Iowa Newborn Screening Program Practitioner's Manual

Iowa Newborn Screening Program (INSP) Contacts

I. ADMINISTRATIVE AND PROCEDURAL INFORMATION:

Center for Congenital and Inherited Disorders

Iowa Department of Public Health

Staff:

Kimberly Noble Piper RN, BS, CPH, CPHG
Executive Officer
Center for Congenital and Inherited Disorders
State Genetics Coordinator
1-800-383-3826
Kimberly.piper@idph.iowa.gov

II. INSP LABORATORY INFORMATION:

Stan Berberich PhD
Program Manager
(319) 335-4500

Tate Kappell
Supervisor
(515) 725-1630

III. FOLLOW-UP AND TREATMENT INFORMATION:

INSP Medical Consultants

- University of Iowa Hospitals and Clinics (UIHC)
  - Department of Pediatrics specialty services:
    - Allergy, Rheumatology and Immunology
    - Endocrinology
    - Hematology
    - Medical Genetics
    - Pulmonology

INSP Medical Director

- Dr. Amy Calhoun MD
  UIHC Department of Pediatrics
  Division of Medical Genetics

Short Term Follow Up (STFU):

- Carol Johnson, Coordinator

Email address
iowanewbornscreening@uiowa.edu

Main Telephone line

(319) 384-5097
Toll free line
866-890-5965

For emergency assistance after hours/weekends/holidays call (319) 356-1616 and ask for geneticist on call

IV. OVERVIEW OF IOWA NEWBORN SCREENING PROGRAM (INSP)

The objective of neonatal screening for metabolic and genetic disorders is the early identification and treatment of affected individuals in order to avoid adverse health consequences such as mental retardation, serious illness, and death.

- 1966 Newborn screening for phenylketonuria (PKU) begins in Iowa
- 1976 Birth Defects Institute (BDI) at the Iowa Department of Public Health is established
- 1983 Legislation passed in Iowa giving the BDI oversight responsibility for the INSP
- 2004 BDI name is changed to Center for Congenital and Inherited Disorders

The Center for Congenital and Inherited Disorders, with assistance from the Advisory Committee, designates the disorders to be screened and regularly evaluates the effectiveness and appropriateness of the program. Information pertaining to the Code of Iowa and the Iowa Administrative Code may be found at:

- Iowa Code: Chapter 136A.
  https://idph.iowa.gov/Portals/1/Files/Genetics/gen_chapter136A.pdf
- Administrative Code: 641, Chapter 4.3
  https://www.legis.iowa.gov/docs/iac/chapter/641.4.pdf

V. RESPONSIBILITIES

- The **attending healthcare provider** listed on the dried blood spot card has the ultimate responsibility for the screening of the newborn and follow-up of abnormal screening results according to Iowa Code. This includes informing the parent/guardian of NBS results (normal and abnormal), and carrying through with recommendations provided by the NBS program unless the provider has a reason to not do so

- **Parents or guardians** may or may not have been educated about NBS. Practitioners should be aware that parents may not have any knowledge about NBS (or remember what they've been told) when you contact them with abnormal results. Parents or guardians may refuse the newborn metabolic screening test, but are required to sign the Iowa Department of Public Health form "Refusal of Iowa Newborn Blood Spot Screening" after thorough discussion of the risks and benefits of testing with the attending healthcare provider.

- The Center for Congenital and Inherited Disorders has designated the **State Hygienic Laboratory** (SHL) as the central screening laboratory for the program.

- The Center for Congenital and Inherited Disorders has designated physicians as program **medical consultants**. The program medical consultants assist attending healthcare providers in confirming a diagnosis, recommending treatment, and advising follow-up care.

- The Center for Congenital and Inherited Disorders requires assurance of **confidentiality and security** of all patient records and program data.

VI. SELECTION OF DISORDERS SCREENED BY THE IOWA NEWBORN SCREENING PROGRAM

Each year the INSP identifies over 100 newborns with one of the disorders screened for by the program.

Many of the disorders we screen for are extremely rare (e.g., 1 in 48,000 live births for classic galactosemia), but without newborn screening many of these would remain undetected until it became too late for treatment to prevent, reduce, or reverse the health problems associated with these disorders.

Decisions for including a disorder in the newborn metabolic screening program are based on the following criteria:

1. There is evidence of substantial public health benefit and acceptance by the public and the medical community.
2. Screening is feasible and cost effective.
3. Satisfactory test methods and laboratory facilities are available.
4. Resources exist to provide counseling and follow-up, and to address other consequences of screening.
5. The disorder is treatable and generally not easily identifiable without screening.
6. If untreated the disorder is likely to result in significant costs to the individual, the family and society.

Secretary's Committee
(http://www.hrsa.gov/advisorycommittees/mchbadvisory/heritabledisorders/)

The Advisory Committee on Heritable Disorders in Newborns and Children (Committee) was established under the Public Health Service Act, Title XI, § 1109 (42 U.S.C. 300b-10), as amended by the Newborn Screening Saves Lives Reauthorization Act of 2014 (P.L. 113-240).The mission of the Advisory Committee on Heritable Disorders in Newborns and Children is to reduce morbidity and mortality in newborns and children who have, or are at risk for, heritable disorders. The Committee advises the Secretary, U.S. Department of Health and Human Services on the most appropriate application of universal newborn screening tests, technologies, policies, guidelines, and standards. The Committee has established a Recommended Uniform Screening Panel (RUSP) of core conditions and secondary conditions which states are encouraged to include in their state newborn screening panels.

VII. LIST OF CORE CONDITIONS CURRENTLY SCREENED FOR IN IOWA:

Provider facts sheets for all of these disorders can be accessed electronically here:
https://idph.iowa.gov/Iowa-Newborn-Screening-Program/For-Providers-and-Professionals/Conditions-Screened

- **Endocrine**:
  - Congenital adrenal hyperplasia (CAH)*
  - Primary congenital hypothyroidism (CH)*
- **Classic galactosemia** (GALT)*
- **Biotinidase deficiency** (BIOT)*
- **Cystic fibrosis** (CF)*
- **Severe combined immune deficiency** (SCID)*
- **Hemoglobinopathies**
  - Sickle Cell anemia (Hb SS)*
  - Hemoglobin SC disease (Hb SC)*
  - Sickle beta-thalassemia (Hb Sβ)*
- **Amino Acidemias**
  - Argininosuccinic aciduria (ASA)*
  - Citrullinemia, type I (CIT)*
  - Homocystinuria (HCY)*
  - Maple syrup urine disease (MSUD)*
  - Classic phenylketonuria (PKU)*
  - Tyrosinemia, type I (TYR-1)*
- **Organic Acidemias**
  - Glutaric acidemia type I (GA-1)*
  - 3-hydroxy 3-methylglutaric aciduria (HMG)*
  - Isovaleric acidemia (IVA)*
  - 3-methylcrotonyl-CoA carboxylase (3-MCC)*

- Methylmalonic acidemia—cobalamin disorders (Cbl-A,B) & methylmalonyl-CoA mutase deficiency (MUT)
- βeta-ketothiolase (βKT)*
- Propionic acidemia (PROP)*
- Holocarboxylase synthetase deficiency (MCD)

➢ **Fatty Acid Oxidation Disorders**

- Carnitine uptake defect & Carnitine transport defect (CUD)*
- Long-chain L-3 hydroxyacyl-CoA dehydrogenase (LCHAD)*
- Medium-chain acyl-CoA dehydrogenase deficiency (MCAD)
- Trifunctional protein deficiency (TFP)*
- Very long-chain acyl-CoA dehydrogenase deficiency (VLCAD)*

[*Secretary's Advisory Committee on Heritable Disorders in Newborns and Children (SACHDNC) Recommended Uniform Screening Panel - Core Panel]

VIII. Expanded Screening

Over thirty disorders can be screened simultaneously from a single blood spot specimen using tandem mass spectrometry technology (TMS or MS/MS). The Iowa Newborn Screening Program began a pilot study in October 2001 for the disorders detectable by MS/MS. Almost all Iowa infants born after October 2001 have been screened for all currently known MS/MS detectable disorders unless a parental waiver was signed.

Individuals found to have one of the detectable disorders by newborn screening are treated by dietary management, monitoring, and/or amino acid and vitamin supplementation to prevent or significantly reduce clinical symptoms.

The disorders screened by tandem mass spectrometry fall into three categories of inheritable metabolic disorders:

Amino Acid Disorders

Individuals with amino acid disorders have a deficiency in one of several pathways or cycles involved in protein metabolism. For amino acid disorders detectable by MS/MS, early treatment allows for the prevention of brain damage, mental retardation, coma, seizures, autistic-like disorders, and even death.

- Argininosuccinic aciduria (ASA)

- Citrullinemia, type I (CIT)
- Homocystinuria (HCY)
- Maple syrup urine disease (MSUD)
- Classic phenylketonuria (PKU)
- Tyrosinemia, type I (TYR-1)

Fatty Acid Oxidation Disorders

Individuals with fatty acid oxidation disorders are unable to break fats down into energy because of specific enzyme deficiencies essential in the fatty acid metabolic pathway. Normally, fat is broken down into energy by enzymes. This energy keeps the body running whenever it runs outs of its main source of energy, which is glucose. It is crucial that individuals with these disorders don't have prolonged fasting. Prolonged fasting can lead to life threatening hypoglycemia. It is estimated that 1 to 2/100 "SIDS" cases are the result of an undiagnosed fatty acid oxidation disorder. Newborn detection of the disorders and early treatment allows for prevention of the symptoms. Treatment includes avoidance of fasting, dietary management of fat intake and L-Carnitine supplementation for most of the disorders. Carnitine is needed to take toxic products out of the body so that an individual does not have irreversible damage. Insurance companies typically cover L-Carnitine supplementation. Individuals with specific fatty acid oxidation disorders, such as 3-Hydroxyacyl CoA Dehydrogenase Deficiency (LCHAD) or Very-Long-Chain Acyl-CoA Dehydrogenase Deficiency (VLCAD) require Medium Chain Triglycerides (MCT) oil.

- Carnitine uptake defect & Carnitine transport defect (CUD)
- Long-chain L-3 hydroxyacyl-CoA dehydrogenase (LCHAD)
- Medium-chain acyl-CoA dehydrogenase deficiency (MCAD)
- Trifunctional protein deficiency (TFP)
- Very long-chain acyl-CoA dehydrogenase deficiency (VLCAD)

Organic Acid Disorders

Organic acid disorders occur because of alterations in pathways of intermediary metabolism for amino acids, carbohydrates, and fatty acids. Babies with an organic acid disorder cannot remove certain waste products from their blood. Newborn detection of the disorders and early treatment allows for prevention of symptoms, which include neonatal hypotonia, respiratory acidemia, respiratory acidosis, muscle atrophy, seizures, developmental delays, coma, and death. Carnitine supplementation and dietary management is used to treat individuals with

many of the disorders. Treatment of methylmalonic acidemia (MMA) may require medical food supplementation.

- Glutaric acidemia type I (GA-1)
- 3-hydroxy 3-methylglutaric aciduria (HMG)
- Isovaleric acidemia (IVA)
- 3-methylcrotonyl-CoA carboxylase (3-MCC)
- Methylmalonic acidemia—cobalamin disorders (Cbl-A,B) & methylmalonyl-CoA mutase deficiency (MUT)
- βeta-ketothiolase (βKT)
- Propionic acidemia (PROP)
- Holocarboxylase synthetase deficiency (MCD)

IX. IMPORTANT NEWBORN SCREENING CONSIDERATIONS

- **Newborn screening tests are not diagnostic!**

- Some of these disorders are considered **time critical disorders**
  - Babies with one of these conditions may have only hours before the onset of a health crisis that can cause death or permanent disability!
  - The time critical disorders are:
    - Congenital adrenal hyperplasia
    - Congenital hypothyroidism
    - Galactosemia
    - Most of the Metabolic disorders
  - The time critical disorders are the ONLY presumptive positive results that are called out emergently on weekends or holidays…**IF YOU RECEIVE A CALL from newborn screening program on a weekend or a holiday, we expect PROMPT action to be taken…timeliness in newborn screening can save a baby's life!!**
  - See expanded section on Timeliness in Blood Spot Newborn Screening

- The possibility of a false negative or false positive result must always be considered.

- Due to biologic variability, some affected infants may have normal screening results (a false negative screening result).

- False positive results may be due to immature endocrine or enzyme function in the newborn, the stress of birth on an infant, or the specimen being collected prior to 24 hours after birth. INSP establishes screen cutoff values, which keep the number of false positives at a minimum, yet minimizes the likelihood of an affected newborn being missed.

- A newborn screen may detect specific mutations only (e.g., CAH due to 21-hydroxylase or 11-beta-hydroxylase deficiency and not other variants).

- **In almost all circumstances, treatment should not be initiated without consultation with program medical consultants**. Treatment prior to diagnostic confirmation may interfere with confirmatory testing. Moreover, it may cause irreversible harm to the infant.

X. Timeliness in Blood Spot Newborn Screening

Why is Timeliness in Newborn Screening Important?

Some of the disorders we screen for are life threatening. We refer to these disorders as "time critical" disorders, because babies with one of these conditions may have only hours before the onset of a health crisis that can cause death or permanent disability.

This is why collecting the screen as close to 24 hours is so important. If we can narrow the time from collection of the baby's sample to when the critical lab result is known and acted on, we can intervene and help minimize or prevent any serious complications for the baby.

This is also why it is very important to get the screen sent to the newborn screening lab for testing the same day it is collected. Timeliness in newborn screening SAVES BABIES' LIVES!

What are the time critical disorders?

- Congenital Adrenal Hyperplasia
- Congenital Hypothyroidism
- Galactosemia
- Metabolic Disorders (most)

The time critical disorders are the only presumptive positive results that are called out on the weekend or holidays. **If you receive a call from the newborn screening program on a weekend or holiday, we expect prompt action to be taken because your timely response could save a baby's life if they have one of these time critical disorders!**

Who is Responsible for Timeliness in Blood Spot Screening?

If you have a reason to read the practitioner's manual, then **YOU** are one of the people involved in the newborn screening process and you have a role to play in timeliness in newborn screening.

Some common stakeholders include:

- staff in the mother/baby units;
- staff in the NICU,
- staff in the hospital lab, especially in the mail out area;
- phlebotomists;
- risk managers/QI staff;
- hospital administrators;
- baby's PCP and staff;
- the person who's name is listed on the dried blood spot card;
- the parents;
- the staff of the newborn screening program

What Can I Do to Improve Timeliness in Newborn Screening?

- Ascertain which babies are eligible to be screened each day (babies that will be 24 hours and 1 minute old).
- Make a plan not only to get these babies screened, but to make sure that the screen is able to dry for at least 3 hours (horizontally on a clean, dry surface) and sent to the newborn screening lab through the courier service *the same day it is collected*.
    - **HINT:** Find out when the newborn screening courier comes to your facility and work backwards to determine the optimal time for collecting newborn screens in your facility to allow for a minimum 3 hour drying time and still allow them to go out on the courier the same day!
- Some hospitals in Iowa have formed their own "timeliness teams" to address specific timeliness issues at their facility. The Iowa Newborn Screening Program strongly encourages this and is happy to provide technical assistance/education to these teams.

What is the Newborn Screening Program Doing to Improve Timeliness in Newborn Screening?

The Iowa Newborn Screening Program (INSP) has the distinction of being known as the timeliest newborn screening program in the United States!

Here are some of the things that the program is doing to improve timeliness in newborn screening:

- The newborn screening program works 7 days a week (courier, lab, follow up, and consultants)
- INSP set a goal for the lab to receive all newborn screens =< 60 hours after birth
- Provides education to birthing facilities, midwives, PCPs, parents, etc.
- Provides hospitals/birthing centers/midwives with monthly or quarterly data on how they are performing for meeting the state timeliness goal
- Provides technical assistance when requested
- Sharing stories with how others have improved timeliness
- Hosts webinars on timeliness
- Participates in national timeliness projects
- Awarded funding to improve timeliness in newborn screening from the Health Services Research Administration/Association of Public Health Laboratories

Is Timeliness Important for Confirmatory Testing, Repeat Screens and Referrals?

- **Yes!**
- Confirmatory tests should be collected as soon as possible after the PCP is notified, ideally within 24 hours.
- The timing for requested repeat screens is between Days 3-7 from notification.
- Referrals to specialists and Cystic Fibrosis Centers for sweat tests should be done within 24 hours from notification.

XI. Baby Matching in the State of Iowa

In order to ensure every infant in Iowa receives a dried blood spot newborn screen the INSP will perform a review of birth certificate registrations from the Bureau of Health Statistics at the IDPH and records of newborn screening tests from the State Hygienic Laboratory newborn screening data system. If there is concern a screen was not obtained on and infant the INSP will follow up with the infant's birth provider and primary care provider to have infant screened as soon as possible.

XII. Refusal by Parents/Guardians of Newborn Screening

Should a parent or guardian refuse the screening, said refusal shall be documented in the infant's medical record, and the parent or guardian shall sign the refusal of screening form. The birthing facility or attending health care provider shall email or fax the signed refusal of screening form to the central laboratory within six days of the refusal. The birthing facility or attending health care provider may submit refusal forms via the courier service established for the transportation of newborn screening specimen collection forms.

The form can be found here:

https://idph.iowa.gov/Portals/1/userfiles/35/NBS%20blood%20spot%20refusal_1.pdf

XIII. Factors affecting the newborn screen:

	Early Collection	Transfusion	Heat/ Humidity	TPN	Steroids/ Other Medication (ex: certain antibiotics)	Prematurity	Weight
CH	x				x		
CAH	x						x
BT		x	x		x		
GALT		x	x		x		
HB		x			x		
IRT		x			x		
TMS	x			x	x	x	
TREC						x	

- **Early Collection:**
  A screening specimen collected before 24 hours of age could give false positive or false negative test results. Blood specimens should be collected from newborns between 24-48 hours and 5 days of age. We are encouraging collection as soon after 24 hours as possible to allow for more timely identification of life-threatening metabolic disorders.
  Exceptions to the 24-hour rule: A newborn screen should always be collected prior to transfusion, transfer, or discharge. Facilities responsible for transferring an infant should collect a newborn screen prior to the transfer unless the baby is critically ill and doing so would interfere with life sustaining measures. Failure to obtain a screen prior to transfer can result in the baby's screen being missed.

- **Transfusions:**
  Red blood cell (RBC) transfusions interfere with the interpretation of some newborn metabolic screening results. Whenever possible, the newborn screen should be

collected prior to a RBC transfusion, even if less than 24 hours of age. IF an infant was transfused at the time of collection, a follow-up filter paper specimen must be collected at least 8 weeks after the last transfusion.

- **Heat and Humidity:**
  Because some of our lab assays directly measure enzyme activity, exposure to direct sunlight, heat, and/or high levels of humidity can cause these enzyme levels to degrade too rapidly to allow for accurate testing. A dried blood spot specimen should never be left to dry in a vehicle or other place where it can be exposed to extreme temperature and humidity variations.

- **Total Parenteral Nutrition (TPN):**
  Infants on some types of TPN may show elevated levels of amino acids (e.g., phenylalanine). Indication of TPN status on the collection form is necessary for clarifying some test results.

- **Hormone (Steroid) Therapy:**
  Steroids administered to the mother during pregnancy, or to the infant immediately after birth, can interfere with congenital adrenal hyperplasia test results. Contact the endocrine consultants regarding management for these situations, (319) 356-2838.

- **Thyroid Medications:**
  When thyroid medications are administered to the mother during pregnancy, Congenital Hypothyroidism screening results are not reliable. Contact the Pediatric Endocrinology Consultants regarding management for these situations, (319) 356-2838

- **Prematurity:**
  SCID screening in Iowa is done through T-cell receptor excision circle (TREC) analysis. SCID is a lack of T cells which makes an infant extremely susceptible to infections. TRECs (T-cell receptor excision circles) are pieces of DNA produced in the thymus. Premature infants frequently have lower TREC levels compared to term infants. This finding can be secondary to several factors including time for T-cell maturation in the thymus, medications given prior to delivery which might reduce T-cell numbers, and/or dilutional factors related to sample collection from an indwelling catheter.

- **Infant's Weight:**
  Transient elevations of 17-OHP (the analyte for the congenital adrenal hyperplasia - CAH screen) may occur in pre-term and low birth weight babies. Because of this, four weight related 17-OHP ranges are in place to minimize the number of false positive results. Without a weight indicated on the collection form, CAH results cannot be reported. If the weight is inadvertently omitted you can fax the weight at

time of collection to the lab and we will reissue the report based on the new information. The fax number is 515/243-3071.

XIV. **How to Complete Iowa Newborn Screening Cards (electronic version of this section can be accessed here:**
https://idph.iowa.gov/Portals/1/userfiles/35/Newborn%20Screening%20Collection%20Cards-8_5x11%20V2%20%281%29.pdf

General Information

It is extremely important to fill out the screening card accurately and completely. *Inaccurate or missing information may adversely affect screening results and/or the ability to quickly contact the infant's care provider in the event of an abnormal screening result.* ***Any delay may put the child's health at risk.***

The specimen submitter is legally responsible for the accuracy and completeness of the information on the newborn screening card.

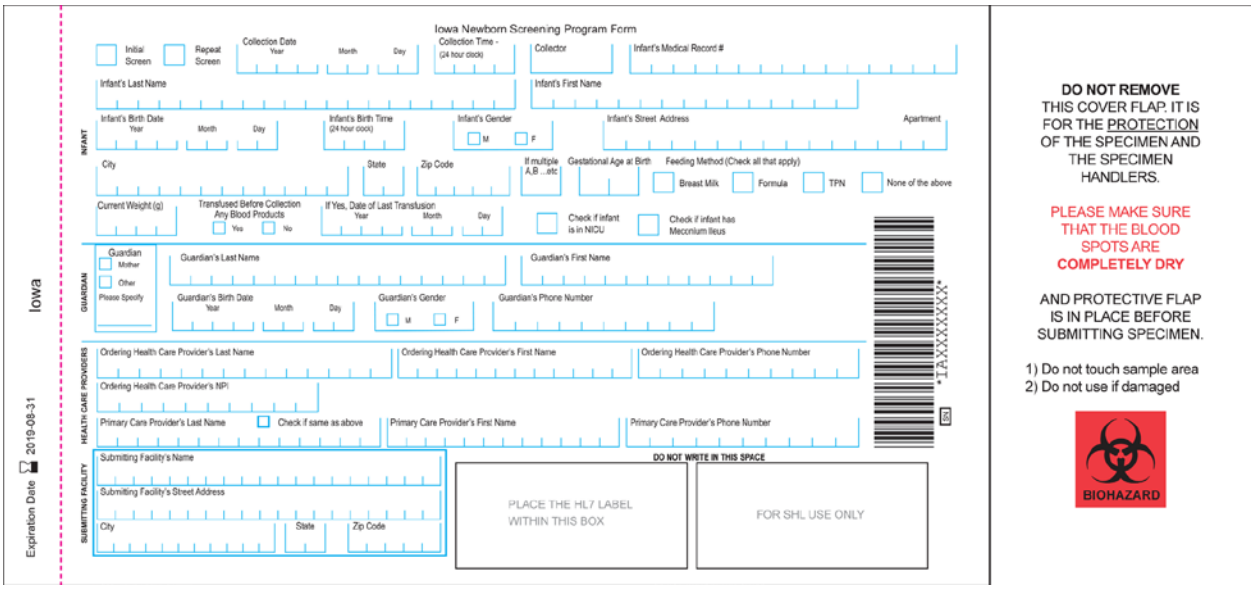
Remember:

- Write firmly in blue or black ink to ensure that all information is transferred between carbon copies.
- Remove the second ply for the facility's records.

For questions, please call the

State Hygienic Laboratory at 515-725-1630.

Hours: Monday - Friday 8:00 a.m. to 4:30 p.m.



Sample Information

Do not place stickers/labels or write in the lower right-hand side of the card in the area that says "FOR SHL USE ONLY"

- Place the HL7 (Health Level 7) label in the designated box if your facility electronically orders newborn screening tests. Leave this box empty if your facility does not electronically order newborn screening tests.
- The box "**For SHL Use Only**" is used by the newborn screening lab. Do not write or apply stickers/labels in this area.

Initial Screen vs. Repeat Screen:

- Check the appropriate box: "Initial" or "Repeat."
- Initial screen is the first submission.
- Repeat screen(s) are any subsequent submission(s) received after the initial screen, even if the resubmission is due to poor quality/specimen rejection, prior early collection samples, etc.

Collection Date:

- Use an eight-digit format (yyyy/mm/dd) for the newborn's date of collection. For example, a sample collected on March 9, 2015, would be recorded as 2015 03 09.

Collection Time:

- Always use 24-hour clock (HH:MM) when entering the time of collection.
- Validity of test results are specific to the exact age (in hours) of the infant, so an accurate time of collection is crucial.

Collector:

- Use unique identifier (initials, last name, employee ID number, etc.) for the person collecting the sample. Each facility can determine its own unique identifier for internal use.

Infant Information

Infant Medical Record Number:

- Write the infant's medical record number.
- **Do not record the mother's medical record number.**

Infant's Last Name:

- Write the infant's last name.
- It is important to list the infant's last name regardless of whether the guardian(s) has chosen a first name.
- Do not assume that the infant's last name is the same as the mother's last name. Record the last name the infant will go by at discharge.
- Providing an incorrect name could potentially cause a delay in reporting abnormal results and impact the health of the infant.

Infant's First Name:

- Record infant's first name, if known.
- If the guardian(s) have not yet chosen a first name, leave this field blank.
- Providing an incorrect name could potentially cause a delay in reporting abnormal results and impact the health of the infant.

Infant's Birth Date:

- Use an eight-digit format (yyyy/mm/dd) for the infant's date of birth. For example, an infant born on March 9, 2015, would be recorded as 2015 03 09.

Infant's Birth Time:

- Always use 24-hour clock (HH:MM) when entering the time of birth. For example, the time for a baby born at 4:15 p.m. would be recorded as 16:15.
- Validity of test results are specific to the exact age (in hours) of the infant, so an accurate birth time is crucial.

Infant's Gender:

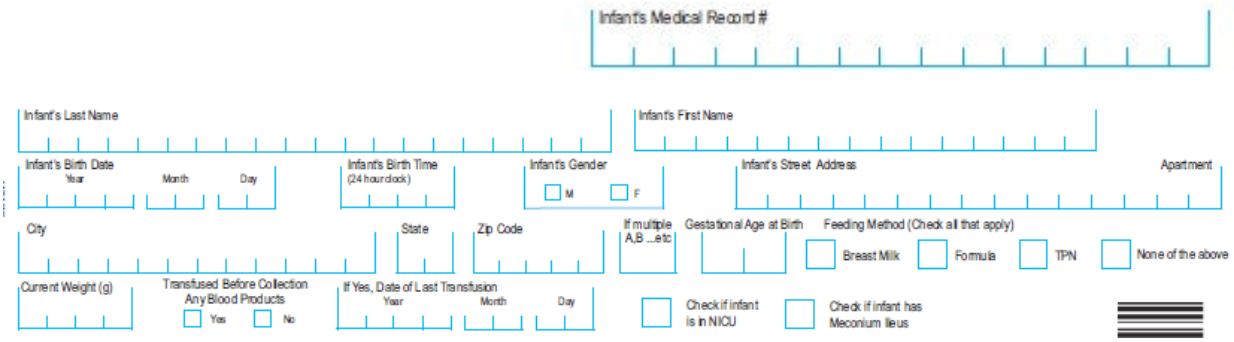
- Mark "M" for male or "F" for female. If unknown or ambiguous genitalia, write "Unknown" in the Infant's Gender box.
- This helps with the identification of the baby.

Infant's Street Address:

- Record where the infant will reside.
- Use complete address, city, state and zip code.
- In the event of an adoption or other guardianship, record the address where the infant will reside.
- Accurate contact information is crucial for contacting the guardian in the event of an abnormal result or a need for retesting.

If Multiple A, B…etc.:

- If the infant is one of a set of multiple births (twins, triplets, etc.) record the birth order of the infant. For example, if the infant was the first born in a set of triplets, write "A", in the box. For the third born infant, write "C" in the box.
- If single birth, leave blank, put a line through the field or cross it out.
- This field is not in reference to the birth order of ALL pregnancies but the <u>birth order of this one pregnancy</u>.



Gestational Age at Birth:

- Record the infant's week of gestation at time of birth. Record in completed weeks only, no rounding up.

- Accurate gestational age is critical for analyzing the results of newborn screening tests. This includes all collections - initial and repeat screens.
- If unknown, write “Unknown.”

Feeding Method:

- Check all types of feeding that apply within the last 24 hours. For example, if the infant has received both Total Parenteral Nutrition (TPN) and breast milk in the last 24 hours, check both boxes.
- Breast milk includes milk sourced from biological mother or donor milk.
- TPN includes, but is not limited to, Neonatal Venous Nutrition (NVN), Peripheral Parenteral Nutrition (PVN), Hyperalimentation (Hyperal), Starter TPN, any supplementation that includes amino acids, and/ or any additional TPN products not mentioned.
- If infant is receiving fluids only and/or no other feeding method listed, check “None of the above.”
- Formulas include all special formulas and additives (e.g. Human Milk Fortifier, Beneprotein, etc.).

Current Weight (g):

- Record the infant’s weight in grams at time of specimen collection.
- Do not leave blank. It is important to correctly record the infant’s weight for accurate test results.

Transfusion (Any Blood Products):

- This field **MUST** be marked “Yes” or “No” because transfusion status affects results. Missing information could lead to delays. If the infant was given any blood product BEFORE newborn screen collection, check “Yes.” If the infant was NOT transfused or transfused after collection check “No.”
- Write the date of the most recent transfusion. If infant has received multiple transfusions, you only need to record the most recent date of transfusion.
- Use an eight-digit format (yyyy/mm/dd) for the most recent transfusion date. For example, infant was last transfused on March 9, 2015, recorded as 2015 03 09.
- Transfusion includes ALL blood products including, but not limited to, red blood cells, plasma, immunoglobulins and platelets.
- If baby received a transfusion before delivery (intrauterine), mark “Yes” and record the date of the most recent transfusion.

Check if infant is in NICU:

- Check the box if the patient is in Neonatal lntensive Care/ Pediatric Intensive Care Unit (NICU/PICU) or another high-acuity level care unit at time of collection.
- If infant is not in NICU/PICU, leave blank.

Check if infant has Meconium Ileus:

- Meconium ileus is known to interfere with the screening for cystic fibrosis. If meconium ileus is suspected, the screening algorithm for cystic fibrosis will change.
- Check the box ONLY IF the infant has or is suspected of having meconium ileus.
- If no meconium ileus is suspected, leave blank.

Guardian Information

Guardian is considered the person with the legal authority to care for the infant. In most cases, this is the birth mother but can include other legal guardian relationships if birth mother is not the legal guardian.

Guardian Box:

- Mother is in reference to biological mother. If biological mother is legal guardian, check "Mother."
- If legal guardian is any other relation other than biological mother, mark "Other."
- If the infant is in the custody of the biological mother, provide the mother's information as the guardian. If the mother is not a legal guardian, provide legal guardian information.
- If other, record relation under "Please Specify." Examples of "other" include adoptive parent, human services, adoption agency, grandparent, etc.

Guardian Last Name and First Name:

- Record the guardian's last name followed by first name.
- In the event of an adoption, record the name of the legal guardian (adoptive parent, adoption agency, social worker, etc.).
- If infant was born via surrogacy, provide the name of the legal guardian who will take care of infant post-delivery.
- Accurate identifying information is crucial for contacting the guardian in the event of an abnormal result or a need for retesting.
- In the event that the infant will be held in protective services, record the name of the infant's social worker or legal guardian.

Guardian's Birth Date:

- Use an eight-digit format (yyyy/mm/dd) for the guardian's date of birth. For example, a guardian born on March 9, 2015, would be recorded as 2015 03 09.
- In the event of an adoption, write the date of birth of the adoptive parent.

Guardian's Gender:

- Check "M" for Male or "F" for Female.

Guardian's Phone Number:

- Record the guardian's phone number (including area code) at which he/she most easily can be reached in case of emergency.
- In the event that infant is not in the custody of birth parents, provide contact information for the legal guardian.
- In the event of an adoption, record the phone number of the case worker here.
- In the event that the infant will be held in protective services, record the phone number of the legal guardian or social worker. *Make sure the number provided will be answered on weekends and holidays in case of emergencies*.
- Accurate contact information for a guardian is important to ensure that the infant can receive follow-up testing and/or care in the event of an abnormal result. Make sure the guardian's number provided will be answered on weekends and holidays in case of emergencies.

Health Care Provider Information

Ordering Health Care Provider's Name:

- Record the name of the health care provider ordering the infant's newborn screen, using last name followed by first name.

Ordering Health Care Provider's Phone Number:

- Provide the phone number (including area code) for the health care provider ordering the infant's newborn screen.
- This information may be used to contact the provider with abnormal test results and follow-up information.

Ordering Health Care Provider's National Provider Identifier Number (NPI)

- Provide the Ordering Health Care Provider's National Provider Identifier number to help correctly identify the correct provider.
- This information may be known by lab staff or billing staff at your facility.

Primary Care Provider Responsible for Infant Follow-Up After Discharge:

- If the Primary Care Provider is the same as the Ordering Health Care Provider, check the box "Check if same as above."
- If the Primary Care Provider is different from the Ordering Health care provider, record the name of the Primary Care Provider, using last name followed by first name.
- If the provider is not known at the time of specimen collection, be sure to write down the name of the clinic where the guardian(s) plan to take the newborn for his or her first well child check.
- Do not write the name of the provider who completed rounds on the newborn in the hospital.
- Correctly recording this information is critical. The Newborn Screening Program needs the name of the primary care provider to make sure follow-up of abnormal results is completed.

Primary Care Provider's Phone Number:

- Provide the phone number (including area code) for the infant's primary care provider.

- This information is used to contact the provider with abnormal test results and follow-up information.

Submitter Information

<u>Apply the pre-printed labels</u> supplied by the State Hygienic Laboratory with the collection forms:

Verify that the label matches your submitter name and address.

- Do not share forms or labels with other submitters as this can lead to results being sent to wrong facilities/providers/midwives.
- The submitter information provided is used for result reporting purposes as well as billing. Provide accurate and complete information.

<u>If no label is available:</u>

Submitting Facility Name:

- Record the name of the hospital, clinic or midwife who collected the specimen.

Submitting Facility's Complete Address:

- Write the street address of the submitter (vital because many institutions have the same name and/or are part of a larger affiliation).
- Write the city, state and zip code.

Refusals:

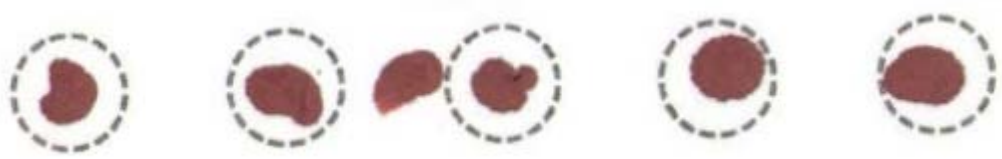
- It is possible for people to refuse screening, though it is important that education on the importance of screening is emphasized before the decision is made. If the family still chooses to refuse screening, you will have them sign the refusal form, and then fax it to 1-319-384-5116.
- Refusal form can be found at http://idph.iowa.gov/genetics/provider/newborn-screening

XV. REJECTION OF SPECIMENS BY STATE HYGIENIC LABORATORY (SHL):

Reasons WHY specimens are rejected:

1. Specimen quantity insufficient for testing.

- Possible causes:
  - Removing filter paper before blood has completely filled circle or before blood has soaked through to the other side.
  - Applying blood to the filter paper with a capillary tube.
  - Allowing filter paper to come in contact with gloved or ungloved hands and/or substances such as hand lotion or powder, which may interfere with absorption.



2. Specimen received in the lab > 9 days from collection date.

- Possible causes:
  - The specimen may have been lost or misdirected in the mail.
  - Specimens may have been batched for several days before being mailed. **Do not hold or batch specimens. Mail within 24 hours after collection. Facilities are encouraged to use overnight delivery.**

3. Specimen appears clotted or layered.

- Possible causes:
  - Applying more than one drop of blood to the same filter paper circle.
  - Filling circle from both sides of filter paper.

(Layered specimen)

(Clotted specimen)

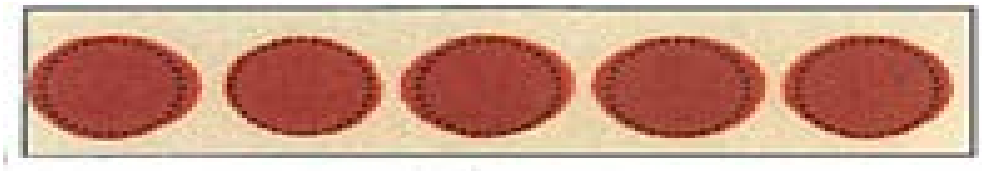
4. Specimen appears scratched or abraded.

- Possible causes:
  - Applying blood with a capillary tube or other device.

5. Specimen not dry before mailing.

- Possible causes:

• Mailing specimen before drying for a minimum of three to four hours.



6. Specimen appears over saturated or unevenly saturated.

- Possible causes:
  - Applying excess blood to the filter paper, usually with a device.
  - Applying blood to both sides of the filter paper.

(Over saturation)

(Uneven saturation)

7. Specimen appears diluted, discolored, or contaminated.

- Possible causes:
  - Squeezing or "milking" of area surrounding the puncture site.
  - Allowing filter paper to come in contact with gloved or ungloved hands, or substances such as alcohol, formula, antiseptic solutions, water, hand lotion, or powder, etc., either before or after blood specimen collection.
  - Exposing blood spots to direct heat.

8. Specimen exhibits serum rings.

- Possible causes:
    - Not wiping alcohol from puncture site before making skin puncture.
    - Allowing filter paper to come in contact with alcohol, hand lotion, etc.
    - Squeezing area surrounding puncture site excessively.
    - Drying specimen improperly.
- Applying blood to filter paper with a capillary tube

XVI. FREQUENTLY ASKED QUESTIONS

What is the purpose of the Iowa Newborn Screening Program (INSP)?

The purpose of the Iowa Newborn Screening Program (INSP) is to screen all newborns in Iowa for genetic and metabolic disorders than can lead to serious health consequences. By early identification of these disorders, a newborn can be treated before symptoms appear, preventing intellectual disability, serious illness, and death.

What is the chance that a baby will actually have one of the disorders detectable by screening?

The chance that a baby will have one of these disorders is very small. In the rare cases when a disorder is found, early diagnosis and treatment can usually prevent the problems associated with these disorders. All abnormal screen results should be taken seriously and recommended follow-up should be done as soon as possible.

Who decides which disorders are included on the Iowa's newborn metabolic screening panel?

The Center for Congenital and Inherited Disorders of the Iowa Department of Public Health is responsible for deciding the list of disorders. A Congenital and Inherited Disorders Advisory Committee, made up of doctors, nurses, legislators, parents and consumers, advises the Center regarding which disorders to include, based on nationally

accepted criteria. The Iowa State Board of Health provides final approval for the addition of new disorders to the screening panel.

Is there a charge for repeat screening?

Although there is a charge for the initial screen, the Iowa Newborn Screening Program does not charge for repeat screens. However, facilities collecting the repeat screen may have specimen collection charges, such as lab drawing fees.

Why is it necessary to retest some babies?

Premature babies may have immature enzyme systems or thyroid functioning. It may be necessary to monitor their progress to be certain they reach normal levels. Unnecessary repeat testing can be avoided by collecting blood specimens 24 hours after birth, before a transfusion, and using correct specimen collection procedures.

Why was the screening specimen reported as poor quality when I know there was plenty of blood in the circles?

All tests performed by INMSP are calibrated to an expected blood volume contained in a 1/8-inch punch of filter paper. There must be an even penetration of blood for the test to be accurate. This means soaking through the filter paper with ONE application and filling the entire circle. Refer to section "REJECTION OF SPECIMENS BY STATE HYGIENIC LABORATORY (SHL)".

Submitting a poor quality specimen results in the inconvenience of recollecting another specimen and delays the screening of the newborn. **This places the newborn at risk for delayed diagnosis of a metabolic condition**. It is important that another sample is collected from the newborn as soon as possible.

Why do some newborn screens have "false positive" results?

False positive results may be due to immature endocrine or enzyme function in the newborn, the stress of birth on an infant, or the specimen being collected prior to 24 hours after birth. INSP establishes screen cutoff values, which keep the number of false positives at a minimum, yet minimizes the likelihood of an affected newborn being missed.

What do I do if the parents refuse the screen?

Should a parent or guardian refuse the screening, said refusal shall be documented in the infant's medical record, and the parent or guardian shall sign the refusal of screening form. The birthing facility or attending health care provider shall submit the signed refusal of screening form to the central laboratory within six days of the refusal. The birthing facility or attending health care provider may submit refusal forms via the courier service established for the transportation of newborn screening specimen collection forms.

The refusal form can be found on the Iowa Department of Public Health's website Iowa Newborn Screening Page:
https://idph.iowa.gov/Portals/1/userfiles/35/NBS%20blood%20spot%20refusal_1.pdf

If newborn metabolic screening is not done for some reason in the first week of life, is it worthwhile to still screen the baby later?

Yes. While some disorders may begin to be expressed and some damage may have already occurred, treatment begun at any time will always be beneficial to the infant. Additionally, the family should be made aware of the infant's metabolic disorder, its genetic implications, and given appropriate counseling. Ideally, all babies should be screened in the first week of life, but screening a baby later is better than never screening at all.

Is there an age limit for newborn metabolic screening?

Infants can be screened for all disorders up to one year of age. CH and CAH ranges apply to the newborn period, and interpretation of results from specimens collected after the newborn period should be performed in consultation with the appropriate specialist. A specimen received on a child greater than one year of age will not have CH and CAH reported.

Will breast-feeding alter the results of the newborn screen?

Breast milk is an adequate source for protein challenge and should not adversely affect results of the newborn screen.

What do I do if a baby has moved here from out of state?

Collect another specimen if you don't have documentation that the infant had a newborn screen prior to the move.

Do I need to repeat the screen if the infant is receiving antibiotics?

No. Antibiotics do not interfere with current screening methodologies.

Whose responsibility is it to advise the parents about the screen?

The licensed attending health care provider has the ultimate responsibility for ensuring that an infant under their care has newborn screening. A parent or guardian should be informed of the type of specimen collected, how it is obtained, the nature of the disorders being screening, and the consequences of treatment and non-treatment. The responsibility includes following up on any abnormal screening results.

Can newborn screening be done if a baby is born at home?

Yes. Parents should arrange with their doctor, nurse, hospital, or midwife to have a newborn screening specimen collected. The Bureau of Vital Records at the Iowa Department of Public Health distributes newborn screening collection forms and parent brochures with their home birth registration packets. The specimens should be collected between 24 hours and 5 days of age.

What are the usual turn-around times for newborn metabolic screening test results?

Test results are routinely mailed to submitting facilities within two to three days after the receipt of the specimen. Presumptive positive (clinically significant) test results are phoned to the health care provider listed on the collection form within 24 hours of obtaining the result

What if I need to talk with someone at the lab or one of the consultants?

Refer to the **Iowa Newborn Screening Program (INSP) Contacts** section at the beginning of this Manual for a list of telephone numbers.

XVII. CHRONOLOGY OF NEWBORN SCREENING IN IOWA

- **1965**—State Legislature enacted a law which recommended testing infants for Phenylketonuria (PKU).
- **1966**—The University Hygienic Laboratory (UHL) began providing PKU testing services to the Child Development Clinic-Department of Pediatrics at The University of Iowa. In addition to the testing, the University Hygienic Laboratory initiated a PKU performance evaluation program for clinical labs in Iowa utilizing both the Guthrie Assay and an automated quantitative fluorometric analysis.
- **1979**—Analytical testing transferred in April 1979 from University Hygienic Laboratory's Consultation and Development Division in Iowa City to the Des Moines branch laboratory's biochemical services section. Testing is voluntary throughout Iowa.
- **1980**—Pilot testing initiated at several large hospitals for four diseases: Galactosemia, PKU, MSUD, and Hypothyroidism. (Federal grant funding).
- **1981**—Newborn Screening was made available to all infants.
- **1982**—The UHL was designated "Iowa's Central Screening Authority". Federal funding ceased and the UHL began “fee for service”. Private or hospital laboratories were still authorized to perform screening tests if they followed UHL Central Authority protocol and reported their results to the Birth Defects Institute of the Iowa State Department of Health.
- **1983**—Amendment to 136A of Iowa Code - Authorized Birth Defects Institute (BDI) of The Iowa State Department of Health (ISDH) to establish policy for newborn screening in Iowa. UHL screened 56% of recorded births. Screening is now mandatory at either the central laboratory (UHL) or an approved laboratory.
- **1984**
    - Last ½ of fiscal year the UHL won contract as the Central Screening Laboratory. All hospitals are now required to send specimens to UHL only.
    - Collection guidelines were changed from 72 hours after birth to 48 hours.
- **1985**—Monthly editorials of laboratory Hotline utilized for presentation of statistical data and notices related to neonatal screening.
- **1987**—Pilot program initiated for testing hemoglobin disorders (May 1987 - Dec. 1987) at high-risk urban areas.
- **1988**—In February Hemoglobin screening is initiated statewide.
- **1989**—Iowa participated in the blinded national survey of the prevalence of HIV infection in childbearing women.

- **1990**—Pilot testing began in March for Congenital Adrenal Hyperplasia (CAH) and lasted 13 months.
- **1991**—CAH testing added to INMSP in April.
- **1992**—July, North Dakota contracts with UHL to conduct screening of newborns. Screening done for all tests except Hemoglobins.
- **1993**—The INMSP laboratory evaluated new microtiter assays for Hypothyroidism and Congenital Adrenal Hyperplasia. (DELFIA modular system)
- **1994**—Pilot studies were conducted on automated procedures for Phenylalanine and Galactosemia. Information from the study was presented at the 10th National Neonatal Screening Symposium in Seattle, Washington.
- **1995**
    - The INMSP laboratory introduces automated quantitative screening for PKU and GALT.
    - Maple Syrup Urine Disease was dropped from the INMSP test battery
    - Collection guidelines were changed from 48 hours after birth to 24 hours
- **1996**—New DELFIA (modular system) technologies for Hypothyroidism and Congenital Adrenal Hyperplasia were introduced in the laboratory (TSH only as primary screen - dropped T4). These procedures replaced radioactive techniques with an accurate and more rapid turnaround time for our participants.
- **1997**—The INMSP laboratory purchased a Bio-Rad HPLC as an added screening method for Hemoglobinopathy testing.
- **1999**
    - A new Y2K compliant Database was installed that also gave the follow-up staff access via the World Wide Web.
    - The laboratory purchased a Tandem Mass Spectrometer instrument to begin studying the efficacy of testing for MCAD (medium chain acyl-CoA dehydrogenase) deficiency.
- **2000**—Sept 1 Iowa and ND began pilot testing for MCADD.
- **2001**
    - August 1, MCAD deficiency testing became routine (mandatory) for IA.
    - 2001—October 1, IA began pilot testing the Expanded MS/MS Panel.
- **2002**
    - March, IA began pilot testing Biotinidase
    - July1, IA added Biotinidase testing and changed the method of testing PKU from Isolab fluorometric to MS/MS
    - July, Nebraska contracts for MS/MS testing.
    - Nov. 15, ND started pilot testing for Expanded MS/MS.

- **2003**
  - April 1, Biotinidase, Hemoglobinopathies, and MCADD added to the ND screening panel.
  - Aug. 1, IA began reporting the Expanded MS/MS Panel.
- **2004**
  - August 5, ND began reporting the Expanded MS/MS Panel.
  - June 3, 2004 IA & ND removed 5 OxoPro and 2,4 Dienoyl-CoA Reductase Deficiency from expanded panel.
- **2005**
  - July 18, IRT/DNA testing was begun for the implementation phase of the Cystic Fibrosis pilot for Iowa (reported HET's and DFNT but not negatives).
  - September 8 began screening LA specimens due to Hurricane Katrina using a reduced MS/MS panel and no CAH.
  - Sept. 9, IA & ND removed Ornithine & Glycine from the MS/MS Panel.
- **2006**
  - ND adds CF to screening panel Jan. 1
  - Feb 1, Iowa began using CDS Courier
  - August 1 added CAH panel to LA
  - Iowa began reporting for CF Sept. 1
- **2007**
  - June 1, Iowa began screening for SD using same panel as Iowa/North Dakota and using ICS Courier;
  - Began screening CF for LA July 1
  - July 1 – Changed IRT cut-off from highest 5% to < 65 to reflex to CFTR (DNA)
  - November 10, last day received LA samples for full panel (continued CF until August 31, 2008)
- **2008—**June 1 – ND began using ICS Courier
- **2009**
  - April – TYR type I (SUAC) pilot began (MS/MS)
  - Dec 7 – no longer testing upper 5% for 17-OHP and TSH
  - Began new CAH kit (new ranges)
- **2010—**April – TYR type I (SUAC) officially part of NBS Panel
- **2011—**March – Stopped requesting repeat screens for HB traits
- **2013—**June – Pilot screening for SCID began (Iowa only)
- **2014—**July 1 – SCID officially part of NBS panel (Iowa only)
- **2015—**September 1-SCID officially part of NBS panel for SD
- **2016—**July – ND begins screening for SCID

- **2018—**July 1 -- SHL begins screening specimens for Alaska; added molecular testing for CPT1A Artic Variant
- **2020 –** July 1 – Pilot screening for SMA began (Iowa and ND)