MISSOURI NEWBORN SCREENING

2009 Annual Report



Missouri Department of Health and Senior Services

Governor Jay Nixon
Margaret T. Donnelly, Director

Acknowledgments

The Missouri State Genetic Advisory Committee and its ancillary Newborn Screening Standing Committee, Sickle Cell Standing Committee, Cystic Fibrosis Standing Committee and Newborn Hearing Screening Standing Committee play a vital role in supporting the activities of the Missouri Department of Health and Senior Services Newborn Screening Program.

The expertise the committees provide is complemented by department staff who are dedicated to helping Missouri children receive the best care available when diagnosed with one of the serious medical conditions detectable through screening tests.

Missouri Department of Health and Senior Services
Division of Community and Public Health
Section for Healthy Families and Youth
Bureau of Genetics and Healthy Childhood
and
State Public Health Laboratory

Table of Contents

What is Newborn Screening?

Newborn screening is a great example of a public health program aimed at the early identification of conditions and the timely intervention by health care providers to eliminate or reduce associated mortality and morbidity. It is the goal that every newborn be screened for certain harmful or potentially fatal disorders that aren't otherwise apparent at birth.

With a simple blood screen, doctors can often tell whether newborns have certain conditions that could eventually cause problems. Screening can often identify serious or life-threatening conditions before symptoms begin. Many of these disorders are metabolic in nature, which means they interfere with the body's ability to use nutrients to produce energy and maintain healthy tissues.

Other types of disorders that may be detected through newborn screening include problems with hormones or blood disorders. These metabolic and other inherited disorders can interfere with an infant's normal physical and mental development in a variety of ways. In some instances they can even lead to death.

Newborn screening tests are required to be collected before a newborn leaves the hospital. The screening involves taking a few drops of blood by pricking the baby's heel and collecting the blood on a filter paper. The paper is sent to the State Newborn Screening Laboratory at the Missouri State Public Health Laboratory for testing. The results are sent back to the hospital of birth and the physician of record. If results are considered to be out of normal range, the family will be contacted for further testing of the baby's blood.

The goal of Missouri's newborn screening program is for every newborn to be screened for certain harmful or potentially fatal disorders that aren't otherwise apparent at birth.

Many changes have been instituted since newborn screening became a standard practice more than 40 years ago. Missouri and other states mandate newborn screening of all infants born within their borders. Affected newborns typically appear normal at birth with no sign of any disorder until a developmental disability or death occurs. Upon detection of a condition, specialists formulate a plan of medical management that allows most affected newborns to develop normally.

Newborn screening is a model for public health-based population genetic screening. It is recognized nationally and internationally as an essential public health program that provides for the best outcomes for the nation's most vulnerable population.

A hearing screen is also part of Missouri's newborn screening program. The screening is usually done while the newborn is sleeping and involves placing a tiny earphone in the baby's ear and measuring his or her response to sound. The baby experiences no discomfort from this procedure. Results from the hearing screening are provided immediately. The results tell the health care staff if further screening or an audiological assessment might be necessary.

Missouri Newborn Blood Spot Screening

Missouri's newborn blood spot program saw a number of accomplishments in 2009, including:

Biotinidase Deficiency Screening
Missouri's Newborn Screening (NBS) Laboratory successfully completed its first full year of biotinidase deficiency screening. During the year approximately 80,000 newborns were screened, and 18 were confirmed to have biotinidase deficiency. This screening test has a positive predictive value (PPV) of 69 percent and is currently the least expensive screening test performed by the NBS Lab. Biotinidase deficiency is also a very simple and inexpensive condition to treat once it is diagnosed.

Discontinuation of the T4 Assay
On April 1, 2009 the NBS Lab discontinued the thyroxine (T4) assay for screening primary congenital hypothyroidism, thus using only the thyroid stimulating hormone (TSH) assay. For the past 20 years, the NBS Lab has been conducting dual testing (T4 and TSH) on every newborn. In the past few years, the sensitivity and specificity of the TSH assay has improved greatly, and it has been determined that the additional utility of the T4 assay was questionable and no longer cost beneficial. Dropping the T4 assay has saved the laboratory more than $200,000 per year in costs. It has not reduced the sensitivity of screening for primary congenital hypothyroidism, yet it has eliminated false positive screening results that originated from using only the T4 assay.

NBS Laboratory Contingency Plan
In partnership with other states, the NBS Lab has completed a third year of validating and drilling an emergency response plan to continue its critical testing in the event of any disaster that may leave the laboratory inoperable, along with a plan to help other states that may need assistance from Missouri should they experience a disaster. The emergency drills are conducted using the framework of the Emergency Management Assistance Compact (EMAC), a compact that has been ratified by Congress with all 50 states as members.

The NBS Lab utilized State Public Health Laboratory, Department of Health and Senior Services and State Emergency Management Agency (SEMA) emergency response personnel throughout the drills. The NBS Lab has now successfully conducted emergency backup testing drills for newborn screening with the states of Iowa, Minnesota, Kansas and Oklahoma and has a thoroughly written and validated newborn screening emergency response plan.

Missouri successfully completed its first full year of biotinidase deficiency screening in 2009.

Evaluation of the Genetic Screening Processor
Missouri was one of two states chosen to perform evaluations on a new screening processor. The beginning of these evaluations started in late 2008. A genetic screening processor (GSP) will replace three current testing platforms in the newborn screening lab, thereby freeing up much-needed space for future newborn screening tests.

In 2009, Missouri evaluated GSP kits for galactosemia and congenital adrenal hyperplasia. The U.S. Food and Drug Administration cleared the GSP testing platform, the GSP TSH kit (which was used in late 2008 for congenital hypothyroidism screening), and the GSP GALT kits for galactosemia screening. These kits, along with the GSP, are now ready to be marketed to other newborn screening labs in the United States due to Missouri's endeavors.

Follow-up of Newborns with Abnormal Results
Missouri successfully extended contracts with all of the genetic tertiary centers, hemoglobinopathy centers and cystic fibrosis centers to continue partnering with them in following-up on newborns having an abnormal newborn screen. The partnership has worked exceptionally well and has ultimately benefitted Missouri families in achieving timely intervention in the care of their newborn. A total of 414 infants were referred to the genetic tertiary centers, hemoglobinopathy centers and cystic fibrosis centers to follow-up on infants considered to be high or moderate risk as a result of their newborn screening results. From these referrals, 166 infants were confirmed positive for a disorder.

Newborn Screening Conference
A one-day conference, "Newborn Screening – What Providers and Parents Need to Know," was held in Jefferson City in April 2009 for health care providers and parents. The conference was funded by a grant from the Heartland Regional Genetics Collaborative. Topics discussed at the conference pertained to newborn blood spot screening, newborn hearing screening and children with special health care needs.

The target audience for the conference included primary care providers, pediatricians, nurses, audiologists, social workers, and other allied health care professionals that work with newborns as well as children with special health care needs and their parents. There were two conference tracks, one for health care providers to increase their knowledge of disorders screened on the Missouri newborn screening panel and a second to provide parents with technical assistance in working with health care providers and organizing parent support groups. Ninety-one people attended the event.

Evaluations from those attending the conference showed it to be beneficial for providers in that it increased their knowledge of newborn screening issues and gave them the opportunity to network with other health care professionals in managing the various disorders detected through newborn screening. Parent comments indicated the conference increased their awareness of organizations and support groups available statewide and nationally.

Newborn Screening Sample Storage – Focus Groups
Missouri passed legislation in 2007 directing the State Public Health Laboratory to store newborn screening samples for five years. The law also allows the stored samples to be used for anonymous research.

Focus groups about the legislative changes were held around the state. The goal of the focus groups was to:

- Determine knowledge and attitudes of the public about their awareness of newborn screening;
- Determine attitudes about newborn screening sample storage to determine the best way to let parents know their options of storing their child's sample and using it for research; and
- Document parent feedback regarding the issue and develop policies and procedures on the methodology of the sample storage and research.

Methodology
In 2009, six focus groups were across the state to obtain knowledge and attitudes of parents and other interested parties. They were held in the western, eastern, central and southern regions of the state. The focus group questions were taken from the Michigan Newborn Screening and Blood Trust Initiative Project. The facilitator guide and some questions were modified to meet the needs of the Missouri Newborn Screening Program. The focus group participants also completed a survey with the same questions once the group discussion was completed.

In addition, surveys were sent to a random sample of parents of children who had a newborn screening to determine their knowledge and attitude of newborn screening and the sample storage and research process. A total of 750 surveys were mailed with approximately 50 returned due to incorrect addresses. Of the remaining 700 surveys, 94 were returned. This was a 13 percent return rate, which was not as good as expected. A second round of surveys was not sent due to lack of funds.

The total number of focus group participants was 83. Fifty-one percent were within the ages of 18 to 20; 29 percent were within the ages of 21 to 29; 9 percent were within the ages of 30 to 39; and 1 percent was 40 and over. The majority of the focus group participants were of reproductive age. As for racial differences, the majority of participants were African-Americans (52 percent). The second largest group was whites (26 percent). The remaining participants were: Native American, 8 percent; Asian, 2 percent; other, 15 percent; and no response, 1 percent.

Findings
Overall comments from the focus group participants indicated that the majority of participants were not aware of the newborn screening program or sample storage law; the majority favored using the leftover newborn screening samples for research; and the research had to be done in academic settings rather than in the private sector. Most importantly, the majority of the participants really did not care how the Department of Health and Senior Services obtained their permission but that they be allowed to make the decision one way or the other. They were not adamant about the options except that they be given options.

When asked what they were going to do with the knowledge they now possessed about newborn screening and sample storage, they said they were going to tell their families and friends about it. Many participants also took the brochures that were brought to the focus group meetings.

The survey results were a little different when compared with the response of the focus groups because the survey was sent to mothers who had recently had a baby. Sixty-six percent indicated that they knew about newborn screening. However, 94 percent were not aware of the sample storage law. Approximately 79 percent were in favor of using the leftover samples for research.

Overall, it appears that parents of newborn babies understood the importance of newborn screening and were in favor of using the samples for research irrespective of types of research or populations who will benefit.

Next Steps

In calendar year 2009, Missouri screened for all 29 core conditions recommended by the American College of Medical Genetics and the March of Dimes. When considering secondary conditions, a total of 67 disorders can be detected through newborn bloodspot screening.

Missouri will be closely monitoring the recommendations of the American College of Medical Genetics in the coming years as recommendations for further screening are made. Newborn screening continues to evolve as advancements are made in the technology to detect disorders and as emerging treatments are discovered or known treatments are modified for treating people affected by these disorders.

In 2009, the Missouri Legislature passed HB 716, known as the Brady Allen Cunningham Act. The bill directs the department to screen by July 2012 for the following five lysosomal storage diseases (LSDs): Krabbe disease, Pompe disease, Gaucher disease, Niemann-Pick disease and Fabry disease. The Department of Health and Senior Services is exploring ways to comply with the law.

Missouri Newborn Screening Disorders

Newborn screening disorders tested and reported in Missouri are:

- Biotinidase deficiency (BIO)
- Classical galactosemia (GALT)
- Congenital adrenal hyperplasia (CAH)
- Congenital primary hypothyroidism (CH)
- Cystic fibrosis (CF)
- Amino Acid Disorders
  - Arginemia (ARG, arginase deficiency)
  - Argininosuccinate acidemia (ASA, argininosuccinase)
  - Citrullinemia type I (CIT-I, argininosuccinate synthetase)
  - Citrullinemia type II (CIT-II, citrin deficiency)
  - Defects of biopterin cofactor biosynthesis (BIOPT-BS)
  - Defects of biopterin cofactor regeneration (BIOPT-RG)
  - Homocystinuria (HCY, cystathionine beta synthase)
  - Hyperphenylalaninemia (H-PHE)
  - Hypermethioninemia (MET)
  - Maple syrup urine disease (MSUD, branched-chain ketoacid dehydrogenase)
  - Phenylketonuria (PKU, phenylalanine hydroxylase)
  - Tyrosinemia type I (TYR-1, fumarylacetoacetate hydrolase)*
  - Tyrosinemia type II (TYR-II, tyrosine aminotransferase)
  - Tyrosinemia type III (TYR-III, hydroxyphenylpyruvate dioxygenase)
- Fatty Acid Disorders
  - Carnitine acylcarnitine translocase deficiency (CACT)
  - Carnitine uptake defect (CUD, carnitine transport defect)*
  - Carnitine palmitoyl transferase deficiency I (CPT-1a)
  - Carnitine palmitoyl transferase deficiency II (CPT-II)
  - Dienoyl-CoA reductase deficiency (DE-RED)
  - Glutaric acidemia type II (GA-II, multiple acyl-CoA dehydrogenase deficiency)
  - Long-chain hydroxyacyl-CoA dehydrogenase deficiency (LCHAD)
  - Medium-chain acyl-CoA dehydrogenase deficiency (MCAD)
  - Medium-chain ketoacyl-CoA thiolase deficiency (MCKAT)
  - Medium/Short chain L-3-hydroxy acyl-CoA dehydrogenase deficiency (M/SCHAD)
  - Short-chain acyl-CoA dehydrogenase deficiency (SCAD)
  - Trifunctional protein deficiency (TFP)
  - Very long-chain acyl-CoA dehydrogenase deficiency (VLCAD)
- Organic Acid Disorders
  - 2-Methyl-3-hydroxybutyric aciduria (2M3HBA)
  - 2-Methylbutyryl-CoA dehydrogenase deficiency (2MBG, SBCAD)
  - 3-Hydroxy 3-methylglutaric aciduria (HMG, 3-Hydrox 3-methylglutaryl-CoA lyase)
  - 3-Methylcrotonyl-CoA carboxylase deficiency (3-MCC)
  - 3-Methylglutaconic aciduria (3MGA, Type I hydratase deficiency)
  - Beta ketothiolase (BKT, mitochondrial acetoacetyl-CoA thiolase, short-chain ketoacyl thiolase)
  - Glutaric acidemia type I (GA-1, glutaryl-CoA dehydrogenase)

- Isobutyryl-CoA dehydrogenase deficiency (IBG)
- Isovaleric acidemia (IVA, Isovaleryl-CoA dehydrogenase)
- Malonic acidemia (MAL, malonyl-CoA decarboxylase)
- Methylmalonic acidemia (CBL A,B; vitamin B12 disorders)
- Methylmalonic acidemia (CBL C,D)
- Methylmalonic acidemia (MUT, methylmalonyl-CoA mutase)
- Multiple carboxylase deficiency (MCD, holocarboxylase synthetase)
- Propionic acidemia (PROP, propionyl-CoA carboxylase)

- Hemoglobinopathies
  - Sickle cell disease (Hb S/S)
  - Sickle hemoglobin-C disease (Hb S/C)
  - Sickle beta zero thalassemia disease
  - Sickle beta plus thalassemia disease
  - Sickle hemoglobin-D disease
  - Sickle hemoglobin-E disease
  - Sickle hemoglobin-O-Arab disease
  - Sickle hemoglobin Lepore Boston disease
  - Sickle HPFH disorder
  - Sickle "Unidentified"
  - Hemoglobin-C beta zero thalassemia disease
  - Hemoglobin-C beta plus thalassemia disease
  - Hemoglobin-E beta zero thalassemia disease
  - Hemoglobin-E beta plus thalassemia disease
  - Hemoglobin-H disease
  - Homozygous beta zero thalassemia disease
  - Homozygous-C disease
  - Homozygous-E disorder
  - Double heterozygous beta thalassemia disease

- Others
  - Hearing

The Missouri Newborn Screening Laboratory's goal is to identify infants at risk and in need of diagnostic testing for the above disorders. A normal screening result does NOT rule out the possibility of an underlying metabolic/genetic disease.

For more details about any of the above mentioned disorders and how they are screened by the NBS Lab, visit the State NBS Laboratory website at: http://www.dhss.mo.gov/Lab/Newborn/index.html.

* There is a lower probability of detection of this disorder during the immediate newborn period.

Screening Spotlight: Cystic Fibrosis

The primary purpose of screening newborns for cystic fibrosis (CF) is to identify infants with CF at an early stage so that intervention through nutritional therapy and improved respiratory function can help reduce morbidity and mortality.

Prior to screening newborns for CF, most children with CF were diagnosed by age 2. Now, most children are diagnosed by 2 months of age. Screening newborns allows those who are confirmed positive to begin enzyme replacement at the time of confirmatory diagnosis and start lung therapies at 4 months of age. It also allows appropriate counseling for parents of newborns with CF. Continual observation of the child's health can considerably improve the child's health outcomes, and early treatment can positively impact the child's quality of life and lifespan.

As treatments for CF continue to improve, so does life expectancy for those who have the condition. Now, with specialized medical care, aggressive drug treatments and therapies, and appropriate nutrition, the median age for survival is approximately 37 years.

Missouri started screening for CF on June 1, 2007, after successfully piloting the program for several months. Since that time approximately 25 infants each year have been identified with a form of CF. Since the inception of CF screening in Missouri, there have been a total of 73 infants identified with the condition.

CF causes thick, sticky mucus to build up in the lungs, digestive system and other organs of the body. Early symptoms of CF include meconium ileus, recurrent cough, wheezing, chronic abdominal pain, loose stools, and failure to thrive. Malnutrition often occurs early, by 2 months of age, and lung disease can also begin within 1 to 3 months of age.

Benefits of early diagnosis through newborn screening for CF include:

- Preventing malnutrition and stunted growth
- Preventing micronutrient deficiency (fat-soluble vitamins)
- Delaying progression of lung disease
- Reducing risk for cognitive dysfunction due to malnutrition
- Enhancing quality of care and quality of life
- Reducing costs for diagnosis and possibly treatment
- Avoiding disparities related to gender, race and ethnicity
- Providing genetic counseling for parents

Incidence

CF occurs most commonly among Caucasians and Ashkenazi Jews, but can also affect people of Hispanic, African or Asian descent. About one in every 3,200 Caucasian newborns have CF, and approximately one in 25 are carriers for the condition. The overall prevalence of CF in Missouri is approximately one in 3,000. In Missouri, about 25 newborns per year are confirmed positive for CF.

Inheritance
Cystic fibrosis is inherited in an autosomal recessive pattern. Because CF is an autosomal recessive disorder, the parents of a child with the condition are unaffected, healthy carriers of CF and have one normal gene and one abnormal gene. With each pregnancy, carrier parents have a 25 percent chance of having a child with two copies of the abnormal gene, resulting in CF. Carrier parents have a 50 percent chance of having a child who is an unaffected carrier and a 25 percent chance of having an unaffected, non-carrier child. These risks would hold true for each pregnancy. All siblings of infants confirmed to have CF also should be tested, and genetic counseling services should be offered to the family.

Variant Forms
Currently, there are more than 1,300 mutations of cystic fibrosis. Delta F 508 is the most common genotype for cystic fibrosis.

Methodology
The Newborn Screening Laboratory uses a two-tiered screening system whereby all specimens are tested using immunoreactive trypsinogen (IRT).

Analyte Measured: Immunoreactive Trypsinogen (IRT)
Determination of IRT concentrations from dried bloodspots serves as the basis for the Missouri Newborn Screening test for CF. IRT concentration is high in the blood of infants with CF, presumably from leakage of the protein into the circulation after exocrine pancreatic injury. Some infants that do not have CF may also have elevated levels of IRT in the newborn period, but these levels decrease to normal in the first weeks of life. Infants having persistently high IRT levels in the first weeks of life are considered at risk for CF. Therefore, an elevated IRT level in a newborn screen requires a repeat screen collected after seven days and prior to six weeks of life to determine if a persistent elevation is present. An infant with a persistent IRT elevation needs to be referred to a certified CF Center for diagnostic sweat testing.

Timing Effect
Because IRT concentration is frequently high immediately after birth, specificity is improved if the test is performed after the first day of life. A specimen collected between 24 and 48 hours of life is optimal. If the IRT is elevated in the initial screen, a repeat screen should be collected after seven days of life and before six weeks of life to determine persistent elevations of IRT. Babies that are low birth-weight, premature and sick may require a third or fourth specimen to determine persistently elevated IRT levels.

There is also an age-related decline in IRT levels in children with CF. IRT levels within the normal range will be considered non-interpretable after 3 months of age and will not be reported on the newborn screen.

Confirmation
All babies that demonstrate persistently elevated levels of IRT in the newborn screen should be referred for a sweat test (pilocarpine iontophoresis) at an accredited Cystic Fibrosis Center. The sweat test is the standard diagnostic test for CF. A high salt level in the patients' sweat is a sign of the disease. The Missouri Department of Health and Senior Services contracts with four accredited CF Centers to provide: follow-up on newborns with elevated IRT results; sweat testing; genetic counseling for the parents; and consultation to primary care providers.

These four centers are (in alphabetical order):

- Cardinal Glennon Children's Hospital, St. Louis – 314-268-6439
- Children's Mercy Hospital, Kansas City – 816-983-6628
- St. Louis Children's Hospital, St. Louis – 314-454-2353
- University Hospital & Clinics, Columbia – 573-884-8579

Treatment

To receive optimal treatment, children with CF should be examined by accredited CF centers that offer a comprehensive approach to CF care; can closely monitor the development of respiratory infections; and can provide nutritional and psychosocial support. CF patients follow a strict regimen to treat the disease as well as to reduce contracting outside infections. The treatment regimen can include:

- Enzymes to aid in digestion at time of diagnosis
- Oral and or IV antibiotics to fight infections
- Vitamins to improve general health
- Respiratory therapy such as bronchodilators and other treatments to clean airways and dislodge mucus from the lungs beginning at 4 months of age
- Steroids to reduce inflammation
- Supplemental oxygen therapy
- Liquid nutrition or healthy high calorie diets for weight gain
- Counseling and support

Comment

The screening test for CF is meant to identify infants at risk for the condition and in need of diagnostic sweat testing. A "normal" screen does not rule out the possibility of the disease. A health care provider should remain vigilant to detect CF among children with clinical symptoms. Also, mild or atypical forms of CF and babies with meconium ileus may not demonstrate elevated IRT levels in the newborn period.

Considerations

- Premature or sick infants may have a false-positive screen due to increased stress on the body. These infants may require a third or fourth newborn screen.
- Blood collection with EDTA can result in inaccurate screening results.
- Babies with meconium ileus have an increased likelihood of having CF, but may not have elevated IRT levels in the newborn period.

Confirmation and Treatment

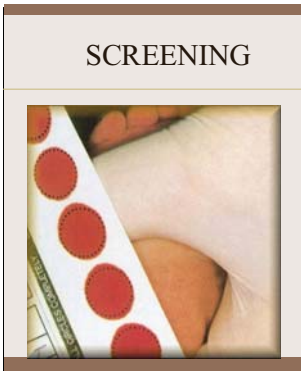
Every infant with two persistently elevated IRT results must have a confirmatory sweat test done in a timely manner. When a newborn screen indicates cystic fibrosis, a definitive diagnosis should be established by a Cystic Fibrosis Foundation accredited care center. All abnormal newborn screening results indicating CF require a sweat test with the results of the diagnosis reported back to the Missouri Department of Health and Senior Services.

Cystic Fibrosis Foundation routine monitoring and care recommendations for infants diagnosed with CF include: encouraging breastfeeding; beginning enzyme replacement and vitamins designated for CF patients upon diagnosis; assessing respiratory symptoms; providing genetic counseling; conducting ongoing measurement of weight, height, and head circumference; discussing tobacco smoke exposure; discussing patient care plan; and educating on infection control.

The Newborn Screening Process

1: TESTING

- The baby's heel is pricked and a few drops of blood are collected on a filter paper 24 to 48 hours after birth.



- The dried blood spot specimen is shipped to the State Public Health Laboratory.
- Specimen is tested for multiple conditions.

2: FOLLOW-UP

- Positive screen results are reported by phone/ fax/letter from lab and follow-up staff to baby's physician. Results are also sent to the appropriate Genetic Tertiary Center in Missouri for follow-up.

- Specimen screening results are entered into data system.
- Baby's physician or health care provider contacts baby's parents.

- Parents bring baby back in for evaluation and more testing at the genetic center.

3: DIAGNOSIS/ INTERVENTION

- Depending on the screen result and the condition screened, repeat or confirmatory testing occurs at the genetic center.

- Parent education for signs/symptoms to watch for is conducted.

- Baby's physician consults with the specialist appropriate to the condition.

4: TREATMENT & MANAGEMENT

- Once diagnosis is made, treatment begins. For some life-threatening conditions, treatment may occur prior to diagnosis – on the recommendation of a specialist.

- Parents receive treatment guidelines/ education. Team support services as appropriate, include:
  - Metabolic dietitian monitoring and consultation
  - Ongoing blood monitoring
  - Referral to early intervention services
  - Pulmonary/CF services
  - Pediatriac endocrine monitoring
  - Pediatric hematology monitoring
  - Genetic counseling and consideration of family testing
  - Other allied health services as needed

Missouri Newborn Hearing Screening

The Centers for Disease Control and Prevention (CDC) recommends that all infants be screened for hearing loss by one month of age. Infants who screen positive for hearing loss should receive an audiologic evaluation by 3 months of age, and infants with confirmed hearing loss should receive early intervention services by 6 months of age.

Provisional 2009 calendar year data for Missouri show:

- 78,631 live births
- 76,526 (97.3 percent) infants screened for hearing loss by one month of age
- 1,311 (1.6 percent) infants screened after 1 month of age
- 1,208 infants failed their final screening (857) or missed a screening (351)
- 438 (51.1 percent) infants that failed their final screening received audiologic evaluation by 3 months of age
- 44 infants diagnosed with a permanent hearing loss
- 30 (68.1 percent) infants received early intervention services by 6 months of age

Note: This data was obtained Aug. 20, 2010, and is subject to change because the process of collecting and analyzing the data is ongoing.

In an effort to reduce loss to follow-up after failure to pass the newborn hearing screening, the Missouri Newborn Hearing Screening Program (MNHSP) expanded a pilot project designed to reduce loss to follow-up after a "refer" result. The program was initiated on July 1, 2008. Pemiscot Memorial Hospital and Twin Rivers Regional Medical Center hearing screening programs agreed to use a script to inform parents of non-passing results and to explain the importance of returning for another screening or for an audiologic evaluation. Additionally, the hospitals made follow-up appointments for these families.

The MNHSP made reminder phone calls to the families prior to the appointment date and sent a letter of notification to each baby's physician. In the summer of 2009, the MNHSP recruited four additional hearing screening programs representing varying sizes and locations: Barnes-Jewish Hospital, Fitzgibbon Hospital, Lake Regional Health Systems and Texas County Memorial Hospital. By the end of 2009, all but one screening program showed reductions in their loss to follow-up rates.

The Centers for Disease Control and Prevention recommends that all infants be screened for hearing loss by one month of age.

In 2009, the MNHSP applied for and received supplemental grant funding from the Health Resources and Services Administration (HRSA) to reduce loss to follow-up by expanding the MOHear Service Coordination joint Missouri Department of Health and Senior Services/Missouri Department of Elementary and Secondary Education (DESE) project. Prior to receiving the additional funding, the MOHear program consisted solely of one hearing loss professional, known as a MOHear, in the western part of the state who assisted the DESE First Steps program in the provision of service coordination to families with an infant recently diagnosed with a permanent hearing loss.

More than 97 percent of newborns in Missouri were screened for hearing loss by one month of age.

In addition to expanding coverage of specialized service coordination in conjunction with the DESE First Steps program, the funding allowed adding resolution of loss to follow-up cases following a refer result or a missed screening to the role of the MOHear. The Department of Health and Senior Services established a contract with Missouri State University (MSU) to establish a program of loss to follow-up coordination and specialized service coordination known as the MOHear Project.

The loss to follow-up component of the project allows for assignment of a MOHear to a region of the state to determine the best way to reduce and reverse the lost to follow-up rates including, but not limited to, setting up screening clinics and providing screenings for those who have failed to return for a rescreening or who missed their screening. Tactics will vary based upon the needs of the community.

In 2009, MSU recruited five MOHears and evaluated loss to follow-up trends in Missouri. MSU concluded that loss to follow-up is a hospital-based issue and, therefore can be addressed by working with specific hospitals. By the end of 2009, plans were in place to provide the new MOHears with education and training needed to meet the goals of the new project.

The specialized service coordination component of the MOHear Project continued in 2009. Working in the western half of the state, the MOHear visited six families in their homes in conjunction with a First Steps service coordinator and acted as a resource person for one primary care physician as well as through phone and email contact.

In conjunction with MSU, the MNHSP surveyed families of infants born in Missouri who failed their initial newborn hearing screening between November 2008 and May 2009. Babies selected for inclusion in the survey did not have any risk factors for hearing loss. Key programmatic findings included:

- 65 percent of the respondents reported that the birth hospital provided them with written information about newborn hearing screening.
- 74 percent of the respondents reported that the birth hospital notified them of the screening result.
- 60 precent of the respondents reported they received an explanation of the importance of early detection. An additional 14 percent were neutral on this question.
- 65 percent of respondents were satisfied with the hearing screening process. An additional 12 percent were neutral.

The authors of the survey, Letitia White, Ph.D. and Brittany Day, sought to examine the effects of parental anxiety on follow-up time after a failed newborn hearing screening. Results indicated that parental anxiety influenced the speed with which families sought follow-up. Families that felt higher degrees of anxiety were more likely to follow-up within

three months, compared to families that did not feel anxious about the screening results. Of the families that did not follow-up within three months, some reported that they did not know who to call to get a follow-up appointment. Additionally, many families reported that they were told after the initial hearing screen that it was unlikely that their baby had a hearing loss. These results suggest that the information provided during the counseling process is important with regards to the timeliness with which families seek follow-up. Families must understand the importance of timely follow-up and should not be given the impression that their baby does not have a hearing loss, even though they failed the newborn screen. Further, a certain amount of anxiety appears to motivate families to follow-up in a timely manner.

Next Steps

The MNHSP will continue to monitor the success of the hospital hearing screening pilot program. If loss to follow-up remains low, the MNHSP will expand the program statewide.

The MOHear Project will go forward in full force in 2010. Following training, the MOHears will begin their regional work in both loss to follow-up management and service coordination. MOHears will work with the hospitals determined to have the highest loss to follow-up rates in their assigned region. Additionally, to launch the statewide availability of MOHear assistance to First Steps service coordination, the MOHear Project will make phone calls, provide written information and offer to speak about the MOHear project at First Steps System Point of Entry (SPOE) offices. Also, when referring a child with hearing loss to the First Steps SPOE, the MNHSP will include a "MOHear Checklist" that will provide the First Steps Service Coordinator with the contact information of the MOHear who works in the child's region. This step will ensure the SPOE knows who to contact for assistance.

Newborn Screening Contact Information

Telephone Contacts:

Newborn Screening Laboratory main number	573-751-2662
Order newborn screening specimen forms; person	573-751-3334
Order newborn screening specimen forms; automated attendant	573-522-4991, Ext. 3226
Genetics and Healthy Childhood, for follow-up information	1-800-877-6246

Web Addresses:

Newborn Screening Laboratory – http://www.dhss.mo.gov/Lab/Newborn/index.html

Newborn Screening Program – http://www.dhss.mo.gov/NewbornScreening/

Newborn Hearing Screening Program – http://www.dhss.mo.gov/NewbornHearing/

Appendix 1: Disorders Confirmed for 2009 and Projected Incidence Rates

DISORDER	DIAGNOSIS CONFIRMED AS POSITIVE AND UNDER MEDICAL CARE	PROJECTED INCIDENCE RATE
Amino Acid Disorders	**6**	**1/8,000***
Arginemia		
Argininosuccinate acidemia		
Citrullinemia type I	1	
Citrullinemia type II		
Defects of biopterin cofactor biosynthesis		
Defects of biopterin cofactor regeneration		
Homocystinuria		
Hypermethioninemia		
Hyperphenylalaninemia	1	
Hyperphenylalaninemia, benign	2	
Maple syrup urine disease		
Maternal PKU		
Phenylketonuria (PKU)	2	1/15,000
Tyrosinemia type I		
Tyrosinemia type II		
Tyrosinemia type III		
Biotinidase Deficiency	**18**	**1/40,000**
Classical galactosemia (GALT)	**2**	**1/50,000**
Congenital adrenal hyperplasia (CAH)	**3**	**1/13,000**
Congenital primary hypothyroidism (CH)	**38**	**1/3,000**
Cystic fibrosis (CF)	**25**	**1/4,000**
Fatty Acid Oxidation Disorders	**17**	**1/10,000***
Carnitine acylcarnitine translocase deficiency		
Carnitine uptake deficiency	3	
Carnitine palmitoyl transferase deficiency I		
Carnitine palmitoyl transferase deficiency II	1	
Dienoyl-CoA reductase deficiency		
Glutaric academia type II		
Long-chain hydroxyacyl-CoA dehydrogenase deficiency	1	
Medium-chain acyl-CoA dehydrogenase deficiency	7	
Medium-chain ketoacyl-CoA thiolase deficiency		
Medium/Short chain L-3 hydroxy acyl-CoA dehydrogenase deficiency		
Short-chain acyl-CoA dehydrogenase deficiency	3	
Trifunctional protein deficiency		
Very-long chain acyl-CoA		

DISORDER	DIAGNOSIS CONFIRMED AS POSITIVE AND UNDER MEDICAL CARE	PROJECTED INCIDENCE RATE
dehydrogenase deficiency	2	
Organic Acid Disorders	**10**	**1/25,000***
2-Methyl-3-hydroxybutyric aciduria		
2-Methylbutyryl-CoA dehydrogenase deficiency		
3-Hydroxy 3-methylglutaric aciduria		
3-Methylcrotonyl-CoA carboxylase deficiency	2	
3-Methylglutaconic aciduria		
Beta ketothiolase		
Glutaric acidemia, type I		
Isobutyryl-CoA dehydrogenase deficiency		
Isovaleric acidemia	1	
Malonic acidemia		
Methylmalonic acidemia (CBL A,B; vitamin B12 disorders)		
Methylmalonic acidemia (CBL, C,D)	2	
Methylmalonic acidemia (MUT, methylmalonyl-CoA mutase)		
Multiple carboxylase deficiency		
Propionic acidemia	1	
Forminioglutamic acid (FIGLU) not a disorder on the newborn screening panel but is found	3	
Secondary aciduria, undetermined metabolic disorder	1	
Hemoglobinopathies	**47**	**1/1,700***
Sickle cell anemia disease (Hb S/S)	22	**1/3,000** Total population **1/400** African-American population
Sickle hemoglobin-C disease (FSC)	16	
Sickle beta zero thalassemia disease		
Sickle beta plus thalassemia disease (FSA)	3	
Sickle hemoglobin-D disease		
Sickle hemoglobin-E disease		
Sickle hemoglobin-O-Arab disease		
Sickle hemoglobin Lepore Boston disease		
Sickle HPFH disorder		
Sickle “Unidentified”		
Homozygous-C disease (FC)	2	
Hemoglobin-C beta zero thalassemia disease		
Hemoglobin-C beta plus thalassemia disease		
Homozygous-E disorder (FE)	2	
Hemoglobin-E beta zero thalassemia disease		
Hemoglobin-E beta plus thalassemia disease		
Homozygous beta zero thalassemia disease	1	
Double heterozygous beta thalassemia disease		

DISORDER	DIAGNOSIS CONFIRMED AS POSITIVE AND UNDER MEDICAL CARE	PROJECTED INCIDENCE RATE
Hemoglobin-H disease (Highly Elevated Barts)		
Other (FSX) compound heterozygous Hb S and G-Taipei	1	

* Combined incidence of all disorders in this category.

Appendix 2: Newborn Screening Laboratory Report – Specimens Received 2009

	Newborn Specimens Received			
	Initial	Repeat	Unsatisfactory	Total Infant Specimens
Jan	6,188	722	99	7,009
Feb	5,977	653	99	6,729
Mar	6,803	809	92	7,704
Apr	6,443	721	71	7,235
May	6,339	659	66	7,064
Jun	7,014	706	89	7,809
Jul	6,992	815	105	7,912
Aug	6,465	760	122	7,347
Sep	7,426	814	103	8,343
Oct	6,562	829	119	7,510
Nov	5,817	737	96	6,650
Dec	6,852	908	158	7,918
Y.T.D.	**78,878 (88.40%)**	**9,133 (10.24%)**	**1,219 (1.37%)**	**89,230**

Appendix 3: Newborn Screening Laboratory Report – Abnormal Results 2009

Disorder		Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Y.T.D.
BIO*	Confirmed	3	1	3	1	2	0	1	1	1	1	2	2	**18**
	Referred	3	1	4	3	2	3	1	2	1	2	2	2	**26**
CAH	Confirmed	0	0	1	0	0	0	1	0	0	0	1	0	**3**
	High Risk	13	5	9	11	3	9	16	3	12	1	2	1	**85**
	Borderline Risk	25	19	29	29	43	40	41	25	35	26	28	43	**383**
CF	Confirmed	2	1	1	1	0	8	5	1	2	1	1	2	**25**
	Referred	12	5	7	11	7	11	5	3	7	9	7	11	**95**
CH	Confirmed	2	1	2	2	6	3	3	4	3	6	0	6	**38**
	High Risk	4	2	4	4	6	3	3	4	3	6	1	6	**46**
	Borderline Risk	63	83	62	62	55	60	54	54	46	56	61	107	**763**
GAL	Confirmed	0	0	0	0	0	0	0	0	1	0	1	0	**2**
	High Risk	2	2	4	0	1	7	4	5	9	3	3	1	**41**
	Borderline Risk	9	11	6	7	9	20	18	22	20	11	7	6	**146**
AA	Confirmed	1	1	0	0	0	2	1	0	0	0	0	1	**6**
	High Risk	1	1	0	0	1	1	0	0	0	0	0	1	**5**
	Moderate Risk	2	0	1	1	0	0	1	2	3	0	1	5	**16**
	Low Risk	55	61	60	53	43	55	69	57	75	55	53	77	**713**
OA	Confirmed	1	0	1	3	0	0	0	1	0	1	1	2	**10**
	High Risk	0	1	0	2	0	0	1	0	0	1	1	0	**6**
	Moderate Risk	3	0	4	3	1	2	1	0	3	4	1	6	**28**
	Low Risk	25	41	28	23	33	29	28	18	15	23	25	28	**316**
FA	Confirmed	0	1	2	1	3	1	1	4	1	1	0	2	**17**
	High Risk	0	1	0	1	0	0	1	2	1	1	0	2	**9**
	Moderate Risk	1	0	4	0	3	3	1	5	4	4	3	2	**30**
	Low Risk	25	33	29	32	17	17	19	23	42	39	41	73	**390**

continued

Disorder		Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Y.T.D.
Hb*	Sickle Cell Disease	4	5	4	1	4	3	2	5	4	5	3	1	**41**
	Other Hemoglobinopathies	2	1	0	1	0	0	1	1	0	0	0	0	**6**
	Abnormal Traits	147	136	143	121	130	149	145	144	158	154	105	147	**1679**
												Total Confirmed		**166**

BIO = biotinidase
CF = cystic fibrosis
GAL = galactosemia
OA = organic acid
Hb = hemoglobinopathies
CAH = congenital adrenal hyperplasia
CH = congenital hypothyroidism
AA = amino acid
FA = fatty acid

*See Appendix 5 for further hemoglobinopathy results.

Average laboratory turnaround times from receipt of specimen to reporting are:

Results	Turnaround Times
High Risk Result*	30 hours
Low/Borderline Risk**	3 - 4 days
Normal Result **	3 - 4 days

* the result is telephoned and faxed to the physician of record
** hard copy reports are mailed to the physician of record and the submitting facility; final abnormal results are also included in this category

Outcome Data - Newborn Screening Specimens and Results

- In 2009 there were 78,878 initial specimens tested in the state newborn screening laboratory. There were a total of 89,230 blood spot specimens received in the laboratory. Specimens received included:

Initial	Repeat	Poor Quality Specimens
78,878	9,133	1,219

- In the process of screening newborns for 66 genetic and metabolic conditions, it is the newborn screening laboratory's role to assess the risk of any abnormal screening results by evaluating the marker analytes present and the levels that were detected. This risk assessment then dictates different levels of action and follow up protocols. The three categories of risk and the number of test results falling in these categories during 2009 were:

High Risk	Moderate Risk	Low/Borderline Risk
360 (0.46%)	54 (0.07%)	2,711 (3.4%)

High Risk - Results are immediately phoned and faxed to the physician of record and to the contracted genetic referral centers for consultation and confirmatory testing. Final laboratory reports are mailed to the facility that submitted the specimen and the physician of record.

Moderate Risk - Results are immediately phoned and faxed to the physician of record and to the contracted genetic referral centers for consultation and confirmatory testing. Final laboratory reports are mailed to the facility that submitted the specimen and the physician of record.

Low/Borderline Risk – Final laboratory results are mailed to the physician of record and submitting facility and a repeat newborn screen is necessary.

- One hundred sixty-six (166) confirmed disorders were diagnosed from these abnormal newborn screening results during 2009.

Appendix 4: 2009 Poor Quality Samples

INCOMPLETE SATURATION: Uneven saturation; blood did not soak through the filter paper. Possible causes: Removing filter paper before blood has completely filled circle or before blood has soaked through to opposite side; improper capillary tube application; allowing filter paper to come in contact with gloved or ungloved hands or substances such as hand lotion or powder, either before or after blood specimen collection.	348
LAYERED CLOTTED OR SUPERSATURATED: Possible causes: Touching the same circle on filter paper to blood drop several times; filling circle on both sides of filter paper; application of excess blood; clotted swirl marks from improper capillary application.	304
DILUTED, DISCOLORED OR CONTAMINATED: Possible causes: Squeezing or milking of area surrounding the puncture site; allowing filter paper to come in contact with gloved or ungloved hands, or substances such as alcohol, formula, antiseptic solutions, water, hand lotion, powder, etc., either before or after blood specimen collection; exposing blood spots to direct heat; allowing blood spots to come in contact with tabletop, etc. while drying the sample.	287
QUANTITY NOT SUFFICIENT: Quantity of blood on filter not sufficient for testing. Possible causes: Removing filter paper before blood has completely filled circle; not allowing an ample sized blood drop to form before applying to filter; inadequate heel stick procedure.	104
BLOOD ON OVERLAY COVER: Overlay cover came in contact with wet blood specimen. Possible causes: Sample is poor quality status because blood soaked from back of filter onto the gold colored backing of the form. The filter circles are designed to hold a specific quantity of blood. If the wet filter is allowed to come in contact with the paper backing of form, blood can be drawn out of filter making the quantitative tests performed by the Newborn Screening Laboratory invalid. It is very important that the wet filter paper does not come in contact with any surface until completely dry.	78
SPECIMEN ABRADED: Filter scratched, torn or abraded. Possible causes: Improper use of capillary tubes. To avoid damaging the filter paper fibers, do not allow the capillary tube to touch the filter paper. Actions such as "coloring in" the circle, repeated dabbing around the circle, or any technique that may scratch, compress, or indent the paper should not be used.	58
OLD SPECIMEN: Specimen greater than 15 days old when received at State Public Health Laboratory.	17
SERUM RINGS: Serum separated into clear rings around blood spot. Possible causes: Card dried vertically (on side) instead of flat; squeezing excessively around puncture site; allowing filter paper to come in contact with alcohol, hand lotion, etc.	8
OTHER UNSUITABLE	5
FILTER AND FORM BARCODES DO NOT MATCH: Barcode on filter does not match barcode on Newborn Screening Form. Collection forms contain barcodes on demographic, hearing and filter portions. The barcodes may not be altered in any way. If incorrect baby is sampled do not remove filter and attach to a different demographic portion. If a sampling error occurs the entire form needs to be voided and sample needs to be recollected on a new form. All barcodes must match laboratory copy, submitter copy, newborn hearing screen, and filter.	3
NO BLOOD: Filter submitted without blood.	2
OLD FORM: Sample received on out-of-date form.	2
MISSING OR INCOMPLETE PATIENT INFORMATION: Missing or incomplete demographic information.	2
LABORATORY ACCIDENT: Unable to test; sample damaged at laboratory.	1
Total Poor Quality Specimens Received	1,219 (1.37%)

Specimens Received:

Initial:	78,878	(88.2%)
Repeat:	9,133	(10.2%)
Unsatisfactory:	1,219	(1.4%)
Whole Blood:	232	(0.3%)
Total:	**89,462**	

Analyses (Tests) Performed:	IEF	HPLC	Total
First Tests:	89,230 (81.3%)	-	89,230 (74.8%)
Retests:	4,429 (4.0%)	4,939 (52.0%)	9,368 (7.9%)
Controls/Standards:	15,790 (14.4%)	4,228 (44.5%)	20,018 (16.8%)
Proficiency Testing:	41 (0.0%)	40 (0.4%)	81 (0.1%)
Whole Blood Tests:	260 (0.2%)	293 (3.1%)	553 (0.5%)
Total:	**109,750**	**9,500**	**119,250**

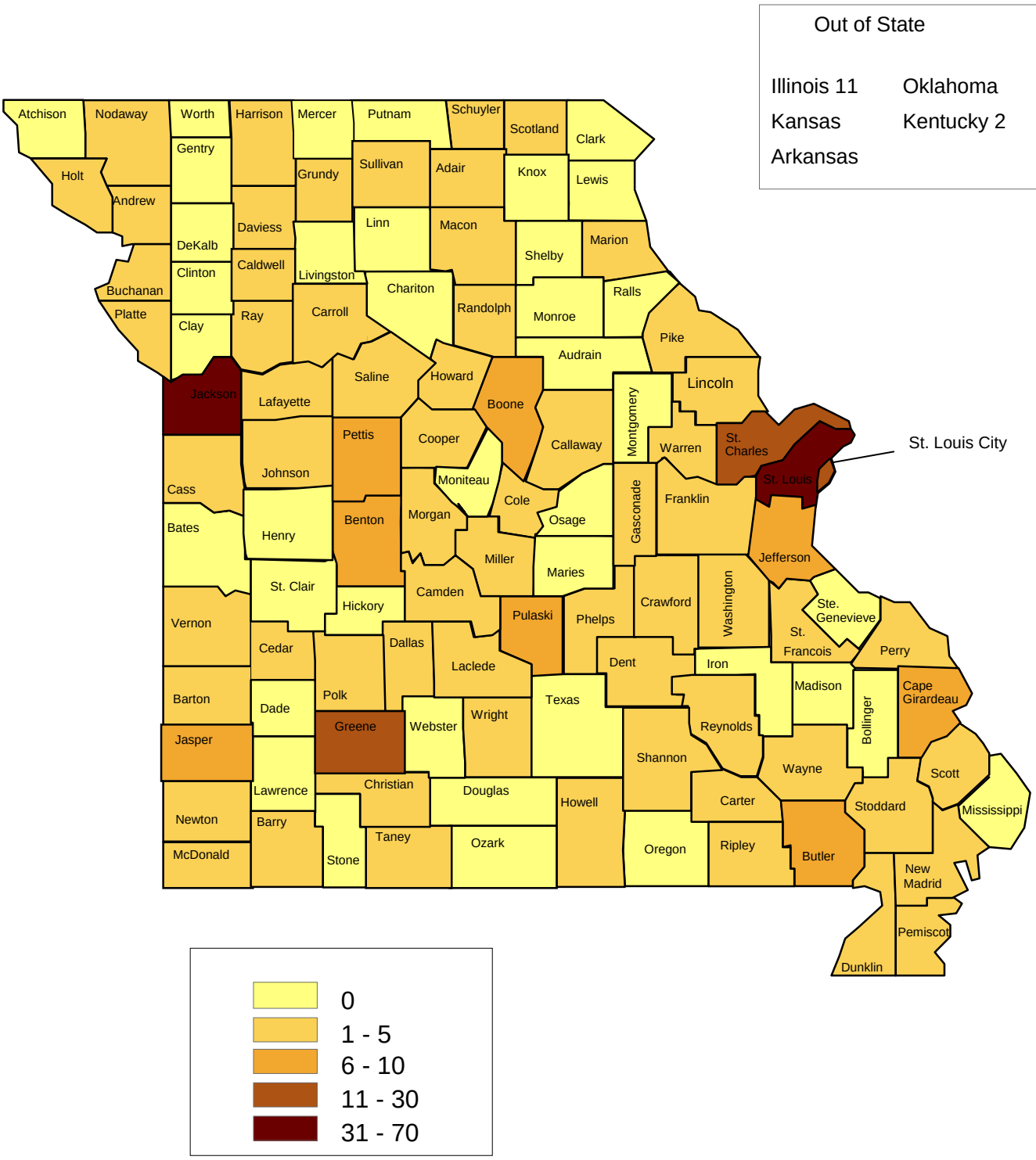
Significant Screening Results = 1,726					
Sickle Cell Disease*		**Other Disease Conditions***		**Trait Conditions**	
FS	22	FC	2	FAS	1021
FSC	16	FE	2	FSAINC	86
FSA	3	F-Only	1	FAC	322
		FSX	1	FCAINC	20
				FAE	40
				FAD	35
				FAX	141
				FACX	5
				Slightly Elevated Barts	6
				Other Trait Condition	3
Total	**41* (2.4%)**	**Total**	**6* (0.3%)**	**Total**	**1,679 (97.3%)**

*Total of 47 possible disease conditions were confirmed.

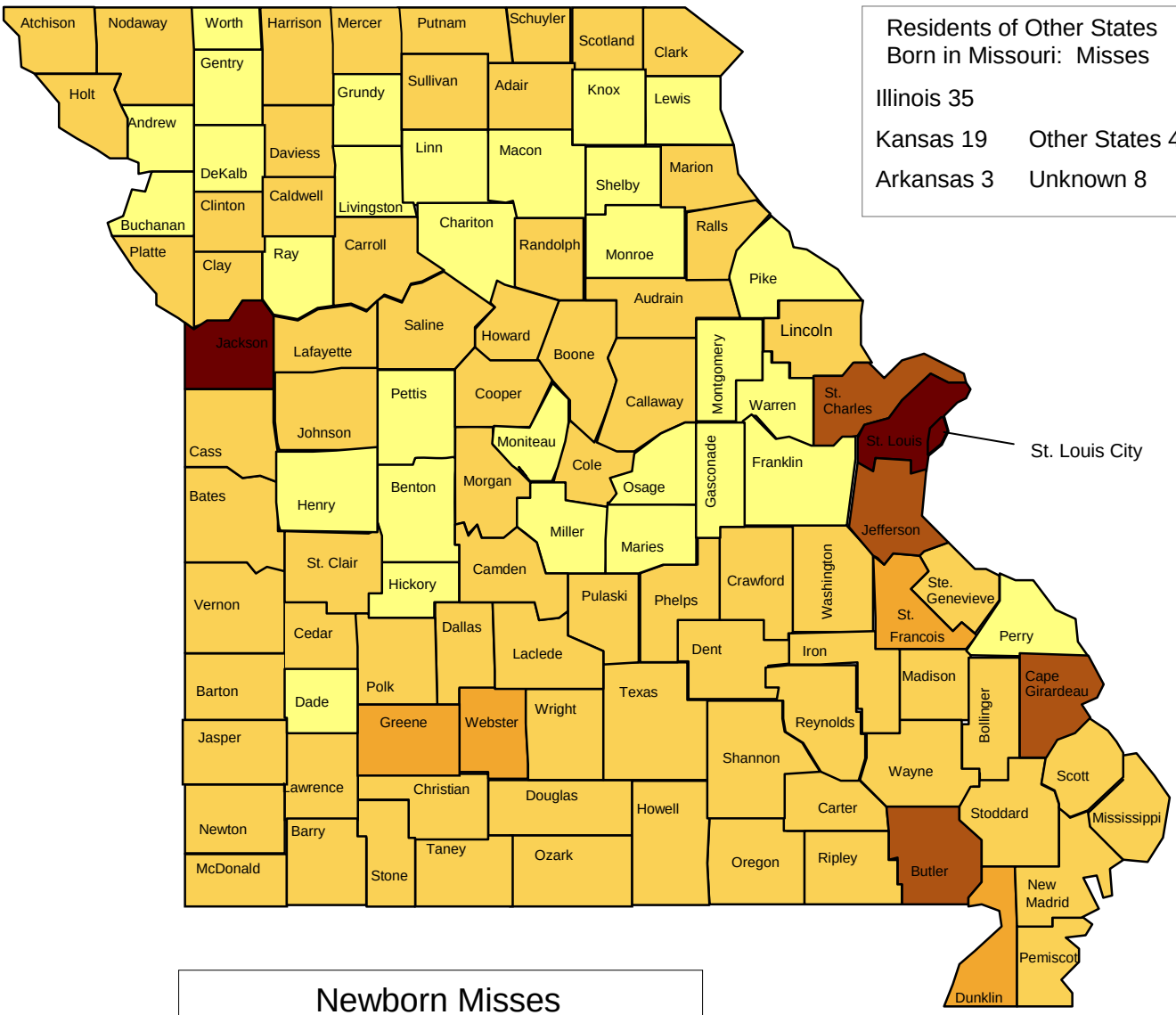
Geographic Follow-up of Significant Disease and Trait Conditions					
Significant Disease Conditions			**"S" Trait Conditions Only (includes repeats)**		
St. Louis Area	29	61.7%	St. Louis Area	670	54.5%
Kansas City Area	14	29.8%	Kansas City Area	357	29.1%
Remainder of MO	4	8.5%	Remainder of MO	202	16.4%
Total	**47****	**100%**	**Total**	**1229**	**100%**

** See Appendix 1.

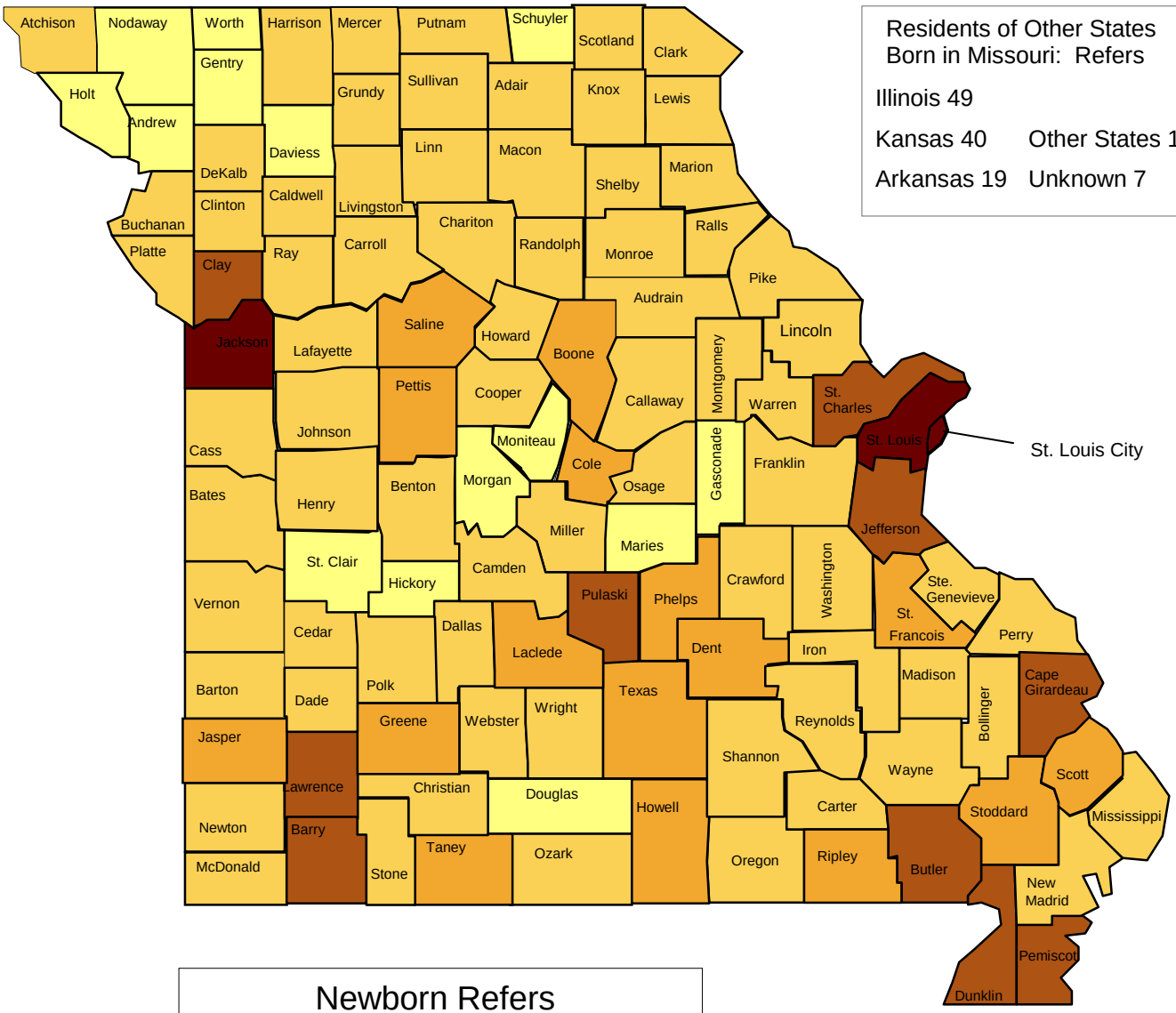
Appendix 6: 2009 Referrals from Missouri Newborn Bloodspot Screening Program



Appendix 7: 2009 Initial Misses from Missouri Newborn Hearing Screening



Appendix 8: 2009 Initial Refers from Missouri Newborn Hearing Screening



Appendix 9: Newborn Screening Satisfaction Surveys

A satisfaction survey of parents was conducted for families of babies having abnormal newborn screening results reported in 2009. Key findings:

Newborn Screening Parent Satisfaction Survey - Parent Response				
	Very Satisfied	Satisfied	Not Satisfied	No Response
Explanation of abnormal tandem mass spectrometry results	75%	25%		
Timeliness on notification of abnormal tandem mass spectrometry screen results	87.5%	12.5%		
Number of follow-up tests or newborn screen results done to determine diagnosis	87.5%			12.5%
Timeliness of follow-up tests and/or newborn screen	75%		25%*	
Answers to parents' questions about the disorders screened and testing methodology	100%			

* Two families had to wait two weeks each to be seen by a genetics professional. Explanation of the two week wait was not stated by the parents.

A satisfaction survey of parents of infants and children receiving services provided by the hemoglobinopathy resource centers was completed in 2007. Key findings:

Hemoglobinopathy Resource Center Satisfaction Survey - Parent Response			
	Very Satisfied	Satisfied	Not Satisfied
Treated with respect	88%	12%	0%
Treatment staff was knowledgeable	86%	14%	0%
Questions/concerns addressed in a timely manner	83%	17%	0%
Staff provided useful referrals and resources	81%	19%	0%
Provided with the services needed	83%	17%	0%
Medical care/services received	78%	22%	0%
Received services or treatment without experiencing any problems	99%	0%	1%*

* Only one response was given for "not satisfied" in the above parent survey: *"Nursing staff and doctors are not nice, sometimes talking to you as if you don't know what you are speaking of."*

Appendix 10: Newborn Hearing Screening Survey

A satisfaction survey of parents of children born in Missouri who failed their initial newborn hearing screening between November 2008 and May 2009 was completed in June 2009. The survey was done in conjunction with a survey written by Letitia White, Ph.D. and Brittany Day designed to examine factors influencing follow-up time after a failed newborn hearing screening for babies in Missouri.

Key findings:

- 77 percent of respondents were satisfied or neutral with the newborn hearing screening process.
- 74 percent of the respondents reported that the birth hospital notified them of the screening result.
- 65 percent of the respondents reported that the birth hospital provided them with the newborn hearing screening program brochure.

Other Results:

- Respondents reported a high level of anxiety when being informed of the results of the initial hospital hearing screening and concerning the retest. Those that reported higher anxiety levels were more likely to follow up in a timely manner.
- Families that felt higher degrees of anxiety were more likely to follow up within three months, compared to families that did not feel anxious about the screening results.
- Of the families that did not follow up within three months, many reported that they did not know who to call to get a follow-up appointment or that they were told that it was unlikely that their baby had a hearing loss.

Missouri Department of Health and Senior Services
P.O. Box 570
Jefferson City, MO 65102
www.dhss.mo.gov