before the advent of newborn screening, women with PKU were severely retarded and often*

*institutionalized so that they bore very few children.*

*Most young women today discontinued the diet during childhood and have not been followed for many years. Since their fertility is now nearly normal, screening has had the paradoxical effect of converting a rare occurrence into a major problem.*

*Indeed, all the social benefits of screening may be neutralized by the birth of retarded children to women who have ended the [PKU] diet.<sup>20</sup>*

More than 3,000 women of childbearing age in the United States have been diagnosed with PKU.<sup>21</sup> In addition, women born prior to implementation of the PKU test—New Jersey did not screen for PKU until 1992—and other women with variants of PKU are at risk of delivering a child impacted by the maternal PKU syndrome.<sup>22</sup>

Altogether, there are approximately 6,000 women who could bear one or more children affected by their mother's high blood phenylalanine levels, according to the Mountain States Regional Genetic Services Network.

The following table shows the number of confirmed PKU cases in each State in 2006 and 2007 along with the national birth rate.

**Table 1. PKU Prevalence**

State	Total 2006 confirmed PKU cases <sup>1</sup>	Total 2007 confirmed PKU cases <sup>2</sup>	Approx. Annual # of Births <sup>3</sup>
Alabama	4	6	58,900
Alaska	0	2	9,800
Arizona	4	3	87,400
Arkansas	3	1	36,800

<sup>1</sup> Cases of Classical PKU, National Newborn Screening and Genetics Resource Center. Accessed February 21, 2008.

<sup>2</sup> Cases of Classical PKU, National Newborn Screening and Genetics Resource Center. Accessed February 21, 2008.

<sup>3</sup> “State Map Page,” National Newborn Screening & Genetics Resource Center, as updated August 2007.

State	Total 2006 confirmed PKU cases <sup>4</sup>	Total 2007 confirmed PKU cases <sup>5</sup>	Approx. Annual # of Births <sup>6</sup>
California	18	12	529,500
Colorado	0		68,500
Connecticut	1	0	42,600
Delaware	0	1	11,300
District of Columbia	0		15,000
Florida	12	5	205,500
Georgia	1		134,600
Hawaii		0	17,500
Idaho	6	2	20,400
Illinois	7	8	177,600
Indiana	11	8	85,500
Iowa	2	2	37,800
Kansas	2	1	39,700
Kentucky	1		52,700
Louisiana	1	4	65,100
Maine	0	0	13,400
Maryland	0	5	68,800
Massachusetts	8	2	81,700
Michigan	3	2	126,000
Minnesota	7	7	73,000
Mississippi	1	2	40,500
Missouri	5	5	76,400
Montana	0		11,000
Nebraska	0		27,000+
Nevada	2	1	32,200
New Hampshire	2		13,900
New Jersey	6	2	111,800
New Mexico	0	1	27,300
New York	3		252,300
North Carolina	5	3	118,200
North Dakota	0	2	8,900
Ohio	10		149,000
Oklahoma	2	2	51,000
Oregon	2	4	46,100
Pennsylvania	8	13	142,950
Rhode Island			13,550
South Carolina	1	2	52,200
South Dakota	1	2	11,000
Tennessee	0	0	82,600
Texas	10	13	374,100
Utah	8	4	50,300
Vermont	0	0	6,100
Virginia	7	2	97,400
Washington	3	5	78,600
West Virginia	0	1	21,100
Wisconsin	4	5	67,400
Wyoming	1	0	5,800
<b>TOTAL CASES</b>	<b>172</b>	<b>141</b>	
<b>2006 Birth Rate</b>	4,224,267		
<b>2007 Birth Rate</b>		4,253,538	

## Newborn Testing Expands Rapidly

Because PKU is such a rare genetic disease, striking only one in every 15,000 children born,<sup>23</sup> some state programs have identified few children with the condition.

In the first three years of screening, Washington, D.C. failed to find even one child with PKU. Policymakers considered diverting the program funding to other priorities.<sup>24</sup> Some states, citing the problems that had emerged with the screening program, and a similar paucity of cases, were also ready to pull the plug on newborn screening.

Newborn screening advocates fought back by pushing to expand testing. Their logic went as follows:

*“[O]nce you’ve pricked the heel and have the blood spot, you can test for other metabolic disorders and get more bang for the buck.”<sup>25</sup>*

That said, most of the other disorders did not have treatment available and “some were not disorders at all, but normal biochemical variants”<sup>26</sup>

These additional tests, many of which have “uncertain” magnitude of benefit<sup>27</sup> were “added casually, with little systematic assessment of their value and risks, and also with little concern for obtaining informed consent.”<sup>28</sup>

## Serious Harm Predicted

Early advocates of newborn screening had plans to take screening well beyond PKU—to delve deep into the DNA of every newborn baby. The inventor of the PKU test, Dr. Robert Guthrie, argued that:

*[T]he conquest of PKU is important not only for itself, but because it serves as an open door to a whole new era of preventive medicine*

<sup>4</sup> Cases of Classical PKU, National Newborn Screening and Genetics Resource Center. Accessed February 21, 2008.

<sup>5</sup> Cases of Classical PKU, National Newborn Screening and Genetics Resource Center. Accessed February 21, 2008.

<sup>6</sup> “State Map Page,” National Newborn Screening & Genetics Resource Center, as updated August 2007.

*based upon new understanding of medical genetics.*<sup>29</sup>

Proponents of newborn screening said the program was “bound to progress toward control of the other inborn errors of metabolism associated with mental retardation.”<sup>30</sup> The predicted expansion of newborn screening began slowly, but has recently exploded around the country.

“Without careful assessment of the benefits and risks, often without the review of institutional review boards, and generally without concern for obtaining informed consent or even the opportunity for informed refusal,”<sup>31</sup> state health officials regularly add to the list of conditions for which children are screened. According to Dr. Norman Fost:

*So we now already have many states including Wisconsin, that does routine testing without consent, without prior research, for dozens of conditions using tandem mass spectrometry.*

*And I predict, unless there is some dramatic change in the way we think about these things, the way we do these things, that multi-array DNA testing will occur within the next few years, as soon as the cost comes down to make it efficient to do it.*

*This, to me, is a calamity involving every child in America. The amount of mischief. The amount of harm, psychosocial harm that will occur to families and children, not to mention medical harm, is, in my view, going to be quite extensive.*<sup>32</sup>

Around the United States, infants are already tested for 16 - 53 conditions (*see table on next page*). Most include the controversial test for cystic fibrosis, which is incurable—and most do not require parent consent.

## Next: DNA Chip Testing

Newborn screening “represents the largest single application of genetic testing in medicine.”<sup>33</sup> It is also considered the first population-wide genetic testing program.<sup>34</sup>

The 1997 Task Force on Genetic Testing defines “genetic test” as including “[p]renatal, **newborn** and carrier screening, as well as testing in high risk families.”<sup>35</sup> [*my emphasis*] Such screening is actually genetic testing:

*The development of genetic-based technologies promises to make screening...a simple establishing of the fact of a genetic predisposition to disease or genetic abnormality.*<sup>36</sup>

Genetic screening with a DNA chip is right around the corner.

A silicon DNA chip is a “thumbnail-sized invention” which is photochemically covered with “thousands of nucleotide sequences attached to the chip in a grid pattern.” (*online animation*)<sup>37</sup>

Strands of an individual’s DNA are washed across the tiny chip and a computerized laser scans the chip. Where the individual’s DNA strands “stick” to the chip tells a technician what genes are in the individual’s DNA sample.<sup>38</sup>

Some screening proponents envision a day when every infant’s entire genome is essentially unwrapped and registered at birth.<sup>39</sup>

The DNA chip can accomplish that goal. As written in the Journal of Medical Ethics by Wolfram Henn, MD, Consultant Clinical Geneticist, at the Germany-based Institute of Human Genetics,

*Earlier than expected even by most experts, the ‘DNA chip’ appears to overcome the technical limitations of genetic mass screening through the synthesis of computer and DNA technologies...The DNA chip allows the testing of many more genetic*

*parameters in a much shorter time and at much lower prices than conventional gene analysis...*

*The whole procedure only takes a few hours. This “massively parallel” approach to genome analysis addresses a huge amount of genetic parameters from one blood or tissue sample in a single step. Any human tissue is suitable as the DNA source, including chorionic villi for prenatal testing.*

*The developers are optimistic that within a few years they will be able to offer the automatic analysis of any given individual’s complete genetic complement by a set of DNA chips.<sup>40</sup>*

### No Consent Required

Such testing disregards the future choices of the child, essentially violating his or her right “not to know.”<sup>41</sup>

Once reaching adulthood, will children be pleased to discover that their DNA—their private genetic code—has been dissected, disclosed, and registered with state government?

Standard medical practice requires informed consent for medical tests. The Institute of Medicine (IOM) has recommended explicit consent for genetic testing, including PKU and all other newborn screening tests.<sup>42</sup> Yet, informed parent consent is only required in Maryland and Wyoming.<sup>43</sup>

While some, but not all, states give parents the right to refuse testing, most parents are not told and do not know they have that right.<sup>44</sup>

Moreover, few states require that parents be informed that newborn screening is genetic testing, or that the testing is conducted by the government.

Genetic test results, and increasingly the newborn’s DNA-filled dried blood spots, which are used to conduct the testing, are cataloged and retained by state governments without parent knowledge or consent.

Ownership is an issue.<sup>45</sup> States may consider the blood spots to be state property, available for genetic research and other purposes—without consent.

**Table 2. No Consent<sup>7</sup>**

State	Consent for Newborn Testing Required <sup>8,9</sup>	Number of Mandated Conditions for Testing <sup>10</sup>	Newborn Testing for Cystic Fibrosis <sup>11</sup>
Alabama	N	39	Y
Alaska	N	45	Y
Arizona	N	28	Y
Arkansas	N	30	Y
California	N	50	Y
Colorado	N	49	Y
Connecticut	N	46	Offered/By Request
Delaware	N	44	Y
District of Columbia	N	52	Y
Florida	N	35	Y
Georgia	N	44	Y
Hawaii	N	45	Y
Idaho	N	45	Y
Illinois	N	48	Y
Indiana	N	50	Y
Iowa	N	50	Y
Kansas	N	30	Y
Kentucky	N	31	Y
Louisiana	N	30	Y
Maine	N	40	Y
Maryland	Y	50	Y
Massachusetts	N	37	Y
Michigan	N	49	Y
Minnesota	N	53	Y
Mississippi	N	50	Y
Missouri	N	36	Y
Montana	N	43	Y
Nebraska	N	34	Y
Nevada	N	44	Y
New Hampshire	N	35	Y
New Jersey	N	24	Y
New Mexico	N	29	Y
New York	N	51	Y
North Carolina	N	40	N

<sup>7</sup> This table reflects all conditions mandated by law or rule, not: 1) testing states may offer for conditions not mandated, 2) other conditions revealed as byproducts of testing, or 3) required HIV testing (CT, IL, NY).

<sup>8</sup> According to the March 2003 GAO report, “Newborn Screening,” 33 states allow religious objection; 13 states allow objection for any reason; 5 states allow no exemptions. Allowing for objections does not require parents to be informed of the right to object. Only 11 states require parents be informed of the program at the time of screening.

<sup>9</sup> “Newborn Screening.” Government Accountability Office, 3/2003.

<sup>10</sup> “National Newborn Screening Status Report [Updated 09/16/08]” National Newborn Screening and Genetics Resource Center.

<sup>11</sup> “National Newborn Screening Status Report [Updated 09/16/08]” National Newborn Screening and Genetics Resource Center

State	Consent for Newborn Testing Required	Number of Mandated Conditions for Testing	Newborn Testing for Cystic Fibrosis
North Dakota	N	51	Y
Ohio	N	40	Y
Oklahoma	N	53	Y
Oregon	N	34	Y
Pennsylvania	N	16	Offered/By Request
Rhode Island	N	32	Y
South Carolina	N	52	Y
South Dakota	N	49	Y
Tennessee	N	52	Y
Texas	N	30	Not yet implemented
Utah	N	45	N
Vermont	N	34	Y
Virginia	N	28	Y
Washington	N	28	Y
West Virginia	N	33	Y
Wisconsin	N	49	Y
Wyoming	Y	30	Y

*newborn screening with genomic medicine.*<sup>47</sup>

Dr. Henn writes that there exists a “broad international consensus on the importance of voluntariness and medical secrecy as well as the rejection of any kind of discrimination resulting from unfavourable [genetic] test results.” However, he too warns,

*After cost-effectiveness analyses have proven that genetic screening can produce considerable savings even for rather rare diseases which require expensive therapies for affected patients, there is little doubt that health insurers will support extensive screening programmes. The widening of the diagnostic spectrum may also reinforce the already widespread public opinion that the birth of handicapped children should be prevented.*

*Ultimately, the exclusion of prenatally testable conditions from health insurance cover[age] might serve as a sanction instrument for a new kind of economically motivated **negative eugenics** that may well become popular in an era of declining prosperity.*<sup>48</sup> [my emphasis]

To the point, Schulman bluntly asks a rather disturbing question in his paper:

*Why prevent the disease when it would be simpler to prevent the patient?*<sup>49</sup>

### Suppression of Facts & Dissent

As is too often the case, scientific facts and dissenters of compulsory newborn screening are unwelcome.

In the case of the 1960s PKU test, several key facts about PKU were ignored,

### Future Eugenics?

Experts in the field of genetics have become increasingly concerned about the possibility of the newborn screening program leading to eugenics, including attempts to create a “perfectly designed” baby.<sup>46</sup>

Adam Schulman, Ph.D., in a paper written for discussion by The President’s Council on Bioethics, contemplates a worrisome connection between newborn screening and *prenatal* screening. To clarify his concern, he pointedly asks,

*If we test an infant, not in the hope of providing treatment for his condition but with a view to making sure that no further children come in to the family with the same defects, aren’t we in effect telling the child that he was in some ways a regrettable mistake—that, had we known his genetic makeup in advance, we would have tried to prevent his birth?...The blameless intention to diagnose and treat our children’s illnesses will have drifted into the rather more sinister project of purifying future generations of their undesirable members. The specter of “eugenicide” hovers over the eagerly anticipated marriage of*

and concerns by expressed by experts in the fields of genetics and ethics were suppressed.

First, children with elevated phenylalanine levels did not necessarily become mentally retarded. Second, no one knew at what level mental retardation began. Third, older siblings of newborns with elevated levels also had higher levels, but were not retarded.<sup>50</sup>

Moreover, as noted earlier, there was disagreement on the treatment of PKU.

In response to these concerns, the American Academy of Pediatrics wanted to end screening. The group sent a letter to the Secretary of the U.S. Department of Health and Human Services in 1965 asking that the PKU screening mandate be stopped, “because we didn’t understand the significance of the test, and we didn’t know how to regulate the diet,” says Dr. Fost.

He added,

*This letter was suppressed. People were called Luddites who were against newborn screening. The PKU lobbying was very powerful, and testing went on until 1971 when a political scientist named Joseph Cooper uncovered this story through the Freedom of Information Act and led to the appointment of the IOM [Institute of Medicine] Committee whose report was published in 1975 articulating principles for ethically responsible newborn screening, particularly genetic screening or screening for genetic disorders...*

*The only problem is that the guidelines are systematically ignored. That is, newborn screening has expanded like topsy, with the same mistakes that beleaguered the PKU program happening over and over again. That is, numerous screening and treatment programs have been implemented without*

*testing, evaluation of the tests, without any systematic study of the sensitivity, specificity, or predictive value of the test, or of the interventions....<sup>51</sup>*

## **What Evidence?**

Failure to evaluate tests and search for evidence of effectiveness continues today. As states expand screening programs, the efficacy and value of the various screening tests remains unclear.

For instance, there is little evidence that testing and early intervention in children with sickle cell disease is more beneficial than waiting to start treatment when symptoms actually present.<sup>52</sup>

The only randomized clinical trial for newborn screening in the United States, the Wisconsin Cystic Fibrosis project, which studied 600,000 infants<sup>53</sup> from 1985 – 1994, is less than conclusive.<sup>54</sup>

Dr. Savio Woo, in a comment made at the national meeting convened in 2000 to write a consensus statement on newborn screening, appears to underscore the lack of knowledge surrounding the entire newborn screening enterprise:

*As imperfect as science is in telling us exactly when to treat PKU/hyperphenylalaninemia and how long to continue, it is crucial to adopt standards. While those standards may be as imperfect as the science, we can always adjust them based on our experience.<sup>55</sup>*

Diane Paul, writing for the Task Force on Genetic Testing, says screening programs are being “routinized prematurely”<sup>56</sup> before the evidence of effectiveness is in.

The federal Children’s Bureau recognized this concern shortly after PKU screening was mandated when “medico-legal problems” that arose in PKU prevented

“an objective and scientific evaluation” of its treatment.<sup>57</sup>

Paul forthrightly asserts that some of the newborn screening tests “were in effect *research programs* which did not allow for consent on the part of the subjects’ guardians.”<sup>58</sup> [*my emphasis*]

## **Involuntary Research Subjects**

The experimental nature of the newborn genetic screening program is problematic to many experts in the field.

Dr. Fost believes that “screening asymptomatic individuals for genetic abnormalities is not a neutral gathering of information with no effect on the lives of those screened; instead, every screening program must be considered an experiment until benefits and risks have been clarified by well-designed empirical studies.”<sup>59</sup>

While some believe newborn screening provides societal benefit by identifying infants with rare conditions and facilitating research, a group of individuals on behalf of the U.S. Preventive Services Task Force counter that assertion,

*“Mandating screening in order to recruit human research subjects does not conform to standard ethical or privacy requirements... We think that, at the very least, informed decision-making by the parents should be required prior to screening if the primary goal is to identify potential subjects for research.”*<sup>60</sup>

Concerned that “this enormous public health effort” [newborn screening] is based on “limited knowledge,” Dr. Jeffrey R. Botkin suggests blood samples and DNA of newborns collected and retained by state government newborn screening programs—*without parent consent*—could be used by government and other researchers to conduct

research on children years after the blood specimens were collected and stored:

*Children identified as affected through retrospective screening of residual [blood] samples could be traced and their health status measured and compared with that of children identified prospectively through screening...Furthermore, children who were mildly affected and never came to clinical recognition would be identified.”*<sup>61</sup>

While Botkin does not call for consent requirements for this research, he says, “A discussion of the extent and content of parental information or permission for this kind of research would be important.”

## **Who’s Pushing Genetic Testing?**

In testimony before The President’s Council on Bioethics, Dr. Nathan Fost said one-half of the 50 conditions for which the American College of Medical Genetics has recommended testing “have no known association with human disease,”<sup>62</sup> adding that the “UK equivalent of the FDA has recommended implementation of only one of these 50 conditions.”

In fact, the ACMG process was “a flawed process,” according to the May/June 2008 Hastings Report. Problems included a less than transparent process, lack of robust epidemiological data, and failure to fully consider the costs of expansion and potential harm to families, to name a few.<sup>63</sup>

Nevertheless, state government officials and advocacy groups continue the push toward more comprehensive genetic testing of children. They are successful, according to Dr. Fost, because:

*There is no toll gate through which an investigator or an innovator has to go to get these kinds of programs approved. He or she only needs to*

*persuade existing committees and state health departments to simply add another test onto the drop of blood or the drops of blood that now exist for virtually every newborn in America.*<sup>64</sup>

For example, in 2003, the Minnesota Commissioner of Health successfully convinced the state legislature to provide the Minnesota Department of Health with ongoing authority to expand at will the list of genetic conditions for which children are tested.<sup>65</sup>

*“What drives this mania for testing?”* Dr. Fost rhetorically asked The President’s Council on Bioethics.

Answering his own question, he noted pressure from parents of children with rare disorders, commercial interests, and the building of powerful and influential empires in state agencies.

To illustrate, he shared a story. Fost had attended an international newborn screening conference 20 years ago. The World Health Organization was planning to advance newborn screening for cystic fibrosis when there was, as Fost said, no evidence of benefit:

*“My sense of what was going on is that...[for state lab directors] it was another machine. It was another couple of people on their staff whose expanded budget—it was getting more information, possibly some research interest. I don’t think they were getting rich off of it, but they—technicians like to do things. Doctors like to do things. Testers like to test.”*<sup>66</sup>

### **Congress Nationalizes Screening**

Despite concerns long expressed by experts in the genetic and medical and bioethics community, Congress has rapidly

advanced newborn screening and genetic research nationwide. As part of the Children’s Health Act of 2000, the U.S. Congress passed Title XXVI, “Screening for Heritable Disorders.”

More recently, on December 13, 2007, the U.S. Senate passed S. 1858—the “Newborn Screening Saves Lives Act of 2007.” The bill essentially nationalizes the newborn genetic testing program, and provides millions of dollars in taxpayer funding for regional newborn screening research centers.<sup>67</sup>

The U.S. House of Representatives has considered passage of its own version of the bill, H.R. 3825, but instead passed S. 1858 on April 8, 2008.

Two weeks later—just five months ago, on April 24, 2008—President George W. Bush signed the national newborn screening bill into law.

The law makes millions of dollars available to state agencies that comply with genetic testing and other recommendations issued by the federal Advisory Committee on Heritable Disorders in Newborns and Children. The law also makes millions of dollars available for genetic research. The law does not require parent consent.

### **It’s Time to Act**

Medical practice standards have long upheld informed consent, and nearly 15 years ago, the Institute of Medicine recommended explicit informed parent consent for newborn genetic testing, including the controversial PKU test.

For the protection of all children and families, it is time to:

- Require explicit informed written parent consent for newborn genetic testing
- Require that parents be fully informed of the many potential risks associated with genetic testing of children.

- Allow parents to choose and limit what conditions their child is tested for at birth.
- Limit testing to newborn conditions, not adult-onset diseases.
- Require informed written parent consent for government storage, use, and dissemination of newborn blood and DNA.
- Provide individual property rights to the newborn blood and DNA stored in state health departments across the United States.
- Consider making newborn genetic testing a function of the private sector again, rather than a function of government.

## Summary

In an attempt to reduce mental retardation in children, Dr. Robert Guthrie invented a blood test for a rare disease called phenylketonuria (PKU).

The PKU test was an imprecise test, leading to the rescue of some children from mental retardation, but also leading to a multitude of unintended and harmful consequences for other children and their families.

The PKU test has now transitioned into a national newborn genetic testing program for a large and growing number of genetic conditions with little scientific evidence of value.

With the emergence of the DNA chip and online interoperable medical records accessible by government and private industry, sweeping genetic exploration of the DNA and genetic propensities of the more than 4,200,000 children born each year in the United States is possible.

Although most parents remain unaware of the dangers, the threat of genetic discrimination, eugenics, and involuntary participation in genetic research is real.

It is time to provide all children, parents and families with informed written consent

rights, genetic privacy rights, and DNA property rights.

## ENDNOTES

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