MISSOURI
NEWBORN SCREENING

2012 Annual Report



Missouri Department of Health and Senior Services

Governor Jay Nixon
Gail Vasterling, 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.

This project was/is supported by the Health Resources and Services Administrative (HRSA) of the U.S. Department of Health and Human Services (HHS) under grant number and title for grant amount H61MC00071, Universal Newborn Hearing Screening, $255,604.00, 0.0% financed with nongovernmental sources. This information or content and conclusions are those of the author and should not be construed as the official position or policy of, nor should any endorsements be inferred by HRSA, HHS or the U.S. Government.

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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
Missouri State Public Health Laboratory

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What is Newborn Screening?

Newborn screening is a public health program aimed at the early identification of conditions and the timely intervention by health care providers. This early identification and timely intervention is needed 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 and before symptoms appear.

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 tissue. 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.

A small sample of blood is collected from the newborn within 24 to 48 hours of birth and sent to the Missouri Department of Health and Senior Services' State Public Health Laboratory for testing. If newborn screening results are out of the normal range, also known as an abnormal screen, the family will be contacted for further testing of the baby's blood. If a baby is confirmed to have one of the diseases found through newborn screening, specialists will formulate a plan of medical management that allows most affected newborns to develop normally.

Another newborn screening is hearing screening. This is usually done at the hospital prior to hospital discharge. This screen is 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 screen are provided immediately. The results tell the health care staff if further screening or an audiological assessment might be necessary.

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.

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 NBS Laboratory website at: http://health.mo.gov/lab/newborn.

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

Screening Spotlight: DNA Analysis Enhances Newborn Screening for Cystic Fibrosis at the Missouri State Public Health Laboratory

In 2012, the Newborn Screening Laboratory (NBSL) added a second tier DNA mutation assay that significantly increased sensitivity and specificity for the cystic fibrosis (CF) screen. This screening test, which had been the NBSL's greatest challenge in newborn screening (NBS) at the Missouri State Public Health Laboratory (MSPHL) for the last five years, has now advanced to the cutting edge.

Cystic fibrosis (CF) is a life-threatening inherited disease of the mucus and sweat glands. It affects mostly the lungs, pancreas, liver, intestines, sinuses, and sex organs. CF causes the mucus to be thick and sticky. The mucus clogs the lungs causing breathing problems and making it easy for bacteria to grow. This can lead to problems such as repeated lung infections and lung damage.

The symptoms and severity of CF vary widely. Some people have serious problems from birth. Others have a milder version of the disease that does not show up until they are teens or young adults. Symptoms of CF include: very salty-tasting skin; persistent coughing, at times with phlegm; frequent lung infections; wheezing or shortness of breath; poor growth and slow weight gain, in spite of a good appetite; and frequent greasy, bulky stools or difficulty in bowel movements.

There is no cure for CF, but treatments have greatly improved in recent years. Until the 1980s, most deaths from CF occurred in children and teenagers. Today, with improved treatments, some people who have CF are living into their forties, fifties, or older.

Facts about Cystic Fibrosis:

- Cystic fibrosis has an average prevalence of 1 in 3,000 (Missouri incidence), and 1 in 25 Caucasians are carriers of the CF gene.
- Infants with CF need to be screened, diagnosed, and started on treatment within two months to help prevent the onset of illness.
- Early detection and management of CF reduces hospitalizations and significantly improves growth, health, and longevity.
- One of the strongest benefits of screening newborns for CF is preventing malnutrition. Malnutrition, or failure to thrive, is usually the first symptom to appear and sets the stage for all the other complications to follow close behind.
- Before newborn screening for CF, parents and physicians could spend many months trying to figure out a cause for the child's chronic illnesss. By the time the child was finally diagnosed, significant health problems had already begun.
- Since newborn screening for CF has been instituted in the U.S., some people with CF are well into their third decade of life and have remained healthy. Before newborn screening, most of these individuals would have died before reaching middle school age, and this after many years of illness and specialized health care.

Former Cystic Fibrosis Screening Algorithm in Missouri using Immuno-Reactive Trypsinogen (IRT)
Missouri has been screening every newborn for CF since January 2007 using the IRT/IRT screening algorithm. Immuno-Reactive-Trypsinogen (IRT) is the biochemical analyte that is secreted from the pancreas and is elevated at birth in babies with CF. There are other adverse physiological conditions that can also cause an elevation in the IRT, but it has been proven that persistent IRT elevation, or two subsequent NBS with elevated IRT, puts the infant at high risk of having CF. Consequently, if the NBSL detected an IRT elevation on a NBS, a repeat screen after one week of age was required. If the repeat screen also had an elevated IRT, hence IRT/IRT, the infant was referred to a Cystic Fibrosis Foundation accredited CF center for a sweat chloride analysis, or "sweat test". The sweat test is the "gold standard" diagnostic test for CF.

Problems with the IRT/IRT algorithm
Although the IRT/IRT protocol was the only screening test available in the early years, and is often the algorithm that many states (including Missouri) have used to start their CF screening, this algorithm has its draw backs. The IRT/IRT method has a high rate of false positives and, at the same time, a few undetected cases of CF have occurred. It is a balancing act for states to choose an IRT cutoff level that does not completely overwhelm their follow-up with referred cases while frightening too many parents, yet at the same time does not miss true CF cases. This is complicated by the fact that the IRT analyte has one of the highest imprecision records of all the NBS analyte markers. Another issue is that there is a problematic time-lag between the first abnormal IRT and obtaining the repeat screen and consequently a diagnosis. Of the babies that need repeat screens to re-check the IRT level, 4% fail to repeat the NBS and need to be tracked and the parent educated on the need to repeat the NBS. Missouri was one of 12 states in the country that still utilized the IRT/IRT screening process. The majority of these states using IRT/IRT mandate universal repeat screening on all their newborns by law, meaning all babies get a second NBS at one to two weeks of age, so the laboratory is confident of receiving a repeat screen for every newborn.

Benefits of utilizing second tier DNA (aka the IRT/DNA algorithm)
The problems with the IRT/IRT algorithm are virtually eliminated by utilizing second tier DNA testing performed on the initial abnormal NBS samples. With the second tier DNA test, babies with initial screens displaying IRT elevations will be immediately assigned CF mutation testing to ascertain if the baby has one (carrier state) or two CF mutations (affected state) present. Even babies with one mutation are referred for sweat testing to rule out CF, since there are some rare mutations that may not be detectable in the second tier DNA panel. Adding the second tier DNA step allowed the NBSL to significantly increase sensitivity (reduce false negatives) by drastically lowering the IRT cutoff and at the same time tremendously increased specificity (reduce false positives) by ruling out those babies who have an elevated IRT but are not even a carrier.

Parental anxiety experienced from false positive screens has been reduced. The time from birth to diagnosis for CF has considerably decreased thereby greatly benefitting babies affected by CF. The vast majority of affected babies have immediate CF confirmation directly from the NBS blood spot allowing intervention and treatment to be significantly expedited, usually before 10 days of age. In addition, every baby that is referred to the CF center with one mutation is at least a carrier of CF, which allows the parents the opportunity to receive counseling and testing to determine their future risk of having children with CF. Not every CF carrier is detected through NBS because approximately 8% of carriers have an elevated IRT on their NBS; however detecting carriers is not the goal of newborn screening.

The 2nd tier DNA assay that the Missouri NBSL utilizes is a 40 mutation panel of the most common alleles that are seen in the general population. As stated earlier, if only one mutation is found, it does not eliminate the possibility of a second mutation. Over 1,800 mutations have been identified, albeit most of these are harmless. In addition, there are many unique or "family" mutations that are only seen in distinct families. Therefore, any baby with even one mutation is referred for confirmatory sweat testing to rule out CF.

The 2nd tier DNA testing went live on September 4, 2012 and is working very well. The Missouri NBS program, along with all the CF treatment centers in Missouri, are pleased with the addition of 2nd tier molecular testing to Missouri's CF screening process as it has significantly enhanced the sensitivity and specificity of NBS for CF.

Table of the 40 mutation panel utilized by the Newborn Screening Laboratory when an elevated IRT is detected in the primary screening test.

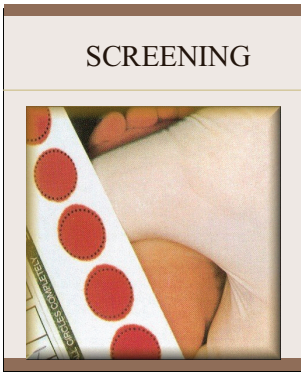
A455E*	R117H*	V520F	1898+1G>A*
delta508F*	R334W*	W1282X*	2183AA>G
delta507F*	R347H	Y122X	2184DELA*
D1152H	R347P*	Y1092XC>A	2789+5G>A*
E60X	R553X*	Y1092XC>G	3120+1G>A*
F508C	R560T*	394delITT	3659delC*
G85E*	R1162X*	621+1G>T*	3849+4A>G
G542X*	S549N	711+1G>T*	3849+10kbC>T*
G551D	S549R A>C	1078delIT	3876delA
N1303K*	S549R T>G	1717-1G>A*	3905insT
Q493X			

*Mutations recommended by the American College of Medical Genetics.

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.

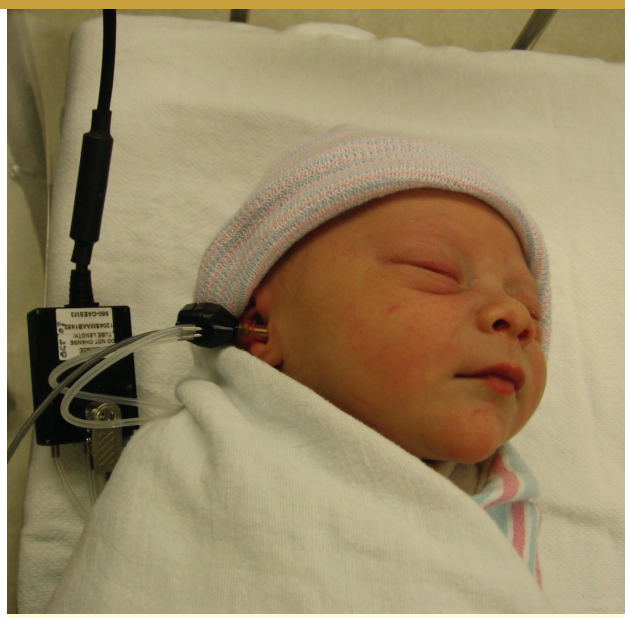
- Parents receive treatment guidelines/ education. Team support services as appropriate, include:
  - Metabolic dietitian monitoring and consultation
  - Ongoing blood monitoring
  - Referral to early intervention services
  - Pulmonary/CF services
  - Pediatriac endocrine monitoring
  - Pediatric hematology 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 1 month of age. Infants who screen positive for possible 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.

2012 calendar year data for Missouri show:

- 76,411 occurrent births (source: DHSS Vital Records)
- 76,202 occurrent births (source: Missouri Health Strategic Architectures and Information Cooperative [MOHSAIC]*)
- 97.9 percent (74,601) screened
- 98.02 percent (73,124) screened by 1 month of age
- 1.91 percent (1,431) failed the final screening
- 56.88 percent (814) of the infants that failed their final screening received audiologic evaluation by 3 months of age
- 100 infants diagnosed with a permanent hearing loss (four lived out-of-state)
- 66 enrolled in Missouri's Part C of the Individual with Disabilities Act (IDEA) program, First Steps
- 60.6 percent (40) of the infants enrolled in First Steps did so by 6 months of age



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

*The difference of 209 births between the occurrent birth count in the program data management system, the Missouri Health Strategic Architectures Information Collaborative (MOHSAIC), and the total occurrent births reported by Vital Records is the result of records that do not yet have an assigned Department Client Number (DCN) and sealed birth records. Records are not released from the Vital Records system to MOHSAIC until the DCN assignment is complete. Non-complete records are due to issues such as paternity and adoptions. Sealed birth records are not displayed or counted in MOHSAIC. This report is based upon MOHSAIC records.

In 2012, the Missouri Newborn Hearing Screening Program (MNHSP) follow-up coordinators (FUP) continued to track newborns through the early hearing detection and intervention (EHDI) process. FUPs continued to notify parents and primary care physicians of "missed" or "refer" (failure to pass the final screening) results and refer infants diagnosed with permanent hearing loss to Missouri's Part C IDEA program, First Steps. In an ongoing effort to reduce loss to follow-up, the MNHSP engaged in improvement activities using the Plan Do Study Act (PDSA) or "small tests of change" technique learned in the National Institute for Children's Health Quality (NICHQ) Collaborative in 2011.

The MNHSP made progress toward statewide electronic entry of initial hearing screening results with funding from a CDC grant. Three hospitals piloted the hearing screening result submission portion of the new Missouri Electronic Vital Records (MoEVR) system. By matching newborn hearing screening results to the birth certificate, the MNHSP will reduce duplicates in MOHSAIC and decrease the amount of time between the initial hearing screening and necessary follow-up by the FUPs.

Also in 2012, the MNHSP developed the document "Missouri Guidelines for Newborn Hearing Screening" and placed it on the DHSS website. The guidelines incorporate best practices related to newborn hearing screening and serve as a model for hospital newborn hearing screening programs.

More than 98 percent of newborns in Missouri were screened for hearing loss by one month of age.

Benchmark Reports, a summary of individual screening program statistics, were compiled and sent to all hospital screening programs by the MNHSP's audiologist consultant. Each report included a discussion of the availability of the MOHear Project to assist with technical difficulties - such as equipment breakdowns - and to supply training in screening techniques in order to reduce the "refer" rate and subsequent loss to follow-up.

The MNHSP arranged a Missouri parent meeting at the national EHDI meeting in St. Louis in March, 2012. Parent networking at that meeting grew into a Missouri Hands and Voices chapter with a "provisional" standing recognized by the national Hands and Voices organization. Hands and Voices is a national, non-profit organization dedicated to supporting families of children who are deaf or hard of hearing – regardless of communication methodologies. Hands and Voices membership includes families who communicate manually and/or orally.

The MNHSP MOHear Project continues to play an important role in the Missouri EHDI system. Funded by a Health Resources and Services Administration (HRSA) grant beginning in 2009, the MOHear Project consists of: 1) unbiased service coordination for families of newborns diagnosed with severe to profound permanent hearing loss; and 2) linkage of newborns to services by regionally-focused efforts at resolving loss to documentation and follow-up at each step of the early hearing detection and intervention process. The effort involves collaboration with the Missouri Department of Elementary and Secondary Education (DESE) and a contract with Missouri State University (MSU) for management of the MOHear Project.

Six professionals comprise the MOHear Project – one manager and five MOHears. The MOHears are professionals (either audiologist, educator of deaf, or speech pathologist) with expertise in the unique needs of infants with hearing loss. In collaboration with DESE's Part C of the IDEA program known as First Steps, System Point of Entry (SPOE) staff contact MOHears to participate in initial intake interviews with the families of infants recently diagnosed with a permanent hearing loss. MOHears offer information about communication modalities to parents based on the principle that parents make the best decisions for their children with hearing loss when they are fully educated about the options available to their child and that the best intervention service for a family is ultimately a family-driven choice. In 2012, SPOES utilized MOHears on 28 occasions. In 2012, the MNHSP added MOHear as an optional choice in the recommendation portion of the audiologic diagnostic form. With the family's permission, this change allows a MOHear to promptly contact family with a recently diagnosed infant with hearing loss.

The MOHears work at reducing loss to follow-up resulted in a steady decrease in loss to follow-up percentages. The loss to follow-up rate following an infant's final "refer" result decreased from 40.8 percent in 2010, to 34.8 percent in 2011, to 32.2 percent in 2012. Activities the MOHears engage in to resolve and prevent loss to

follow-up include the following: phone calls to families believed to be lost to follow-up, individual outpatient screenings, rescreening clinics, visits to hospitals to review procedures and conduct trainings, equipment loans, contact with audiology clinics in order to solicit recent diagnostics, and contact with physician offices to ensure correct screening procedures and reporting.

Next Steps

The MOHear Project will expand its outreach by meeting with SPOEs to explain the benefits of including a MOHear in the initial intake interviews. The MOHears will use PowerPoint presentations and informational packets to assist in the building of SPOE MOHear relationships.

Due to the success of hospital hearing screening program Benchmark Reports as an informational and teaching tool, the audiologist consultant will develop Benchmark Reports for audiology clinics and midwives.

The MNHSP will continue to engage in improvement activities using the NICHQ PDSA “small tests of change” technique. The MNHSP will seek to include external partners in the process.

Newborn Screening Contact Information

Telephone Contacts:

Newborn Screening Laboratory main number	573-751-2662
Order newborn screening specimen forms	573-751-3334
Genetics and Healthy Childhood, follow-up information	800-877-6246

Web Addresses:

Newborn Screening Laboratory – http://health.mo.gov/lab/newborn

Newborn Screening Program – http://health.mo.gov/newbornscreening

Newborn Hearing Screening Program – http://health.mo.gov/newbornhearing

Appendix 1: Disorders Confirmed for 2012 and Projected Incidence Rates

DISORDER	DIAGNOSIS CONFIRMED AS POSITIVE AND UNDER MEDICAL CARE	PROJECTED INCIDENCE RATE
Amino Acid Disorders	**9**	**1/8,000***
Arginemia		
Argininosuccinate acidemia		
Citrullinemia type I		
Citrullinemia type II		
Defects of biopterin cofactor biosynthesis		
Defects of biopterin cofactor regeneration		
Homocystinuria		
Hypermethioninemia	1	
Hyperphenylalaninemia	2	
Hyperphenylalaninemia, benign	1	
Maple syrup urine disease	1	
Maternal PKU		
Phenylketonuria (PKU)	4	
Tyrosinemia type I		
Tyrosinemia type II		
Tyrosinemia type III		
Biotinidase Deficiency (BIOT)	**15**	**1/5,500***
Partial biotinidase deficiency	12	
Profound biotindase deficiency	3	
Congenital adrenal hyperplasia (CAH)	**1**	**1/20,000**
Congenital primary hypothyroidism (CH)	**49**	**1/1,600**
Cystic fibrosis (CF)	**28**	**1/3,200**
Fatty Acid Oxidation Disorders	**25**	**1/5,000***
Carnitine acylcarnitine translocase deficiency		
Carnitine uptake deficiency		
Carnitine palmitoyl transferase deficiency I		
Carnitine palmitoyl transferase deficiency II		
Dienoyl-CoA reductase deficiency		
Glutaric academia type II		
Long-chain hydroxyacyl-CoA dehydrogenase deficiency		
Maternal carnitine uptake deficiency	1	
Medium-chain acyl-CoA dehydrogenase	13	

DISORDER	DIAGNOSIS CONFIRMED AS POSITIVE AND UNDER MEDICAL CARE	PROJECTED INCIDENCE RATE
deficiency		
Medium-chain ketoacyl-CoA thiolase deficiency		
Medium/Short chain L-3 hydroxy acyl-CoA dehydrogenase deficiency		
Short-chain acyl-CoA dehydrogenase deficiency	7	
Trifunctional protein deficiency		
Very-long chain acyl-CoA dehydrogenase deficiency	4	
Galactosemia (GALT)	**7**	**1/50,000****
Classical galactosemia	2	
Duarte galactosemia	5	
Krabbe Disease	**3**	**1/400,000*****
Genotype of unknown significance	2	
Krabbe unknown risk of onset	1	
Organic Acid Disorders	**5**	**1/9,000***
2-Methyl-3-hydroxybutyric aciduria		
2-Methylbutyryl-CoA dehydrogenase deficiency		
3-Hydroxy 3-methylglutaric aciduria		
3-Methylcrotonyl-CoA carboxylase deficiency		
3-Methylglutaconic aciduria		
Beta ketothiolase		
Glutaric acidemia, type I	1	
Isobutyryl-CoA dehydrogenase deficiency		
Isovaleric acidemia		
Malonic acidemia		
Methylmalonic acidemia (CBL A,B; vitamin B12 disorders)		
Methylmalonic acidemia (CBL, C,D)		
Methylmalonic acidemia (MUT, methylmalonyl-CoA mutase)		
Multiple carboxylase deficiency		
Propionic acidemia		
Forminioglutamic acid (FIGLU) not a disorder on the newborn screening panel but is found	4	
Hemoglobinopathies	**47**	**1/1,700***
Sickle cell anemia disease (Hb S/S)	21	**1/3,000** Total population **1/400** African-American population
Sickle hemoglobin-C disease (FSC)	16	

DISORDER	DIAGNOSIS CONFIRMED AS POSITIVE AND UNDER MEDICAL CARE	PROJECTED INCIDENCE RATE
Sickle beta zero thalassemia disease		
Sickle beta plus thalassemia disease (FSA)	1	
Sickle hemoglobin-D disease		
Sickle hemoglobin-E disease	1	
Sickle hemoglobin-O-Arab disease		
Sickle hemoglobin Lepore Boston disease		
Sickle HPFH disorder		
Sickle "Unidentified"		
Homozygous-C disease (FC)	1	
Hemoglobin-C beta zero thalassemia disease		
Hemoglobin-C beta plus thalassemia disease		
Homozygous-E disorder (FE)	4	
Hemoglobin-E beta zero thalassemia disease		
Hemoglobin-E beta plus thalassemia disease		
Homozygous beta zero thalassemia disease		
Double heterozygous beta thalassemia disease		
Hemoglobin-H disease (Highly Elevated Barts)	1	
Other (FSX) compound heterozygous Hb S and G-Taipei	2	

*****Combined incidence of all disorders in this category

**Incidence only for classical galactosemia

***Severe Infantile Krabbe based on New York's experience

Appendix 2: Newborn Screening Laboratory Report
Samples Received 2012

	Newborn Samples Received			
	Initial	**Repeat**	**Poor Quality**	**Total Infant Samples**
Jan	6,228	1,108	151	7,487
Feb	5,668	996	144	6,808
Mar	6,017	1,119	105	7,241
Apr	5,718	979	95	6,792
May	6,587	1,119	74	7,780
Jun	6,164	1,094	90	7,348
Jul	7,091	1,159	83	8,333
Aug	6,833	1,201	96	8,130
Sep	6,137	1,098	81	7,316
Oct	6,980	1,246	137	8,363
Nov	6,006	1,091	131	7,228
Dec	5,707	987	148	6,842
Y.T.D.	**75,136 (83.79%)**	**13,197 (14.72%)**	**1,335 (1.49%)**	**89,668**

Appendix 3: Abnormal Results 2012

Disorder		Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Y.T.D.
BIO	Confirmed	1	0	2	0	2	1	2	2	1	0	0	3	**14**
	High Risk	1	0	2	0	4	1	2	2	1	0	0	4	**17**
	Borderline	0	0	4	3	2	3	3	2	0	1	1	0	**19**
CAH	Confirmed	0	0	0	0	1	0	0	0	0	0	0	0	**1**
	High Risk	1	2	2	3	2	5	2	3	0	3	0	2	**25**
	Borderline	62	55	64	51	60	44	41	48	55	52	51	44	**627**
CF	Confirmed	4	2	1	1	5	1	1	4	5	1	2	1	**28**
	Referred	15	10	3	8	11	5	1	7	15	11	18	23	**127**
	Initial IRT	36	37	38	30	32	33	29	31	65	61	57	49	**498**
CH	Confirmed	3	7	3	5	0	3	5	3	8	4	3	5	**49**
	High Risk	3	10	3	5	1	5	6	7	9	4	5	6	**64**
	Borderline	112	115	85	65	62	72	81	89	97	131	102	92	**1103**
GAL	Confirmed	0	1	0	0	1	0	2	1	0	0	1	0	**6**
	High Risk	0	1	0	0	1	2	2	1	0	0	1	0	**8**
	Borderline	1	0	2	2	5	3	10	4	2	3	4	5	**41**
AA	Confirmed	1	1	1	0	2	0	1	1	1	0	0	1	**9**
	High Risk	1	3	2	0	2	0	1	1	1	1	1	1	**14**
	Moderate I	2	1	0	2	1	0	0	0	1	0	3	1	**11**
	Low Risk	33	56	56	59	60	44	57	46	31	35	34	41	**552**
OA	Confirmed	0	1	0	1	0	0	0	1	2	2	0	0	**7**
	High Risk	0	0	0	0	0	0	0	1	0	1	0	0	**2**
	Moderate I	4	3	1	0	1	0	0	0	1	3	2	2	**17**
	Low Risk	30	27	36	36	42	39	34	33	43	50	47	48	**465**
FA	Confirmed	2	1	2	2	1	0	2	6	2	4	2	1	**25**
	High Risk	0	1	0	1	0	0	2	6	3	5	1	1	**20**
	Moderate I	3	6	5	3	5	1	3	3	3	1	4	0	**37**
	Low Risk	52	42	35	32	48	48	56	51	33	47	43	42	**529**
Hb	Sickle Cell	5	2	0	1	3	3	3	8	4	5	4	1	**39**
	Other Hem	1	0	3	0	2	1	0	0	0	0	1	0	**8**
	Abnormal '	139	126	117	107	118	123	148	148	143	146	98	120	**1533**
LSD	Confirmed	0	0	0	0	0	0	0	0	1	0	2	0	**3**
	High Risk	0	0	0	0	0	0	0	0	1	3	2	1	**7**
	Krabbe Po	0	0	0	0	0	0	0	3	0	2	1	2	**8**

BIO = biotinidase deficiency		CF = cystic fibrosis			GAL = galactosemia		OA = organic acid		Hb = Hemoglobinopathies			**Total Confirmed**		**189**
CAH = congenital adrenal hyperplas		CH = congenital hypothyroidism			AA = amino acid		FA = fatty acid		LSD = lysosomal storage disorder					

Appendix 4: Outcome Data – Newborn Screening Samples and Results

- In 2012 there were 75,136 babies tested in the state newborn screening laboratory. There were 89,668 blood spot samples received in the laboratory. Samples received included:

Initial	Repeat	Poor Quality
75,136	13,197	1,335

- 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 by evaluating the marker analytes 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 2012 were:

High Risk	Moderate Risk	Low / Borderline Risk
284 (0.38%)	65 (0.09%)	3,336 (4.4%)

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 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 with a comment that a repeat newborn screen is necessary.

- One hundred and eighty-nine (189) confirmed disorders were diagnosed from these abnormal newborn screen results during 2012.

Appendix 5: 2012 Poor Quality Samples

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 size blood drop to form before applying to filter; inadequate heel stick procedure.	54
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.	529
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.	38
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.	459
DILUTED, DISCOLORED OR CONTAMINATED: Possible causes: Squeezing or milking of area surrounding the puncture site; allowing filter paper to come into 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 into contact with tabletop, etc. while drying the sample.	186
OLD SPECIMEN: Specimen greater than 15 days old when received at State Public Health Laboratory.	28
NO BLOOD: Filter submitted without blood.	6
OLD FORM: Sample received on out-of-date form.	7

FILTER AND FORM BARCODES DO NOT MATCH: Bar code on filter does not match bar code 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 paper 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.	1
MISSING, INCOMPLETE OR CONFLICTING PATIENT INFORMATION: Missing, incomplete or conflicting demographic information.	3
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.	14
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 into contact with the paper backing of from, blood can be drawn out of filter making the quantative tests performed by the Newborn Screening Laboratory invalid. It is very important that he wet filter paper does not come into contact with any surface until completely dry.	10
Total Poor Quality Samples Received	1,335 (1.49%)

Appendix 6: Hemoglobinopathy Report 2012

Specimens Received:

Initial:	75,136	(83.6%)
Repeat:	13,197	(14.7%)
Unsatisfactory:	1,335	(01.5%)
Whole Blood:	215	(00.3%)
Total:	**89,883**	

Significant Results = 1,580					
Sickle Cell Disease		**Other Disease Conditions**		**Trait Conditions**	
FS	21	FCA	1	FAS	996
FSA	1	FE	4	FSAINC	53
FSC	16	Highly Elevated Barts	1	FAC	272
FSE	1	FSX	2	FCAINC	23
				FAE	22
				FAD	34
				FAX	124
				FASX	3
				FACX	1
				Slightly Elevated Barts	4
				Other Trait condition	1
Total	**39 (2.5%)**	**Total**	**8 (0.5%)**	**Total**	**1,533 (97.0%)**

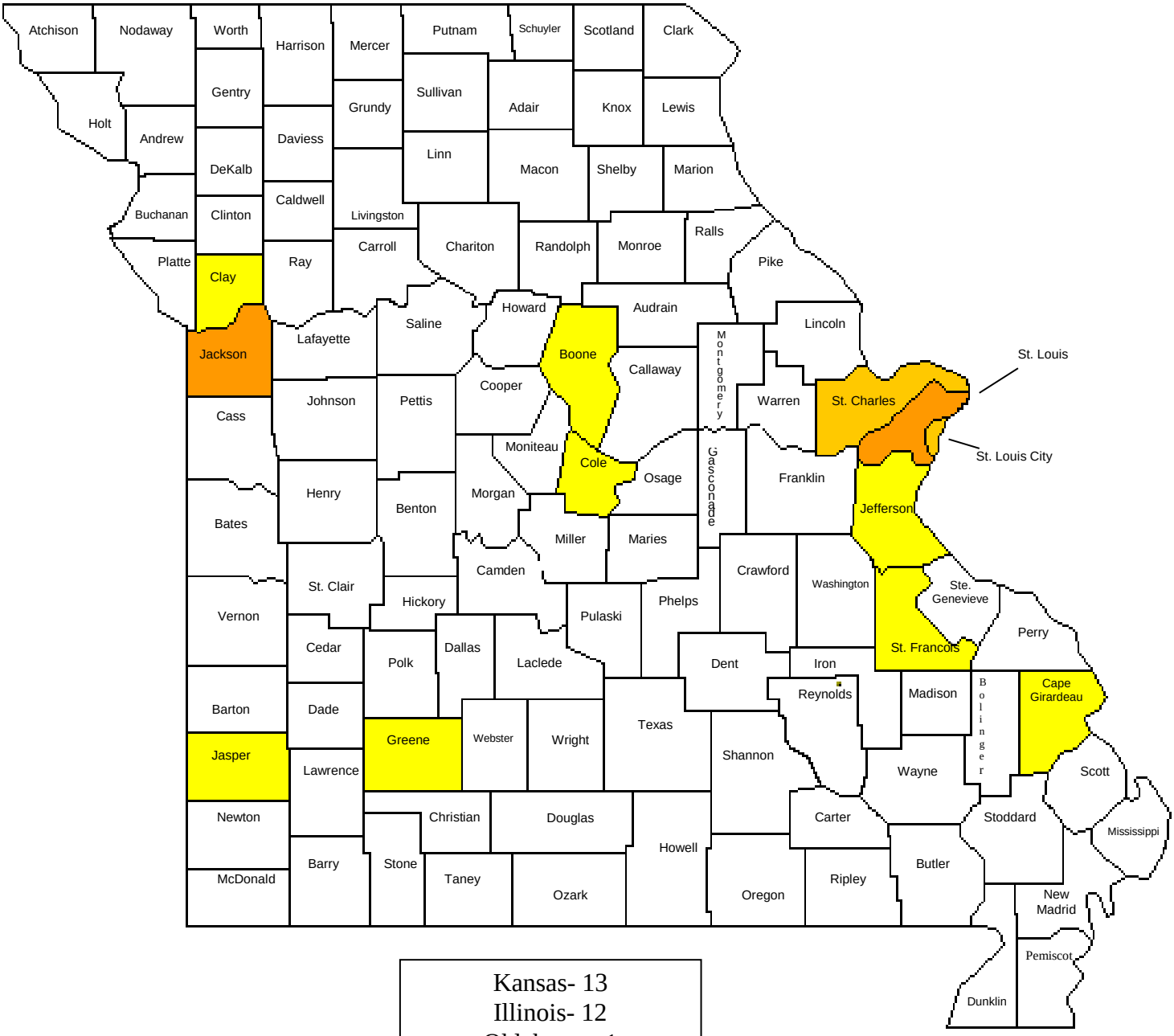
Geographic Follow-up of Significant Disease

Significant Disease Conditions		
St. Louis Area	37	**79%**
Kansas City Area	7	**15%**
Remainder of MO	3	**6%**
Total	**47****	**100%**

**See Appendix 1

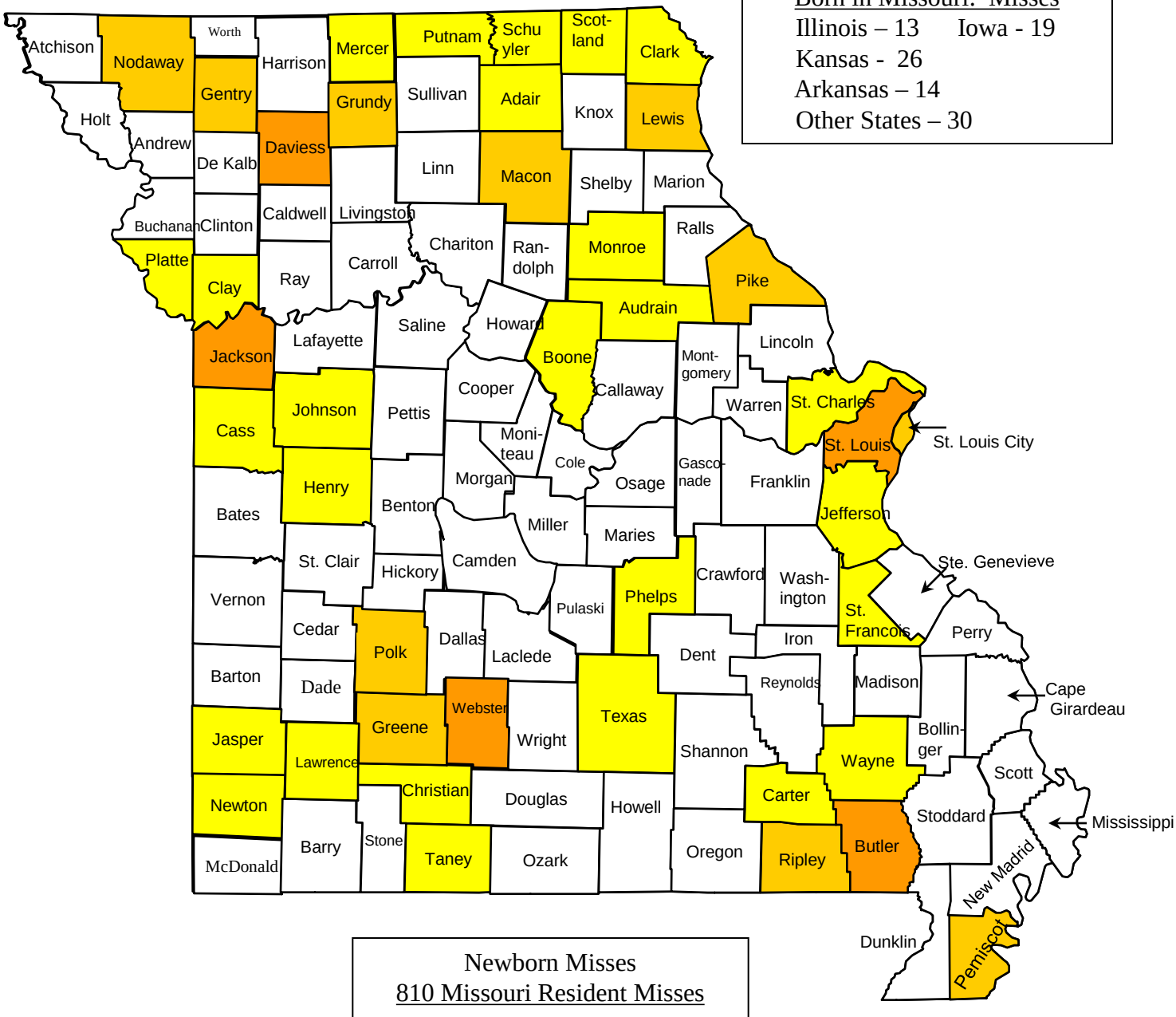
Hemoglobinopathies	**47**	
Sickle cell disease (Hb S/S)	21	**1/3,000** Total population; **1/400** African-American population
Sickle hemoglobin-C disease	16	
Sickle beta zero thalassemia disease		
Sickle beta plus thalassemia disease	1	
Sickle hemoglobin-D disease		
Sickle hemoglobin-E disease	1	
Sickle hemoglobin-O-Arab disease		
Sickle hemoglobin Lepore Boston disease		
Sickle HPFH disorder		
Sickle “Unidentified”	2	
Homozygous-C disease		
Hemoglobin-C beta zero thalassemia disease		
Hemoglobin-C beta plus thalassemia disease	1	
Homozygous-E disorder	4	
Hemoglobin-E beta zero thalassemia disease		
Hemoglobin-E beta plus thalassemia disease		
Homozygous beta zero thalassemia disease		
Double heterozygous beta thalassemia disease		
Hemoglobin-H disease	1	

Appendix 7: Number of Newborns with Abnormal Screens Referred for Follow-up by County in 2012



Appendix 8: Number of Newborns that Missed a Hearing Screening by County During 2012

Residents of Other States
Born in Missouri: Misses
Illinois – 13 Iowa - 19
Kansas - 26
Arkansas – 14
Other States – 30



Newborn Misses
810 Missouri Resident Misses

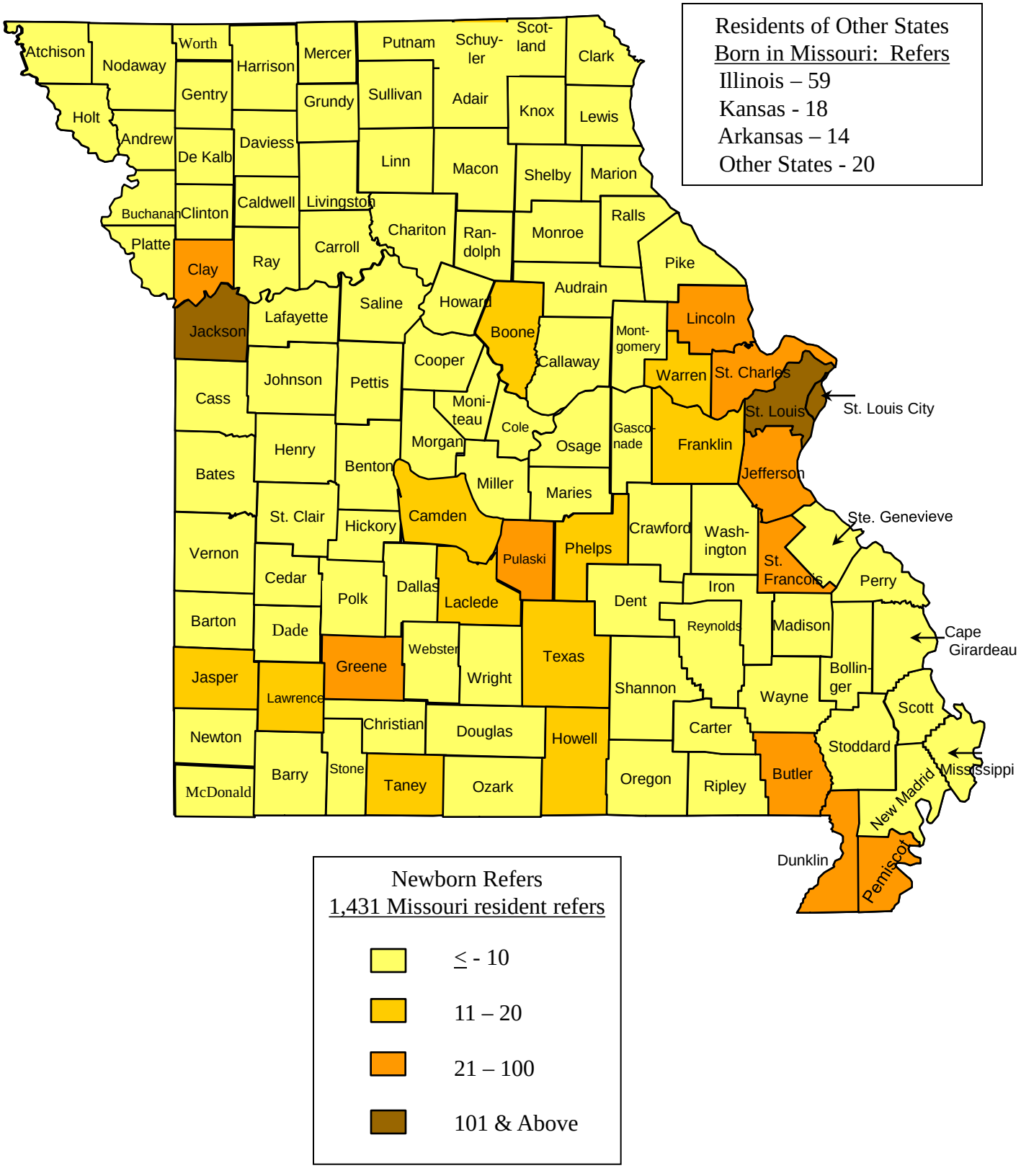
< - 6

6 – 10

11 – 20

21 - 93

Appendix 9: Number of Newborns Referred after a Hearing Screen by County in 2012



Appendix 10: Newborn Screening Satisfaction Surveys

A satisfaction survey of parents was conducted for families of babies having abnormal newborn screening results reported in 2012. Key findings:

Newborn Screening Parent Satisfaction Survey			
	Very Satisfied	Satisfied	Not Satisfied
Staff explained my baby's condition in a way I could understand	87%	13%	
Able to ask questions and discuss decisions about my baby's health care	100%		
Offered reassurance and support	93%	7%	
The treatment staff was knowledgeable	100%		
My questions and concerns were addressed in a timely manner	93%	7%	
The staff provided me with useful referrals and resources	87%	13%	
Received high quality care during my appointments	80%	20%	

A satisfaction survey of parents and children receiving services provided by the hemoglobinopathy resource centers was completed in 2011*. Key findings:

Hemoglobinopathy Resource Center Satisfaction Survey – Parent Response			
	Very Satisfied	Satisfied	Not Satisfied
Treated with respect	95%	5%	0%
Treatment staff was knowledgeable	91%	9%	0%
Questions/concerns addressed in a timely manner	83%	16%	1%
Staff provided useful referrals and resources	77%	20%	3%
Provided with the services needed	89%	9%	2%
Medical care/services received	87%	11%	2%
Received services or treatment without experiencing any problems	95%	0%	5%

Reasons parents/responded as not satisfied with services were because of a long wait time.
*Hemoglobinopathy survey is conducted every other year. Next survey will be done in 2013.

Appendix 11: Newborn Hearing Screening Survey

A satisfaction survey of parents of children born in Missouri who failed their initial newborn hearing screening between October 2011 and December 2011 was completed in March 2012*. The survey examined factors influencing the follow-up time between a failed newborn hearing screening and a repeat screening or an audiologic evaluation.

Key findings:

- 66% of the respondents reported that the birth hospital provided them with written information about the hearing screening prior to the hearing screening (an increase of 1% from the 2009 survey).
- 91% of the respondents reported that the birth hospital notified them of the screening result (an increase of 17% from the 2009 survey).
- 66% of the respondents reported that the hospital staff explained the importance of knowing whether a baby has a hearing loss early in life. (This question will be asked again in the 2013 survey.)

*2011 survey data. Survey conducted every two years.

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