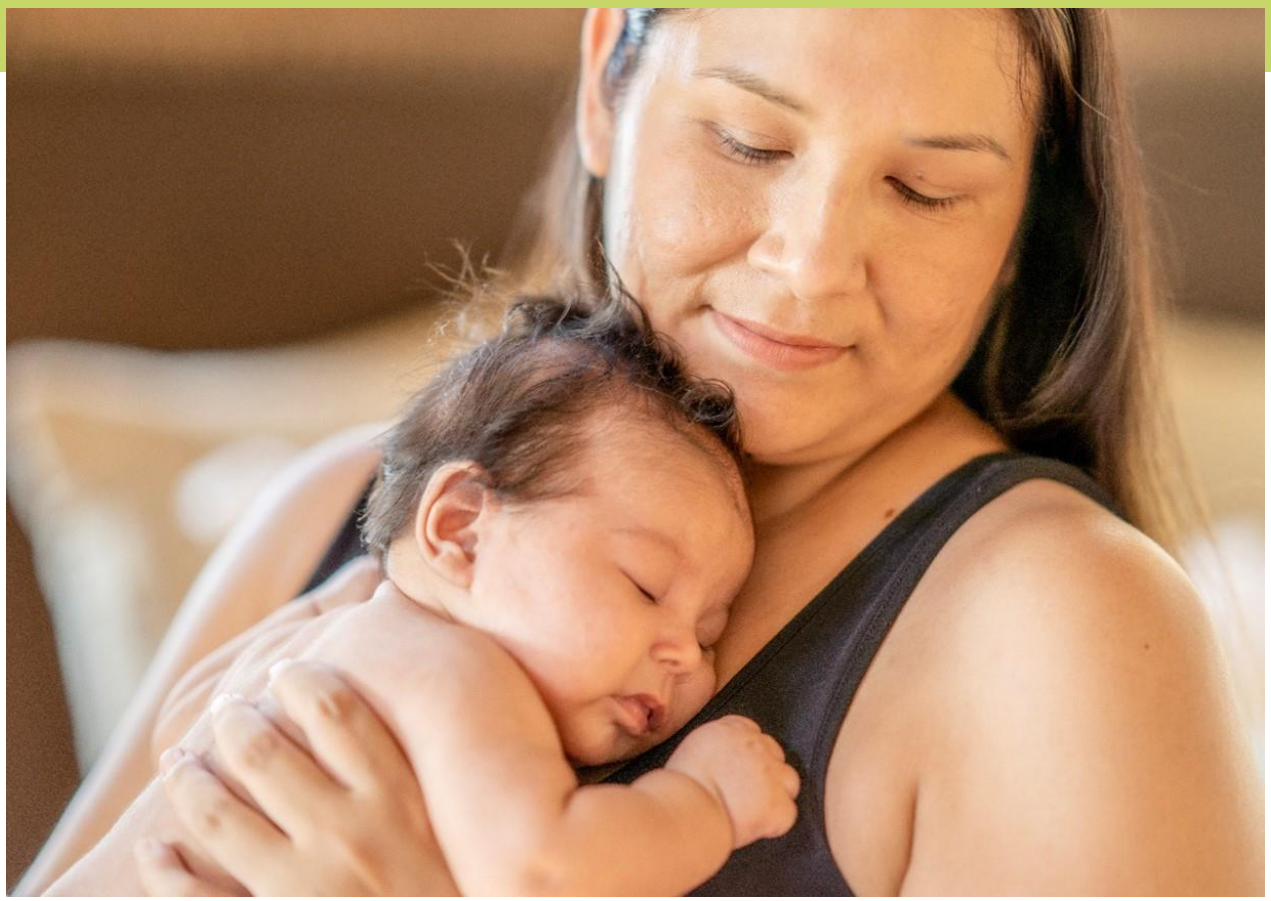

Status Report to the General Assembly

Adding Conditions to the Iowa Newborn Screening Panel

Division of Public Health

Center for Congenital and Inherited Disorders

December 2024

IOWA Health and Human Services

This report is submitted pursuant to Iowa Code section 135A.3A(5), which states:

5. The department shall submit a status report to the general assembly, annually, by December 31, regarding all of the following:

a. The current conditions included in the newborn screening.
b. Any new conditions currently under consideration or recommended by the advisory committee for inclusion in the newborn screening.
c. Any new conditions considered but not recommended by the advisory committee in the prior twelve-month period and the reason for not recommending any such conditions.
d. Any departmental request for additional program capacity or resources necessitated by the inclusion of a recommended new condition in the newborn screening.
e. Any delay and the reason for the delay by the advisory committee in complying with the specified twelve-month time frame in considering or recommending the inclusion of a new condition in the newborn screening to the department.
f. Any delay and the reason for the delay by the department in complying with the specified eighteen-month time frame in including a new condition in the newborn screening following receipt of a recommendation from the advisory committee recommending the inclusion of such condition.

A. Current Conditions on the Iowa Newborn Screening Panel

In 2024, one new condition was added to the Iowa newborn screening panel: Krabbe disease. With the addition of Krabbe disease, the Iowa newborn screening panel includes all conditions on the federal Recommended Uniform Screening Panel (RUSP).

The Iowa Newborn Screening Program currently screens Iowa newborns for the following conditions:

Amino Acidemias and Urea Cycle Disorders

- (ASA) Argininosuccinic aciduria*
- (CIT) Citrullinemia, type 1 or ASA Synthetase Deficiency*
- (HCY) Homocystinuria (cystathionine beta synthetase)*
- (MSUD) Maple Syrup Urine Disease*
- (PKU) Classic Phenylketonuria*
- (TYR-1) Tyrosinemia, type I*
- (ARG) Argininemia**
- (BIOPT-BS) Defects of biopterin cofactor biosynthesis**
- (CIT-II) Citrullinemia, type II**
- (BIOPT-REG) Defects of biopterin cofactor regeneration**
- (H-PHE) Benign hyperphenylalaninemia**
- (MET) Hypermethioninemia**
- (TYR II) Tyrosinemia, type II**

- (TYR III) Tyrosinemia, type III**

Organic Acidemias

- (GA-1) Glutaric acidemia type I*
- (HMG) 3-Hydroxy 3-methylglutaric aciduria *
- (IVA) Isovaleric acidemia*
- (3-MCC) 3-Methylcrotonyl-CoA carboxylase*
- (Cbl-A,B) Methylmalonic acidemia (cobalamin disorders, vitamin B12 disorders)*
- (βKT) βeta-Ketothiolase*
- (MUT) Methylmalonic Acidemia (methylmalonyl-CoA mutase)*
- (PROP) Propionic acidemia*
- (MCD) Holocarboxylase synthetase*
- (2M3HBA) 2-Methyl-3-hydroxybutyric aciduria**
- (2MBG) 2-Methylbutyrylglycinuria**
- (3MGA) 3-Methylglutaconic aciduria**
- (Cbl-C, D) Methylmalonic acidemia with homocystinuria**
- (MAL) Malonic acidemia**

Fatty Acid Oxidation Disorders

- (CUD) Carnitine uptake defect (Carnitine transport defect)*
- (LCHAD) Long-chain L-3 hydroxyacyl-CoA dehydrogenase*
- (MCAD) Medium chain acyl-CoA dehydrogenase*
- (TFP) Trifunctional protein deficiency*
- (VLCAD) Very long-chain acyl-CoA dehydrogenase*
- (CACT) Carnitine acylcarnitine translocase**
- (CPT-Ia) Carnitine palmitoyltransferase type I**
- (CPT-II) Carnitine palmitoyltransferase type II**
- (GA2) Glutaric acidemia type II**
- (MCAT) Medium-chain ketoacyl-CoA thiolase**
- (M/SCHAD) Medium/Short chain L-3-hydroxyacyl-CoA dehydrogenase**

Endocrine

- (CAH) Congenital adrenal hyperplasia*
- (CH) Primary Congenital hypothyroidism*

Lysosomal Storage Disorders

- Pompe Disease (glycogen storage disease type II)*
- (MPSI) Mucopolysaccharidosis Type I*
- (MPS II) Mucopolysaccharidosis Type II*
- **Krabbe disease (globoid leukodystrophy)***

Hemoglobinopathies

- (Hb SS) S,S Disease (Sickle Cell Anemia)*
- (Hb S/C) S,C Disease*
- (HB S/βTh) S, βeta-thalassemia*
- (Var Hb) Variant hemoglobinopathies**

Other

- (BIOT) Biotinidase deficiency*
- (CF) Cystic Fibrosis*
- (GALT) Classic Galactosemia*
- (SCID) Severe Combined Immunodeficiency*
- (HEAR) Hearing loss*
- (CCHD) Critical Congenital Heart Disease*
- (SMA) Spinal Muscular Atrophy*
- X-Linked Adrenoleukodystrophy (XALD)*
- (GAMT) Guanidinoacetate methyltransferase deficiency*

*Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC) Recommended Uniform Screening Panel (RUSP) - Core Panel. The ACHDNC is an advisory board of pediatricians, geneticists, and medical experts charted by the U.S. Department of Health and Human Services to report regularly on newborn and childhood screening practices, recommend improvements in the national newborn and childhood screening programs, and complete other legislatively authorized activities to improve health outcomes for babies.

**ACHDNC Recommended Uniform Screening Panel (RUSP) - Secondary Targets. Conditions on the secondary target list are not directly targeted by screening but are routinely identified through screening for disorders on the Core Panel (by-products of screening for the core conditions).

B. New Conditions Currently under Consideration or Recommended by the Congenital and Inherited Disorders Advisory Committee for Inclusion in the Iowa Newborn Screening Panel

The former Congenital and Inherited Disorders Advisory Committee (CIDAC) established a standing subcommittee for the management of the Iowa newborn screening panel. This subcommittee was charged with management of the newborn screening panel by ensuring all conditions included in the RUSP as of January 1, 2022, are included in the panel; reviewing and making recommendations to the Department about new conditions for inclusion in the panel; and regularly evaluating the effectiveness and appropriateness of the panel.

The subcommittee used an evidence-based review framework for the review of conditions for addition to the Iowa newborn screening panel. This includes using a decision matrix to qualify the review to make a recommendation to the Department regarding the addition of the condition to the panel.
The subcommittee expands during the review of a condition to include ad hoc members with experience and expertise in the condition under review.

During March through June 2024, the subcommittee reviewed Krabbe disease as a new condition for the Iowa newborn screening panel. Members of an ad hoc work group for the Krabbe disease review included a parent of children with an inherited condition, a medical geneticist with experience in treating patients with Lysosomal Storage Disorders (LSDs – includes Krabbe disease), Iowa Newborn Screening Program (INSP) administrative, laboratory, follow-up and genetic counseling staff, and the chair of CIDAC. An Iowa parent of children with Krabbe disease provided expert and experience testimony to the work group.

The ad hoc work group recommended to CIDAC the addition of Krabbe disease to Iowa's panel. CIDAC membership unanimously voted to accept the recommendation and added Krabbe disease to the Iowa newborn screening panel, with a Level A2 recommendation: "Screening for the condition has a high certainty of significant net benefits and screening has high or moderate feasibility. INSP has developmental readiness to screen within 18 months." It is expected that universal screening for Krabbe disease will begin by July 1, 2025.

With the dissolution of the Congenital and Inherited Conditions Advisory Committee effective July 1, 2024, the responsibility for oversight of the management of the Iowa newborn screening panel has been placed with the Council for Health and Human Services (Council). On November 21, 2024, the Council voted to establish the Congenital and Inherited Disorders Ad Hoc Committee (Committee). The Committee will meet on an ad hoc basis to review new conditions for Iowa's newborn screening panel, and to conduct an annual evaluation of the effectiveness of the newborn screening panel.

C. New conditions considered but not recommended by the advisory committee in the prior twelve-month period and the reason for not recommending any such conditions

There are no conditions that have been considered, but not recommended for inclusion in the newborn screening panel at this time.

D. Departmental request for additional program capacity or resources necessitated by the inclusion of a recommended new condition in the newborn screening

Department – The Director of the Center for Congenital and Inherited Disorders (Director), Iowa HHS Division of Pubic Health, has assumed the additional administrative work of CIDAC and the Subcommittee (now the Council for Health and Human Services Congenital and Inherited Disorders Ad Hoc Committee) regarding the activities required by Iowa Code chapter 136A. The Director is responsible to recruit Committee members and ad hoc condition reviewers; conduct research; draft documents; provide supporting resources such as references to applicable laws and federal recommendations and evidence-based information about new conditions; set agendas and take meeting notes; convene the meetings; and communicate all activities to the Department, Committee members, and other stakeholders. This administrative work will need to be sustained through a reallocation of the Director's time, or the addition of staff, as new conditions are added to the RUSP and to support continued review of Iowa's newborn screening panel.
It should be noted that Committee members and ad hoc reviewers serve on a volunteer basis and receive no compensation for their commitment. The average time commitment for a Committee member to this effort was 20-40 hours over the last year.

State Hygienic Laboratory (SHL) – Due to an increasing number of tests, the SHL newborn screening laboratory purchased an additional instrument to increase its capacity to conduct tandem mass spectrometry (MS/MS) testing. There will be an increase in costs for calibration and maintenance of the instruments utilized for testing of the new condition. Screening for Krabbe disease will use existing equipment and staff but will require re-validation of the existing lysosomal storage disorder testing panel. The addition of new conditions requires the purchase of new reagents and testing kits. An adjustment to the newborn screening fee in 2025 will be required to account for the increased costs.

Short-term Follow-up (STFU) – Physician experts for Krabbe disease will serve as the medical consultants for the new disorder. There is a need to educate newborn screening stakeholders about Krabbe disease. This requires developing educational resources (brochure inserts, notices to birthing facilities, newsletter articles, press releases, etc.) as well as additional staff time to carry out these tasks. While no additional STFU or genetic counselors are needed to staff the caseload work of adding Krabbe disease, staff workload will need to be reallocated to complete the necessary educational/informational tasks.

Additional Resources Needed as New Conditions Are Added

Fixed costs for implementation of newborn screening are increasing. The SHL is currently close to capacity in its physical space to accommodate the additional

equipment, supporting instruments and staff for testing new conditions. As new conditions are added, SHL will need to purchase additional testing equipment, such as those used for tandem mass spectrometry (MS/MS); and 2nd tier testing to validate the newborn screening results for these conditions is often molecular-based and requires specific space, equipment and staff. The SHL will need building modifications to continue to expand.

Short-term Follow-Up staff will need to engage medical consultants with experience in caring for newborns with the new condition to advise the SHL on testing methodology and cut-offs, establish standard treatment algorithms, and manage the care of the newborn.

The addition of new conditions increases the volume of newborn screening testing so SHL and STFU will need to hire more staff accordingly.

E. Delay and the reason for the delay by the advisory committee in complying with the specified twelve-month time frame in considering or recommending the inclusion of a new condition in the newborn screening to the department

There has been no delay in complying with the twelve-month time frame in considering or recommending the inclusion of a new condition in the newborn screening panel to the Department.

F. Any delay and the reason for the delay by the department in complying with the specified eighteen-month time frame in including a new condition in the newborn screening following receipt of a recommendation from the advisory committee recommending the inclusion of such condition

It has taken a large effort to add six new conditions to Iowa's newborn screening panel since 2022, and SHL staff have needed to commit a considerable amount of time to building new test methodologies and screening protocols and validating the tests. The SHL and STFU program are in the final stages of test validation and protocol development for MPS II and Krabbe disease. Once these tasks are complete, an implementation pilot for these two conditions will begin (target date of February 2025). The testing platform for Krabbe disease is the same as what is required for MPS II, so test development for Krabbe disease was moved ahead of GAMT in the test development queue. Once the implementation pilot for MPS II and Krabbe disease has begun staff will be able to turn their full attention to GAMT. The test development for GAMT will require re-calibration and validation of other conditions on the same testing platform as GAMT, which may take up to an additional four to five months to complete.

Review of the Iowa Newborn Screening Panel

The Committee will convene at least annually to review the effectiveness and appropriateness of the current newborn screening panel.