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Status Report to the General Assembly

Adding Conditions to the Iowa Newborn Screening Panel

Center for Congenital and Inherited Disorders, Division of Public Health

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Citation for Required Status Report

The 89th General Assembly of the State of Iowa enacted Chapter 1023 Congenital and Inherited Disorders —Screening of Newborns S.F. 2345 – An Act Relating to the Newborn Screening. Chapter 1023 of Iowa Acts.

New Section 136A.3A Subsection 5 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.

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Status Report of Adding Conditions to the Iowa Newborn Screening Panel

The State of Iowa Department of Health and Human Services is pleased to provide this status report on adding conditions to the Iowa newborn screening panel to the General Assembly of the State of Iowa.

Current Conditions on the Iowa Newborn Screening Panel

In 2023, three new conditions were added to the Iowa newborn screening panel: Pompe disease, Mucopolysaccharidosis Type 1 (MPSI), and X-linked Adrenoleukodystrophy (XALD). This ensures that all conditions included in the federal Recommended Uniform Screening Panel (RUSP) as of January 1, 2022, are included in the Iowa newborn screening panel.

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*

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*
- **Pompe Disease***
- **Mucopolysaccharidosis Type I (MPSI)***
- **X-Linked Adrenoleukodystrophy (XALD)***

*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).

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

The Congenital and Inherited Disorders Advisory Committee (CIDAC) established a standing subcommittee for the management of the Iowa newborn screening panel. This subcommittee is 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 developed an evidence-based review framework for the review of conditions for addition to the Iowa newborn screening panel and built a decision matrix to qualify the review in order to make a recommendation to the Department regarding the addition of the condition to the panel.

The subcommittee expanded during the review of a condition to include ad hoc members with experience and expertise in the condition under review.

In accordance with 136A.3A subsection 4.b., the CIDAC's Subcommittee for the Management of the Iowa Newborn Screening Panel (Subcommittee) commenced evidence-based reviews and made recommendations regarding the inclusion of two conditions within twelve months of the addition of those conditions to the RUSP.

Mucopolysaccharidosis Type II (MPS II) was added to the RUSP in August 2022, and the Subcommittee with ad hoc members began an evidence-based review in December 2022. In March 2023, the Subcommittee made a Level A2 recommendation to add MPSII to Iowa's newborn screening panel. Level A2 states: "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."

The Subcommittee chair presented the recommendation to CIDAC at the April 2023 meeting. CIDAC members agreed with the recommendation and voted to add MPS II to Iowa's panel. Iowa Newborn Screening Program staff at the State Hygienic Laboratory (SHL) and the Short-Term Follow-up (STFU) Program are currently building the capacity to screen for MPS II. It is expected that a universal MPSII newborn screening pilot will begin in July 2024.

Guanidinoacetate N-methyltransferase (GAMT) was added to the RUSP in January 2023. The Subcommittee with ad hoc members began reviewing GAMT in June 2023 and presented a Level A3 recommendation to CIDAC to add GAMT to Iowa's panel at CIDAC's meeting in October 2023. Level A3 states: "Screening for the condition has a high certainty of significant

net benefits and screening has high or moderate feasibility. Screening readiness would take longer than 18 months." CIDAC membership accepted the recommendation with the recognition that universal screening for GAMT will take longer than 18 months to implement. Justification for the delay in implementing GAMT screening is described later in this document.

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, by CIDAC for inclusion in the newborn screening panel at this time.

DEPARTMENTAL REQUEST FOR ADDITIONAL PROGRAM CAPACITY OR RESOURCES NECESSITATED BY THE INCLUSION OF A RECOMMENDED NEW CONDITION IN THE NEWBORN SCREENING

Department – The Executive Officer of the Center for Congenital and Inherited Disorders has assumed the additional administrative work of CIDAC and the Subcommittee regarding the activities required in the relevant sections of S.F. 2345. This includes collaborating with the CIDAC chair and vice chair to recruit Subcommittee and ad hoc members; 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 CIDAC chairs, Subcommittee members, and other stakeholders. This administrative work will need to be sustained through a reallocation of the Executive 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 CIDAC members and Subcommittee members serve on a volunteer basis and receive no compensation for their commitment. To date, the average time commitment for Subcommittee members to this effort is 20-40 hours over the last year.

State Hygienic Laboratory (SHL) – No new instruments or staff will be required to complete testing for MPS II. There will be an increase in costs for calibration and maintenance of the instruments utilized for testing of the new conditions. Screening for GAMT will use existing equipment and staff, but will require re-validation of the existing amino acid testing panel. The addition of these new conditions requires the purchase of new reagents and testing kits. An adjustment to the newborn screening fee will be required to account for the increased costs.

Short-term Follow-up (STFU) – Physician experts for MPS II and GAMT will serve as the medical consultants for these additional disorders. There is also a need to educate newborn screening stakeholders about these new disorders. 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 these new disorders, 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 in order 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.

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 by CIDAC 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.

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

The State Hygienic Laboratory and Short-Term Follow-Up program are unable to begin preparations for implementation of universal newborn screening for GAMT until implementation for MPS II has occurred. It has taken a large effort to add three new conditions in a short amount of time, and SHL staff have needed to commit a large amount of time to building new test methodologies and validating the tests. Once MPS II screening is implemented, staff will be able to turn their attention to GAMT. The addition of GAMT will require re-calibration and validation of the other conditions on the same testing platform as GAMT, which may take up to nine months to a year to complete.