COLORADO
Department of Public Health & Environment

To: Members of the State Board of Health

From: Gregory Bonn, Newborn Screening Operations Mgr., and Emily Travanty, PhD, Scientific and Interim Director, Colorado State Public Health Laboratory

Through: Scott Bookman, ***SB***
Director, Division of Disease Control and Public Health Response (DCPHR)

Date: January 20, 2021

Subject: Request for a Rulemaking Hearing concerning Proposed Amendments to 5 CCR 1005-4, Newborn Screening and Second Newborn Screening

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In preparation for a Public Rulemaking Hearing, please find copies of the following documents:

a) Proposed Amendments to 5 CCR 1005-4,
b) Statement of Basis and Purpose and Specific Statutory Authority,
c) Regulatory Analysis, and
d) Early Stakeholder Engagement

The Colorado Newborn Screening Program (CONBSP) provides initial and second newborn screening services for 36 rare genetic and metabolic conditions. Dried blood spot (DBS) specimens are collected by hospitals, midwives, and pediatricians who submit the specimens for testing in the Colorado State Public Health Laboratory (State Laboratory). The CONBSP screens approximately 68,000 newborns in Colorado, Wyoming, and parts of Arizona each year. All 68,000 newborns receive a first screen for all 36 genetic and metabolic conditions. About 64,000 newborns receive a routine second screen to retest for two conditions: Congenital Hypothyroidism (CH) and Congenital Adrenal Hyperplasia (CAH). Additionally, all previous abnormal results and previous unsatisfactory specimens (specimens without enough blood to test, for example) also receive a second screen.

Newborns identified at risk through screening are connected to contracted follow-up specialists who guide the newborn's family and primary care provider on appropriate next steps. Each year, the CONBSP identifies approximately 80-100 newborns with one of the conditions on the screening panels, i.e. there are approximately 80-100 true positive

screening results per year across all conditions screened. In addition to true positive cases more than affected 700 newborns are identified each year. Carriers of hemoglobin trait, immune deficiencies, and other disorders are indicated by newborn screening. True positive newborns and affected newborns face health issues that are best recognized and treated early. Disorder outcomes, without early intervention can lead to death, disability and failure to thrive. Early diagnosis and intervention stops the costly search for a diagnosis once irreversible damaging signs and symptoms manifest.

The program is proposing three changes to the current rule that will bring the Colorado newborn screening panel into alignment with the current conditions on the Recommended Uniform Screening Panel (RUSP). The RUSP is a list of disorders that the Secretary of the Department of Health and Human Services (HHS) recommends for states to screen as part of their state universal newborn screening (NBS) programs. The proposed additions are as follows:

- Adding Glycogen Storage Disease Type II (Pompe Disease) to the Colorado newborn screening panel. This disease was added to the RUSP in 2015.
- Adding Mucopolysaccharidosis Type 1 (MPS1) to the Colorado newborn screening panel. This disease was added to the RUSP in 2015.
- Adding X-linked Adrenoleukodystrophy (XALD) to the Colorado newborn screening panel. This disease was added to the RUSP in 2016.

The rule changes are proposed in response to two factors:

1. CDPHE regularly reviews national recommendations for newborn screening and seeks full alignment with the conditions recommended for screening on the RUSP.
2. Stakeholders of the CONBSP advocated for the inclusion of additional conditions on Colorado's newborn screening panel.

Colorado stakeholders proposed legislation in 2018 (HB 18-1006) to allow the CONBSP to increase fees and establish funds necessary to establish the required infrastructure to provide testing for the disorders that were on the RUSP and not yet tested by the CONBSP. The fee increase was implemented to improve the Laboratory Information Management System (LIMS), expand laboratory space, purchase equipment, and add staff in order for the CONBSP to add the remaining conditions on the RUSP. In 2018, there were three disorders that were part of the RUSP, that were not on the CONBSP panel: Pompe, MPS1 and X-ALD. This rulemaking proposes the inclusion of these three conditions.

The Department has contacted a wide variety of stakeholders to solicit input on these proposed amendments; the Department remains committed to stakeholder engagement during the rulemaking period.

Changes to rule language appear in ALL CAPS.

STATEMENT OF BASIS AND PURPOSE AND SPECIFIC STATUTORY AUTHORITY
for Amendments to 5 CCR 1005-4,
Newborn Screening and Second Newborn Screening

The Department is proposing amendments to this rule that will bring the Colorado newborn screening panel into alignment with the current conditions on the Recommended Uniform Screening Panel (RUSP). The proposed additions are as follows:

- Adding Glycogen Storage Disease Type II (Pompe Disease) to the Colorado newborn screening panel.
- Adding Mucopolysaccharidosis Type 1 (MPS1) to the Colorado newborn screening panel.
- Adding X-linked Adrenoleukodystrophy (XALD) to the Colorado newborn screening panel.

The Newborn Screening and Second Newborn Screening rule performs the following functions, it:

- Defines key terms,
- Establishes procedures for the collection and submission of blood spot specimens for testing,
- Establishes procedures for laboratory testing, reporting, and follow-up services for newborn screening and second newborn screening,
- Establishes requirements for quality control and education, and
- Lists conditions covered by the newborn screening and second newborn screening panels.

Together, these definitions, procedures and requirements establish roles and responsibilities for the genetic and metabolic testing portion of Colorado's Newborn Screening Program.

Proposed Change for Initial Screening

Of the 36 conditions presently included in the initial newborn screening panel, six (phenylketonuria, hypothyroidism, abnormal hemoglobins, galactosemia, cystic fibrosis, biotinidase deficiency) are identified in statute. The remainder was added by the Board of Health, in accordance with the criteria put forth in section 25-4-1004(1)(c), C.R.S. The Department undertakes a review, when a condition is recommended for inclusion on the newborn screening panel, consistent with the criteria laid out in statute.

In the table below, the Department evaluates the suitability of Pompe, MPS1, and X-ALD for population-wide newborn screening in Colorado using the four (4) criteria in Section 25-4-1004(1)(c), C.R.S. and proposes their addition to this rule.

Summary of Analysis for Population-wide Newborn Screening for Pompe, MPS1, and XALD			
Statutory Language	**Summary of CDPHE Findings**		
	Pompe	**MPS1**	**XALD**
The condition for which the test is designed presents a significant danger to the health of the infant or his family and is amenable to treatment	Criterion met The condition causes physical damage and/or death. Treatments and medical interventions are available and improve outcomes.	Criterion met The condition causes physical damage and/or death. Treatments and medical interventions are available and improve outcomes.	Criterion met The condition causes physical damage and/or death. Treatments and medical interventions are available and improve outcomes.
The incidence of the condition is sufficiently high to warrant screening	Criterion met Incidence is 1 in 40,000 similar to other conditions on the current CONBSP panel.	Criterion met Incidence is 1 in 100,000 similar to other conditions on the current CONBSP panel.	Criterion met Incidence is 1 in 17,000 similar to other conditions on the current CONBSP panel.
The test meets commonly accepted clinical standards of reliability, as demonstrated through research or use in another state or jurisdiction	Criterion met Currently there are multiple FDA authorized screening methods. Screening is performed in 24 U.S. states or territories.	Criterion met Currently there are multiple FDA authorized screening methods. Screening is performed in 22 U.S. states or territories.	Criterion met Currently there are FDA authorized screening methods. Screening is performed in 19 U.S. states or territories.

The cost-benefit consequences of screening are acceptable within the context of the total newborn screening program	Criterion met Ongoing screening costs for the condition are similar to other conditions on the current CONBSP panel.	Criterion met Ongoing screening costs for the condition are similar to other conditions on the current CONBSP panel.	Criterion met Ongoing screening costs for the condition are similar to other conditions on the current CONBSP panel.

Pompe Disease:

(I) The condition for which the test is designed presents a significant danger to the health of the infant or his family and is amenable to treatment;

Pompe is an autosomal recessive genetic condition. It is considered a lysosomal storage disorder because people with Pompe have lysosomes that lack or have lower activity of the enzyme called acid alpha-glucosidase (GAA). GAA aids in the breakdown of certain types of complex sugars known as glycogen. Lack or limited GAA causes undigested sugar molecules and other harmful substances to build up in cells throughout the body, resulting in a variety of symptoms.

The severity and age of onset of Pompe differ depending on the form. Signs of classic infantile-onset Pompe begin before or shortly after birth and include:

- Muscle weakness (myopathy)
- Poor muscle tone (hypotonia)
- Cardiomyopathy (enlarged heart)
- Failure to gain weight and grow at expected rate (failure to thrive)
- Difficulty breathing
- Trouble feeding
- Respiratory infections
- Hearing problems

Signs of non-classic infantile-onset Pompe usually occur by age one and include:

- Delayed motor skills
- Progressive muscle weakness (myopathy)
- Difficulty breathing

Late-onset Pompe may develop in childhood, adolescence, or even adulthood. It is also associated with progressive muscular weakness and difficulty breathing. However, the symptoms are usually milder and progress more slowly infantile-onset Pompe.

When Pompe is detected early and proper treatment is started immediately, many babies with the condition are able to live longer lives with improved cardiac function, improved muscle strength, improved growth and development. This is why newborn screening for Pompe is so important.

(II) The incidence of the condition is sufficiently high to warrant screening;

Pompe is estimated to affect 1 in every 40,000 newborn babies in the United States. Worldwide, the incidence of this condition varies depending on ethnicity and geographic region. African Americans are estimated to be affected at 1 in every 14,000.

A confirmed case of Pompe was last reported to Colorado Responds to Children with Special Needs (CRCSN) in 2018. Lower affected rates are noted in states without newborn screening. Children are generally not coded correctly (using the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10) coding), misdiagnosed or passed away prior to diagnosis. The Children's Hospital Colorado currently has 3 patients diagnosed with Pompe under their care.

Incidence rate of the condition is sufficiently high and comparable to other disorders currently on the Colorado Newborn Screening Program (CONBSP) panel.

(III) The test meets commonly accepted clinical standards of reliability, as demonstrated through research or use in another state or jurisdiction; and

Since Pompe was added to the RUSP in 2015 there are multiple platforms now available for first tier testing. In addition, Food and Drug Administration (FDA)-authorized digital microfluidics and mass spectrometry kits are available with wide spread use in the United States. Quality and reliability of these tests has improved over the years. The ability to multiplex or test for other conditions simultaneously using these testing platforms allows for additional savings. Currently Pompe is being tested in 24 U.S. states or territories.

(IV) The cost-benefit consequences of screening are acceptable within the context of the total newborn screening program.

There are four categories of costs:

Laboratory Costs: Laboratory costs for Pompe will be supported by a continuation of the Centers for Disease Control and Prevention (CDC) NewDisorders Grant. This grant provides initial cost for equipment, Laboratory Information Management System (LIMS) modification, and validation testing. Pompe and MPS I can be multiplexed and cost savings can occur if they are added at the same time in order to optimize reagents, staff time and create one LIMS modification. The laboratory costs of adding Pompe screening are estimated in the table below:

Item	Startup or Recurring	Cost
LIMS Modification*	Startup	$15k-30k
Equipment Modernization		
Digital Fluidics Systems*	Startup	$40,000
Laboratory Staff (FTE)*	Startup (.5 FTE)	$12,000
Laboratory Staff (FTE)*	Recurring (0.25 FTE)	$1,000/month
Reagents		
Validation*	Startup	$20k
Daily Screening**	Recurring	$11,300/month

*Note cost savings for adding Pompe and MPS I at the same time. Startup costs, LIMS, and validation reagents are one-time cost due to multiplexing assay.
** Based on 68,000 samples per year at $2.00 per sample.

Costs associated with the Department contracting with medical experts to provide follow-up services for Pompe: CONBSP expects to find 2-4 newborns a year when testing for Pompe, with an average follow-up cost of $1,000-$3,000 per newborn. Annual costs of approximately $12,000.

Costs associated with confirmatory testing and genetic tests to assess Pompe: Genetic testing is provided by the vendor of the first tier testing method at no additional cost. Follow-up enzyme level testing cost would range from $100-$145 per sample.

Costs associated with treatment of individuals diagnosed with Pompe, i.e. treatment of true positives: Early diagnosis and treatment results in improved clinical outcomes and prolonged survival of individuals with Pompe Disease including improving cardiac function, respiratory issues, and muscle weakness.

Treatment costs are covered by insurance once the child is diagnosed and recommended by a medical professional. Early diagnosis allows for treatment to begin and limits the effects of the disorder on the child. Delayed care increases costs over the lifetime of the child.

Current Recommended Treatments:

- Enzyme Replacement Therapy (ERT) with recombinant human GAA (Myozyme®, alglucosidase alfa). This treatment aims to replace the enzyme that is missing in patients with Pompe Disease thus preventing the build-up of glycogen in organs. ERT improves cardiac function, muscle weakness, and breathing issues. ERT effectively reverses cardiomyopathy, improves motor development, and improves overall survival (Chien et al 2020). Early initiation of ERT in patients with infantile onset Pompe disease is essential for a good outcome. In addition, some patients with infantile-onset Pompe disease may also need immunomodulation therapy prior to ERT to improve how their body responds to therapy.
    - Estimated Costs:
        - ERT once every 2 weeks
            - $100,000-$300,000 per year plus infusion facility cost
            - Weight-based so newborns on lower side of cost estimate
- Physical Therapy - Physical therapy will be necessary to help infants, children, and adolescents develop motor skills, maintain range of motion, and strengthen muscles and joints.
- Respiratory Therapy – Respiratory Therapy improves the respiratory status of most patients with infantile onset Pompe disease. However, some patients may still experience lung infections and breathing difficulties requiring some breathing assistance and monitoring by pulmonology.

Mucopolysaccharidosis type I (MPS I)

(I) The condition for which the test is designed presents a significant danger to the health of the infant or his family and is amenable to treatment;

MPS I is an inherited condition that affects many different parts of the body. It is considered a lysosomal storage disorder because people with MPS I have lysosomes that lack or have lower activity of the enzyme called alpha-L-iduronidase (IDUA). IDUA aids with the breakdown of certain types of complex sugars, glycosaminoglycans (GAGs). Lack or limited IDUA enzymes cause undigested sugar molecules and other harmful substances to build up in cells throughout the body, resulting in many signs and symptoms of MPSI.

Early Signs of MPS I include:

- Soft out-pouching around the belly-button (umbilical hernia) or lower abdomen (inguinal hernia)
- Large head (macrocephaly)

- Distinctive facial features that appear “coarse”
- Developmental delay and learning disabilities
- Swollen abdomen (due to enlarged liver and spleen)
- Clouding of the eye (corneal clouding)
- Hearing loss
- Frequent congestion

Life expectancy in MPS I is varied. Individuals with attenuated MPS I can have a reasonably normal lifespan while severely affected individuals may die before becoming teenagers. The most common cause of death is heart or respiratory failure.

(II) The incidence of the condition is sufficiently high to warrant screening;

The severe form of mucopolysaccharidosis type I occurs in about 1 in 100,000 newborns. The attenuated form is less common and occurs in approximately 1 in 500,000 newborns.

In October 2020, MPS I was added to the reportable conditions for Colorado Responds to Children with Special Needs (CRCSN). Prior to this date cases were not reported. The Children’s Hospital Colorado currently has 7 patients diagnosed with MPS I under their care. Incidence rate of the condition is sufficiently high and comparable to other disorders currently on the CONBSP panel.

(III) The test meets commonly accepted clinical standards of reliability, as demonstrated through research or use in another state or jurisdiction; and

Since MPS I was added to the RUSP in 2016 there are multiple platforms now available for first tier testing. FDA-authorized digital microfluidics and mass spectrometry kits are available with wide spread use in the United States. Quality and reliability of these tests has improved over the years. The ability to multiplex or test for other conditions simultaneously using these testing platforms allows for additional savings. Currently MPS I is being tested in 22 states or territories.

(IV) The cost-benefit consequences of screening are acceptable within the context of the total newborn screening program.

There are four categories of costs:

Laboratory costs: Laboratory costs for MPS I will be supported by a continuation of the CDC NewDisorders Grant. This grant provides initial cost for equipment, LIMS modification, and validation testing. Pompe and MPS I can be multiplexed and cost savings can occur if they are added at the same time in order to optimize reagents, staff time and create one LIMS modification. The laboratory costs of adding MPS I screening are estimated below:

Item	Startup or Recurring	Cost
LIMS Modification*	Startup	$15k-30k
Equipment Modernization		
Digital Fluidics Systems*	Startup	$40,000
Laboratory Staff (FTE)*	Startup (.5 FTE)	$12,000
Laboratory Staff (FTE)*	Recurring (0.25 FTE)	$1,000/month
Reagents		
Validation*	Startup	$20k
Daily Screening**	Recurring	$11,300/month

*Note cost savings for adding Pompe and MPS I at the same time. Startup costs, LIMS, and validation reagents are one-time cost due to multiplexing assay.
**Based on 68,000 samples per year at $2.00 per sample.

Costs associated with the Department contracting with medical experts to provide follow-up services for MPS I: CONBSP expects to find 1-2 newborns a year when testing for MPS I, with an average follow-up cost of $1,000-$3,000 per newborn. Annual costs for $6,000.

Costs associated with confirmatory testing and genetic tests to assess MPS I: Genetic testing is provided by the vendor of the first tier testing method at no additional cost. Follow-up enzyme level testing cost would range from $100-$145 per sample.

Costs associated with treatment of individuals diagnosed with MPS I, i.e. treatment of true positives:

Treatment costs are covered by insurance once the child is diagnosed and recommended by a medical professional. Early diagnosis allows for treatment to begin and limits the effects of the disorder on the child. Delayed care increases costs over the lifetime of the child.

Current Recommended Treatments:

- Enzyme Replacement Therapy (ERT) - This treatment is administered by intravenous solution (IV) weekly to replace or supplement the missing or low enzymes. ERT is not a cure, it slows progression and may improve growth, joint movement, sleep apnea, respiratory function, pain levels, vision, and liver/spleen enlargement.
    - Estimated Costs Attenuated MPS I:
        - Weekly
        - $100,000-300,000 per year plus infusion facility costs
        - Weight based so newborns on lower side of cost estimate
- Hematopoietic Stem Cell Transplantation (HSCT) -HSCT has become the gold standard for the treatment of the severe form of MPS I in patients diagnosed and treated before 2–2.5 years of age.
    - Estimated Costs:
        - Severe MPS I (neurological involvement)
        - Cost $1,000,000
            - ERT often used while waiting for HSCT then up to 6 months following transplant (approx. 1 year)
- Physical Therapy - Physical therapy is a very important part of treating the signs and symptoms of MPS I. Consistent physical therapy early on can help preserve mobility and lessen pain and joint stiffness.
- Surgeries - Recommend surgeries to improve the child's quality of life. Removal of the tonsils and adenoids and insertion of ventilating (ear) tubes can prevent some upper respiratory infections and may reduce hearing loss. Hearing aids may be recommended for some individuals. Children with mild to severe MPS I may develop a buildup of fluid in the brain (hydrocephaly), a surgery to relieve the pressure inside the skull may be recommended.

ALD or X-ALD

(I) The condition for which the test is designed presents a significant danger to the health of the infant or his family and is amenable to treatment;

Adrenoleukodystrophy (ALD) or X-Linked Adrenoleukodystrophy (X-ALD) occurs when certain fats (very long chain fatty acids, or VLCFAs) cannot be broken down in the body. These fats build up and affect how the body normally functions. This disease largely affects the nervous system and adrenal glands. When an individual has ALD, the buildup of VLCFAs may disrupt the fatty covering (myelin) of the nerve cells in the brain and spinal cord causing the myelin to breakdown, which reduces the ability of the nerves to relay information to the brain. Without myelin, the nervous system cannot function properly causing for example difficulties swallowing or weakness in the legs. However, these symptoms vary depending on the type and age of onset and other factors which are not well understood. In addition, the build of VLCFAs damages the outer layer of the adrenal glands (adrenal cortex).

Adrenoleukodystrophy is caused by mutations or changes in the ABCD1 gene. This gene provides instructions for making the protein, adrenoleukodystrophy (ALDP), which transports VLCFAs into peroxisomes. Peroxisomes are small sacs inside cells that break down VLCFAs and other molecules.

When the ABCD1 gene has a mutation or change, there is not enough ALDP being made, so VLCFAs are not transported and broken down correctly. This causes a buildup of VLCFAs in the body, which damages the myelin and the adrenal glands leading to the symptoms seen in ALD.

ALD is inherited in an X-linked pattern, meaning the mutated or changed gene is located on the X chromosome, one of the two sex chromosomes in each cell. Females have two X chromosomes in each cell. Males have one X chromosome and one Y chromosome, so one mutated or changed copy of the ABCD1 gene is enough to cause ALD.

Female carriers of ALD (females with one non-working copy of the gene and one working copy) have been shown to experience the signs and symptoms of X-ALD more often than expected. Some carriers may show no symptoms, others may have mild symptoms, and others may have more significant symptoms in adulthood.

There are three different typical presentations of ALD.

- Boys with childhood cerebral X-ALD (cALD) usually start showing symptoms when they are between 4 and 10 years old. Symptoms start with attention deficit disorder/hyperactivity and then progress to the symptoms listed under condition characteristics. The condition progresses very quickly, and the child usually passes away a few years after symptoms first appear, although some with intensive medical treatment may survive longer. Recent advances are beginning to change the outlook for boys affected cALD however. The development of cALD may be detected by changes on special imaging called magnetic resonance imaging (MRI) months to years in advance of seeing symptoms. Boys who develop these changes may be referred for effective therapy (see below). Symptoms can begin as early as age 2 but more commonly between ages 4-10 years old. Early symptoms may include:
    - Difficulty swallowing
    - Vision problems; crossed eyes
    - Hearing loss
    - Difficulty reading, writing, understanding speech, and comprehending written and spoken material
    - Aggressive behavior
    - Hyperactivity
    - Adrenocortical insufficiency or Addison's disease; adrenal glands do not produce enough steroid hormones
    - Poor coordination

- Changes in muscle tone; spasms and spasticity
- Seizures
- Worsening nervous system deterioration
- Decreased fine motor control
- Paralysis
- Coma

- Men with adrenomyeloneuropathy (AMN) start showing symptoms around age 20 years old or older. Most individuals with AMN, but not all, have adrenocortical insufficiency. About 10-20% of individuals in this condition will have severe brain and nervous system damage causing an early death. Women who carry ALD may develop similar symptoms. Early symptoms may include:
  - Urinary and genital tract disorders
  - Progressive stiffness and weakness in the legs (paraparesis)

- Adrenal insufficiency or Addison's disease occurs in 90% of males with ALD and can present as early as 6 months of age. Addison's disease prevents the body from handling stress, but can be treated with a replacement dose of a corticosteroid taken daily, as well as stress doses when needed. Symptoms can begin anytime from early childhood to adulthood. While it would appear to be less severe than the neurologic presentations, it is a serious condition and requires appropriate medical management. If left untreated, a person affected by Addison disease may go into a coma. Most individuals with Addison disease will go on to develop some neurologic aspects with time. Early symptoms may include:
  - Decreased appetite
  - Darker areas of skin color or pigment
  - Vomiting
  - Loss of weight and muscle mass
  - Muscle weakness
  - Low blood sugar
  - If left untreated, this condition can result in a severe situation referred to as an adrenal crisis.

More than twenty percent of women who are carriers show some symptoms of ALD. These often appear later than in men, but may be as severe. Some women may never show any symptoms. Adrenal insufficiency is not typically seen in women.

Children with childhood cerebral ALD (cALD) will have ongoing neurological deterioration. Unless HCT (stem cell bone marrow transplantation) is done early, the child will continue to lose neurologic abilities. Sadly without HCT, most children with cALD will die before age ten. The best results from HCT are seen if the transplant is performed when the beginning changes to the brain are detected by MRI but before physical symptoms are seen.

The other forms of ALD are milder, and will progress over decades. AMN may result in early death due to nervous system deterioration, but Addison disease can be managed through regular testing and treatment with replacement corticosteroid.

(II) The incidence of the condition is sufficiently high to warrant screening;

ALD affects 1 in 17,000 individuals (males and females) worldwide, regardless of race, ethnicity and geography. ALD affects males more severely and is more common in males because it is an X-linked condition. However, 20-40% of women who are carriers have symptoms in adulthood.

In October 2020, ALD was added to the reportable conditions for CRCSN; prior to this date cases were not reported. Children's Hospital Colorado currently follows 11 male patients (4 of which are post-transplant) and 12 female carriers. Incidence rate of the condition is sufficiently high and comparable to other disorders currently on the CONBSP panel.

(III) The test meets commonly accepted clinical standards of reliability, as demonstrated through research or use in another state or jurisdiction; and

Since ALD was added to the RUSP in 2016 there is an FDA-authorized mass spectrometry kit available in the United States. Quality and reliability of these tests have improved over the years. The ability to multiplex or test for other conditions simultaneously using these testing platforms allows for additional savings. Currently, ALD is being tested in 19 U.S. states or territories.

(IV) The cost-benefit consequences of screening are acceptable within the context of the total newborn screening program.

There are four categories of costs:

Laboratory costs: The laboratory testing costs of ALD are minimal due to the ability of the laboratory to multiplex the test with its current mass spectrometry testing. The additional cost will be covered by a continuation of the CDC New Disorders grant. The grant will cover validation and LIMS costs. No new equipment or full time equivalent staff (FTE) will be required to support the testing once implemented. The laboratory costs of adding ALD screening are estimated below:

Item	Startup or Recurring	Cost
LIMS Modification*	Startup	$15k-30k
No New Equipment Needed	Startup	$0
Laboratory Staff (FTE)*	Startup (.5 FTE)	$12,000
Laboratory Staff (FTE)*	Recurring (0.0 FTE)	$0
Reagents		
Validation*	Startup	$20k
Daily Screening	Recurring	$600/month

Costs associated with the Department contracting with medical experts to provide follow-up services for ALD. CONBSP expects to find 4-6 newborns a year when testing for ALD, with an average follow-up cost of $2,000-$4,000 per newborn. Annual costs for $24,000.

Costs associated with confirmatory testing and genetic tests to assess ALD. CONBSP expects to find 4-6 newborns a year when testing for ALD, with an average follow-up cost of $1,000 per newborn. Annual costs of $6,000.

Costs associated with treatment of individuals diagnosed with ALD, i.e. treatment of true positives.

Treatment costs are covered by insurance once the child is diagnosed and recommended by a medical professional. Early diagnosis allows for treatment to begin and limits the effects of the disorder on the child. Delayed care increases costs over the lifetime of the child.

Current Recommended Treatments:

- Steroids - Individuals who have adrenal insufficiency need to have regular adrenal gland testing, and can be treated effectively with replacement corticosteroids.
    - Estimated Costs:
        - $600-$800 annually.

- Serial magnetic resonance imaging (MRI)- Individual will require a MRI every 6 months starting at age 2 and end at around age 10. Changes or abnormal MRI findings indicate onset of cALD and warrants treatment.
    - Estimated Costs:
        - $6,500 per visit for approximately $104,000 total over 8 years.
- Allogeneic hematopoietic cell transplantation (HCT) or Stem Cell Transplantation - HCT is a treatment that may halt the progression of cALD in children if the disease is diagnosed and treated early.
    - Estimated Costs:
        - $1,000,000 for HCT
- Other Treatments
    - Other treatments include medication to help relieve symptoms like stiffness and seizures, and physical therapy, which can help relieve muscle spasms and reduce muscle rigidity.
    - There is currently a clinical trial for gene therapy which may be another method to stop the progression of ALD.
    - The compound Lorenzo's oil does lower VLCFA in the blood. It is considered an investigational agent and its role in altering manifestations of the disease is under study.

Specific Statutory Authority.

Sections 25-4-1004(1)(c)(I-IV), C.R.S

Is this rulemaking due to a change in state statute?

__X____ Yes, the bill number is HB18-1006. Rules are ___ authorized _XX__ required.

_____ No

Does this rulemaking include proposed rule language that incorporate materials by reference?

_____ Yes ___ URL

__X____ No

Does this rulemaking include proposed rule language to create or modify fines or fees?

_____ Yes

__X____ No

Does the proposed rule language create (or increase) a state mandate on local government?

_X__ No.

- The proposed rule does not require a local government to perform or increase a specific activity for which the local government will not be reimbursed;
- The proposed rule requires a local government to perform or increase a specific activity because the local government has opted to perform an activity, or;
- The proposed rule reduces or eliminates a state mandate on local government.

REGULATORY ANALYSIS
for Amendments to 5 CCR 1005-4
Newborn Screening and Second Newborn Screening

1. A description of the classes of persons affected by the proposed rule, including the classes that will bear the costs and the classes that will benefit from the proposed rule.

Group of persons/entities Affected by the Proposed Rule	Size of the Group	Relationship to the Proposed Rule Select category: C/S/B
Colorado's Newborns	~63,400/yr	B
Parents/Families of Colorado's Newborns	~500,000	B
Birthing Facilities	~100	S
Physicians identified on NBS demographic slips	~4,000	S/B
Midwives	~150	S
Pediatricians and Family Medicine Physicians	~5,000[1]	S/B
Patient Advocacy Groups, e.g. March of Dimes, NORD,	~6	S
Adult Patients with Rare Diseases	~500,000[2]	S
Clinical Specialists currently contracted with CDPHE to provide follow-up services	~20	C/S
Large Reference Laboratories	~2	S
Colorado Department of Health Care Policy and Financing	~5	S

1. *Colorado Physician Workforce Profile* **2016** Association of American Medical Colleges.
2. *Genetic and Rare Diseases Information Center* U.S. Department of Health and Human Services accessed at https://rarediseases.info.nih.gov/diseases/pages/31/faqs-about-rare-diseases on 6/21/2019.

While all are stakeholders, groups of persons/entities connect to the rule and the problem being solved by the rule in different ways. To better understand those different relationships, please use this relationship categorization key:

C = individuals/entities that implement or apply the rule.
S = individuals/entities that do not implement or apply the rule but are interested in others applying the rule.
B = the individuals that are ultimately served, including the customers of our customers. These individuals may benefit, be harmed by or be at-risk because of the standard communicated in the rule or the manner in which the rule is implemented.

More than one category may be appropriate for some stakeholders.

2. To the extent practicable, a description of the probable quantitative and qualitative impact of the proposed rule, economic or otherwise, upon affected classes of persons.

Economic outcomes
Summarize the financial costs and benefits, include a description of costs that must be incurred, costs that may be incurred, any Department measures taken to reduce or eliminate these costs, any financial benefits.

C: The Department will incur costs related to the proposed rule.

Pompe Disease:

Laboratory Costs: Laboratory costs for Pompe will be supported by a continuation of the Centers for Disease Control and Prevention (CDC) NewDisorders Grant. This grant provides initial cost for equipment, Laboratory Information Management System (LIMS) modification, and validation testing. Pompe and MPS I can be multiplexed and cost savings can occur if they are added at the same time in order to optimize reagents, staff time and create one LIMS modification. The laboratory costs of adding Pompe screening are estimated in the table below:

Item	Startup or Recurring	Cost
LIMS Modification*	Startup	$15k-30k
Equipment Modernization		
Digital Fluidics Systems*	Startup	$40,000
Laboratory Staff (FTE)*	Startup (.5 FTE)	$12,000
Laboratory Staff (FTE)*	Recurring (0.25 FTE)	$1,000/month
Reagents		
Validation*	Startup	$20k
Daily Screening**	Recurring	$11,300/month

*Note cost savings for adding Pompe and MPS I at the same time. Startup costs, LIMS, and validation reagents are one-time cost due to multiplexing assay.
** Based on 68,000 samples per year at $2.00 per sample.

Costs associated with the Department contracting with medical experts to provide follow-up services for Pompe: Colorado Newborn Screening Program (CONBSP) expects to find 2-4 newborns a year when testing for Pompe, with an average follow-up cost of $1,000-$3,000 per newborn. Annual costs for $12,000.

Costs associated with confirmatory testing and genetic tests to assess Pompe: Genetic testing is provided by the vendor of the first tier testing method at no additional cost. Follow-up enzyme level testing cost would range from $100-$145 per sample.

MPS I:

Laboratory costs: Laboratory costs for MPS I will be supported by a continuation of the CDC NewDisorders Grant. This grant provides initial cost for equipment, LIMS modification, and validation testing. Pompe and MPS I can be multiplexed and cost savings can occur if they are added at the same time in order to optimize reagents, staff time and create one LIMS modification. The laboratory costs of adding MPS I screening are estimated below:

Item	Startup or Recurring	Cost
LIMS Modification*	Startup	$15k-30k
Equipment Modernization		
Digital Fluidics Systems*	Startup	$40,000
Laboratory Staff (FTE)*	Startup (.5 FTE)	$12,000
Laboratory Staff (FTE)*	Recurring (0.25 FTE)	$1,000/month
Reagents		
Validation*	Startup	$20k
Daily Screening**	Recurring	$11,300/month

*Note cost savings for adding Pompe and MPS I at the same time. Startup costs, LIMS, and validation reagents are one-time cost due to multiplexing assay.
** Based on 68,000 samples per year at $2.00 per sample.

Costs associated with the Department contracting with medical experts to provide follow-up services for MPS I: CONBSP expects to find 1-2 newborns a year when testing for MPS I, with an average follow-up cost of $1,000-$3,000 per newborn. Annual costs for $6,000.00.

Costs associated with confirmatory testing and genetic tests to assess MPS I: Genetic testing is provided by the vendor of the first tier testing method at no additional cost. Follow-up enzyme level testing cost would range from $100-$145 per sample.

ALD or X-ALD:

Laboratory costs: The laboratory testing costs of ALD are minimal due to the ability of the laboratory to multiplex the test with its current mass spectrometry testing. The additional cost will be covered by a continuation of the CDC New Disorders grant. The grant will cover validation and LIMS costs. No new equipment or full-time equivalent staff (FTE) will be required to support the testing once implemented. The laboratory costs of adding ALD screening are estimated below:

Item	Startup or Recurring	Cost
LIMS Modification*	Startup	$15k-30k
No New Equipment Needed	Startup	$0
Laboratory Staff (FTE)*	Startup (.5 FTE)	$12,000
Laboratory Staff (FTE)*	Recurring (0.0 FTE)	$0
Reagents		
Validation*	Startup	$20k
Daily Screening	Recurring	$600/month

Costs associated with the Department contracting with medical experts to provide follow-up services for ALD. CONBSP expects to find 4-6 newborns a year when testing for ALD, with an average follow-up cost of $2,000-$4,000 per newborn. Annual costs for $24,000.

Costs associated with confirmatory testing and genetic tests to assess ALD. CONBSP expects to find 4-6 newborns a year when testing for ALD, with an average follow-up cost of $1,000 per newborn. Annual costs of $6,000.

Costs associated with treatment of individuals diagnosed with ALD, i.e. treatment of true positives.

Please describe any anticipated financial costs or benefits to these individuals/entities.

S: There are no costs to health care facilities and providers submitting specimens as this portion of the process is unchanged. The Department of Health Care and Policy may incur additional costs; this is discussed in #3 below.

B: Patients and families will incur treatment costs when the newborn screen result for Pompe, MPS I, and/or ALD is positive.

Costs associated with treatment of individuals diagnosed with Pompe, i.e. treatment of true positives: Early diagnosis and treatment results in improved clinical outcomes and prolonged survival of individuals with Pompe Disease including improving cardiac function, respiratory issues, and muscle weakness.

Treatment costs are covered by insurance once the child is diagnosed and recommended by a medical professional. Early diagnosis allows for treatment to begin and limits the effects of the disorder on the child. Delayed care increases costs over the lifetime of the child.

Current Recommended Treatments:

- Enzyme Replacement Therapy (ERT) with recombinant human GAA (Myozyme®, alglucosidase alfa). This treatment aims to replace the enzyme that is missing in patients with Pompe Disease thus preventing the build-up of glycogen in organs. ERT improves cardiac function, muscle weakness, and breathing issues. ERT effectively reverses cardiomyopathy, improves motor development, and improves overall survival (Chien et al 2020). Early initiation of ERT in patients with infantile onset Pompe disease is essential for a good outcome. In addition, some patients with infantile-onset Pompe disease may also need immunomodulation therapy prior to ERT to improve how their body responds to therapy.
    - Estimated Costs:
        - ERT once every 2 weeks
        - $100,000-$300,000 per year plus infusion facility cost
        - Weight-based so newborns on lower side of cost estimate
- Physical Therapy - Physical therapy will be necessary to help infants, children, and adolescents develop motor skills, maintain range of motion, and strengthen muscles and joints.
- Respiratory Therapy – Respiratory Therapy improves the respiratory status of most patients with infantile onset Pompe disease. However, some patients may still experience lung infections and breathing difficulties requiring some breathing assistance and monitoring by pulmonology.

Costs associated with treatment of individuals diagnosed with MPS I, i.e. treatment of true positives:

Treatment costs are covered by insurance once the child is diagnosed and recommended by a medical professional. Early diagnosis allows for treatment to begin and limits the effects of the disorder on the child. Delayed care increases costs over the lifetime of the child.

Current Recommended Treatments:

- Enzyme Replacement Therapy (ERT) - This treatment is administered by intravenous solution (IV) weekly to replace or supplement the missing or low enzymes. ERT is not a cure, it slows progression and may improve growth, joint movement, sleep apnea, respiratory function, pain levels, vision, and liver/spleen enlargement.
    - Estimated Costs Attenuated MPS I:
        - Weekly
        - $100,000-300,000 per year plus infusion facility costs
        - Weight based so newborns on lower side of cost estimate

- Hematopoietic Stem Cell Transplantation (HSCT) -HSCT has become the gold standard for the treatment of the severe form of MPS I in patients diagnosed and treated before 2–2.5 years of age.
    - Estimated Costs:
        - Severe MPS I (neurological involvement)
        - Cost $1,000,000
            - ERT often used while waiting for HSCT then up to 6 months following transplant (approx. 1 year)
- Physical Therapy - Physical therapy is a very important part of treating the signs and symptoms of MPS I. Consistent physical therapy early on can help preserve mobility and lessen pain and joint stiffness.
- Surgeries - Recommend surgeries to improve the child's quality of life. Removal of the tonsils and adenoids and insertion of ventilating (ear) tubes can prevent some upper respiratory infections and may reduce hearing loss. Hearing aids may be recommended for some individuals. Children with mild to severe MPS I may develop a buildup of fluid in the brain (hydrocephaly), a surgery to relieve the pressure inside the skull may be recommended.

Costs associated with treatment of individuals diagnosed with ALD, i.e. treatment of true positives.

Treatment costs are covered by insurance once the child is diagnosed and recommended by a medical professional. Early diagnosis allows for treatment to begin and limits the effects of the disorder on the child. Delayed care increases costs over the lifetime of the child.

Current Recommended Treatments:

- Steroids - Individuals who have adrenal insufficiency need to have regular adrenal gland testing, and can be treated effectively with replacement corticosteroids.
    - Estimated Costs:
        - $600-$800 annually.
- Serial magnetic resonance imaging (MRI)- Individual will require a MRI every 6 months starting at age 2 and end at around age 10. Changes or abnormal MRI findings indicate onset of cALD and warrants treatment.
    - Estimated Costs:
        - $6,500 per visit for approximately $104,000 total over 8 years.
- Allogeneic hematopoietic cell transplantation (HCT) or Stem Cell Transplantation - HCT is a treatment that may halt the progression of cALD in children if the disease is diagnosed and treated early.
    - Estimated Costs:
        - $1,000,000 for HCT
- Other Treatments
    - Other treatments include medication to help relieve symptoms like stiffness and seizures, and physical therapy, which can help relieve muscle spasms and reduce muscle rigidity.
    - There is currently a clinical trial for gene therapy which may be another method to stop the progression of ALD.

- The compound Lorenzo's oil does lower VLCFA in the blood. It is considered an investigational agent and its role in altering manifestations of the disease is under study.

Non-economic outcomes

Summarize the anticipated favorable and non-favorable non-economic outcomes (short-term and long-term), and, if known, the likelihood of the outcomes for each affected class of persons by the relationship category.

S: Pediatricians and family medicine physicians will benefit from timely detection and connection to medical experts when serving a child with a Pompe, MPS1, and/or ALD screen positive result.

Advocacy organizations, parents and adult patients with rare genetic conditions might see the addition of Pompe, MPS I, and/or ALD as a sign of the state's awareness of rare disorders and the state's willingness to help populations at risk.

Reference laboratories and other screening programs benefit from shared learning of operations and the clinical interpretation of results.

B: Newborns will benefit from improved quality of life when connected to care in a timely manner. The parents of newborns will benefit from a screening method that determines risk and can help prevent a diagnostic odyssey. Variations in symptoms and onset are not currently as clearly defined, based on testing and genetic results. Extended monitoring of the newborn may be required without a clear determination of expected onset.

African-American population will benefit from improved healthcare outcomes for a disorder that is more prevalent in their population.

3. The probable costs to the agency and to any other agency of the implementation and enforcement of the proposed rule and any anticipated effect on state revenues.

A. Anticipated CDPHE personal services, operating costs or other expenditures:

With the multiplexed approach to Pompe and MPS I screening, the Department will incur approximately $102,000 in one-time costs (setting up the Laboratory Information Management System (LIMS), algorithm validation, equipment) and $23,600 in monthly on-going expenditures. See table below:

Item	Startup or Recurring	Cost
LIMS Modification*	Startup	$15k-30k
Equipment		
Digital Fluidics Systems*	Startup	$40,000
Laboratory Staff (FTE)*	Startup (.5 FTE)	$12,000
Laboratory Staff (FTE)*	Recurring (0.25 FTE)	$1,000/month
Reagents		
Validation*	Startup	$20k
Daily Screening**	Recurring	$22,600/month

Costs associated with the Department contracting with medical experts to provide follow-up services for Pompe: Colorado Newborn Screening Program (CONBSP) expects to find 2-4 newborns a year when testing for Pompe, with an average follow-up cost of $1,000-$3,000 per newborn. Annual costs for $12,000.

Costs associated with confirmatory testing and genetic tests to assess Pompe: Genetic testing is provided by the vendor of the first tier testing method at no additional cost. Follow-up enzyme level testing cost would range from $100-$145 per sample.

Costs associated with the Department contracting with medical experts to provide follow-up services for MPS I: CONBSP expects to find 1-2 newborns a year when testing for MPS I, with an average follow-up cost of $1,000-$3,000 per newborn. Annual costs for $6,000.00.

Costs associated with confirmatory testing and genetic tests to assess MPS I: Genetic testing is provided by the vendor of the first tier testing method at no additional cost. Follow-up enzyme level testing cost would range from $100-$145 per sample.

With the multiplexed approach to ALD screening, the Department will incur approximately $62,000 in one-time costs (setting up the Laboratory Information Management System (LIMS), algorithm validation, equipment) and $600 in monthly on-going expenditures. See table below:

Item	Startup or Recurring	Cost
LIMS Modification*	Startup	$15k-30k
No New Equipment Needed	Startup	$0
Laboratory Staff (FTE)*	Startup (.5 FTE)	$12,000
Laboratory Staff (FTE)*	Recurring (0.0 FTE)	$0
Reagents		
Validation*	Startup	$20k
Daily Screening	Recurring	$600/month

Costs associated with the Department contracting with medical experts to provide follow-up services for ALD. CONBSP expects to find 4-6 newborns a year when testing for ALD, with an average follow-up cost of $2,000-$4,000 per newborn. Annual costs for $24,000.

Costs associated with confirmatory testing and genetic tests to assess ALD. CONBSP expects to find 4-6 newborns a year when testing for ALD, with an average follow-up cost of $1,000 per newborn. Annual costs of $6,000.

Anticipated CDPHE Revenues:

For the addition of Pompe, MPS I, and ALD, CDPHE has received funding from the CDC to aid with implementing population-wide newborn screening for these disorders. The addition of any condition presently on the RUSP but not yet implemented in Colorado would satisfy the funding requirements for the CDC grant. Recurring expenses will be supported by the Newborn Screening and Genetic Counseling Cash Fund (NBS Cash Fund); this fee is set by the Executive Director of the Department. The fee is currently $111.00 and sufficient to support the addition of these disorders. This fee is paid by the named submitter of an initial newborn screening specimen.

Anticipated personal services, operating costs or other expenditures by another state agency:

The Food and Drug Administration (FDA) approved treatments for Pompe and MPS I are expensive and many of the children diagnosed with these disorders require health care coverage under Medicaid. Health First Colorado, the State Medicaid Program, is already covering these costs for children that are diagnosed following clinical presentation of symptoms, therefore additional costs associated with treatment therapy is not anticipated. Additionally, early identification and treatment prior to clinical presentation of symptoms will reduce irreversible damage and thereby reduce ongoing costs associated with ancillary medical expenses.

The FDA approved treatments for ALD are expensive and many of the children diagnosed with the disorder require health care coverage under Medicaid. Health First Colorado, the State Medicaid Program, is already covering these costs for children that are diagnosed following clinical presentation of symptoms. Additional costs associated with MRI monitoring up to $104,000 may be incurred. Without this additional monitoring early identification and treatment prior to clinical presentation of symptoms would not be possible. Early identification will reduce the possibility of death or irreversible damage and thereby reduce ongoing costs associated with ancillary medical expenses. Hematopoietic cell transplantation when indicated by MRI monitoring would be an additional cost of approximately $1,000,000. Additional treatment costs are normally not incurred for these children when the expected outcome at this stage, without monitoring is death. Late HCT treatment based on a diagnosis only prior to signs and symptoms has a significantly lowered success rate.

Anticipated Revenues for another state agency: N/A

4. A comparison of the probable costs and benefits of the proposed rule to the probable costs and benefits of inaction.

Along with the costs and benefits discussed above, the proposed revisions:

_X__ Comply with a statutory mandate to promulgate rules.
___ Comply with federal or state statutory mandates, federal or state regulations, and department funding obligations.
_X__ Maintain alignment with other states or national standards.
___ Implement a Regulatory Efficiency Review (rule review) result
_X_ Improve public and environmental health practice.
_X_ Implement stakeholder feedback.
___ Advance the following CDPHE Strategic Plan priorities:

Goal 1, Implement public health and environmental priorities
Goal 2, Increase Efficiency, Effectiveness and Elegance
Goal 3, Improve Employee Engagement
Goal 4, Promote health equity and environmental justice
Goal 5, Prepare and respond to emerging issues, and
Comply with statutory mandates and funding obligations

Strategies to support these goals:
___ Substance Abuse (Goal 1)
___ Mental Health (Goal 1, 2, 3 and 4)
___ Obesity (Goal 1)
___ Immunization (Goal 1)
___ Air Quality (Goal 1)
___ Water Quality (Goal 1)
_X__ Data collection and dissemination (Goal 1, 2, 3, 4, 5)
___ Implement quality improvement/a quality improvement project (Goal 1, 2, 3, 5)
___ Employee Engagement (Goal 1, 2, 3)
_X_ Decisions incorporate health equity and environmental justice (Goal 1, 3, 4)
___ Detect, prepare and respond to emerging issues (Goal 1, 2, 3, 4, 5)

___ Advance CDPHE Division-level strategic priorities.

African-American population will benefit from improved healthcare outcomes for Pompe, a disorder that is more prevalent in their population. There are more than 240,000 African-Americans in Colorado and historically they have been underserved by the healthcare community. Early genetic studies for newborn screening focused on Northern European populations and neglected disorders frequently found in minority populations. Equity in healthcare is a Department priority.

The costs and benefits of the proposed rule will not be incurred if inaction was chosen.

Costs and benefits of inaction not previously discussed include: N/A

5. A determination of whether there are less costly methods or less intrusive methods for achieving the purpose of the proposed rule.

The Department is not aware of less costly approaches that could be implemented in a timely manner. By implementing a multiplexed, FDA-authorized test for screening the CONBSP is selecting an efficient and cost-effective approach to newborn screening.

6. Alternative Rules or Alternatives to Rulemaking Considered and Why Rejected.

For the addition of Pompe, MPS I and ALD, the department also considered keeping its newborn screening panel in its current form. This would mean newborns with these disorders who would benefit most from early diagnosis would not be identified through newborn screening. Families which are aware of the risks posed by these disorders could opt for prenatal screening or commercial newborn screening. However, this would be inconsistent with the Department's focus on health equity. Children identified with these disorders through the natural progression of the disease are still likely to be treated, so newborn

screening is not likely to inflate treatment costs for the broader healthcare system. In fact, because children who start treatment earlier generally have better outcomes than those who start treatment later, it is possible the overall costs of care will be lower for children treated sooner and reduce the child's reliance on medical interventions or equipment to maintain quality of life.

7. To the extent practicable, a quantification of the data used in the analysis; the analysis must take into account both short-term and long-term consequences.

https://www.babysfirsttest.org/newborn-screening/conditions/mucopolysaccharidosis-type-i

https://www.babysfirsttest.org/newborn-screening/conditions/pompe

https://www.hrsa.gov/advisory-committees/heritable-disorders/rusp/index.html

https://www.hrsa.gov/sites/default/files/hrsa/advisory-committees/heritable-disorders/rusp/previous-nominations/pompe-exsum.pdf

https://www.hrsa.gov/sites/default/files/hrsa/advisory-committees/heritable-disorders/rusp/previous-nominations/mps-i-27-june-2018.pdf

https://www.hrsa.gov/sites/default/files/hrsa/advisory-committees/heritable-disorders/rusp/previous-nominations/x-ald-27-june-2018.pdf

https://www.newsteps.org/data-resources/state-profiles

Hans C. Andersson Newborn Screening + Enzyme Replacement Therapy = Improved Lysosomal Storage Disorder: Outcomes in Infantile-Onset Pompe Disease The Journal of Pediatrics, Volume 166, Issue 4, April 2015, Pages 800-801

Eisengart, J.B., Rudser, K.D., Xue, Y. *et al.* Long-term outcomes of systemic therapies for Hurler syndrome: an international multicenter comparison. *Genet Med* 20, 1423–1429 (2018). https://doi.org/10.1038/gim.2018.29

Kemper, A., Brosco, J., Comeau, A. *et al.* Newborn screening for X-linked adrenoleukodystrophy: evidence summary and advisory committee recommendation. *Genet Med* 19, 121–126 (2017). https://doi.org/10.1038/gim.2016.68

Wiens K, Berry SA, Choi H, Gaviglio A, Gupta A, Hietala A, Kenney-Jung D, Lund T, Miller W, Pierpont EI, Raymond G, Winslow H, Zierhut HA, Orchard PJ. A report on state-wide implementation of newborn screening for X-linked Adrenoleukodystrophy. Am J Med Genet A. 2019 Jul;179(7):1205-1213. doi: 10.1002/ajmg.a.61171. Epub 2019 May 10. PMID: 31074578; PMCID: PMC6619352.

STAKEHOLDER ENGAGEMENT
for Amendments to
5 CCR 1005-4
Newborn Screening and Second Newborn Screening

State law requires agencies to establish a representative group of participants when considering to adopt or modify new and existing rules. This is commonly referred to as a stakeholder group.

Early Stakeholder Engagement:
The following individuals and/or entities were invited to provide input and included in the development of these proposed rules:

Organization	Representative Name and Title (if known)
National Organization for Rare Disorders / Family Member	Nick Kirchhof, Colorado Volunteer State Ambassador
Children's Hospital Colorado / University of Colorado	Dr. Cullen Dutmer, Immunology
Children's Hospital Colorado / University of Colorado	Dr. Scott Sagel, Cystic Fibrosis
Wyoming Department of Health	Carleigh Soule, Newborn Screening and Genetics Coordinator
Wyoming Department of Health	Eighmey Zeeck, Women and Infant Health Program Manager
Rocky Mountain Endocrinology	Dr. Aristides Maniatis
Children's Hospital Colorado / University of Colorado	Dr. Stacey Martiniano, Cystic Fibrosis
Children's Hospital Colorado / University of Colorado	Erica Wright, Genetic Counselor
Children's Hospital Colorado / University of Colorado	Dr. Jennifer Barker, Endocrine
Children's Hospital Colorado / University of Colorado	Melissa Gibbons, Genetic Counselor
Children's Hospital Colorado / University of Colorado	Dr. Peter Baker, Inherited Metabolic Disease (IMD)
Children's Hospital Colorado / University of Colorado	Shawn McCandles, IMD
UC Health	Dr. Mary Kohn
University of Colorado / Sickle Center	Donna Holstein, Nurse
University of Colorado / Sickle Center	Dr. Kathryn Hassell
Primary Care Partners Grand Junction	Dr. Patrice Whistler, Pediatrics
Family Member of Affected Individual	Lori Wise
UC Health	Anne Behring, Nurse
Center for Public Health Innovation	Yvonne Kellar-Guenther
Colorado Department of Public Health and Environment	Scott Bookman, Laboratory Services Division Director
Colorado Department of Public Health and Environment	Emily Travanty, PhD, Laboratory Services Division Scientific

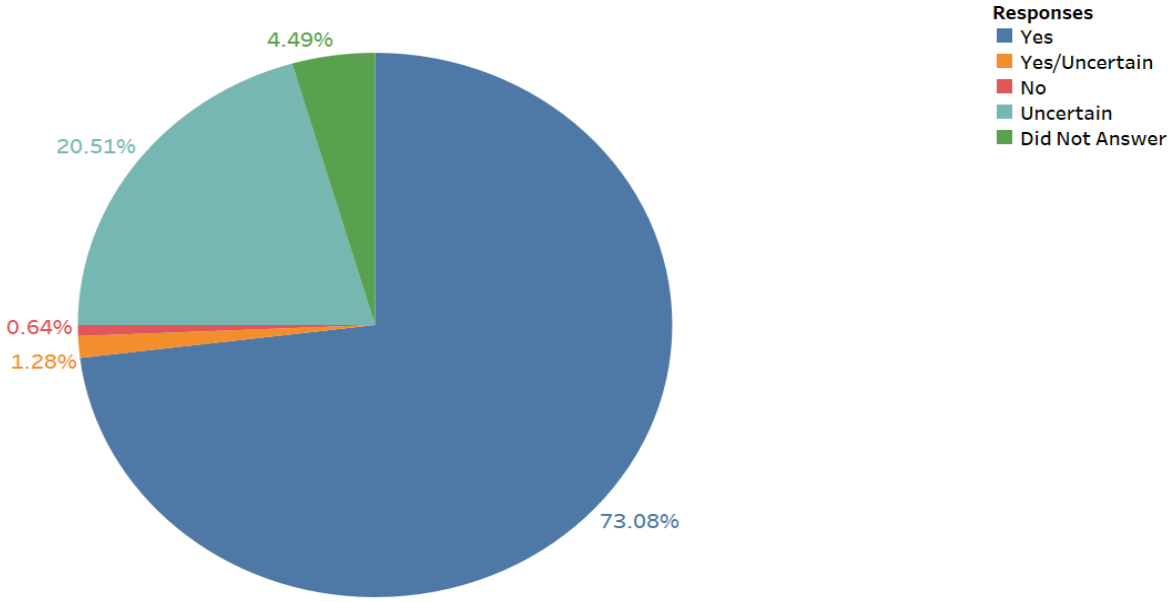
	Director
Colorado Department of Public Health and Environment	Gregory Bonn, Newborn Screening (NBS) Operations Manager
Colorado Department of Public Health and Environment	Rachel Rodriguez, NBS Supervisor
Colorado Department of Public Health and Environment	Kathy Inkhamfong, NBS Program Assistant
Colorado Department of Public Health and Environment	Abena Watson-Siriboe, NBS Scientist
Colorado Department of Public Health and Environment	Kendra Jones, NBS Scientist

The Department's outreach to stakeholders has been ongoing with open communication among all stakeholder groups. The CONBSP hosts quarterly stakeholder meetings. Additionally, in 2019 the CONBSP established a stakeholder survey to determine the interest and priority of adding conditions to the CONBSP panel. The survey was posted on the CONBSP website, shared in the monthly newsletter, added to email signatures and provided to stakeholder groups.

On January 28, 2020 the focus of the stakeholder meeting was the addition of the remaining three conditions currently on the RUSP not on the CONBSP panel. Experts in testing and treatment of these conditions provided detailed information to inform the stakeholder discussion. Stakeholders expressed their interest in adding these three conditions to the Newborn Screening Panel at this time.

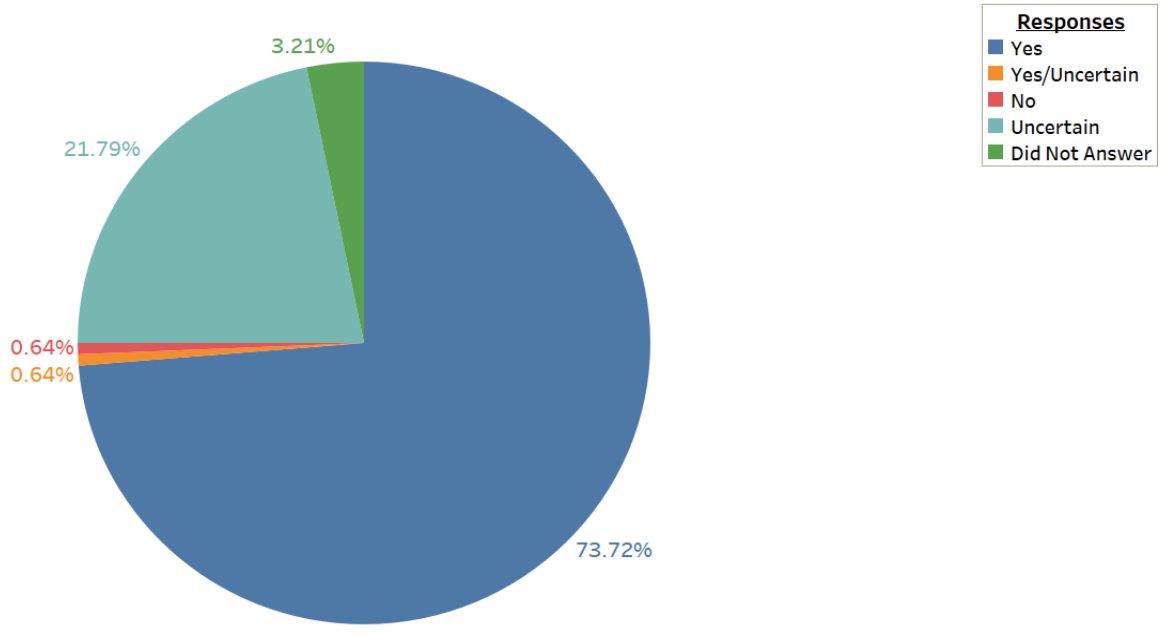
All subsequent quarterly stakeholder meetings have allowed for continued discussion regarding the addition of these three conditions. Stakeholder support for the addition of the conditions has remained consistent.

Stakeholder Responses to the Addition of Pompe



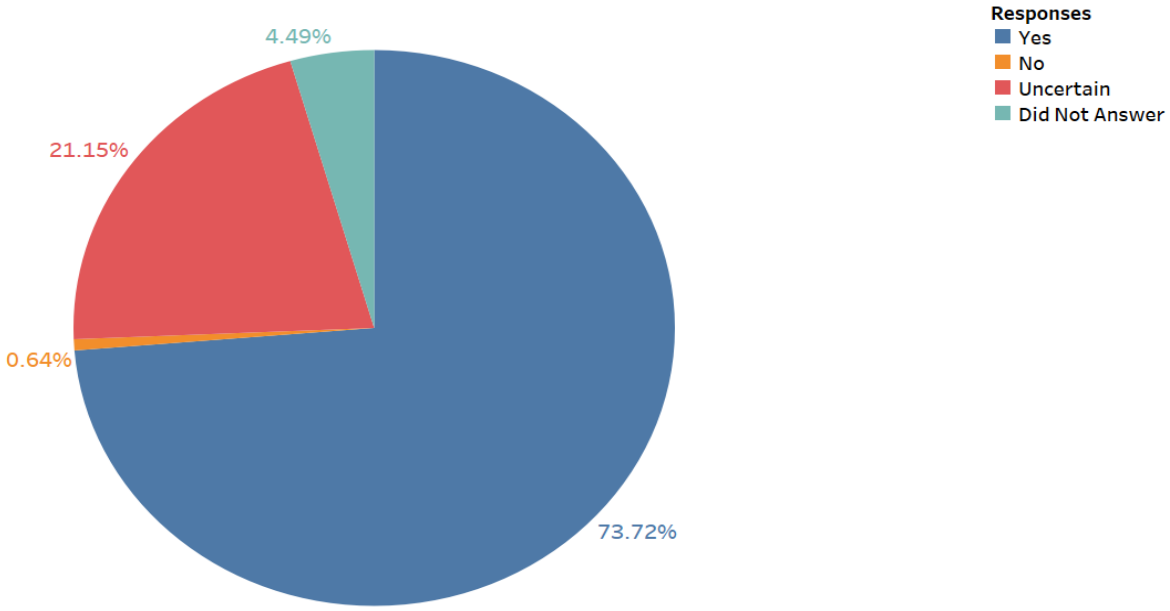
% of Total Count Email Addresses. Color shows details about Should Pompe Disease be added to the Colorado Newborn Screening panel?1. The marks are labeled by % of Total Count Email Addresses.

Stakeholder Responses for the Addition of MPS-I



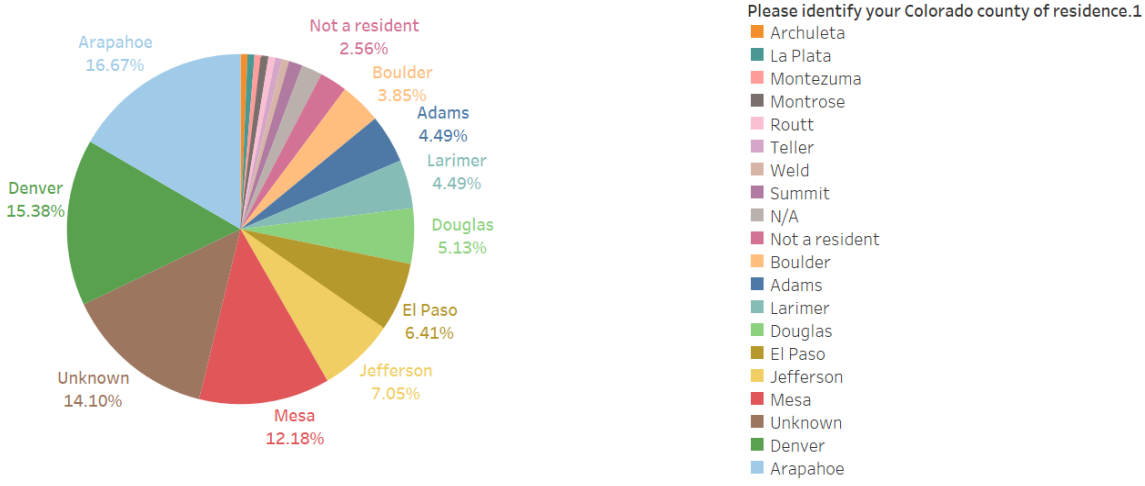
% of Total Count Email Addresses. Color shows details about Should Mucopolysaccharidosis Type I (MPS-1) be added to the Colorado Newborn Screening panel?1. The marks are labeled by % of Total Count Email Addresses.

Stakeholder Response to the Addition of X-ALD

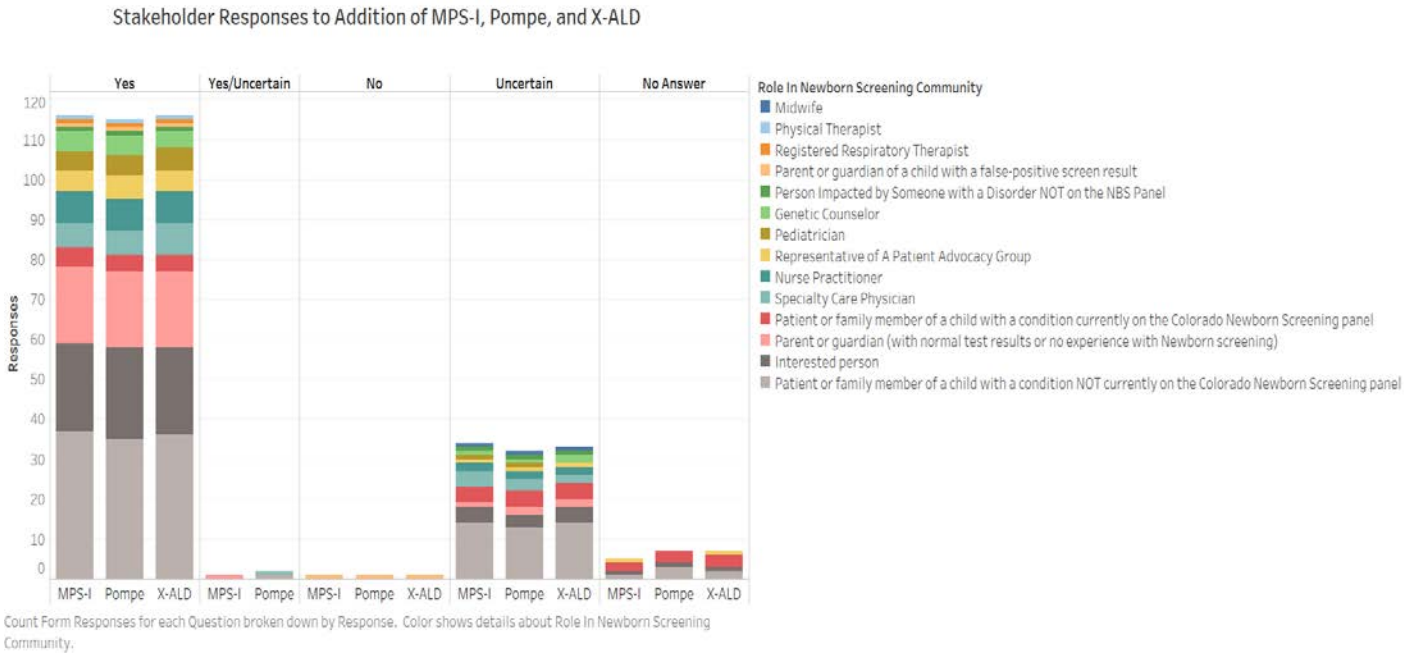


% of Total Count Email Addresses. Color shows details about Should X-linked Adrenoleukodystrophy (X-ALD) be added to the Colorado Newborn Screening panel?1. The marks are labeled by % of Total Count Email Addresses.

Stakeholder Responses by County



Total Responses: 156



Stakeholder Group Notification

The stakeholder group was provided notice of the rulemaking hearing and provided a copy of the proposed rules or the internet location where the rules may be viewed. Notice was provided prior to the date the notice of rulemaking was published in the Colorado Register (typically, the 10th of the month following the Request for Rulemaking).

_X_ Not applicable. This is a Request for Rulemaking Packet. Notification will occur if the Board of Health sets this matter for rulemaking.

____ Yes.

Summarize Major Factual and Policy Issues Encountered and the Stakeholder Feedback Received. If there is a lack of consensus regarding the proposed rule, please also identify the Department's efforts to address stakeholder feedback or why the Department was unable to accommodate the request.

To date, no major factual or policy issues have been encountered. The Department is committed to continued communication with stakeholders throughout the rulemaking period.

Please identify the determinants of health or other health equity and environmental justice considerations, values or outcomes related to this rulemaking.

Overall, after considering the benefits, risks and costs, the proposed rule:

Select all that apply.

	Improves behavioral health and mental health; or, reduces substance abuse or suicide risk.	X	Reduces or eliminates health care costs, improves access to health care or the system of care; stabilizes individual participation; or, improves the quality of

			care for unserved or underserved populations.
	Improves housing, land use, neighborhoods, local infrastructure, community services, built environment, safe physical spaces or transportation.		Reduces occupational hazards; improves an individual's ability to secure or maintain employment; or, increases stability in an employer's workforce.
	Improves access to food and healthy food options.		Reduces exposure to toxins, pollutants, contaminants or hazardous substances; or ensures the safe application of radioactive material or chemicals.
X	Improves access to public and environmental health information; improves the readability of the rule; or, increases the shared understanding of roles and responsibilities, or what occurs under a rule.	X	Supports community partnerships; community planning efforts; community needs for data to inform decisions; community needs to evaluate the effectiveness of its efforts and outcomes.
	Increases a child's ability to participate in early education and educational opportunities through prevention efforts that increase protective factors and decrease risk factors, or stabilizes individual participation in the opportunity.		Considers the value of different lived experiences and the increased opportunity to be effective when services are culturally responsive.
X	Monitors, diagnoses and investigates health problems, and health or environmental hazards in the community.		Ensures a competent public and environmental health workforce or health care workforce.
	Other:_____ _____		Other:_____ _____

HOUSE BILL 18-1006

BY REPRESENTATIVE(S) Hamner and Liston, Arndt, Becker K., Bridges, Buckner, Danielson, Esgar, Exum, Garnett, Gray, Hansen, Jackson, Kennedy, Lee, McLachlan, Michaelson Jenet, Pabon, Pettersen, Roberts, Rosenthal, Winter, Young, Duran, Coleman, Ginal, Hooton, Kraft-Tharp, Melton, Salazar, Valdez;
also SENATOR(S) Gardner and Moreno, Aguilar, Court, Crowder, Fields, Jahn, Jones, Kefalas, Kerr, Lambert, Lundberg, Martinez Humenik, Merrifield, Priola, Tate, Todd, Zenzinger.

CONCERNING MODIFICATIONS TO THE NEWBORN SCREENING PROGRAM ADMINISTERED BY THE DEPARTMENT OF PUBLIC HEALTH AND ENVIRONMENT, AND, IN CONNECTION THEREWITH, MAKING AN APPROPRIATION.

Be it enacted by the General Assembly of the State of Colorado:

SECTION 1. In Colorado Revised Statutes, **repeal** part 8 of article 4 of title 25.

SECTION 2. In Colorado Revised Statutes, **amend** 25-4-1002 as follows:

25-4-1002. Legislative declaration. (1) The general assembly

Capital letters or bold & italic numbers indicate new material added to existing statutes; dashes through words indicate deletions from existing statutes and such material not part of act.

hereby finds and declares that:

(a) RECENT NEWBORN SCREENING INNOVATIONS ARE CONSIDERED AMONG THE GREATEST PUBLIC HEALTH ACHIEVEMENTS OF THE TWENTY-FIRST CENTURY;

(b) SCIENTIFIC RESEARCH HAS DEMONSTRATED THAT NEWBORN SCREENING NOT ONLY SAVES LIVES AND IMPROVES DEVELOPMENTAL OUTCOMES BUT ALSO CONTRIBUTES TO COST SAVINGS FOR FAMILIES, HEALTH CARE SYSTEMS, AND THE STATE;

(c) NEWBORN SCREENING INCLUDES CONDITIONS FOR WHICH DIAGNOSIS AND TREATMENT MUST BE IMPLEMENTED IN A TIMELY MANNER IN ORDER TO ACHIEVE MAXIMUM BENEFIT FOR THE CHILD;

(d) NEWBORN SCREENING IS AN APPROPRIATE PUBLIC HEALTH FUNCTION TO PROVIDE NECESSARY EDUCATIONAL SERVICES TO HEALTH CARE PROVIDERS, FAMILIES, AND COMMUNITIES SO THAT APPROPRIATE RESOURCES AND INFORMATION ARE AVAILABLE;

(e) NEWBORN SCREENING IS A PUBLIC HEALTH FUNCTION THAT IDENTIFIES NEWBORNS AT RISK OF CERTAIN CONDITIONS OR HEARING LOSS, AS WELL AS NEWBORNS WHO DO NOT RECEIVE SCREENING, AND APPROPRIATELY CONNECTS THEM TO CARE;

(f) AN EFFECTIVE NEWBORN SCREENING PROGRAM IS DEPENDENT UPON A STRONG SYSTEM OF EDUCATION AND COORDINATION AMONG PRIMARY CARE PROVIDERS, HOSPITALS, SPECIALTY CARE PROVIDERS, PATIENT AND FAMILY SUPPORT ORGANIZATIONS, PUBLIC HEALTH LABORATORY STAFF, AND PUBLIC HEALTH PROFESSIONALS;

~~(a)~~ (g) State policy regarding newborn screening and genetic counseling and education should be made with full public knowledge, in light of expert opinion, and should be constantly reviewed to consider changing medical knowledge and ensure full public protection;

~~(b)~~ (h) Participation of persons in NEWBORN SCREENING PROGRAMS OR genetic counseling programs in this state should be wholly voluntary, and ~~that~~ all information obtained from persons involved in ~~such~~ THESE programs ~~or in newborn screening programs~~ in the state ~~should~~ MUST be

held strictly confidential. FAMILY PARTICIPATION IN THE FOLLOW-UP SUPPORT AND ASSISTANCE SERVICES IS VOLUNTARY.

(i) HEARING LOSS OCCURS IN NEWBORN INFANTS MORE FREQUENTLY THAN ANY OTHER HEALTH CONDITION FOR WHICH NEWBORN INFANT SCREENING IS REQUIRED;

(j) EIGHTY PERCENT OF THE LANGUAGE ABILITY OF A CHILD IS ESTABLISHED BY THE TIME THE CHILD IS EIGHTEEN MONTHS OF AGE, AND IT IS VITALLY IMPORTANT TO SUPPORT THE HEALTHY DEVELOPMENT OF LANGUAGE SKILLS;

(k) EARLY DETECTION, EARLY INTERVENTION, AND TREATMENT OF HEARING LOSS IN A CHILD ARE HIGHLY EFFECTIVE IN FACILITATING A CHILD'S HEALTHY DEVELOPMENT IN A MANNER CONSISTENT WITH THE CHILD'S AGE AND COGNITIVE ABILITY;

(l) CHILDREN WITH HEARING LOSS WHO DO NOT RECEIVE EARLY INTERVENTION AND TREATMENT FREQUENTLY REQUIRE SPECIAL EDUCATIONAL SERVICES, WHICH, FOR THE VAST MAJORITY OF CHILDREN IN THE STATE WITH HEARING NEEDS, ARE PUBLICLY FUNDED; AND

(m) APPROPRIATE TESTING AND IDENTIFICATION OF NEWBORN INFANTS WITH HEARING LOSS WILL FACILITATE EARLY INTERVENTION AND TREATMENT AND WILL THEREFORE SERVE THE PUBLIC PURPOSES OF PROMOTING THE HEALTHY DEVELOPMENT OF CHILDREN AND REDUCING THE NEED FOR ADDITIONAL PUBLIC EXPENDITURES.

SECTION 3. In Colorado Revised Statutes, 25-4-1003, **amend** (2) introductory portion and (2)(e) as follows:

25-4-1003. Powers and duties of state board and executive director - newborn screening programs - genetic counseling and education programs - rules. (2) The executive director of the department ~~of public health and environment~~ shall comply with the following provisions:

(e) All information gathered by the department ~~of public health and environment,~~ or by other agencies, entities, and individuals conducting programs and projects on newborn screening and genetic counseling and

education, other than statistical information and information ~~which~~ THAT the ~~individual~~ PARENT OR GUARDIAN OF A NEWBORN allows to be released through ~~his~~ THE PARENT'S OR GUARDIAN'S informed consent, ~~shall be~~ IS confidential. Public and private access to ~~individual~~ NEWBORN patient data ~~shall be~~ IS limited to data compiled without the ~~individual's~~ NEWBORN'S name. THE INFORMATION GATHERED PURSUANT TO THIS SUBSECTION (2)(e) DOES NOT RESTRICT THE DEPARTMENT FROM PERFORMING FOLLOW-UP SERVICES WITH NEWBORNS, THEIR PARENTS OR GUARDIANS, AND HEALTH CARE PROVIDERS.

SECTION 4. In Colorado Revised Statutes, 25-4-1004, **amend** (1)(b), (1)(c) introductory portion, and (2); and **add** (1.5) and (3) as follows:

25-4-1004. Newborn screening - advisory committee - rules. (1) (b) ~~On or after April 1, 1989, all~~ Infants born in the state of Colorado shall be tested for the following conditions: Phenylketonuria, hypothyroidism, abnormal hemoglobins, galactosemia, cystic fibrosis, biotinidase deficiency, and such other conditions as the STATE board ~~of health~~ may determine meet the criteria set forth in ~~paragraph (c) of this subsection (1). Appropriate specimens for such testing shall be forwarded by the hospital in which the child is born to the laboratory operated or designated by the department of public health and environment for such purposes~~ SUBSECTION (1)(c) OF THIS SECTION. THE BIRTHING FACILITY WHERE THE INFANT IS BORN SHALL FORWARD ALL APPROPRIATE SPECIMENS TO THE LABORATORY OPERATED OR DESIGNATED BY THE DEPARTMENT. The physician, nurse, midwife, or other health professional attending a birth outside a ~~hospital shall be~~ BIRTHING FACILITY IS responsible for ~~the collection~~ COLLECTING and forwarding ~~of such~~ THE specimens. The LABORATORY SHALL FORWARD THE results of the testing ~~shall be forwarded~~ directly to the physician, PRIMARY CARE PROVIDER, or other ~~primary~~ health care provider AS NEEDED for the provision of such information to the parent, ~~or~~ parents, OR GUARDIANS of the child. The results of any testing or follow-up testing pursuant to section 25-4-1004.5 may be sent to the immunization tracking system authorized by section 25-4-2403 and accessed by the physician or other primary health care provider. The state board ~~of health~~ may discontinue testing for any condition listed in this ~~paragraph (b)~~ SUBSECTION (1)(b) if, upon consideration of criteria set forth in ~~paragraph (c) of this subsection (1)~~ SUBSECTION (1)(c) OF THIS SECTION, the STATE board finds that the public health is better served by not testing infants for that condition. TESTING UNDER THIS SUBSECTION (1)(b) IS NOT

REQUIRED IF THE PARENT OR LEGAL GUARDIAN OBJECTS.

(c) The STATE board ~~of health~~ shall use the following criteria to determine whether ~~or not~~ to test infants for conditions ~~which~~ THAT are not specifically enumerated in this subsection (1):

(1.5) IF THE DEPARTMENT DEEMS THAT NEW CONDITIONS FOR WHICH AN INFANT MUST BE TESTED SHOULD BE ADDED, THE DEPARTMENT SHALL REPORT THE ADDED CONDITIONS TO THE GENERAL ASSEMBLY DURING ITS PRESENTATION IN ACCORDANCE WITH THE "STATE MEASUREMENT FOR ACCOUNTABLE, RESPONSIVE, AND TRANSPARENT (SMART) GOVERNMENT ACT", PART 2 OF ARTICLE 7 OF TITLE 2. THE DEPARTMENT SHALL ALSO NOTIFY THE JOINT BUDGET COMMITTEE AND THE HEALTH AND HUMAN SERVICES COMMITTEE OF THE SENATE AND THE HEALTH, INSURANCE, AND ENVIRONMENT COMMITTEE AND THE PUBLIC HEALTH CARE AND HUMAN SERVICES COMMITTEE OF THE HOUSE OF REPRESENTATIVES, OR THEIR SUCCESSOR COMMITTEES, WITHIN SIXTY DAYS AFTER THE DEPARTMENT RECOMMENDS A NEW CONDITION AND INCLUDE THE ADDED CONDITIONS IN THE DEPARTMENT'S ANNUAL BUDGET REQUEST SUBMITTED TO THE GENERAL ASSEMBLY EACH NOVEMBER 1.

(2) The executive director of the department of public health and environment shall assess a fee ~~which~~ THAT is sufficient to cover the DIRECT AND INDIRECT costs of ~~such~~ THE testing REQUIRED BY THIS SECTION and to accomplish the other purposes of this part 10. ~~Hospitals shall~~ BIRTHING FACILITIES MAY assess a reasonable fee to be charged the parent, ~~or~~ parents, OR GUARDIANS of the infant to cover the costs of handling the specimens, the reimbursement of laboratory costs, and the costs of providing other services, INCLUDING THE CONNECTION OF FOLLOW-UP SERVICES AND CARE TO INFANTS IDENTIFIED AS AT RISK THROUGH SCREENING, necessary to implement the purposes of this part 10.

(3) THE STATE BOARD SHALL PROMULGATE RULES CONCERNING THE REQUIREMENTS OF THE NEWBORN SCREENING PROGRAM FOR GENETIC AND METABOLIC DISORDERS, INCLUDING:

(I) IN ADDITION TO THOSE CONDITIONS LISTED IN SUBSECTION (1)(b) OF THIS SECTION, ANY OTHER CONDITIONS FOR WHICH TESTING MUST OCCUR;

(II) OBTAINING SAMPLES OR SPECIMENS FROM NEWBORN INFANTS

REQUIRED FOR THE TESTS PRESCRIBED BY THE STATE BOARD; AND

(III) THE HANDLING AND DELIVERY OF SAMPLES OR SPECIMENS FOR TESTING AND EXAMINATION.

SECTION 5. In Colorado Revised Statutes, 25-4-1004.5, **amend** (2)(b), (3)(a) introductory portion, (3)(a)(V), (3)(b) introductory portion, and (3)(c); **repeal** (1); and **add** (2)(c) and (3)(b.5) as follows:

25-4-1004.5. Follow-up testing and treatment - second screening - fee - rules. (1) ~~The general assembly finds that:~~

~~(a) Newborn screening authorized by section 25-4-1004 is provided for every newborn in the state;~~

~~(b) Newborn testing is designed to identify metabolic disorders that cause mental retardation and other health problems unless they are diagnosed and treated early in life;~~

~~(c) In order to ensure that children with metabolic disorders are able to lead as normal a life as possible and to minimize long-term health care costs for such children, it is necessary to provide centralized follow-up testing and treatment services;~~

~~(d) For over twenty-five years the follow-up testing and treatment services were provided by a federal grant that was discontinued June 30, 1993. Since that time, follow-up testing and treatment services have been limited. If alternative sources of funding are not provided, those services will be eliminated.~~

~~(e) A nominal increase of the fee on newborn screening to cover the costs of providing follow-up and referral services would allow for those services to be continued;~~

~~(f) Over the past ten years, many children with serious health conditions have received timely diagnosis and treatment as a result of the newborn screening required by this part 10. Such screening has averted the possibility of life-long institutionalization of some children and substantial related health care costs. The general assembly further finds, however, that many infants who are screened early in life may exhibit false or inaccurate~~

~~results on certain newborn screening tests. The general assembly therefore finds and declares that subsequent newborn screening will provide more accurate and reliable test results for the timely and effective diagnosis and treatment of certain health conditions in newborn infants and the best interests of children in Colorado will be served by a new screening program that routinely tests all newborns twice.~~

(2) (b) ~~On and after July 1, 1994,~~ The executive director of the department ~~of public health and environment~~ shall increase the newborn screening fee as provided in section 25-4-1004 (2) so that the fee is sufficient to include the costs of providing FIRST AND SECOND SPECIMEN TESTS WITH SECOND-TIER TESTING IF NECESSITATED BY THE RESULTS OF THE SCREENING IN ORDER TO REDUCE THE NUMBER OF FALSE POSITIVE TESTS AND TO PROVIDE follow-up and referral services to families with a newborn whose test results under a newborn screening indicate a GENETIC OR metabolic disorder. ~~Follow-up services include comprehensive diagnostic testing. The increase shall not exceed five dollars, except that it may be adjusted annually to reflect any change in the Denver-Boulder consumer price index. Any fees collected shall be subject to the provisions of section 25-4-1006.~~

(c) THE STATE BOARD SHALL PROMULGATE RULES TO ESTABLISH AND MAINTAIN APPROPRIATE FOLLOW-UP SERVICES ON POSITIVE SCREEN CASES IN ORDER THAT MEASURES MAY BE TAKEN TO PREVENT DEATH OR INTELLECTUAL OR OTHER PERMANENT DISABILITIES. THE FOLLOW-UP SERVICES MUST INCLUDE IDENTIFICATION OF NEWBORNS AT RISK FOR GENETIC AND METABOLIC CONDITIONS, COORDINATION AMONG MEDICAL PROVIDERS AND FAMILIES, CONNECTING NEWBORNS WHO SCREEN POSITIVE TO TIMELY INTERVENTION AND APPROPRIATE REFERRALS TO SPECIALISTS FOR FOLLOW-UP AND DIAGNOSTIC TESTING, AND ADDITIONAL DUTIES AS DETERMINED BY THE DEPARTMENT.

(3) (a) ~~On and after July 1, 1996, all~~ Infants born in the state of Colorado who receive newborn screening pursuant to section 25-4-1004 (1) ~~shall~~ MUST have a second specimen taken to screen for the following conditions:

(V) Such other conditions as the state board ~~of health~~ may determine meet the criteria set forth in section 25-4-1004 (1)(c) and require a second screening for accurate test results.

(b) The ~~executive director of the department of public health and environment~~ STATE BOARD is authorized to promulgate rules ~~regulations,~~ and standards for the implementation of the second specimen testing specified in this subsection (3), including: ~~but not limited to the following:~~

(b.5) THE LABORATORY OPERATED BY THE LABORATORY SERVICES DIVISION IN THE DEPARTMENT, OR THE LABORATORY DESIGNATED BY THE DEPARTMENT, AS APPLICABLE, MUST REMAIN OPEN A MINIMUM OF SIX DAYS PER WEEK EVERY WEEK OF THE YEAR.

(c) On and after July 1, ~~1996~~ 2018, the executive director of the department of public health and environment may adjust the newborn screening fee set forth in section 25-4-1004 (2) so that the fee is sufficient to cover the costs associated with the second screening described in this subsection (3). ~~Any increase shall be in addition to the fee described in subsection (2) of this section and shall not initially exceed five dollars and seventy-five cents but may be adjusted annually to reflect any actual cost increase associated with the administration of the second screening. Any fees collected pursuant to this paragraph (c) shall be subject to the provisions of section 25-4-1006~~ MONEY IN THE NEWBORN SCREENING AND GENETIC COUNSELING CASH FUNDS IS EXEMPT FROM SECTION 24-75-402 THROUGH JULY 1, 2021.

SECTION 6. In Colorado Revised Statutes, 25-4-1004.7, **amend** (2)(a)(I) introductory portion, (2)(a)(I)(A), (2)(a)(I)(C), (2)(a)(II), (3)(a), and (5); **repeal** (1), (2)(a)(I)(B), (3)(b), and (4)(a); and **add** (7), (8), (9), (10), and (11) as follows:

25-4-1004.7. Newborn hearing screening - advisory committee - report - rules. (1) ~~(a) The general assembly finds, determines, and declares:~~

~~(I) That hearing loss occurs in newborn infants more frequently than any other health condition for which newborn infant screening is required;~~

~~(II) That eighty percent of the language ability of a child is established by the time the child is eighteen months of age and that hearing is vitally important to the healthy development of such language skills;~~

~~(III) That early detection of hearing loss in a child and early~~

~~intervention and treatment has been demonstrated to be highly effective in facilitating a child's healthy development in a manner consistent with the child's age and cognitive ability;~~

~~(IV) That children with hearing loss who do not receive such early intervention and treatment frequently require special educational services and that such services are publicly funded for the vast majority of children with hearing needs in the state;~~

~~(V) That appropriate testing and identification of newborn infants with hearing loss will facilitate early intervention and treatment and may therefore serve the public purposes of promoting the healthy development of children and reducing public expenditure; and~~

~~(VI) That consumers should be entitled to know whether the hospital at which they choose to deliver their infant provides newborn hearing screening.~~

~~(b) For these reasons the general assembly hereby determines that it would be beneficial and in the best interests of the development of the children of the state of Colorado that newborn infants' hearing be screened.~~

(2) (a) (I) There is hereby established an advisory committee on hearing in newborn infants ~~for the purpose of collecting the informational data specified in paragraph (b) of subsection (3) of this section, and~~ for the purpose of REVIEWING INFORMATION AND STATISTICS GATHERED DURING THE NEWBORN HEARING SCREENING PROGRAM AND providing recommendations to ~~hospitals~~ BIRTHING FACILITIES, other health care institutions, the department, ~~of public health and environment,~~ and the public concerning, but not necessarily limited to: ~~the following:~~

(A) ~~Appropriate methodologies to be implemented~~ BEST PRACTICES for hearing screening of newborn infants, which ~~methodologies shall~~ PRACTICES MUST be objective and physiologically based and ~~which shall~~ MUST not include a requirement that the initial newborn hearing screening be performed by an audiologist; AND

(B) ~~The number of births sufficient to qualify a hospital or health institution to arrange otherwise for hearing screenings; and~~

(C) Guidelines AND BEST PRACTICES for reporting and the means to assure that identified children receive referral for appropriate follow-up services.

(II) The advisory committee on hearing in newborn infants ~~shall~~ MUST consist of at least ~~seven~~ NINE members. ~~who shall be appointed by~~ The executive director of the department ~~of public health and environment~~ SHALL APPOINT MEMBERS TO THE ADVISORY COMMITTEE. Members appointed to the committee ~~shall~~ MUST have training, experience, or interest in the area of hearing ~~conditions~~ LOSS in children AND SHOULD INCLUDE REPRESENTATIVES FROM RURAL AND URBAN AREAS OF THE STATE, A PARENT WHO HAS A CHILD WITH HEARING LOSS, A REPRESENTATIVE OF A PATIENT AND FAMILY SUPPORT ORGANIZATION, A REPRESENTATIVE OF A HOSPITAL, A REPRESENTATIVE FROM AN ORGANIZATION REPRESENTING CULTURALLY DEAF PERSONS, AN AMERICAN SIGN LANGUAGE EXPERT WHO HAS EXPERIENCE IN EVALUATION AND INTERVENTION OF INFANTS AND YOUNG CHILDREN, AND PHYSICIANS AND AUDIOLOGISTS WITH SPECIFIC EXPERTISE IN HEARING LOSS IN INFANTS.

(3) (a) It is the intent of the general assembly that ~~newborn hearing screening be conducted on no fewer than ninety-five percent of the infants born in hospitals~~ INFANTS BORN IN THE STATE BE SCREENED FOR HEARING LOSS using procedures recommended by the advisory committee on hearing in newborn infants, created in subsection (2) of this section. Toward that end, every licensed or certified ~~hospital~~ BIRTHING FACILITY shall educate the parents of infants born in such ~~hospitals~~ BIRTHING FACILITIES of the importance of screening the hearing of newborn infants and follow-up care. Education ~~shall not be~~ IS NOT considered a substitute for the hearing screening described in this section. ~~Every licensed or certified hospital shall report annually to the advisory committee concerning the following:~~ SCREENING FOR HEARING LOSS UNDER THIS SUBSECTION (3)(a) IS NOT REQUIRED IF THE PARENT OR LEGAL GUARDIAN OBJECTS.

~~(I) The number of infants born in the hospital;~~

~~(II) The number of infants screened;~~

~~(III) The number of infants who passed the screening, if administered; and~~

~~(IV) The number of infants who did not pass the screening, if administered.~~

(b) ~~The advisory committee on hearing in newborn infants shall determine which hospitals or other health care institutions in the state of Colorado are administering hearing screening to newborn infants on a voluntary basis and the number of infants screened.~~

~~(I) to (IV) Repealed.~~

(4) (a) ~~If the number of infants screened falls below eighty-five percent, the board of health shall promulgate rules requiring hearing screening of newborn infants pursuant to section 24-4-103, C.R.S., of the "State Administrative Procedure Act".~~

(5) A physician, nurse, midwife, or other health professional attending a birth outside a hospital or institution shall MAKE EVERY PROFESSIONAL EFFORT, AS DEFINED BY THE BOARD, INCLUDING FOLLOWING UP AT SCHEDULED POSTPARTUM APPOINTMENTS, TO ENSURE THAT THE HEARING SCREENING IS PERFORMED WITHIN THIRTY DAYS OF THE BIRTH AND SHALL provide information, as established by RULE OF the department, to parents regarding ~~places where the parents may have their infants' hearing screened and~~ the importance of ~~such~~ THE screening. THE PHYSICIAN, NURSE, MIDWIFE, OR OTHER HEALTH PROFESSIONAL WHO PERFORMS THE SCREENING SHALL PROVIDE A REPORT OF ANY SCREENING TO THE PARENT OR GUARDIAN OF THE INFANT, THE PRIMARY CARE PROVIDER OF THE INFANT, AND THE DEPARTMENT. SCREENING FOR HEARING LOSS UNDER THIS SUBSECTION (5) IS NOT REQUIRED IF THE PARENT OR LEGAL GUARDIAN OBJECTS.

(7) UPON RECEIPT OF SUFFICIENT FINANCIAL RESOURCES IN THE NEWBORN HEARING SCREENING CASH FUND, AS DETERMINED BY THE DEPARTMENT, TO SUPPORT A NEW INFORMATION TECHNOLOGY SYSTEM FOR THE PURPOSE OF MANAGING THE NEWBORN HEARING SCREENING PROGRAM, THE DEPARTMENT SHALL PROCURE AN INFORMATION TECHNOLOGY SYSTEM AND PROMULGATE RULES IN ORDER TO IMPLEMENT THE SYSTEM.

(8) (a) THE STATE BOARD OF HEALTH SHALL PROMULGATE RULES THAT REQUIRE EACH OF THE FOLLOWING WITH INFORMATION PERTINENT TO THIS SECTION TO REPORT THE RESULTS OF INDIVIDUAL SCREENING TO THE DEPARTMENT:

(I) A BIRTHING FACILITY; OR

(II) ANOTHER FACILITY OR PROVIDER.

(b) THE RULES MUST INCLUDE A REQUIREMENT THAT THE BIRTHING FACILITY INCLUDE THE RESULTS OF THE HEARING SCREENING IN THE ELECTRONIC MEDICAL RECORD OF THE NEWBORN. THE INFORMATION SYSTEM REQUIRED IN SUBSECTION (7) OF THIS SECTION MUST ALLOW THE RESULTS OF OUTPATIENT RESCREENINGS TO BE REPORTED TO THE DEPARTMENT AND TO THE PARENT OR GUARDIAN OF THE NEWBORN.

(9) (a) THE STATE BOARD OF HEALTH SHALL PROMULGATE RULES TO ESTABLISH AND MAINTAIN APPROPRIATE FOLLOW-UP SERVICES FOR NEWBORNS AT RISK OF HEARING LOSS. THE FOLLOW-UP SERVICES MUST INCLUDE IDENTIFICATION OF NEWBORNS AT RISK FOR HEARING LOSS, COORDINATION AMONG MEDICAL AND AUDIOLOGY PROVIDERS AND FAMILIES, CONNECTING NEWBORNS TO TIMELY INTERVENTION, APPROPRIATE REFERRALS TO SPECIALISTS FOR FOLLOW-UP AND DIAGNOSTIC TESTING, AND ADDITIONAL DUTIES AS DETERMINED BY THE DEPARTMENT.

(b) THE FOLLOW-UP SERVICES MUST PROVIDE THE PARENTS WITH INFORMATION AND RESOURCES SO THAT THE PARENTS CAN, IN A TIMELY MANNER, LOCATE APPROPRIATE DIAGNOSTIC AND TREATMENT SERVICES FOR THE NEWBORN.

(c) THE DEPARTMENT SHALL ALSO PROVIDE APPROPRIATE TRAINING, ON A PERIODIC BASIS, TO BIRTHING FACILITIES AND MIDWIVES ON THE DEPARTMENT'S SCREENING PROGRAM.

(d) THE INFORMATION GATHERED BY THE DEPARTMENT, OTHER THAN STATISTICAL INFORMATION AND INFORMATION THAT THE PARENT OR GUARDIAN OF A NEWBORN ALLOWS TO BE RELEASED THROUGH THE PARENT'S OR GUARDIAN'S INFORMED CONSENT, IS CONFIDENTIAL. PUBLIC ACCESS TO NEWBORN PATIENT DATA IS LIMITED TO DATA COMPILED WITHOUT THE NEWBORN'S NAME. AUDIOLOGISTS AND OTHER HEALTH PROFESSIONALS PROVIDING DIAGNOSTIC SERVICES TO NEWBORNS AND THEIR FAMILIES MAY ACCESS THE INFORMATION, ON A NEWBORN-SPECIFIC BASIS, FOR THE PURPOSE OF ENTERING FOLLOW-UP INFORMATION. THE INFORMATION GATHERED IN ACCORDANCE WITH THIS SUBSECTION (9)(d) DOES NOT RESTRICT THE DEPARTMENT FROM PERFORMING FOLLOW-UP SERVICES WITH

NEWBORNS, THEIR PARENTS OR GUARDIANS, AND HEALTH CARE PROVIDERS.

(10) (a) THE DEPARTMENT SHALL DEVELOP AND PUBLISH MATERIALS ON ITS WEBSITE FOR USE IN EDUCATING AND TRAINING ON CYTOMEGALOVIRUS, REFERRED TO AS "CMV", THAT INCLUDE THE FOLLOWING:

(I) THE ESTIMATED INCIDENCE OF CMV;

(II) THE TRANSMISSION OF CMV TO PREGNANT WOMEN OR WOMEN WHO MAY BECOME PREGNANT;

(III) BIRTH DEFECTS CAUSED BY CONGENITAL CMV;

(IV) METHODS OF DIAGNOSING CONGENITAL CMV;

(V) AVAILABLE PREVENTIVE MEASURES TO AVOID THE INFECTION IN WOMEN WHO ARE PREGNANT OR MAY BECOME PREGNANT;

(VI) RESOURCES AND EVIDENCE-BASED TREATMENT AS THEY BECOME AVAILABLE FOR FAMILIES OF CHILDREN BORN WITH CMV; AND

(VII) ANY FEDERAL OR STATE REQUIREMENTS REGARDING TESTING FOR CMV.

(b) SUBJECT TO AVAILABLE APPROPRIATIONS, THE DEPARTMENT SHALL PROVIDE TECHNICAL ASSISTANCE AND TRAINING REGARDING CMV TO HEALTH CARE FACILITIES AND HEALTH CARE PROVIDERS UPON REQUEST.

(11) THE EXECUTIVE DIRECTOR OF THE DEPARTMENT MAY ASSESS A FEE THAT IS SUFFICIENT TO COVER THE ONGOING DIRECT AND INDIRECT COSTS OF ALL INITIAL NEWBORN HEARING SCREENING AND FOLLOW-UP SERVICES AND TO ACCOMPLISH THE OTHER PURPOSES OF THIS SECTION, WHICH FEE SHALL BE DEPOSITED INTO THE NEWBORN HEARING SCREENING CASH FUND CREATED IN SECTION 25-4-1006 (3). BIRTHING FACILITIES MAY ASSESS A REASONABLE FEE TO BE CHARGED THE PARENT OR GUARDIAN OF THE NEWBORN TO COVER THE COSTS OF PROVIDING SERVICES NECESSARY TO IMPLEMENT THE PURPOSES OF THIS SECTION.

SECTION 7. In Colorado Revised Statutes, **amend** 25-4-1005 as

follows:

25-4-1005. Exceptions. Nothing in the provisions of this part 10 shall be construed to require the testing or medical treatment for the minor child of any person WHO HAS PERSONAL OBJECTION TO THE ADMINISTRATION OF THE TESTS OR TREATMENT or of any person who is a member of a well-recognized church or religious denomination and whose religious convictions in accordance with the tenets or principles of ~~his~~ THE church or religious denomination are against medical treatment for disease or physical defects. ~~or has a personal objection to the administration of such tests or treatment.~~

SECTION 8. In Colorado Revised Statutes, 25-4-1006, **amend** (1); and **add** (3) and (4) as follows:

25-4-1006. Cash funds. (1) All ~~moneys~~ MONEY received from fees collected pursuant to this part 10, EXCEPT FOR THE MONEY RECEIVED PURSUANT TO SECTION 25-4-1004.7, shall be transmitted to the state treasurer, who shall credit ~~the same~~ IT to the newborn screening and genetic counseling cash funds, which funds are hereby created. Such ~~moneys~~ MONEY shall be utilized for expenditures authorized or contemplated by and not inconsistent with the provisions of this part 10 relating to newborn screening, follow-up care, and genetic counseling and education programs and functions. All ~~moneys~~ MONEY credited to the newborn screening and genetic counseling cash funds shall be used as provided in this part 10 and shall not be deposited in or transferred to the general fund of this state or any other fund.

(3) THERE IS HEREBY CREATED THE NEWBORN HEARING SCREENING CASH FUND FOR THE PURPOSE OF COVERING THE ONGOING DIRECT AND INDIRECT COSTS ASSOCIATED WITH THE ADMINISTRATION OF THE NEWBORN HEARING SCREENING PROGRAM. ALL MONEY COLLECTED PURSUANT TO SECTION 25-4-1004.7 SHALL BE TRANSMITTED TO THE STATE TREASURER, WHO SHALL CREDIT IT TO THE NEWBORN HEARING SCREENING CASH FUND. THE MONEY IN THE CASH FUND AT THE END OF ANY FISCAL YEAR SHALL REMAIN IN THE CASH FUND AND SHALL NOT BE CREDITED OR TRANSFERRED TO THE GENERAL FUND OR ANY OTHER FUND. IN ADDITION, THE GENERAL ASSEMBLY MAY APPROPRIATE MONEY FROM THE GENERAL FUND TO THE DEPARTMENT TO IMPLEMENT THE NEWBORN HEARING SCREENING PROGRAM.

(4) MONEY IN THE NEWBORN SCREENING AND GENETIC COUNSELING CASH FUNDS AND THE NEWBORN HEARING SCREENING CASH FUND ARE EXEMPT FROM SECTION 24-75-402 THROUGH JULY 1, 2021.

SECTION 9. In Colorado Revised Statutes, **add** 25-4-1002.5 as follows:

25-4-1002.5. Definitions. AS USED IN THIS PART 10, UNLESS THE CONTEXT OTHERWISE REQUIRES:

(1) "BIRTHING FACILITY" MEANS A GENERAL HOSPITAL OR BIRTHING CENTER LICENSED OR CERTIFIED PURSUANT TO SECTION 25-1.5-103.

(2) "DEPARTMENT" MEANS THE DEPARTMENT OF PUBLIC HEALTH AND ENVIRONMENT.

(3) "STATE BOARD" MEANS THE STATE BOARD OF HEALTH IN THE DEPARTMENT.

SECTION 10. In Colorado Revised Statutes, 24-75-302, **amend as amended by House Bill 18-1173** (2.3)(c); **amend as added by House Bill 18-1173** (2.3)(d); and **add** (2.3)(e) as follows:

24-75-302. Capital construction fund - capital assessment fees - calculation - information technology capital account. (2.3) In addition to the sums transferred pursuant to subsections (2) and (2.5) of this section, the state treasurer and the controller shall transfer a sum as specified in this subsection (2.3) from the general fund to the information technology capital account created in subsection (3.7) of this section, as enacted by House Bill 15-1266, as money becomes available in the general fund during the fiscal year beginning on July 1 of the fiscal year in which the transfer is made. Transfers between funds pursuant to this subsection (2.3) are not appropriations subject to the limitations of section 24-75-201.1. The amounts transferred pursuant to this subsection (2.3) are as follows:

(c) On July 1, 2017, nineteen million eight hundred fifty-five thousand five hundred fifteen dollars; ~~and~~

(d) On April 1, 2018, two million eight hundred eighty-eight thousand five hundred twenty-nine dollars; AND

(e) ON JULY 1, 2018, SEVEN HUNDRED THOUSAND DOLLARS.

SECTION 11. Capital construction appropriation. (1) For the 2018-19 state fiscal year, $700,000 is appropriated to the department of public health and environment for use by the center for health and environmental information. This appropriation is from the information technology capital account within the capital construction fund created in section 24-75-302 (3.7), C.R.S. To implement this act, the center may use this appropriation for capital construction related to an information technology system for hearing loss screening. Any money appropriated in this subsection (1) not expended prior to July 1, 2019, is further appropriated to the division for the 2019-20 and 2020-21 state fiscal years for the same purpose.

(2) For the 2018-19 state fiscal year, $1,162,500 is appropriated to the department of public health and environment for use by the laboratory services division. This appropriation is from the newborn screening and genetic counseling cash funds created in section 25-4-1006 (1), C.R.S. To implement this act, the division may use this appropriation for capital construction related to laboratory space expansion and equipment purchase. Any money appropriated in this subsection (2) not expended prior to July 1, 2019, is further appropriated to the division for the 2019-20 and 2020-21 state fiscal years for the same purpose.

SECTION 12. Appropriation. For the 2018-19 state fiscal year, $89,222 is appropriated to the department of public health and environment for use by the center for health and environmental information. This appropriation is from the newborn hearing screening cash fund created in section 25-4-1006 (3), C.R.S., and is based on the assumption that the center will require an additional 1.0 FTE. To implement this act, the center may use this appropriation for the birth defects monitoring and prevention program.

SECTION 13. Effective date. This act takes effect July 1, 2018.

SECTION 14. Safety clause. The general assembly hereby finds,

determines, and declares that this act is necessary for the immediate preservation of the public peace, health, and safety.

Crisanta Duran
SPEAKER OF THE HOUSE
OF REPRESENTATIVES

Kevin J. Grantham
PRESIDENT OF
THE SENATE

Marilyn Eddins
CHIEF CLERK OF THE HOUSE
OF REPRESENTATIVES

Effie Ameen
SECRETARY OF
THE SENATE

APPROVED 3:24 PM 6/4/18

John W. Hickenlooper
GOVERNOR OF THE STATE OF COLORADO

DEPARTMENT OF PUBLIC HEALTH AND ENVIRONMENT

Laboratory Services Division

NEWBORN SCREENING AND SECOND NEWBORN SCREENING

5 CCR 1005-4

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SECTION 2: NEWBORN SCREENING REQUIREMENTS FOR NAMED SUBMITTERS

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2.4 List of Conditions for Newborn Screening

The Laboratory shall conduct screening tests for the following conditions:

2.4.1 Phenylketonuria
2.4.2 Congenital Hypothyroidism
2.4.3 Hemoglobinopathies
2.4.4 Galactosemia
2.4.5 Cystic Fibrosis
2.4.6 Biotinidase Deficiency
2.4.7 Congenital Adrenal Hyperplasia
2.4.8 Medium Chain Acyl-CoA Dehydrogenase Deficiency
2.4.9 Very Long Chain Acyl-CoA Dehydrogenase Deficiency
2.4.10 Long-Chain L-3-Hydroxy Acyl-CoA Dehydrogenase Deficiency
2.4.11 Trifunctional Protein Deficiency
2.4.12 Carnitine Acyl-Carnitine Translocase Deficiency
2.4.13 Short Chain Acyl-CoA Dehydrogenase Deficiency
2.4.14 Carnitine Palmitoyltransferase II Deficiency
2.4.15 Glutaric Acidemia Type 2
2.4.16 Arginosuccinic Acidemia
2.4.17 Citrullinemia
2.4.18 Tyrosinemia
2.5.19 Hypermethionemia
2.4.20 Maple Syrup Urine Disease
2.4.21 Homocystinuria
2.4.22 Isovaleric Acidemia
2.4.23 Glutaric Acidemia Type 1
2.5.24 3-Hydroxy-3-Methylglutaryl-CoA Lyase Deficiency
2.4.25 Multiple Carboxylase Deficiency
2.4.26 3-Methylcrotonyl-CoA Carboxylase Deficiency
2.4.27 3-Methylglutaconic Aciduria
2.4.28 Methylmalonic Acidemias
2.4.29 Propionic Acidemia
2.4.30 Beta-Ketothiolase Deficiency
2.4.31 Carnitine Uptake Defect
2.4.32 Arginase Deficiency

2.4.33 Malonic Acidemia
2.4.34 Carnitine Palmitoyltransferase Deficiency 1a
2.4.35 Severe Combined Immunodeficiency
2.4.36 Spinal Muscular Atrophy due to homozygous deletion of exon 7 in Survival Motor Neuron 1 gene
2.4.37 GLYCOGEN STORAGE DISEASE TYPE II (POMPE DISEASE)

2.4.38 MUCOPOLYSACCHARIDOSIS TYPE 1 (MPS1)

2.4.39 X-LINKED ADRENOLEUKODYSTROPHY (X-ALD)