PROPOSAL
FOR
EXPANDED NEWBORN SCREENING
IN
ARKANSAS

October 2006

DIVISION OF HEALTH
ARKANSAS DEPARTMENT OF HEALTH AND HUMAN SERVICES

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EXECUTIVE SUMMARY

A. Introduction

Since the late 1960's, Arkansas, by joining other States with legislation, has recognized the value of a newborn screening program to prevent or reduce risks of mental retardation, other permanent disabilities and early death. Since the 1990's the State has required[1] that all its newborn infants be screened for eight[2] conditions (See Table 1):

- hearing loss,
- galactosemia (an abnormal concentration of sugar in the blood),
- hypothyroidism (a thyroid hormone deficiency),
- phenylketonuria (a chemical disorder), and
- sickle cell disease and three other related abnormalities of red blood cells.

Except for hearing loss, these disorders are the focus of the State's "metabolic screening program."

In 2003 and 2005 Arkansas passed enabling legislation to expand its newborn screening ("**NBS**") program: To wit,

> …if reliable and efficient testing techniques are available, all newborn infants shall be tested for other genetic disorders of metabolism by employing procedures approved by the State Board of Health.[3]
>
> [The Division of Health] shall establish and maintain a program of reviewing and following up on positive cases so that measures may be taken to prevent mental retardation or other permanent disabilities.[4]

In addition, the Legislature mandated, subject to funding that was not provided, the inclusion of cystic fibrosis in the NBS program.[5]

In this report the Division of Health ("**DOH**") of the Arkansas Department of Health and Human Services advocates:

1. Expansion of the State's newborn screening program to include 21 "Core" Conditions and 25 "Secondary" Conditions, because they are "genetic disorders of metabolism"[6] for which "efficient and reliable testing" methods exist and appropriate DOH procedures will be provided by the Board of Health.

2. Provision for an increased fee to permit the proposed expansion of newborn screening, including cystic fibrosis.

A properly funded expansion will align Arkansas's newborn screening program with current national recommendations.

B. Newborn Screening: The Current Program in Arkansas

Under the State's current newborn screening program, a baby born in a hospital has a hearing check and a blood sample drawn from a heel-stick. The hearing test result and blood sample are sent to the DOH, which records the hearing test result and, in its Public Health Laboratory, tests the blood sample for the seven genetic and metabolic conditions described above. When an abnormal test is reported, the DOH Child Health staff notifies the baby's physician or, if necessary the family, of the abnormality. DOH short-term follow-up also assures that 1) the baby has been retested, 2) the condition accurately diagnosed, and 3) the baby referred to the appropriate health service for the needed care. Babies with confirmed abnormalities are entered into DOH's long-term follow-up system. In 2005, the hearing screening program confirmed that 68 babies had moderate or profound hearing loss in one or both ears, and in 2004, the metabolic screening program confirmed that 44 babies had a genetic disorder of metabolism. The DOH charges hospitals $14.83 to test each blood specimen sent to the Public Health Laboratory. This fee covers part of the laboratory costs, and none of the short-term and long-term follow-up costs. Additional support comes from federal grants that are not likely to continue.

C. Newborn Screening: The Current National Recommendations

New laboratory testing methods are available to screen for additional genetic disorders. In addition, the Centers for Disease Control ("**CDC**") and the Health Resources and Services Administration ("**HRSA**"), together with medical specialists and other experts, have combined to develop new screening recommendations ("**Policy**") whose adoption will increase uniformity among State programs. The Policy recommends that all States screen for 29 "Core" conditions ("**Core Conditions**"), seven[7] of which are already screened in Arkansas, and one of which, cystic fibrosis, remains an unfunded mandate (See Table 1). All Core Conditions are detectable by efficient and reliable screening tests and can be treated (See Exhibit "A"). The Policy also recommends that States report another 25 Secondary conditions ("**Secondary Conditions**") as they may be coincidentally revealed during the screening for Core Conditions. Many States have begun to implement these new recommendations. (See Part C in Tables 1 and 2).

D. DOH Recommendations for Expansion in Arkansas

The DOH recommends to the Board of Health and the Arkansas Legislature that the Public Health Laboratory screen for the 21 additional Core Conditions as well as for cystic fibrosis, and initially report the 25 Secondary Conditions. The Board of Health is authorized by Arkansas law to include new conditions that are "genetic disorders of metabolism".

E. Expansion: Its Anticipated Cost and Funding

For NBS expansion, the DOH must purchase equipment and supplies, hire personnel, contract with medical experts in the State, set up a database, and educate professionals and the public. To fully fund this program will require a fee increase from the current $14.83 to $89.25 per baby tested. For each newborn infant screened, hospitals must pay the DOH this fee, and may obtain reimbursement from Medicaid and private health insurers.[8] The DOH is obligated to "[m]onitor positive test results and assist in treatment and care of affected [newborns]…."[9]

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I. INTRODUCTION AND PURPOSE

The miracle of birth brings to families a sense of pride and hope for the future. Little is more important to parents than knowing that their new baby is healthy. Their physician can best offer this reassurance with a thorough assessment of the child's health. After a careful medical history and physical examination, laboratory studies provide a wealth of information unavailable by any other means. For newborn babies, the number of medical conditions detectable within the first month of life has risen dramatically due to laboratory advances.

Ultimately, the purposes of expanding newborn screening programs are three: 1) to reduce suffering and untimely death from newborn disorders, 2) to reduce parental anxiety and loss of work time caring for a chronically ill child, and 3) to lessen societal costs in terms of health care, special education, and loss of productivity due to workforce reduction. This report sets forth the evidence supporting the proposed expansion of Arkansas' newborn screening program.

II. THE HISTORY OF NEWBORN SCREENING

Newborn screening of infants for certain disorders began 40 years ago for phenylketonuria (PKU).[10] From the 1960s onward, screening programs for phenylketonuria became the standard of medical care in the United States. Subsequently screening for additional conditions became accepted, if: 1) a test was available and affordable, 2) the condition evaded clinical recognition early in its course, and 3) harmful health consequences could be prevented or reduced by early treatment.[11] Hypothyroidism at birth causes mental retardation yet is preventable by thyroid medication.[12] Galactosemia, a disorder of sugar metabolism causing mental retardation, can be treated with diet and lifestyle modifications.[13] Sickle-cell disease commonly causes life-threatening crises that can be avoided or controlled by treatment. PKU, hypothyroidism, sickle-cell disease and galactosemia are included in all States' screening programs[14] (See Table 1, Part C). Scientific advances, including development of new laboratory methods for mass screening[15] have continued to spur States' interest in screening for many other disorders, which are briefly described in Exhibit "A" (See also Part C of Tables 1 and 2).

While many States throughout the United States have added new diseases to their screening programs, they have done so inconsistently.[16] These programmatic differences, and the resulting inequities for newborns in different states, have gained national attention. Health leaders, especially in the National Foundation March of Dimes, are working to bring uniformity to newborn screening across all state programs.

III. RECENT ADVANCES IN LABORATORY TESTING AND NATIONAL RECOMMENDATIONS FOR EXPANDED SCREENING

Three laboratory procedures developed in recent decades have opened the way to screening for more illnesses. A laboratory test to detect biotinidase deficiency has been available since the 1980s.[17] Tandem mass spectrometry ("**MS-MS**") has the capacity for rapid screening of large numbers of blood specimens for many disorders and is very cost-efficient.[15] Cystic fibrosis screening is achieved using molecular genetic techniques.[18] Each of these three testing methods utilizes the single heel-prick blood sample taken from the newborn. Using but a portion of a

newborn's blood sample, the MS-MS equipment, in a single run, can test for forty-six of the Core and Secondary Conditions included in the proposed expansion, along with two of the disorders (galactosemia and phenylketonuria) in the State's current NBS program.

In the late 1990s, the CDC and HRSA[16] began to work with medical and laboratory specialists, administrators, ethicists, public health lawyers, and consumer groups to develop recommendations for State screening programs. Later HRSA contracted with the American College of Medical Genetics ("**ACMG**")[16] to bring this process to fruition. The ACMG coordinated the Newborn Screening Expert Group to conduct an in-depth review of medical and laboratory science as well as a survey of all States' screening programs. Their report ("**Report**") was published in *Genetics in Medicine* [16] and *Pediatrics*.[19]

The Report recommends that all State newborn screening programs test for 29 "Core Conditions", and report on 25 "Secondary Conditions" that may be revealed in the course of testing for a Core Condition (See Tables 1 and 2). Each of the "Core" conditions has 1) an efficient screening test and 2) effective treatments that can prevent much sickness and even early death. Arkansas law now provides for the state to screen for eight[20] of the recommended 29 Core conditions (See Table 1). However, funding to screen for only 7 is currently available. "Secondary" conditions are disorders that, while lacking an effective treatment or a well-known natural history, are clinically significant, because they help the physician accurately diagnose a Core disorder, or they reveal that a newborn without symptoms is a gene-carrier whose offspring may have symptoms of the genetic condition.

IV. ETHICAL ISSUES

Ethical consideration regarding newborn screening focuses on four basic principles: *Autonomy*, *Beneficence*, *Non-maleficence*, and *Justice*.[21] Newborn screening maximizes *autonomy,* if it presents parents with a choice to have or not to have their infant screened. Parental option is provided by AR law.[1] Newborn screening maximizes *beneficenc*e, if it reliably identifies conditions before sickness begins, if the conditions cause serious illness when left untreated, and if the available treatments are effective in preserving good health. All Core conditions meet this test. (See Table 1) Newborn screening achieves *non-maleficence,* if the testing procedure carries minimal risk. The stick of the baby's heel to obtain a few drops of blood is only momentarily painful and significant side effects are very rare. Testing achieves *non-maleficence* when done in a way that minimizes parental anxiety. Any laboratory result other than "normal" creates anxiety for the parents. Because laboratory tests that screen for very rare disorders may report specimens as "possibly abnormal," the baby must be tested a second time to verify the true presence or absence of the illness. Until the final result is available, parental concern mounts. For this reason, parents need to understand that the initial test is a screen, not a diagnosis. Definitive testing for newborns having a positive screen test must quickly be achieved. One circumstance brings *maleficence* poignantly into question: a baby is screened and found to have a disease for which no treatment is known. If a baby is not tested for such a condition, then parental anxiety is avoided until the disease becomes apparent, if it ever does. Another view is that even with no known treatment, the parent can be provided with anticipatory guidance about what to prepare for and expect. Informed of an abnormal test result, the physician and parent can avoid the "diagnostic odyssey", a lengthy, expensive search to explain a perplexing illness. Newborn screening maximizes *justice,* if it is made equally

available to all newborns, and if there is widespread access to medical care for the illness identified. Arkansas law and rule provide widespread access. Justice is enhanced by protections against discrimination in employment, education, and insurance. State and Federal law provide these protections. Broader justice to society as a whole occurs when early treatment avoids high medical costs and the need for long-term special education.

V. OTHER STATES' EXPERIENCE WITH EXPANDED NBS PROGRAMS

Within the last ten years, numerous States have expanded their newborn screening programs (See Part C, Tables 1 and 2). North Carolina has the longest experience.[22] Over a seven-year period 944,078 babies were screened. Among these infants 219 were confirmed to have a positive test: 99 had fatty acid oxidation disorders, 58 had organic acid disorders, and 62 had amino acid disorders (See Exhibit "A"). If Arkansas's experience were similar to that of North Carolina, about nine babies a year would be confirmed to have one of these disorders. California developed a pilot program and screened[23] approximately 375,000 newborns, finding 51 with one of these disorders. Applying this rate to Arkansas's approximate 38,000 annual births, Arkansas's expanded program would identify an additional six babies per year having one of these diseases. California also reported the cost and benefit of its expanded screening, based on its then-current $78.00 fee per screened infant. California's study concluded that *averted* costs, due to long-term medical treatment and special education for mental retardation and other disabilities, exceeded the cost of screening and treatment by 47 million dollars in the best-case scenario, and by 18.9 million dollars in the worst-case scenario. If these costs and savings were applied to Arkansas, the range of savings would be between 1.9 million and 4.7 million dollars annually.

VI. NEWBORN SCREENING IN ARKANSAS: SOME RECENT HISTORY

In 2005 the Arkansas Newborn Hearing Screening program reported 38,358 newborns were delivered in the State, of whom 98.0% received hearing screening by a hospital or a community audiologist. [24] Among those screened, 1581 (4.3%) were referred for follow-up testing and 68 had confirmed hearing loss. Arkansas's newborn metabolic screening program screened 37,118 newborns in 2004[25] and 779 of them had positive initial screens. Subsequent testing confirmed 44 (0.12%) had disease: 29 babies had red blood cell disorders (not counting sickle trait), 11 had hypothyroidism, three had phenylketonuria, and one had galactosemia (See Exhibit "A").

VII. ARKANSAS LAW GOVERNING NEWBORN SCREENING

Arkansas Code §20-15-302 on newborn testing provides, in summary, that:

> All newborn infants shall be tested for phenylketonuria, hypothyroidism, galactosemia, sickle cell anemia and, if funding exists, cystic fibrosis. If reliable and efficient testing techniques are available, all newborn infants shall be tested for other genetic disorders of metabolism by employing procedures approved by the State Board of Health. Medicaid shall reimburse the hospital for these tests as well as for the hospital's *per diem* for the newborn. All positive test results shall be sent to the DOH. The DOH shall establish and maintain a program of reviewing and following up on positive cases to prevent mental

retardation and other permanent disabilities. Information compiled for this purpose may be used by the DOH and others designated by the DOH, but may not disclose the identity of any person. The DOH shall provide educational programs among physicians, hospitals, public health nurses, and the public concerning the disorders covered in this section. Parents and legal guardians may opt out of testing on medical, religious, or philosophical grounds.

Arkansas Code §20-15-304 on DOH administration of NBS provides, in summary, that:

The DOH shall prescribe the tests to be done; promulgate regulations with the Insurance Commissioner; determine the persons or institutions to obtain the blood specimens; determine the amount to be charged for the laboratory testing and the manner of billing; furnish copies of the law and regulations to physicians, hospitals and other providers required to perform the tests; establish a central laboratory to perform analysis of the specimens; report the findings; monitor test results and assist in treatment of affected infants; and disseminate information and advice to the public concerning the disorders.

Arkansas Code §20-35-103, nondisclosure of genetic information provides, in summary, that:

No research records of individuals shall be subject to subpoena or discovery in civil suits except where it is the basis for the suit. No records shall be disclosed to employers or health insurers without informed written consent of the individual. Specimens may be shared for research purposes, only when the person's name or social security number is not attached, or when the person has given written consent. It is permissible to publish the results of genetic studies as long as no individual subject is identified.

Arkansas Code §23-79-129 on insurance coverage of infants provides, in summary, that:

Every accident and health insurance policy, contract, or plan shall include coverage for the newborn infant children of the insured from the moment of birth; shall include coverage of illness, injury, congenital defects and premature birth; and shall include coverage of newborn screening tests.

Arkansas Code §23-66-320 on genetic nondiscrimination in insurance, in summary:

Limits insurers' right to require genetic testing for underwriting decisions; and the right to make underwriting decisions around genetic information, "except to the extent and in the same way as insurers make coverage changes for loss caused by other medical conditions" and increased risks.

Arkansas Code §11-5-403 on employers' use of genetic information states, in summary, that:

An employer shall not seek to obtain or use a genetic test or genetic information of the employee or prospective employee for restricting any right or benefit otherwise due.

VIII. THE STRUCTURE AND FINANCING FOR AN EXPANDED NEWBORN SCREENING PROGRAM IN ARKANSAS

DOH proposes that the 21 Core Conditions and the 25 Secondary Conditions listed in Tables 1 and 2, as well as cystic fibrosis, be added to Arkansas's NBS screening program. Part A in each of Table 1 and Table 2 sets forth the genetic and metabolic nature of the condition; Part B, the frequency that each disorder will be found in Arkansas; and Part C, the number of States (including the District of Columbia) currently screening for each condition.

To implement the expanded screening program in Arkansas and to insure that affected newborns receive the care they need, the following program components will be required:

1. Laboratory testing and reporting,
2. Medical diagnosis of abnormal findings with clinical recommendations for care,
3. Follow-up to assure that each affected newborn receives adequate and ongoing care,
4. Education of appropriate professionals and parents about these conditions,
5. The creation and maintenance of a newborn screening registry to track conditions and evaluate program performance.

Since the Board of Health's approval in 1995, the fee paid by each hospital delivering babies has been $14.83 per newborn screened ("**Fee**"). To date, the Fee has covered only a portion of the cost of Arkansas's current screening program comprising the eight conditions set forth in Table 1, and sickle cell trait (See Table 1, Footnote 6). Current staffing includes two and one-half full-time nurses who provide follow-up care to assure that children with abnormal laboratory results receive confirmatory diagnostic studies and that the families are informed about the condition and the medical attention it requires.

An increase in the Fee is required to finance the proposed expanded screening program. It is estimated that, in the expanded program, the initial screens of 38,000 newborns will yield approximately 3,550 abnormal test results, including about 1200 hemoglobinopathies (See Exhibit "A", and Part B. of Tables 1 and 2), primarily sickle cell trait. Each abnormal test result will require the DOH's follow-up investigation and in many cases confirmatory diagnostic testing. Once a case is identified (*i.e.*, an abnormal test result is confirmed), the DOH's duties require it to assure that appropriate medical care is provided, that the infant is entered into the DOH database, and that appropriate parent and physician education is provided. The Arkansas Public Health Laboratory's capacity to screen for the expanded program will require additional staff, equipment and supplies. The total annual budget for the expanded newborn screening program, including laboratory, follow-up and administrative costs, is projected to be $3,391,373, if 38,000 newborns and their parents are served in Arkansas. Consequently, the Fee must be increased to $89.25, an amount that is in line with charges applied by other States (See Table 3). Regarding the State fees listed in Table 3, it should be noted that some States do not perform newborn screening in their public health laboratories, but contract privately, and that some States who do perform screening in their own laboratories fund the program from other state resources or grants. The proposed NBS expansion leaves as it is the State's current system for hospital payment, and reimbursement, of the Fee. (See text at Endnote 8).

IX. CONCLUSION

Nationally, great changes are occurring in state newborn screening programs. Federal agencies have partnered with expert groups of physicians, laboratory practitioners, and public health professionals to develop recommendations for uniformity among newborn screening programs, so that all babies, regardless of where they are born in the United States, have the same opportunity for life expectancy and quality of life. Arkansas has a documented need to expand its screening program, and applicable state law directs the Board of Health to expand it for "other genetic disorders of metabolism" for which "efficient and reliable testing methods" exist. The 29 nationally recommended Core Conditions and the 25 Secondary Conditions satisfy the Arkansas statutory prerequisites, and the DOH will implement and operate the expanded program with procedures worthy of approval by the Board of Health. Other States have demonstrated that an expanded program will identify more affected babies, and create cost-savings through early treatment before illness does lasting harm. Arkansas health leaders have urged expansion of newborn screening in our State. The DOH is prepared and eager to expand and operate the program once the Board of Health authorizes this action and the General Assembly provides the necessary regulatory review and appropriation.

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X. EXHIBIT AND TABLES

EXHIBIT "A" GLOSSARY OF CONDITIONS***

Biotinidase (BIOT) Biotinidase deficiency, due to the lack of the enzyme biotinidase, results in the body's inability to use vitamin B substances absorbed by the intestines. Insufficient biotin causes several other critical enzyme systems to malfunction. Affected newborns appear normal, but develop critical symptoms after the first weeks or months of life. Symptoms include floppiness, seizures, developmental delay, hair loss, skin rash, hearing loss, and vision loss. Metabolic acidosis can result in coma and death. A daily biotin dietary supplement can prevent all symptoms.	**Congenital Adrenal Hyperplasia (CAH)** CAH is a group of disorders caused by the deficiency of an adrenal enzyme resulting in decreased production of two important hormones. One helps the body respond to stressful events, and the other helps maintain body fluids and salts. Without enough of these hormones, affected newborns may appear normal, but can quickly develop symptoms including lethargy, vomiting, muscle weakness and dehydration. In severe cases death may occur within a few weeks if left untreated. Infants with milder forms of the disorder are at risk for reproductive and growth difficulties. If detected early, and treated well with medication, affected infants should have normal growth and development.	**Cystic Fibrosis (CF)** In cystic fibrosis the body cannot make an important protein involved in using chloride ions, which are an ingredient in table salt. The major clinical consequences are the production of abnormally thickened mucous secretions in the lungs and digestive systems of affected newborns. Breathing and digestion become severely compromised and lead to multiple hospitalizations. With early detection and lifelong comprehensive treatment plans, infants diagnosed with CF can be expected to live longer and in a better state of health than in the past.	**Galactosemia (GALT)** Galactosemia results from a deficiency in the enzyme needed to metabolize galactose, a milk sugar. Newborns typically appear normal; however, within a few days to two weeks after initiating milk feedings, vomiting, diarrhea, lethargy, jaundice and liver damage develop. Untreated, the disorder may result in developmental retardation, liver enlargement, growth failure, cataracts, and, in severe cases, death. With early detection and strict adherence to a galactose-free diet, affected infants can be expected to achieve satisfactory general health.
Homocystinuria (HCY) Homocystinuria is caused by an enzyme deficiency of the amino acid homocysteine. Major clinical features include eye and vision defects, mental retardation, bone thinning and blood clots. The eye and vision defects appear in 80% of affected children by age 15. Blood thinning and clots can cause death in 50% of affected people by age 20, rising to 75% by age 30. With early detection, strict dietary management, and vitamin supplements, normal growth and development should occur.	**Hemoglobinopathies (Hbgs)** Hemoglobinopathies are inherited abnormalities in blood cell proteins that carry oxygen. The abnormal protein causes the red cells to assume a crescent shape called "sickling" which makes them hard and sticky. These changes prevent red cells from moving smoothly through the body. The most catastrophic abnormal hemoglobin conditions are sickle cell anemia and sickle beta thalassemia. Affected newborns appear normal, but anemia develops in the first few months of life, followed by increased susceptibility to infection, and slow growth rates. Appropriate medical care, including penicillin prophylaxis, vaccinations, and long-term management, can minimize sickle cell disease complications.	**Phenylketonuria (PKU)** Phenylketonuria is the result of an inability to break down the amino acid, phenylalanine, found in food protein. Infants may appear normal in the first few months of life, but left untreated, PKU can cause mental and motor retardation, an underdeveloped brain, poor growth rate, and seizures. With early detection and proper dietary treatment, growth and development should be normal. Hyperphenylalaninemia can occur in several forms, some mild, some very severe. The severe form is referred to as PKU. The milder form is sometimes called "benign hyperphenylalaninemia" (H-Phe).	**Congenital Hypothyroidism (CH)** Congenital hypothyroidism is due to an inability to produce adequate amounts of thyroid hormone. Left untreated, this congenital deficiency of thyroid hormone can result in mental retardation and stunted growth. Newborns may appear normal up to three months of age. If detected early (before three weeks) and maintained on appropriate levels of thyroid hormone medication, infants diagnosed with CH should have normal growth and development.
Maple Syrup Urine Disease (MSUD) Maple Syrup Urine Disease is an enzyme deficiency disorder. Newborns typically appear normal, but by the first week of life can experience feeding difficulties, lethargy, and failure to thrive. Left untreated, MSUD can lead to progressive neurological problems, acidosis, seizures, and sudden breathing cessation that can rapidly lead to coma and death. Severe effects can be avoided with early detection and treatment. Strict dietary management, dietary supplements, and close developmental monitoring and assessment are needed	**Amino Acid Disorders (AAD)** Amino acid metabolism disorders are a group of inherited conditions in which protein metabolism is disrupted. Onset of symptoms may occur shortly after birth or after an apparently normal neonatal period. The symptoms may occur in episodes with normal periods in between. The clinical onset may include unusual urine odors, irritability, poor feeding, changes in muscle tone, lightened pigmentation, failure to thrive, jaundice, or liver enlargement. Other symptoms include vomiting, lethargy, seizures, and coma. Treatment of amino acid metabolism disorders includes a low-protein diet strictly controlling intake of specific amino acids. Amino acid disorders include 6 Core Conditions **(ASA, CIT-1, HCY, MSUD, PKU, and TYR-1**) and **8** Secondary Conditions (**ARG, BIOPT-BS, BIOPT-RG, CIT-2, H-PHE, MET, TYR-2,** and TYR-3).	**Fatty Acid Oxidation Disorders (FAOD)** Fatty Oxidation Disorders are genetic metabolic deficiencies in which a missing or malfunctioning enzyme prevents the body's oxidizing (breakdown) of fatty acids to make energy. The body's main energy source is a sugar, glucose. When glucose runs out, fat normally is broken down into energy. However, that energy is not readily available to children and adults with a fatty acid disorder. Undiagnosed and untreated, these disorders can lead to serious complications affecting the liver, heart, and eyes; general muscle development; and possibly to death. Symptoms of a metabolic "crisis", sometimes stress-induced, include vomiting, diarrhea, lethargy and difficulty breathing. These disorders include 5 Core **Conditions (CUD, LCHAD, MCAD, TFP, VLCAD**) and 8 Secondary Conditions (CACT, CPT-1a, CPT-2, DE-RED, GA-2, MCKAT, M/SCHAD, and SCAD).	**Organic Acid Disorders (OAD)** Organic acidemias are a group of inherited metabolic disorders that lead to accumulation of organic acids in biological fluids, e.g., blood and urine. The accumulation disturbs the acidity of the body and causes alterations in metabolic chemical reactions. These disorders can cause intoxication-like symptoms such as vomiting, dehydration, and coma. Some patients may have too little sugar, too much lactic acid, or too much ammonia in the blood. Chronic symptoms include recurrent vomiting, failure to thrive, floppiness and general developmental delay. Symptoms can be diminished by restricting protein in the diet and, in some cases, supplementation with vitamins and/or carnitine. These disorders include 8 Core Conditions **(GA-1, HMG, IVA, 3-MCC, CBL-A,B, BKT, MUT, PROP, and MCD**), and 6 Secondary Conditions (2M3HBA, 2MBG, 3MGA, Cbl-C, D, IBG, and MAL).

******* With revisions, based on information from the National Newborn Screening Information System at **http://www2.uthscsa.edu/nnsis/**. Accessed October 6, 2006.

TABLE 1 CORE CONDITIONS

PART A: CONDITION STATUS AS GENETIC DISORDER OF METABOLISM [1] ~ PART B: ARKANSAS FREQUENCY OF CONDITION ~ PART C: NO. STATES MANDATING TESTING OF CONDITION

CORE CONDITIONS			Part A: Status of Condition [2] as:		Part B: 2005 Arkansas Frequency						Part C: Mandated NBS Condition
			Metabolic	Genetic							
Program Group of Conditions	Currently Included Conditions in Approximate Order of Frequency		Y/N	Y/N	2005 AR Newborns Screened (*a*)		2005 Newborns in AR with Abnormal[4] Screens (*b*)		2005 Confirmed Positive Cases in AR (*c*)	Ratio: Abnormal[4] Screens to Cases in AR (*c*/*b*)	No. of States (Including D.C.) (as of 9/25/06)
7 Core Conditions Now Mandated and Funded in AR NBS Program	Hearing loss	HEAR	N/A	Many	36,789		1,581		68	23.3	30
	Sickle cell anemia [6]	Hb S/S	Y[3]	Y	37,460		15		15	1.0	51
	Sickle - C disease	Hb S/C	Y[3]	Y	37,460		14		14	1.0	51
	Sickle - S-Beta thalassemia	S/β-thal.	Y[3]	Y	37,460		3		3	1.0	51
	Congenital hypothyroidism	CH	Y[3]	Y	37,460		1,251		11	112.1	51
	Phenylketonuria	PKU	Y[3]	Y	37,460		13		3	4.3	51
	Classic galactosemia	GALT	Y[3]	Y	37,460		47		1	46.0	51
1 Core Condition Mandated but Unfunded in AR NBS Program (to be added) →	Currently not Included (No Funding)		Part A: Status of Condition [2] as:		Part B: US Frequency and AR Estimate						Part C: Mandated NBS Condition
			Metabolic	Genetic	Est. US[7] Annual # Newborns Screened (a)	Est. US[7] Annual # Abnormal[4] Screens (b)	Projected AR Annual # Abnormal[4] Screens (b/a)(38,000)[5]	Est. US[7] Annual # Confirmed Cases (c)	Projected AR Annual # Confirmed Positive Cases (c/a)(38,000)[5]	# Abnormal[4] Screens To # Confirmed Cases (b/c)	No. of States (Including D.C.) (as of 9/25/06)
			Y/N	Y/N							
	Cystic fibrosis	CF	Y[3]	Y	598,413	2,267	144	135	9	16.8	22
21 Conditions Proposed to be Added to Arkansas NBS Program	Congenital Adrenal Hyperplasia	CAH	Y	Y	2,806,013	15,501	210	184	2	84.2	37
	Homocystinuria	HCY	Y	Y	1,860,711	2,836	58	5	0	567.2	37
	Biotinidase	BIOT	Y	Y	1,896,068	2,802	56	81	2	34.6	37
	Carnitine uptake defect	CUD	Y	Y	1,030,482	1,381	51	16	1	86.3	36
	Methylmalonic acidemia (Vitm. B12)	CBL A,B	Y	Y	315,809	411	49	0	0	411+	42
	Maple syrup urine disease	MSUD	Y	Y	1,982,557	2,275	44	16	0	142.2	32
	Propionic acidemia	PROP	Y	Y	1,458,146	1,423	37	11	0	129.4	37
	Methylmalonic acidemia	MUT	Y	Y	1,499,752	1,434	36	17	0	84.4	47
	3-Methylcrotonyl-CoA carboxylase def.	3-MCC	Y	Y	1,458,146	1,238	32	25	1	49.5	37
	Tyrosinemia Type 1	TYR 1	Y	Y	1,326,153	1,095	31	0	0	1,095+	41
	3-methylcrotonyl-CoA carboxylase def.	HMG	Y	Y	1,458,146	1,181	31	1	0	1,181.0	37
	Trifunctional protein def.	TFP	Y	Y	1,264,251	957	29	0	0	957+	37
	Medium-chain acyl-CoA dehydrog. def.	MCAD	Y	Y	2,009,175	1,517	29	114	2	13.3	43
	Isovaleric acidemia	IVA	Y	Y	1,458,146	1,091	28	18	0	60.6	44
	Long-chain 3-OH acyl-CoA dehydrog. def.	LCHAD	Y	Y	1,347,241	997	28	5	0	199.4	36
	Very long-chain acyl-CoA dehydrog. def.	VCLAD	Y	Y	1,458,146	1,078	28	18	0	59.9	37
	Methyl Co-A carboxylase def.	MCD	Y	Y	1,462,533	1,008	26	0	0	1,008+	35
	Beta-ketothiolase deficiency	βKT	Y	Y	1,260,902	863	26	1	0	863.0	37
	Glutaric aciduria Type 1	GA-1	Y	Y	1,458,146	974	25	13	0	74.9	35
	Citrullinemia Type 1	CIT-1	Y	Y	1,625,670	1,009	24	11	0	91.7	34
	Argininosuccinate lyase def.	ASA	Y	Y	2,004,634	975	18	184	0	139.3	37

1. A.C.A.§20-15-302. (a)(1)(A) All newborn infants shall be tested for [PKU], [CH], [GALT], cystic fibrosis, and sickle-cell anemia. (B) In addition, if reliable and efficient testing techniques are available, all newborn infants shall be tested for other genetic disorders of metabolism by employing procedures approved by the State Board of Health. [Emphasis added.] **2.** Unless otherwise noted, data from ACMG report - Newborn Screening: Towards a Uniform Screening Panel and System. Genet Med. 2006; 8(5) Suppl: S12-S25. **3.** A.C.A. §20-15-304 and §23-79-129(a)(2) indicate condition is a disorder "of metabolism". **4.** Includes true and false positives; "false positive" is a positive screening result in an infant who is truly unaffected by the condition's symptoms or by any gene causing the condition. **5.** 38,000 = Est. # AR births per yr. **6.** Sickle cell trait (Hb S/A) is also presently screened in the AR NBS program. A positive Hb S/A case means a newborn will not have Hb S/S symptoms but is an Hb S/S-gene carrier whose offspring may have Hb S/S symptoms. **7.** Data from http://www2.uthscsa.edu/nnsis/. The following are the Hb A/S data for Table 1, Part B: A. 37,460; B. 1187; C. 1204; D. 1187; E. 1204; and F. 1.0.

TABLE 2 25 SECONDARY CONDITIONS FOR PROPOSED EXPANSION OF ARKANSAS NEWBORN SCREENING PROGRAM

PART A: CONDITION STATUS AS GENETIC DISORDER OF METABOLISM [1] ~ PART B: ARKANSAS FREQUENCY OF CONDITION ~ PART C: NO. OF STATES MANDATING TESTING

SECONDARY CONDITIONS		Part A: Status of Condition [2] as:		Part B: Estimated 2005 Arkansas Frequency of Condition						Part C: Mandated NBS Condition
		Metabolic	Genetic							
Condition Name and Abbreviation (Sorted: Highest to Lowest Frequency)		Y/N	Y/N	Estimated US [3] Annual # Newborns Screened (a)	Estimated US [3] Annual # Abnormal [4] Screens (b)	Estimated AR Annual # Abnormal [4] Screens (b/a)(38,000) [5]	Estimated US [3] Annual # of Confirmed Positive Cases (c)	Estimated AR Annual # Confirmed Positive Cases (c/a)(38,000) [5]	Ratio: # US Abnormal [4] Screens To # US Confirmed Positive Cases (b/c)	# of States (Including D.C.) (as of 9/25/06)
2,4 Dienoyl-CoA reductase deficiency	De-Red	Y	Y	271,212	709	99	0	0	709+	18
Methylmalonic acidemia	CBL C,D	Y	Y	1,078,289	1155	41	5	0	231.0	25
Tyrosinemia Type 2	TYR-2	Y	Y	1,135,127	1096	37	2	0	548.0	23
3-Methylglutaconic aciduria	3MGA	Y	Y	806,747	737	35	0	0	737+	23
Short-chain acyl-CoA dehydrog, def.	SCAD	Y	Y	1,316,327	1140	33	35	1	32.6	50
Carnitine palmitoyl transferase def. Type 1	CPT-1a	Y	Y	932,498	779	32	6	0	129.8	12
Carnitine palmitoyl transferase def. Type 2	CPT-2	Y	Y	1,341,213	1050	30	3	0	350.0	12
Carnitine/acylcarnitine translocase def.	CACT	Y	Y	1,336,059	1042	30	1	0	1042.0	21
2-Methylbutyryl-CoA dehydrog. def.	2MBG	Y	Y	995,323	771	29	4	0	192.8	31
Multiple acyl-CoA dehydrog. def.	GA-2	Y	Y	1,341,213	991	28	6	0	165.2	30
Argininemia	ARG	Y	Y	923,100	635	26	1	0	635.0	27
2-Methyl-3-hydroxybutyric CoA dehydrog. deficiency	2M3HBA	Y	Y	669,127	460	26	0	0	460+	9
Medium/short-chain L-3-hydroxy acyl-CoA dehydrogenase	M/SCHA D	Y	Y	343,548	207	23	0	0	207+	18
Malonic aciduria	MAL	Y	Y	591,081	271	17	1	0	271.0	18
Isobutyryl-CoA dehydrog. deficiency	IBG	Y	Y	995,323	736	11	3	0	99.5	31
Citrullinemia Type 2	CIT-2	Y	Y	0	0	0	1 [6]	Not Available (N/A)	N/A	28
Hypermethioninemia	MET	Y	Y	399,900	0	0	0	0	N/A	24
Galactokinase deficiency	GALK	Y	Y	3,259,806	6	0	1	0	6	19
Galactose epimerase deficiency	GALE	Y	Y	3,259,806	383	4	7	0	55	12
Benign hyperphenylalaninemia	H-PHE	Y	Y	N/A	N/A	N/A	N/A	N/A	N/A	9
Biopterin cofactor regeneration	BIOPT-RG	Y	Y	N/A	N/A	N/A	N/A	N/A	N/A	30
Biopterin cofactor synthesis defect	BIOPT-BS	Y	Y	N/A	N/A	N/A	N/A	N/A	N/A	31
Medium-chain ketoacyl-CoA thiolase deficiency	MCKAT	Y	Y	N/A	N/A	N/A	N/A	N/A	N/A	28
Tyrosinemia Type 3	TYR-3	Y	Y	N/A	N/A	N/A	N/A	N/A	N/A	18
Variant hemoglobinopathies (incl. Hb E)	Variant Hbgs	Y [3]	Y	N/A	N/A	N/A	N/A	N/A	N/A	48

1. A.C.A. §20-15-302. (a)(1)(A) All newborn infants shall be tested for [PKU], [CH], [GALT], cystic fibrosis, and sickle-cell anemia. (B) In addition, if reliable and efficient testing techniques are available, all newborn infants shall be tested for other genetic disorders of metabolism by employing procedures approved by the State Board of Health. [Emphasis added.] **2**. Unless otherwise noted, data from ACMG report - Newborn Screening: Towards a Uniform Screening Panel and System. Genet Med. 2006; 8(5) Suppl: S12-S25. **3.** Data from http://www2.uthscsa.edu/nnsis/. **4.** Includes true and false positives; "false positive" is a positive screening result in an infant who is truly unaffected by the condition's symptoms or by any gene causing the condition. **5**. 38,000 = Est. AR births/yr. **6**. Case apparently found clinically, not by screening test.

TABLE 3: STATE NEWBORN SCREENING FEES***

State	Amount	State	Amount	State	Amount	State	Amount
Alabama	$139.33	Illinois	$47.00	Montana	$42.70	Rhode Island	$110.00
Alaska	$55.00	Indiana	$62.50	Nebraska	$35.75	South Carolina	$42.00
Arizona	$30 1st screen $40 2nd screen	Iowa	$77.00	Nevada	$60.00	South Dakota	$99.99
Arkansas	$14.83	Kansas	$0	New Hampshire	$40.00	Tennessee	$47.50
California	$78.00	Kentucky	$53.50	New Jersey	$71.00	Texas	$19.50
Colorado	$59.00	Louisiana	$30.00	New Mexico	$32.00	Utah	$65.00
Connecticut	$28.00	Maine	$52.00	New York	$0	Vermont	$33.30
Delaware	$78.00	Maryland	$42.00	North Carolina	$14.00	Virginia	$53.00
Dist. Of Columbia	$0	Massachusetts	$54.75	North Dakota	$42.50	Washington	$67.50
Florida	$15.00	Michigan	$56.83	Ohio	$55.16	West Virginia	$0
Georgia	$0	Minnesota	$61.00	Oklahoma	$98.70	Wisconsin	$69.50
Hawaii	$47.00	Mississippi	$70.00	Oregon	$54.00	Wyoming	$70.00
Idaho	$25.00	Missouri	$50.00	Pennsylvania	$0		

***Source: http://genes-r-us.uthscsa.edu/resources/consumer/statemap.htm. Accessed October 6, 2006. Some States do not perform newborn screening in their public health laboratories, but contract privately; other States who do perform screening in their own laboratories fund the program from other state resources or grants.

XI. ENDNOTES

[1] State Law prescribes the circumstances in which a parent or legal guardian may refuse to have an infant screened. A.C.A. § 20-15-1104(a) (3) and A.C.A. §20-15-302.

[2] A.C.A. §20-15-1101 et seq., A.C.A. §20-15-1501, and A.C.A. §20-15-302(a)(1)(A).

[3] A.C.A. §20-15-302(a)(1)(B).

[4] A.C.A. §20-15-302(c)(1).

[5] A.C.A. §20-15-302(a)(1)(A) and (f).

[6] Metabolism means the biochemical reactions in the body involving growth, the exchange of energy or the elimination of wastes.

[7] The State's NBS program also screens for the sickle cell trait to determine whether a newborn's offspring may be affected by symptoms of a sickle-cell disease. The sickle cell trait is not an enumerated Core or Secondary Condition.

[8] A.C.A. §20-15-302(2) and §23-79-129(a) (2)(B).

[9] A.C.A. §20-15-304(6)

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[20] Arkansas also screens for the sickle-cell trait; See Endnote 7.

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