TITLE 181 SPECIAL HEALTH PROGRAMS

CHAPTER 2 SCREENING OF INFANTS FOR METABOLIC DISEASES

2-001 SCOPE: These regulations implement the law governing screening of infants for metabolic diseases, Neb. Rev. Stat. §§ 71-519 to 71-524. These regulations define terms; state the requirements for screening for metabolic diseases; specify the diseases for which tests are required; specify the time periods for performance and reporting of results of the tests by physicians, hospitals, laboratories, and births not attended by a physician; and prescribe the mechanism for determining tests, test methods and techniques, and such reports and reporting procedures as are necessary to implement the law.

2-002 DEFINITIONS: As used in these regulations, unless the context otherwise requires:

Argininosuccinic Acidemia (ASA) means a disorder of amino acid metabolism in which an enzyme defect in the urea cycle results in elevated ammonia and citrulline. If not identified and left untreated, infants develop failure to thrive, seizures, lethargy and coma, and later onset of mental retardation.

Beta-ketothiolase Deficiency (also known as Mitochondrial Acetoacetyl-CoA Thiolase Deficiency or 3-Ketothiolase deficiency or BKT) means a disorder of organic acid metabolism in which an enzyme defect results in the accumulation of isoleucine and related metabolites. If not identified and left untreated, metabolic crisis may occur with coma or death, mental retardation, cardiac abnormalities and other physical problems.

Biotinidase Deficiency (BIOT) means a metabolic disease that results in an inability to recycle and conserve the vitamin biotin which, if not identified and left untreated, may lead to mental retardation, seizures, hearing loss, and dermatitis.

Carnitine Uptake Defect (CUD) means a disorder of fatty acid metabolism in which there is a defect in the transport of carnitine into the tissues. This prevents fatty acid metabolism and limits energy production. If not identified and left untreated, patients develop cardiomyopathy, fasting hypoglycemia and muscle disease. (Carnitine Uptake Defect might not be detected during the immediate newborn period.)

Citrullinemia (CIT) means a disorder of amino acid metabolism in which an enzyme defect in the urea cycle results in hyperammonemia and elevated citrulline. If not identified and left untreated, infants develop failure to thrive, vomiting, seizures, lethargy, coma and later onset of mental retardation.

Confirmatory Test means a test or a panel of tests performed following a presumptive positive screening test which provides additional, more specific diagnostic information concerning the existence or non-existence of diseases screened for.

Congenital Adrenal Hyperplasia (CAH) means a genetic disorder which results in the adrenal glands producing too little or no cortisol, insufficient aldosterone, and too much androgen. If not identified and left untreated, this can result in classical salt-losing CAH or an adrenal crisis that can result in sudden death.

Congenital Primary Hypothyroidism (CPH) means a disease characterized by a congenital deficiency or absence of thyroid hormone (thyroxine) which, if not identified and left untreated, may lead to mental and growth retardation.

Cutoff Value means a value on a screening test for a specific metabolic disease which gives a high degree of probability that all newborns with a greater or lower value, depending on the test method, will not have the metabolic disease.

Cystic Fibrosis (CF) means a genetic disorder in which mutations alter the structure, function, or production of a transmembrane chloride channel protein which in turn can affect the function of the lungs, upper respiratory tract, gastrointestinal tract, pancreas, liver, sweat glands, and genitourinary tract. Early diagnosis and treatment results in improved outcomes for affected patients.

Department means the Department of Health and Human Services of the State of Nebraska.

Galactosemia (GALT) means a disease of galactose metabolism which, if not identified and left untreated, may lead to failure to thrive, vomiting, liver disease, cataracts, and mental retardation.

Glutaric Acidemia type I (GAI) means a disorder of organic acid metabolism in which an enzyme defect results in increased glutaric acid and its metabolites. If not identified and left untreated children develop metabolic acidosis, failure to thrive, mental retardation and sudden onset of seizures, spasticity and movement problems.

Hemoglobinopathies (Hb SS, Hb S/βTh, Hb S/C) means a group of genetic disorders characterized by production of abnormal hemoglobin which may cause clinical disease including anemia or oxygen carrying difficulties.

Homocystinuria (HCY) means a disorder of amino acid metabolism in which an enzyme defect results in increased methionine and homocystine. If not identified and left untreated, children can develop mental retardation, vision problems, skeletal abnormalities and strokes.

Hospital means any facility defined under Neb. Rev. Stat. § 71-~~2017.01(2)~~419.

Institutional Review Board (IRB) means an Institutional Review Board qualifying and complying with requirements in the Code of Federal Regulations Title 45 Part 46 Protection of Human Subjects, Effective July 14, 2009.

Isovaleric Acidemia (IVA) means a disorder of amino acid metabolism in which an enzyme defect results in elevations of leucine and isovaleric acid. If not identified and left untreated, it can cause failure to thrive, metabolic acidosis, dehydration, hyperammonemia, and hypoglycemia.

Laboratory means a facility for the biological, microbiological, serological, chemical, immunological, hematological, biophysical, cytological, pathological or other examination of materials derived from the human body for the purpose of providing information for the diagnosis, prevention, or treatment of any disease or impairment of, or the assessment of the health of, human beings. These examinations also include procedures to determine, measure, or otherwise describe the presence or absence of various substances or organisms in the body. Facilities only collecting or preparing specimens (or both) or only serving as a mailing service and not performing testing are not considered laboratories.

Long-chain Hydroxyacyl-CoA Dehydrogenase Deficiency (also known as 3-Hydroxy Long-chain Acyl-CoA Dehydrogenase Deficiency or LCHAD) means a disorder of fatty acid metabolism in which an enzyme defect results in metabolic derangement during periods of prolonged fasting. If not identified and left untreated, it can result in failure to thrive, hypoglycemia, liver disease, cardiomyopathy and possibly death.

Maple Syrup Urine Disease (MSUD) means a disorder of amino acid metabolism in which an enzyme defect allows leucine, isoleucine and valine to accumulate to toxic levels. If not identified and left untreated, it can progress to mental retardation, failure to thrive, seizures, coma, cerebral edema and possibly death.

Medium Chain Acyl-CoA Dehydrogenase Deficiency (MCAD) means a disorder of fatty acid metabolism that results in an inability to metabolize medium-chain fatty acids which, if not identified and left untreated, under conditions of fasting may lead to hypoglycemia, seizures, developmental disability and/or sudden death.

Methylmalonic Acidemia (Mutase Deficiency or MUT or MMA) means a disorder of amino acid metabolism in which various related enzyme defects result in increased methylmalonic acid. If not identified and left untreated, it can result in failure to thrive, metabolic acidosis, dehydration, hyperammonemia, hypoglycemia, mental retardation and possibly death.

Methylmalonic Acidemia (Cbl A and B) means a disorder of vitamin B12 (cobalamin) and amino acid metabolism in which an enzyme defect results in increased methylmalonic acid and homocystine. If not identified and left untreated, it can result in failure to thrive, metabolic acidosis, seizures, anemia, mental retardation and possibly death.

Multiple Carboxylase Deficiency (MCD) means a disorder of biotin vitamin metabolism in which an enzyme defect results in impaired biotin function leading to abnormal metabolism of amino

acids, carbohydrates and lipids. If not identified and left untreated, infants develop metabolic acidosis, seizures, dermatitis, hearing loss, coma, mental retardation and possibly death.

NBSAC-approved protocols mean follow-up practices recommended by the Newborn Screening Advisory Committee and adopted by the Nebraska Newborn Screening Follow-up Program, to rule out or help diagnose conditions in response to screening results that are out of range. For most out-of-range results, only a repeat dried blood spot specimen is needed. For substantially out-of-range results, or results from serial screens that continue to be out of range, other confirmatory specimens and tests often with higher specificity and sensitivity to measure an analyte or analytes are usually recommended.

Newborn means an infant who is 28 days old or less.

Newborn Screening means a laboratory test applied to newborn specimens in a search for newborns with metabolic diseases. Screening will detect a high proportion of newborns with the disease (true positive). Some newborns who do not have the disease will be identified by the screening test as possibly affected (false positive).

NNSP means the Nebraska Newborn Screening Program.

Newborn Screening Advisory Committee means a committee whose membership is determined by the Department Director which is comprised of a minimum of 15 and maximum of 25 stakeholders and representatives from but not limited to the following areas: Newborn and pediatric primary health care providers; medical and allied professionals from the sub-specialities associated with treatment for the disorders screened; clinical laboratorians; and consumers with technical, professional, and/or personal experience with newborn screening for congenital and inherited disorders.

Phenylketonuria (PKU) means a disorder of amino acid metabolism in which an enzyme defect results in increased levels of phenylalanine. If not identified and left untreated, it may lead to mental retardation and seizures.

Propionic Acidemia (PROP or PA) means a disorder of amino acid metabolism in which an enzyme defect results in increased propionic acid. If not identified and left untreated, it can result in failure to thrive, metabolic acidosis, vomiting, dehydration, hyperammonemia, mental retardation and death.

Physician means a person licensed to practice medicine and surgery or osteopathic medicine and surgery pursuant to the Medicine and Surgery Practice Act.

Presumptive Positive means a screening test result that is above or below the cutoff value and/or outside the normal range or value determined by an algorithm for assigning an interpretation of presumptive positive, depending on the test method.

Public Health means the art and science dealing with the protection and improvement of community health by organized community effort and including preventive medicine and sanitary and social science.

Public Health Emergency (the condition that requires the Governor to declare a state of public health emergency) means an occurrence or imminent threat of an illness or health condition, caused by bioterrorism, epidemic or pandemic disease, or a novel and highly fatal infectious agent or biological toxin that poses a substantial risk of a significant number of human fatalities or incidents of permanent or long-term disability (WHO/CDC, 2001). The declaration of a state of public health emergency permits the Governor to suspend state regulations and/or change the functions of state agencies.

Public Health Research is research intended to generate or contribute to generalizable knowledge to improve public health practice. Generalizable knowledge is new information that has relevance beyond the population or program from which it was collected. Intended benefits of the research project may or may not include study participants, but always extend beyond study participants, and usually to society. Data collected exceed requirements for care of the study participants or extend beyond the scope of the activity.

For purposes of defining public health research, "generalizable" does not refer to the statistical concept of population estimation, or to the traditional public health method of collecting information from a sample to understand health in the sampled population. Holding public health activities to a standard of studying every case in order to classify an activity as non-research is not practical or reasonable.

Residual Dried Blood Spots means the portion of the initial or repeat dried blood spot specimen remaining, after all punches have been removed for testing of the specimen for newborn screening purposes.

Severe Combined Immune Deficiencies (SCIDs) means a group of rare congenital immune deficiency states that share a deficiency of T-cell function as their common thread. Deficiency of T-cell function prevents the appropriate coordination of the immune attack on a foreign invader. Effects of untreated disease leads to frequent infections, and some forms are fatal in early childhood.

Submitter means the person who sends the Collection and Reporting (CARE) Form to the testing laboratory for initial, repeat, or confirmatory screening tests, including, but not limited to, the hospital, the laboratory, or the physician.

Test Method means a laboratory examination which measures blood constituents associated with metabolic diseases.

Tyrosinemia (TYR) means a disorder of amino acid metabolism in which various related enzyme defects result in elevation of tyrosine. Effects of untreated disease may include failure to thrive, liver failure, skin and eye lesions, developmental delay or mental retardation. (Tyrosinemia type 1 might not be detected during the immediate newborn period).

Trifunctional Protein Deficiency (TFP) means a disorder of fatty acid metabolism in which a genetic defect results in deficiency of 3 enzymes that act sequentially in fatty acid degradation. During periods of fasting, if not identified and left untreated, children can develop hypoglycemia, failure to thrive, cardiomyopathy, liver disease and death.

Very Long-chain Acyl-CoA Dehydrogenase Deficiency (VLCAD) means a disorder of fatty acid metabolism in which an enzyme defect results in an inability to degrade long-chain fatty acids. If not identified and left untreated, it may lead to fasting hypoglycemia, liver disease, seizures, skeletal myopathy, cardiomyopathy and sudden death.

3-Hydroxy 3-Methyl Glutaric Aciduria (also known as 3-Hydroxy-3-Methylglutaryl-CoA Lyase Deficiency or HMG) means a disorder of organic acid metabolism in which an enzyme defect results in elevation of leucine in the blood and impaired production of ketones. If not identified and left untreated, it can result in mental retardation, metabolic acidosis, hypoglycemia, hyperammonemia, seizures, coma and death.

3-Methylcrotonyl-CoA Carboxylase Deficiency (3MCC) means a disorder of amino acid metabolism in which an enzyme defect results in an inability to metabolize leucine. If not identified and left untreated, it can lead to vomiting, metabolic acidosis, apnea, hyptonia, seizures and possibly death.

2-003 SPECIFICATION OF DISEASES: All infants born in the state of Nebraska must be tested for the group of metabolic diseases of amino acid, fatty acid, vitamin and organic acid metabolism that may be detected from the acylcarnitine and amino acid profiles of tandem mass spectrometry including and in addition to the following diseases:

1. Argininosuccinic Acidemia (beginning July 1, 2008);
2. Beta-ketothiolase Deficiency (beginning July 1, 2008);
3. Biotinidase Deficiency;
4. Carnitine Uptake Defect (beginning July 1, 2008);
5. Citrullinemia (beginning July 1, 2008);
6. Congenital Adrenal Hyperplasia;
7. Congenital Primary Hypothyroidism;
8. Cystic Fibrosis;
9. Galactosemia;
10. Glutaric Acidemia type 1 (beginning July 1, 2008);
11. Hemoglobinopathies;
12. Homocystinuria (beginning July 1, 2008);
13. Isovaleric Acidemia (beginning July 1, 2008);
14. Long-chain Hydroxyacyl-CoA Dehydrogenase Deficiency (beginning July 1, 2008);
15. Maple Syrup Urine Disease (beginning July 1, 2008);
16. Medium Chain Acyl-CoA Dehydrogenase Deficiency;
17. Methylmalonic Acidemia (Mutase Deficiency) (beginning July 1, 2008);
18. Methylmalonic Acidemia (Cbl A and B) (beginning July 1, 2008);
19, Multiple Carboxylase Deficiency (beginning July 1, 2008);
20. Phenylketonuria;
21. Propionic Acidemia (beginning July 1, 2008);
22. Severe Combined Immune Deficiencies, (beginning July 1, 2014);
23~~2~~. Tyrosinemia (beginning July 1, 2008);
24~~3~~. Trifunctional Protein Deficiency (beginning July 1, 2008);
25~~4~~. Very Long-chain Acyl-CoA Dehydrogenase Deficiency (beginning July 1, 2008);
26~~5~~. 3-Hydroxy 3-Methyl Glutaric Aciduria (beginning July 1, 2008); and

27~~6~~. 3-Methylcrotonyl-CoA Carboxylase Deficiency (beginning July 1, 2008).

2-004 SPECIMEN COLLECTION

2-004.01 Specimen Requirements

2-004.01A The specimen requirements of the testing laboratory for each specific analyte must be followed. The testing laboratory must accept only specimens that are dried blood spots that have been collected on the CARE Form.

2-004.01B Collection of dried blood spot specimens must comply with the Clinical and Laboratory Standards Institute (CLSI) "Blood Collection on Filter Paper for Newborn Screening Programs; Approved Standard", most current edition.

Heel stick with direct application is the preferred method. That method is illustrated and described on Attachment 1, which is incorporated into these regulations with this reference. The submitter must forward the dried blood spots to the testing laboratory within 24 hours of specimen collection. On weekends and holidays if no transport service is available, the next earliest available transport service must be used.

2-004.01C Umbilical cord blood must not be used.

2-004.01D Urine must not be substituted for blood specimens.

2-004.02 Collection and Reporting Form (CARE Form): The Collection and Reporting Form (CARE Form), which is attached to these regulations as Attachment 2 and incorporated herein by reference, must be the sole method of dried blood spot specimen collection for all newborn screening. Forms are available from the Department at cost.

2-005 PHYSICIAN DUTIES

2-005.01 Specimen Collection: For all live births, the newborn's physician must cause the collection for testing of a newborn screening specimen for metabolic diseases between 24 to 48 hours of age or immediately prior to the newborn's discharge, whichever occurs first.

2-005.01A Prior to 24 Hours of Age: If the initial specimen for any infant is collected prior to 24 hours of age, the newborn's physician or designee must collect or cause to be collected a repeat amino acid profile and hypothyroidism screening specimen by 7 days of age, regardless of prior test results.

2-005.01B Sick, Low Birth Weight, or Premature Infants: Newborns transferred to neonatal intensive care units (NICU) must have a specimen collected prior to transfer, and information communicated as required at 181 NAC 2-005.01E3. The attending physician at the hospital NICU must verify and otherwise ensure a specimen is collected prior to the provision of any treatment, excluding respiratory treatment. The specimen may be collected prior to 24 hours of age. If the first

specimen is collected at less than 24 hours of age, or if the newborn was less than 2000 grams at birth, a repeat specimen must be collected at 48-72 hours of age. A third specimen must be collected at 28 days of life or upon discharge, whichever occurs first, on all infants less than 2000 grams at birth, or who had any prior abnormal screen result.

2-005.01C Blood Transfusion: If a newborn requires a blood transfusion, even if prior to 24 hours of age, the specimen must be collected before the blood transfusion. The specimen should be collected at the time blood is collected for the typing and cross match prior to transfusion unless a dried blood spot specimen was verified to have been collected prior to the typing and cross match. The newborn's physician or designee must collect or cause to be collected a repeat specimen for the amino acid profile and hypothyroidism screening by 48-72 hours of age if the pre-transfusion specimen was collected at less than 24 hours of age, regardless of prior test results.

2-005.01D No Specimen Collected: Upon notification by the hospital that a newborn was discharged before a screening sample was collected, the newborn's physician or designee must collect or cause to be collected a screening specimen within 48 hours of parental notification.

2-005.01E Newborn Transfer To Another Hospital

2-005.01E1 Before 24 Hours of Age: The physician at the hospital of birth must collect or cause to be collected a blood specimen immediately prior to discharge for testing for metabolic diseases if the newborn is transferred to another hospital, either in- or out-of-state, even if this occurs before the infant is 24 hours of age. If the specimen is collected at less than 24 hours of age, the physician or designee at the hospital of birth must document and inform the receiving physician that a specimen for testing for metabolic diseases was collected prior to 24 hours of age and notify the receiving physician that another specimen must be collected between 48 and 72 hours of age.

2-005.01E2 After 24 Hours of Age: The physician at the hospital of birth must collect or cause to be collected a blood specimen for testing for metabolic diseases from any newborn being transferred to another hospital after the newborn is 24 hours of age and notify the physician upon transfer that a blood specimen for metabolic diseases has been collected. The transferring physician must immediately notify the receiving physician if the specimen needs to be repeated, or if confirmatory testing is required.

2-005.01E3 Transfer Forms: All physicians transferring newborns to another hospital or the physician’s designee at the hospital must notify the receiving physician in writing of the following information and fax a copy of the written information to the NNSP within 24 hours:

1. Date of transfer;
2. Person completing form or other written notification;

3. Hospital of birth;
4. Infant's name;
5. Date and time of birth;
6. Date and time of specimen collection;
7. Transferring physician;
8. Whether the newborn screening specimen was or was not collected at the hospital of birth;
9. Whether the newborn screening specimen was or was not collected prior to 24 hours of age;
10. Whether the newborn was transfused, and if so, whether the specimen was collected prior to transfusion;
11. The type and time of transfusion if the specimen was collected post-transfusion;
12. If the tests have not been performed and an initial specimen needs to be collected;
13. If the specimen was collected prior to 24 hours, or following transfusion, and a repeat specimen needs to be collected;
14. Receiving hospital; and
15. Receiving physician, if known.

The Transfer Form, Attachment 3 of these regulations, may be used to notify the receiving physician and is included as a convenience for the transferring physician.

2-005.02 Unsatisfactory Specimen: Upon receiving notice from the testing laboratory that a specimen is unsatisfactory, the newborn's physician or designee must collect or cause to be collected a repeat specimen within 48 hours of parental notification.

~~2-005.02A The physician or designee must make a reasonable attempt to cause the collection of a repeat specimen. A reasonable attempt includes that the physician or designee must:~~

~~1. Immediately notify the parent, guardian, or custodian by telephone, if possible, and in writing;~~

~~2. If there has been no response within 5 days, notify the parent, guardian, or custodian in writing by certified mail, return receipt requested, or equivalent; and~~

~~3. If there has been no response within 10 days of first notification, notify the Nebraska Newborn Screening Program (NNSP) in writing that obtaining a repeat specimen was not accomplished.~~

2-005.03 Screening Test Results Received: Once the physician receives the results of the newborn screening tests, the physician or designee must place or cause to be placed the results in the newborn's patient record.

2-005.04 Presumptive Positive Screening Test Result: The newborn's physician or

designee must obtain a specimen for repeat or confirmatory testing from the newborn within 48 hours after notification by the testing laboratory of any presumptive positive screening result including out of range, inconclusive or abnormal interpretations. Repeat dried blood spot specimens must be submitted to the newborn screening laboratory that tested the initial specimen in accordance with NBSAC-approved protocols for follow-up. Confirmatory tests must be ordered and confirmatory specimens sent in accordance with NBSAC-approved protocols only to laboratories meeting standards established by the Department on the advice of the Newborn Screening Advisory Committee as set forth in 181 NAC 2-007.01E.

~~2-005.04A The physician or designee must make a reasonable attempt to cause the collection of a repeat specimen. A reasonable attempt includes that the physician or designee must:~~

~~1. Immediately notify the parent, guardian, or custodian by telephone, if possible, and in writing;~~

~~2. If there has been no response within 5 days, notify the parent, guardian, or custodian in writing by certified mail, return receipt requested, or equivalent; and~~

~~3. If there has been no response within 10 days of first notification, notify the NNSP in writing that obtaining a repeat specimen was not accomplished.~~

2-005.04B Specific Responses to Presumptive Positive Screening Test Results

2-005.04B1 Congenital Adrenal Hyperplasia (CAH): If screening test results are positive for CAH, the physician must monitor the newborn for vomiting, poor weight gain, and elevated potassium, and collect or cause to be collected a specimen for a confirmatory test.

2-005.04B2 Congenital Primary Hypothyroidism (CPH): If screening test results are positive for congenital primary hypothyroidism, thyroxine therapy must not be given prior to obtaining confirmatory testing.

2-005.04B3 Cystic Fibrosis: If screening test results are positive for Cystic Fibrosis, the physician must order a repeat or confirmatory test as indicated.

2-005.04B4 Galactosemia: If screening test results are positive for galactosemia, the physician must take the child off milk, place the child on a powder-based soy formula, and then collect or cause to be collected a specimen for a confirmatory test.

2-005.04B5 Medium Chain Acyl-CoA Dehydrogenase Deficiency (MCAD): If screening test results are positive for MCAD, parent(s) should be advised to avoid fasting of the newborn for greater than 4 hours, and the physician should consider carnitine supplementation until confirmatory results are

known.

2-005.04B6 Phenylketonuria: If screening test results are positive for phenylketonuria, formula with reduced or absent phenylalanine must not be given prior to obtaining positive confirmatory phenylalanine and tyrosine levels and other necessary confirmatory tests.

a. Phenylalanine levels of 20 mg/dL (or 1210 µmol/L) or greater on 2 occasions 24 hours or more apart while the infant is on full feeding and a phenylalanine to tyrosine ratio of 10 to 1 or higher is indicative of classical phenylketonuria.

b. Phenylalanine levels of greater than 3.0 mg/dL (or 182 µmol/L) but less than 20 mg/dL (or 1210 µmol/L) on 2 occasions 24 hours or more apart while the infant is on full feeding, and a phenylalanine to tyrosine ratio of 5 to 1 or higher is indicative of nonclassical or variant phenylketonuria.

2-005.05 The physician or designee must make a reasonable attempt to cause the collection of a repeat or confirmatory specimen as appropriate to the situation whenever the initial specimen was; collected at less than 24 hours or after a transfusion; is determined to be unacceptable for testing for any condition on the screening panel; results of any screening test are out of range, presumptive positive, inconclusive or abnormal, or if an infant is found to have been discharged without the screen. A reasonable attempt means that the physician or designee must:

a. Immediately notify the parent, guardian, or custodian by telephone, if possible, and in writing.
b. If there has been no response within 5 days, notify the parent, guardian, or custodian in writing by certified mail, return receipt requested, or equivalent, and
c. If there has been no response within 10 days of first notification, notify the Nebraska Newborn Screening Program (NNSP) in writing that obtaining the specimen was not accomplished.

2-005.05A Enforcement: In the event that a parent fails to respond to notification, the physician must assure that such steps are taken as indicated in 181 NAC 2-009 and Neb. Rev. Stat. § 71-524.

2-005.06 Patient Education: The physician or an individual to whom the physician has delegated authority, must:

2-005.06A Provide information to the newborn's parent/legal guardian about the diseases for which newborn screening tests are required. Patient education materials provided by the Department about the required tests must be used to aid in informing the parent/legal guardian. There is no provision for dissent from or refusal of the required newborn screening tests specified at 181 NAC 2-003.

2-006 HOSPITAL OR OTHER SUBMITTER DUTIES

2-006.01 Collection and Reporting Form (CARE Form): The hospital or other submitter designated by the newborn's attending physician must complete all information and collect the specimen on the CARE Form. The hospital or other submitter must retain the designated copy for inclusion into the newborn's medical record and send the remaining copies to the testing laboratory designated by the Department within 24 hours after specimen collection.

2-006.02 No Specimen Collected: The hospital or other submitter designated by the newborn's attending physician must immediately notify the newborn's physician or designee by telephone and in writing if the newborn was discharged before a screening sample was collected, and document this notification in the newborn's medical record.

2-006.03 No Test Results: The birthing hospital or facility must maintain a monitoring mechanism to track results for all births occurring at or en route and admitted to their facility. If test results are not received by the hospital or other submitter within 10 days after the specimen was submitted to the testing laboratory, the hospital or other submitter must immediately contact the testing laboratory to determine if the testing laboratory received the specimen and performed the appropriate analyses, and document this contact in the newborn's medical record:

2-006.03A If the testing laboratory did not receive a specimen, the hospital or other submitter must immediately notify the physician by telephone and in writing, and document this notification in the newborn's medical record.

2-006.03B If the testing laboratory did receive the specimen and completed the appropriate analyses, a duplicate report must be obtained and placed in the newborn's medical record.

2-006.03C If the testing laboratory did receive the specimen but has not yet performed the appropriate analyses, the hospital or other submitter must immediately notify the NNSP.

2-006.04 Screening Test Results Received: When the hospital or other submitter receives the completed copy of the CARE Form or other record of screening test results from the testing laboratory, the hospital or other submitter must place the screening test results in the newborn's medical record and appropriately retain those results for 25 years from the newborn's date of birth.

2-006.05 Contact Person: The hospital must keep the NNSP informed of the contact person responsible for newborn screening.

2-007 TESTING LABORATORY DUTIES

2-007.01 General Rules

2-007.01A Electronic Transmission: The testing laboratory must report all of the

information on the CARE Form electronically, at its own expense, to the NNSP central database utilizing software developed and provided by the Department or in electronic format that provides complete demographic and test results records for each infant and that provides the reporting functions as specified by the Department in 181 NAC 2-007.02A and in contract. The testing laboratory must provide, at its own expense, the necessary hardware.

2-007.01B Test Performance: The testing laboratory must perform all tests required in the contract between the Department and the laboratory at least six days a week.

2-007.01C Contact Person: The testing laboratory must keep the NNSP informed of the contact person responsible for newborn screening.

2-007.01D Screening Tests: Except as provided in the disaster preparedness plan as required in the contract, the screening tests must be completed only by the laboratory designated by contract with the Department beginning with the effective date of the contract.

2-007.01E Confirmatory Tests: Confirmatory tests may be done by any laboratory including the laboratory designated by the Department as long as it is certified under the Clinical Laboratory Improvement Amendments (CLIA) and meets standards as set forth at 181 NAC 2-007.01E, items 1 and 2. The contracted newborn screening laboratory will append to the laboratory report for all presumptive positive screening results, disorder specific recommendations for immediate testing and clinical follow-up, as approved by the Department and the Newborn Screening Advisory Committee.

1. Confirmatory testing laboratories must be CLIA certified, and maintain data to support validation of the assays and normal reference ranges for neonates and infants for whom confirmatory testing is provided.

2. Confirmatory testing laboratories must provide at a minimum written or electronic laboratory reports back to the specimen submitter that include:

    a. Name of test.
    b. Validated age-appropriate normal reference ranges for the analytes tested when confirming for endocrinopathies (CAH and CPH) and hemoglobinopathies.
    c. Test method and relative amounts of hemoglobins when confirming for hemoglobinopathies.
    d. Identification of ratios when hemoglobins A and S are present.
    e. Test results in quantitative values (except hemoglobins above) and units of measure consistent with units of measure in the normal reference ranges or values.
    f. Interpretation of results appropriate to the age of the newborn or infant.
    g. Name and address where testing was completed.
    h. Name and phone number of reviewer/person providing the

interpretation.

i. Written acknowledgement of conditions that may interfere with the appropriate interpretation of results.

2-007.02 Record Keeping and Reporting: Testing laboratories must maintain records and make reports in the following manner:

2-007.02A Electronic Report: The laboratory must make an electronic report to the Department which includes the following information:

1. All information contained on the CARE Form;

2. The serial number located on the CARE Form;

3. If applicable, identification of any unsatisfactory specimen and the reason for its unsatisfactory nature;

4. Screening, repeat, and confirmatory test results, including numerical data where applicable; and

5. Any notifications to the physician, NNSP, or the submitter.

2-007.02B When Receiving a Specimen: The testing laboratory must enter the data identified in 181 NAC 2-007.02A, items 1 and 2, into the electronic database specified at 181 NAC 2-007.01A at the time of receiving the specimen.

2-007.02C After Individual Test Completion: Tests results must be entered into the database within 24 hours of individual completion.

2-007.02D Transfer of Electronic Report: The testing laboratory must transmit to the Department's electronic database or allow electronic access by the NNSP to all data identified in 181 NAC 2-007.02A at least once every 24 hours.

2-007.02E Transfer of Screening Test Results: Within 24 hours of completing all screening tests on each newborn, the laboratory must return a copy of the completed CARE Form or other record of test results to the hospital or other submitter.

2-007.02F Blood Spot Storage, Use and Disposal Records: The testing laboratory must maintain for 25 years an index or catalog of the residual dried blood spots processed in the laboratory that includes the following information:

1. The serial number or unique identifier of each specimen processed;
2. The test results of each specimen processed;
3. Verification of disposal of specimens not released for research, public health, quality assurance, or diagnostic purposes. This information may be batched by test completion date so long as each serial number or unique identifier can be linked with its test completion date;

4. Date of disposal;
5. Location of disposal if other than the laboratory;
6. For specimens released for public health research, documentation as required at 181 NAC 2-007.08; and
7. Signature of the person who released, disposed of, or witnessed the disposal of the specimen; or for specimens disposed of by a contractor, written evidence that the contract for disposal of residual dried blood spots requires disposal be done in accordance with 181 NAC 2-007.02F, items 3, 4, and 5.

2-007.02G Quality Assurance Reports: The testing laboratory must provide to the NNSP, copies of written reports of participation in and results of appropriate quality assurance proficiency testing programs offered by the Centers for Disease Control and Prevention of the United States Department of Health and Human Services and any other professional laboratory organization.

2-007.03 Unsatisfactory Specimen: If a specimen is unsatisfactory for any reason for any test(s), including but not limited to, being of insufficient volume or quality, the testing laboratory must reject it. Within 24 hours of receiving any unsatisfactory specimen, the testing laboratory must:

1. Notify the submitter and physician or designee by telephone and in writing that the specimen was unsatisfactory and that a repeat specimen must be collected within 48 hours of notification to the parent, guardian, or custodian;

2. Schedule any tests possible on the specimen received in accordance with the testing laboratory's standard operating procedure and testing times; and

3. Enter the applicable information identified in 181 NAC 2-007.02A into the Department's electronic database.

2-007.04 Negative Screening, Negative Repeat Screening, and Negative Confirmatory Test Results: Within 24 hours of obtaining a negative screening, negative repeat screening, or negative confirmatory test result, the testing laboratory must:

1. Send a copy of the CARE Form or other record of test results to the submitter; and

2. Enter the applicable information identified in 181 NAC 2-007.02A into the Department's electronic database.

2-007.05 Presumptive Positive Screening, Positive Repeat Screening, or Positive Confirmatory Test Results: Immediately after obtaining any presumptive positive screening, positive repeat screening, or positive confirmatory test result, the testing laboratory must:

1. Provide test result information to the submitter and physician or designee by telephone and in writing;

2. Utilize the NNSP telephone number provided by the Department and relay the information on the CARE Form and the presumptive positive or positive results; and

3. Enter the applicable information identified in 181 NAC 2-007.02A into the Department's electronic database.

2-007.06 Standardized Laboratory Test Methods: The testing laboratory must use only the standardized test methods provided for in the contract with the Department and the methods used must produce results for which the specified cutoff value and/or algorithms for assigning presumptive positive results is/are appropriate. The screening test approved analytical method, cutoff value and/or algorithms for assigning presumptive positive results (identification protocol) will be specified in the contract between the Department and the laboratory conducting newborn screening testing for the diseases specified in these regulations. Identification protocols used by the performing laboratory must be agreed upon in contract by the Department with the advice of the Newborn Screening Advisory Committee.

The Newborn Screening Advisory Committee is responsible for reviewing technical aspects of the identification protocol for the initial screening test relevant to repeat and confirmatory testing. The Committee must make recommendations for approval, disapproval or revision to identification protocols. The Department has final decision authority for contractually agreed upon tests, analytic methods and identification protocols for normal and abnormal results and reporting specifications.

2-007.07 Storage of Residual Dried Blood Spots: The testing laboratory must store the residual dried blood spots for 90 days. Specimens must be refrigerated in sealed bags of low gas permeability.

2-007.08 Use of Residual Dried Blood Spots: Residual dried blood spots may be used for public health research, further patient diagnostic testing, and public health purposes, for example, but not limited to, quality assurance and improvement of newborn screening practices.

2-007.08A Residual dried blood spots may be used for public health research only when:

1. The Chief Medical Officer and the Newborn Screening Advisory Committee or its proxy sub-committee have reviewed and approved the application for research containing but not limited to the following information:

   a. The full report of the review and approval of the research by a Human Subjects Review or Institutional Review Board
   b. The qualifications of the applicant and of the principal investigator, if other than the applicant, including education, experience, prior publications, and recommendations of professional colleagues

who have knowledge and experience of scientific or medical research;

c, The purpose of the research project, a summary of the project, and the anticipated time of completion of the project;

d. The location where the research project will be conducted and the equipment, personnel, and other resources available to the applicant to carry out the project;

e. The identity of the individual or entity funding the research project, a description of the availability of funds for the research project, and any conditions on the receipt or continuation of the funding;

f. The specific data or biological sample information requested and a description of the use to be made of it and, if subject-identifying data is requested, a substantiation of the need for access to the subject-identifying data;

g. A description of the measures to be taken to secure the data and biological sample information and to maintain the confidentiality of such during the research project, for disposal of the data and biological sample upon completion of the study, and to assure that the results of the study will not divulge or make public, information that will disclose the identity of any individual subject;

h. A written assurance/agreement that the research will be published in the public domain and communication of research results will not be restricted on the basis of the proprietary interests of commercial, private or other partners;

~~h.~~ i. A description of the process that will be used for obtaining written consent from the legally responsible parent or guardian of the individuals whose specimens will be requested;

~~i~~ j. If contact with a subject or subject's parent or legal guardian is planned or expected beyond obtaining consent as required under 181 NAC 2-007.08A1h, substantiation of the need for the contact and a description of the method to be used to obtain permission from the subject or subject's parent or legal guardian for the contact; and;

~~j.~~ k. Such additional information as the Department determines to be necessary to assure that release of data to the applicant is appropriate and consistent with these regulations, Title 181 NAC 2.

l. A Material Transfer Agreement (MTA) between the newborn screening laboratory responsible for the storage and release of specimens and the specimen recipients. The MTA must address prohibitions on secondary transfer and secondary research of DBS without state authorization; data sharing back to the state program; intellectual property rights, publication requirements, and acknowledgement of state resource use in publications".

2. For every specimen released for research, with or without patient identifying information, the laboratory must document:

a. Who had access to the specimen;
b. To whom the specimen was released;
c. The amount of specimen released; and
d. Evidence from the research entity that written consents were obtained from the legally responsible parent or guardian of the individuals whose specimens were released.

3. The blood spot is not released for public health research until after the 90-day storage time. During the 90-day storage time, it must be available for clinical purposes for the patient.

4. Records required at 181 NAC 2-007.08A, items 1 and 2, must be retained for 25 years.

2-007.08B Residual dried blood spots may be used for patient diagnostic testing when the ordering physician files with the laboratory a written request for specimen retrieval and a written authorization for release of the specimen signed by the parent or legal guardian.

2-007.08C Residual dried blood spots may be used for public health purposes as follows.

1. They may be used for quality assurance and improvement of newborn screening practices subject to the following:

a. Only dried blood spots deemed unsatisfactory for testing may be released to the submitting hospital to use as examples of poor specimen quality;
b. The filter paper portion of the CARE form containing the dried blood spots must be detached from the written patient identification part of the form prior to release;
c. The bar code and filter paper serial number linking the dried blood spot to the patient identification information must be removed from the residual dried blood spot prior to release; and
d. Requests for return of unsatisfactory specimens must be made by the submitting facility through the NNSP.

2. They may be used for other public health purposes when:

a. The Chief Medical Officer has determined there is a valid public health purpose;
b. The Chief Medical Officer has informed the Newborn Screening Advisory Committee about the public health use of the residual dried blood spots;
c. Patient information linking the specimen to the patient will be protected;
d. There are assurances that all applicable provisions of federal law will be complied with; and

e. The blood spot is not released or used for the public health purpose until after the 90-day storage time. During the 90-day storage time it must be available for clinical or identification purposes for the patient, unless a public health emergency is declared.

2-007.09 Data Reports: Reported data may be made available by the Department for purposes of research in aggregate statistical form or de-identified anonymous form. Written requests for release of this data for the purposes of research must be made to the NNSP. Review and approval of such requests will be at the discretion of the Chief Medical Officer.

2-007.10 Disposal of Residual Dried Blood Spots: Residual dried blood spots not released under 181 NAC 2-007.08 must be disposed of within 30 days of the end of the 90-day storage time. Destruction of the specimens, by incineration, by autoclaving and shredding, or by some other reasonable and prudent means, must ensure that identifying information cannot be linked to the residual dried blood spots.

2-007.11 Laboratory Provision of Access: Records required at 181 NAC 2-007.02F, 2-007.08, and 2-007.09 must be made available to the Department for inspection upon request.

2-008 BIRTHS NOT ATTENDED BY A PHYSICIAN: In the event a birth is not attended by a physician, the person registering the birth (who may be the parent) must ensure that:

1. The newborn has a newborn screening blood spot specimen collected as set out in 181 NAC 2-005.01 (between 24 and 48 hours of birth);
2. The specimen is submitted to the testing laboratory designated by the Department as set out in 181 NAC 2-006.01 (within 24 hours of collection); and
3. In response to a positive screening result, a confirmatory specimen is submitted to a testing laboratory in accordance with 181 NAC 2-007.01E within 48 hours of receipt of the newborn screening result.

2-009 ENFORCEMENT: Neb. Rev. Stat. § 71-524 provides as follows: In addition to any other remedies which may be available by law, a civil proceeding to enforce section 71-519 may be brought in the district court of the county where the infant is domiciled or found. The attending physician, the hospital or other birthing facility, the Attorney General, or the county attorney of the county where the infant is domiciled or found may institute such proceedings as are necessary to enforce such section. It shall be the duty of the Attorney General or the county attorney to whom the Department of Health and Human Services reports a violation to cause appropriate proceedings to be initiated without delay. A hearing on any action brought pursuant to this section shall be held within 72 hours of the filing of such action, and a decision shall be rendered by the court within 24 hours of the close of the hearing.

2-010 LABORATORY COLLECTION AND REMITTANCE OF FEES: There is hereby

assessed a fee of $10 for each infant screened for the diseases specified in 181 NAC 2-003. The laboratory conducting the tests for such diseases must collect a fee of $10 per infant screened, and submit the amounts collected to the Department for credit to the Department of Health and Human Services Cash Fund on a monthly basis.

Specimen Collection for Newborn Screening

Excerpt from *Blood Collection on Filter Paper for Newborn Screening Programs; Approved Standard—Fifth Edition* (LA4-A5)

1 PREPARATION

1.1 Wash hands vigorously.

1.2 Wear powder-free gloves and change gloves between infants.

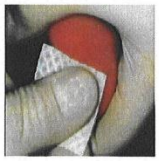
1.3 Confirm identity of infant and ensure that all data elements on the form are complete, accurate, and consistent.

2 SAMPLING TECHNIQUE

2.1 **Warm heel for puncture (incision/stick) site.** Heel warming devices containing an exothermic thermochemical composition are commercially available, or warm site with soft cloth, moistened with warm water **(less than 42 °C)** for three to five minutes. In some situations, warming site may not be necessary to increase blood flow and volume.

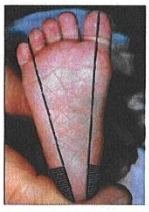
2.2 Position the infant's leg lower than the heart to increase venous pressure.

2.3 Wearing gloves, wipe infant's heel with 70% isopropyl alcohol. ▶ *

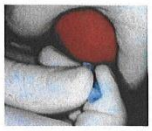


2.4 Allow heel to air dry.

2.5 The puncture should be made within the shaded area as illustrated in the figure to the right. ▶ *



2.6 Using a sterile lancet of recommended length, perform puncture (depth <2.0 mm) as illustrated or use an incision device. An incision device may provide superior blood flow by making a standardized incision 1.0 mm deep by 2.5 mm long. ▶ *



2.7 Gently wipe off first drop of blood with sterile gauze or cotton ball. (Initial drop contains tissue fluids, which might dilute sample.)

2.8 Wait for formation of large blood droplet.

2.9 Apply gentle pressure with thumb around the heel but not near the puncture site, and ease intermittently as drops of blood form.

2.10 Gently touch the filter paper card to the blood drop and fill each printed circle with a SINGLE application of blood. Apply blood to one side only. Observe the saturation of each printed circle as the blood flows through the filter paper. ▶ *

2.11 All used items should be disposed of in an appropriate biohazard container.

2.12 After the specimen is collected, elevate the infant's foot and, using sterile gauze or cotton ball, briefly apply gentle pressure to the puncture site until the bleeding stops. Do not apply adhesive bandages.

2.13 Allow blood specimen to AIR DRY THOROUGHLY, on a horizontally level, nonabsorbent, open surface, such as a drying rack or plastic-coated test tube rack, *for a minimum of three hours* at ambient temperature. Keep specimen away from direct sunlight. (Do not stack or heat.) ▶ †

2.14 After the specimen has dried, place in an approved container for transport. (See local regulations.)

3 PITFALLS

3.1 Failure to allow residual alcohol to dry might dilute the specimen and adversely affect test results.

3.2 Puncturing the heel on posterior curvature will permit blood to flow away from puncture, making proper spotting difficult. DO NOT USE PREVIOUS PUNCTURE SITES.

3.3 *Milking* or squeezing the puncture might cause hemolysis and admixture of tissue fluids with specimen.

3.4 Do not layer successive drops of blood on the target spot. If blood flow diminishes to incompletely fill circles, REPEAT sampling technique 2.1 through 2.10.

3.5 Avoid touching the area within the circle before and after blood collection. Do not allow water, feeding formulas, antiseptic solutions, or powder from gloves or other materials to come into contact with the specimen card before or after use.

3.6 Do not place the specimens in the transport container until thoroughly dry. Insufficient drying adversely affects test results. Use of sealed plastic bags requires desiccation. Ideally, transport specimens within 24 hours of collection.

** Photos reprinted with permission from New York State Department of Health.*

† Photo reprinted with permission from GE Healthcare.

Text describing how to collect an acceptable blood spot specimen reprinted with permission from Clinical and Laboratory Standards Institute.

ATTACHMENT 2

COLLECTION AND REPORTING (CARE) FORM – NEBRASKA NEWBORN SCREENING PROGRAM

Birth Date____/____/____ Time ____:____ (Military)
Collection Date____/____/____ Time ____:____ (Military)
Collector's Initials_____ Gestational Age:_____
Birth Weight_____
NICU Admit ☐ Yes ☐ No
If Yes, is this specimen: ☐ Initial specimen ☐ 48-72° repeat
☐ Other repeat ☐ 28 day/ discharge repeat for a < 2000 gram birth
Has baby EVER been transfused ☐ Yes ☐ No
If Yes, Date last transfused:___/____/____Time____:____(Military)
Baby receiving TPN ☐ Yes ☐ No
If yes, was it interrupted 3 hours before taking this specimen
☐ Yes ☐ No
Baby has Meconium Ileus or other bowel obstruction ☐ Yes ☐ No
Baby on Antibiotics ☐ Yes ☐ No

_____
Baby's last name
_____,_____
First name *Middle*
_____
Patient Record Number
_____
Place of Birth
Home birth ☐ Yes ☐ No Sex ☐ M ☐ F ☐Unknown

_____
Mother's last name
_____,_____
First name *Middle*
_____
Address
_____
City *State* *ZIP*
Mother's Phone_(_____)_____-_____
Mother's DOB____/____/____

NEBRASKA Serial No XXXXX

_____
Name of Submitter/Facility
_____
City *State (if other than NE)*
_____
Name of Ordering Physician
_(_____)_____-_____
Ordering Physician's Phone
_____
Name of Physician following baby post –discharge
_(_____)_____-_____
Post-discharge Physician's Phone

-Allow to air dry horizontally at least 3 hours
-Do not let blood spots touch anything before they are dry
-Ship within 24 hours (when transport available

SHIP TO:

Newborn Screening Laboratory Logo and Address

Date Received

Nebraska Collection and Reporting Form (Care Form)
Serial No XXXXXXXX

Date Reported

Note: Filter paper form not to scale.

ATTACHMENT 3

NEBRASKA NEWBORN SCREENING PROGRAM
NEWBORN TRANSFER FORM

Date of Transfer: _____ Person Completing Form:_____

Hospital of Birth:_____

Infant's Name: _____

Date of Birth: _____ Time of Birth: _____

Date of Specimen Collection:_____ Time of Specimen Collection:_____

Transferring Physician: _____

Newborn Screening Specimen Collected at Hospital of Birth: Yes No

Newborn Screening Specimen Collected Prior to 24 Hours of Age: Yes No

Infant transfused? Yes No

If yes, was specimen collected prior to transfusion? Yes No

If collected post-transfusion, indicate type: _____ and time of transfusion ___:___

Receiving Hospital: _____

Receiving Physician:_____

Person Receiving Form:_____

ATTENTION RECEIVING PHYSICIAN: If the newborn screening tests have not been performed or tests need to be repeated when you take charge of the infant, you are responsible for ordering a specimen and returning the results recorded on this form to the hospital of birth.

Forward one copy of this form to the receiving hospital and fax one copy to:

Nebraska Newborn Screening Program
Department of Health & Human Services
P.O. Box 95026
Lincoln, NE 68509
Fax 402-471-1863