COLORADO
Department of Public Health & Environment

To: Members of the State Board of Health

From: Dr. Emily Travanty, PhD, Scientific and Deputy Division Director, Colorado State Public Health Laboratory
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Interim Director, Office of Emergency Preparedness and Response
Division of Disease Control and Public Health Response (DCPHR)

Through: Tony Cappello, PhD, Director, DCPHR ***TC***

Date: April 15, 2020

Subject: **Emergency Rulemaking Hearing**
Proposed Amendments to 5 CCR 1005-4, *Newborn Screening and Second Newborn Screening*.

Please find copies of the following documents: Statement of Basis and Purpose and Specific Statutory Authority, Regulatory Analysis, Stakeholder Engagement, and Proposed Amendments to 5 CCR 1005-4, Newborn Screening and Second Newborn Screening.

The Colorado Newborn Screening Program (CONBSP) provides initial and second newborn screening services for 38 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 38 genetic and metabolic conditions. About 64,000 newborns receive a routine second screen to retest for three conditions: Congenital Hypothyroidism (CH), Congenital Adrenal Hyperplasia (CAH), Hemoglobinopathies (Hgb). 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.

Section 25-4-1004.5(3), C.R.S. requires second specimens be submitted for Hemoglobinopathies (Hgb). This is communicated in the rule at Section 3.3.3. Section 25-4-1004.5(3)(b), C.R.S., authorizes the Board to promulgate rules regarding exceptions to the necessity for a second specimen test. The Department requests Hgb be added to the list of conditions with exceptions at Section 3.2.2.2. Under the proposed rule change, the second newborn screening for Hgb would only occur on a subset of specimens meeting certain criteria rather than routinely on all specimens.

Based on a need to free up resources to focus on COVID-19 testing, the availability of more accurate and efficient Hgb testing, and a review of 2017-2019 data collected to determine whether clinical outcomes justify the maintenance of current practices, the State Laboratory has determined that it can safely exclude Hgb from routine second screening requirements without compromising the ability to accurately identify newborns with Hgb. In 2019, using the new Hgb testing instruments and processes, only one newborn out of 64,016 was identified to have Hgb on a second screen; a review of the newborn's history and additional testing revealed samples were mislabeled at a submitter's facility. Testing was repeated on the newborn's samples submitted for the first and second screen. Future testing under the proposed rule changes would provide the same outcome since all abnormal results will be retested.

This emergency rulemaking is imperatively necessary for the preservation of public health, safety, and welfare. Due to the unprecedented demands on the State Laboratory due to COVID-19 testing for the foreseeable future, the State Laboratory can no longer afford to perform unnecessary testing that does not provide benefit to newborns or families. Removing this second screening will allow the State Laboratory to allocate more resources to the COVID-19 response without compromising patient care. Thus, the Department is requesting an emergency rulemaking so that the proposed reduction in second screening may be effective upon adoption.

Changes to rule language appear in ALL CAPS, highlighted language, and strikethroughs.

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

Basis and Purpose.

The Department is proposing emergency rules to address lab resource reallocation in order to optimize Lab response to the COVID19 pandemic.

The *Newborn Screening and Second Newborn Screening* rule (5 CCR 1005-4) establishes:

a) Definitions of key terms,
b) Procedures for the collection and submission of blood spot specimens for testing,
c) Procedures for laboratory testing, reporting, and follow-up services for newborn screening and second newborn screening,
d) Requirements for quality control and education, and
e) 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.

Section 25-4-1004.5(3), C.R.S. requires second specimens be submitted for Hemoglobinopathies (Hgb). This is communicated in the rule at Section 3.3.3. Section 25-4-1004.5(3)(b), C.R.S., authorizes the Board to promulgate rules regarding exceptions to the necessity for a second specimen test. The Department requests Hemoglobinopathies (Hgb) be added to the list of conditions with exceptions at Section 3.2.2.2 of this rule.

Currently Hemoglobinopathies are tested on every sample for both the initial and second screen. Hemoglobinopathies is the medical term for a group of blood disorders and diseases that affect red blood cells. These disorders include both sickle cell disease (SCD) and thalassemia. Under the proposed rule change, the second newborn screening for Hgb would only occur on a subset of specimens rather than routinely on all specimens. Second newborn screening specimen means a second specimen collected from a newborn between 8 and 14 days after birth for the purpose of conducting a second screening. Whether a second screen specimen is screened for Hgb would depend on the initial Hgb result. An abnormal screen result for an initial screen would trigger screening of the second screen specimen, including AF (Adult Hgb greater than Fetal Hgb) results. AF results on an initial newborn screen indicate that the child was transfused and the current CONBSP workflow retests all assays again on the second screen sample. This is the approach currently used for second screening of four other conditions: 1) Biotinidase Deficiency (BIO), 2) Classical Galactosemia (GALT), 3) Cystic Fibrosis (CF), and 4) Phenylketonuria (PKU). Historically, these conditions were tested on all second screen samples and a similar workflow change was successfully implemented.

The Colorado Newborn Screening Program (CONBSP) regularly conducts reviews of data to determine whether clinical outcomes justify the maintenance of current practices. Such regular reviews, often using data collected over several years, are important in light of the program's

collective efforts to improve clinical outcomes and the clinical value of the screening results, perform timely testing, incorporate new technology, and identify cost savings.

In 2017, the CONBSP acquired a Bio-Rad Variant High Performance Liquid Chromatography (HPLC) system for second screen testing of Hgb. Prior to this, Hgb testing was performed by Isoelectric Focusing (IEF) gels only, which is time consuming, subjective, and lacks traceability. HPLC was added to the Hgb algorithm as a second screen to confirm abnormal results obtained by first screen IEF testing. This improved testing process eliminated subjective reporting of abnormal results. In 2018, additional HPLC instruments were added and a Laboratory Information Management System (LIMS) build out was completed to move HPLC to first screen testing and IEF to second screen testing. This process change improved traceability and decreased staff hands on testing time. Validation and implementation of the new process was completed in early 2019.

Based on a need to free up resources to focus on COVID-19 testing, the use of more accurate and efficient Hgb testing, and a review of 2017-2019 data collected to determine whether clinical outcomes justify the maintenance of current practices, the State Laboratory has determined that it can safely exclude Hgb from routine second screening requirements without compromising the ability to accurately identify newborns with Hgb. In 2019, 64,016 second screens were performed and only one newborn was found to have abnormal results on the first screen and normal results on the second screen; a review of the newborn's history and additional testing revealed samples were mislabeled at a submitter's facility. Testing was repeated on the newborn's samples submitted for the first and second screen. Future testing under the proposed rule changes would provide the same outcome since all abnormal results will be retested. Should the proposed rule change be adopted, the State Laboratory will implement procedures such that all abnormal Hgb results will be retested.

This emergency rulemaking is imperatively necessary for the preservation of public health, safety, and welfare. Due to the unprecedented demands on the State Laboratory requiring COVID-19 testing for the foreseeable future, the State Laboratory can no longer afford to perform unnecessary testing that does not provide benefit to newborns or families. Removing this second screening will allow the State Laboratory to allocate more resources to the COVID-19 response without compromising patient care. Thus, the Department is requesting an emergency rulemaking so that the proposed reduction in second screening may be effective upon adoption.

Emergency Rulemaking Finding and Justification:

An emergency rule-making, which waives the initial Administrative Procedure Act noticing requirements, is necessary to comply with state law. Emergency rulemaking is authorized pursuant to Section 24-4-103(6), C.R.S. due to the emergent nature of the COVID 19 pandemic.

1. The World Health Organization (WHO) declared COVID-19 a global health emergency on January 30, 2020: https://www.who.int/news-room/detail/30-01-2020-statement-on-the-second-meeting-of-the-international-health-regulations-(2005)-emergency-committee-regarding-the-outbreak-of-novel-coronavirus-(2019-ncov)

2. The World Health Organization declared COVID-19 a pandemic on March 11, 2020: https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020
3. Governor Polis issued a written State of Emergency for Colorado on March 11, 2020: https://drive.google.com/file/d/1szJfU9WF36-lCVgRhXMAnJdlQyTSG83e/view
4. President Trump declared the COVID-19 pandemic an emergency declaration pursuant to section 501 (b) of the Robert T. Stafford Disaster Relief and Emergency Assistance Act on March 13, 2020: https://www.whitehouse.gov/presidential-actions/proclamation-declaring-national-emergency-concerning-novel-coronavirus-disease-covid-19-outbreak/

This emergency rule shall become effective upon adoption on April 15, 2020. It will be effective for no more than 120 days after its adoption unless made permanent through a rulemaking that satisfies the Administrative Procedure Act noticing requirements.

Specific Statutory Authority

These rules are promulgated pursuant to the following statutes: Sections 25-4-1004(1)(c)(I-IV) and 25-4-1004.5(3)(b)(V), C.R.S with consideration of 25-4-1003(2)(a).

Is this rulemaking due to a change in state statute?

_____ Yes, the bill number is _____. Rules are ___ authorized ___ required.
___X___ 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 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.

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

__X_ No

___ Yes.

Has an elected official or other representatives of local governments disagreed with this categorization of the mandate?

___Yes

_X_ No. If “yes,” please explain why there is disagreement in the categorization.

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 proposed rule**
The Colorado Newborn Screening Program (CONBSP) Staff	16	C
Colorado's Newborns	~63,000	B
Parents/Families of Colorado's Newborns	~63,000	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	S/B
Patient Advocacy Groups, e.g. March of Dimes	1	S
Adult Patients with Rare Diseases	~500,000	S/B
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	1	S

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.

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

C: CONBSP expects to save an average of $125,000/year on the High Performance Liquid Chromatography (HPLC) kits for second screen samples and 780 staff hours to perform second screen Hgb testing. These resources can be put toward COVID-19 testing or could help offset costs associated with adding new conditions (HB18-1006 mandates that we review these new conditions).

S: There may be some minimal cost savings if additional specimens are not needed for Hgb second specimen testing.

B: No additional cost. There may be some minimal cost savings if additional specimens are not needed for Hgb second specimen testing. The investment in new technologies by the program resulted in fewer false positives and has reduced unnecessary medical appointments. Benefits of cost containment, improved testing methods and instruments under the current process would eventually lead to fee increases, due to increased reagent costs for the new method. Removal of unnecessary testing would offset cost of regular increases in testing reagents and staffing.

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, B: Fewer unsatisfactory specimens (specimens without enough blood to test, for example) would lower the impact of sample recollections for newborns, parents, and medical providers. Each sample collection requires an in-person visit to a medical facility.

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: N/A

Anticipated CDPHE Revenues: N/A

B. Anticipated personal services, operating costs or other expenditures by another state agency: N/A

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.

___ Comply with a statutory mandate to promulgate rules.

_X_ Comply with federal or state statutory mandates, federal or state regulations, and department funding obligations.

___ Maintain alignment with other states or national standards.

___ Implement a Regulatory Efficiency Review (rule review) result

_X_ Improve public and environmental health practice.

___ Implement stakeholder feedback.

_X_ 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)

_X_ Implement quality improvement or a quality improvement project (Goal 1, 2, 3, 5)

___ Employee Engagement (Goal 1, 2, 3)

___ Decisions incorporate health equity and environmental justice (Goal 1, 3, 4)

_X_ Detect, prepare and respond to emerging issues (Goal 1, 2, 3, 4, 5)

_X__ Advance CDPHE Division-level strategic priorities. (Goal 2,5)

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.

   Rulemaking is proposed when it is the least costly method or the only statutorily allowable method for achieving the purpose of the statute. The benefits, risks and costs of these proposed revisions were compared to the costs and benefits of other options. A rule change is required for CONBSP to alter the tests performed on either first or second newborn screens; thus rulemaking is the only option.

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

   The Department considered leaving the HgB process as is and or waiting to request this change during a standard rulemaking scheduled for early 2021. This was rejected due to the need to free up resources to focus on COVID testing as much as possible and minimize unnecessary testing. As part of the CONBSP's effort to continuously review its practices and the available technology for process improvement, new Hgb testing instruments and processes were implemented beginning in mid-2017. These improvements have increased the reliability of Hgb testing and diminishes the value and need for the second screen testing. The cost-benefit analysis highlights the unnecessary expense associated with the current method. Moreover, the current process wastes DBS material unnecessarily, thereby increasing the risk that screening will not be completed on a specimen. The cost of continuing to perform HgB on every second screen would be $125,000/year with the current method. Emergency rulemaking is the only current path that allows us to quickly make these needed changes at this extraordinary time.

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.

   CONBSP regularly conducts reviews of data collected over years of screening to determine whether clinical outcomes justify the maintenance of current practices. Such regular reviews are important in light of the program's collective efforts to improve clinical outcomes, to improve the clinical value of our screening results, to perform testing timely, to incorporate new technology, and to identify cost savings.

   The CONBSP is one of twelve (12) states that performs routine second screening. Second screening provides a number of benefits that include identification of missed abnormal results from the first screen, routine collection process for borderline results, and a routine method to obtain at least one screen in case of unsatisfactory first screens. Improved testing methods and patient sample tracking have lessened the need for second screen testing for some disorders. Conversely, second screen testing for Congenital Hypothyroidism and Congenital Adrenal Hyperplasia continues to identify cases that tested normal on the first screen.

In 2017, the CONBSP updated the testing method for Hemoglobinopathies and resolved prior testing method shortcomings. The implementation of HPLC testing increased reliability and traceability, while lowering the false positive rate due to technologist subjective interpretation of results. Review of the results since the implementation of HPLC demonstrate no missed abnormal cases due to testing. In 2019, 64,016 second screens were performed and only one newborn was found to have abnormal results on the first screen and normal results on the second screen. A review of the newborn's history and additional testing revealed samples were mislabeled at a submitter's facility. All testing was repeated on both newborn's samples. Future testing under the proposed rule changes would provide the same outcome since all abnormal results will be retested.

2019 Data	Normal Results	Abnormal Results Hgb	Total Samples Tested
1st Screen	69,309	776	70,085
2nd Screen	63,332	684	64,016

Note: Difference in total samples is due to failure to submit the second screen. All but two (2) of the 64,016 second screen results matched their corresponding first screen results.

Subjective Abnormal Hgb Result	Abnormal Total 2015	Abnormal Total 2016	Abnormal Total 2017	Abnormal Total 2018	Abnormal Total 2019
F + A + Bart's	168	287	289	3	0
F + A + U	168	168	198	128	90
F + U	7	0	1	1	0
F+U+A	70	84	56	0	0
Totals	413	539	544	132	90

Note: F= Fetal HgB, A = Adult Hgb, Bart's= Abnormal Hgb Variant, and U= Unknown Abnormal Hgb Variant. Order of pattern is based on the estimated quantity of each Hgb variant.

The program spends an average of $10,417/month or $125,000/year on the HPLC kits for second screen samples. Additional costs are attributable to consumables and laboratory staff FTE. Staff time to set-up, test, and review each sample plate of Hgb is approximately 50 minutes per plate. This requires approximately 2.5 hours per day and 6

days per week of NBS staff time. In 2019, the CONBSP dedicated at least 780 hours to population based testing for second screen Hgb testing.

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)**
Colorado Sickle Cell Treatment and Research Center	Dr. Kathryn Hassell and Donna Holstein, RN, BSN
Colorado Newborn Screening Stakeholder Group	226 active members

The Department distributed information about the proposed changes to stakeholders who are regularly engaged in Newborn Screening discussions hosted by the State Laboratory on March 26, 2020. This stakeholder list includes Colorado Health Care Providers, Advocacy Groups, Local Public Health Agencies, the Colorado Department of Education, and Clinical or Laboratory partners. Stakeholder feedback was also collected through a virtual meeting held on March 31.

Based on the email sent to stakeholders on March 26, 2020, the Department received four supportive comments and two comments asking for clarification. In addition, the Department held a virtual meeting on March 31, 2020 to discuss this proposed change with stakeholders and to solicit feedback.

Information about the 2020 emergency rulemaking and about how to submit feedback to the Department has been publicized on the State Laboratory website. The Department will continue to collect feedback for the permanent rulemaking hearing in August 2020.

Stakeholder Group Notification

_X__ Not applicable. This is an Emergency Rulemaking. If adopted, notification will occur if the Board of Health for the permanent rulemaking hearing.
____ Yes. This is selected for the rulemaking to document that timely division notification occurred.

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.

No major factual or policy issues were encountered.

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

By evaluating the effectiveness of the current approach to second screens for Hgb, the Department is meeting its mandate to provide newborn screening in the most efficient and cost-effective manner possible. By reducing the CONBSP's screening expenses for Hgb without significantly increasing the risk of a false negative Hgb result, the Department is freeing resources of the CONBSP to strengthen other aspects of the program, which should benefit all newborns screened under the program.

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

	Improves behavioral health and mental health; or, reduces substance abuse or suicide risk.		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:_____

DEPARTMENT OF PUBLIC HEALTH AND ENVIRONMENT

Laboratory Services Division

NEWBORN SCREENING AND SECOND NEWBORN SCREENING

5 CCR 1005-4

Emergency rules adopted by the Board of Health _____, 2020. Effective _____.

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SECTION 3: SECOND NEWBORN SCREENING REQUIREMENTS FOR NAMED SUBMITTERS

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3.2 Notification, Specimen Collection, Handling and Submission

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3.2.2 Section 25-4-1004.5(3)(b)(V), C.R.S. allows exceptions to testing of second newborn screening specimens. Second newborn screening specimen testing is not required for the conditions identified at 3.3.1, 3.3.3, 3.3.4, 3.3.5 and 3.3.6 unless: an unsatisfactory specimen was submitted for an initial newborn screening specimen; a screen positive result was obtained on an initial newborn screening specimen from the same newborn; there is no record of a satisfactory initial newborn screening specimen submission, or; for 3.3.1 only, the initial newborn screening specimen from the same newborn was collected before 24 hours of life.

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3.3 List of Conditions for Second Newborn Screening

The Laboratory shall conduct screening tests for the following conditions:

3.2.1 Phenylketonuria

3.2.2 Congenital Hypothyroidism

~~3.3.3 Hemoglobinopathies~~

3.3.3~~4~~ Galactosemia

3.3.4~~5~~ Cystic Fibrosis

3.3.5~~6~~ Biotinidase Deficiency

3.3.6~~7~~ Congenital Adrenal Hyperplasia

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