SCR 16 and HCR 34 of the 2019 Regular Session of the Louisiana Legislature

Costs and benefits of adding Mucopolysaccharidosis Type 1, Pompe Disease, and Spinal Muscular Atrophy to the Louisiana Newborn Screening Panel

Summary of Findings

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LOUISIANA DEPARTMENT OF HEALTH

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Executive Summary

Each year in Louisiana, approximately 63,000 infants are tested for genetic and metabolic conditions. Approximately 1,500 babies require further testing and, of these, about 170 are diagnosed with a disorder. The purpose of screening newborns for inherited and congenital disorders is to detect any conditions that can be harmful or fatal as soon as possible and to provide treatment as expeditiously as possible. During the 2019 Regular Session of the Louisiana legislature, the Louisiana Department of Health (LDH) was charged with studying the potential addition of three conditions to the state's Newborn Screening Panel: Mucopolysaccharidosis Type I (MPS I), Glycogen Storage Disorder Type II (Pompe), and Spinal Muscular Atrophy (SMA). This report summarizes the state's process for assessing the costs, benefits and readiness to incorporate these tests into the state's newborn screening panel. Please note that this study focuses on the costs of testing and follow-up to the point of diagnosis and linkage to treatment. The costs associated with treatment will be projected in conjunction with the Medicaid program as part of the testing implementation process.

Background

House Concurrent Resolution (HCR) 34 of the 2019 Regular Session urges and requests the Louisiana Department of Health (LDH) to study the costs and benefits associated with the potential addition of Mucopolysaccharidosis Type I (MPS I) and Glycogen Storage Disorder Type II (Pompe) disease to the state's newborn screening panel. Additional steps are to report findings of the study to the legislative committees on health and welfare, and to add these conditions to the newborn screening panel expeditiously when funding for this purpose is available. Additionally, Senate Concurrent Resolution (SCR) 16 of the 2019 Regular Session urges and requests LDH to take such actions as are necessary to add Spinal Muscular Atrophy (SMA) to the newborn screening panel.

The Louisiana Department of Health (LDH) Office of Public Health (OPH) Genetic Diseases Program ("Genetics") is housed within the Bureau of Family Health. The Genetics Program is responsible for Louisiana's newborn heel stick screening and follow-up program in accordance with the pertinent legislation and rules. Services provided by this program include: a) provision of testing and follow-up for genetic disorders mandated on the Louisiana Newborn Screening Panel, b) Genetic and Sickle Cell clinics in regional parish health units and c) special formula for patients with metabolic disorders.

As a part of the newborn heel stick screening program, the Genetics Program oversees **the Louisiana Genetic Diseases Program Advisory Committee (GDPAC)**. Established in 1967 under LAC 48.v.6901, 6303, one charge of this group is to consult with OPH on the promulgation of rules and regulations necessary to conduct the genetic diseases program and set the policy and scope of genetics services in Louisiana, including adding new conditions to the Louisiana Newborn Screening Panel. Members of GDPAC are appointed by the OPH Assistant Secretary and include representation from: a) all medical schools within the state; b) the disciplines of genetics, pediatrics, obstetrics, hematology, endocrinology and pulmonology; c) representation from OPH including, but not be limited to nutrition, laboratory, social work, children's special health services, maternal and child health and the physicians connected with these programs; and d) two consumer representatives. The committee is required to be assembled annually, however the committee voted to begin convening quarterly during the Fall 2019 meeting. The new quarterly meeting schedule was established to ensure timely review and deliberation of tests for potential inclusion in the state's Newborn Screening Panel.

The Louisiana Genetic Diseases Program Advisory Committee's deliberations start with a review of national recommendations. The United States Department of Health and Human Services (HHS) Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC) is the national body charged with making recommendations that guide states in the development of their newborn screening programs. This national committee convenes regularly to discuss conditions recommended by parent advocates, organizations, and experts for inclusion in the Recommended Uniform Screening Panel (RUSP), the list of disorders that HHS endorses for potential inclusion in state newborn screening programs. Once a group nominates a condition, the following steps take place through the ACHDNC:

- *Nomination and Prioritization Workgroup:* The Committee's Nomination and Prioritization (N&P) Workgroup reviews the completed Nomination Package and compiles a summary for Committee consideration. The Committee decides if sufficient evidence is available, and votes to assign, or not assign, the nominated condition to the external Condition Review Workgroup. Nominators whose conditions are not assigned to the Condition Review Workgroup are provided with feedback.
- *Condition Review Workgroup:* The external Condition Review Workgroup completes a systematic evidence-based review, provides updates, and presents a final report to the Committee on assigned conditions.
- *Committee Deliberations and Vote:* The Committee discusses and deliberates on the evidence presented by the Condition Review Workgroup. The Committee uses a decision matrix (to guide their final decisions.) Then the Committee votes to recommend or not recommend adding the nominated condition to the RUSP for consideration by the Secretary of Health and Human Services. Nominators whose conditions are not recommended for addition to the RUSP are provided with feedback.
- *Final Decision:* The Secretary of Health and Human Services makes the final decision on whether to add, or not add, a recommended condition to the RUSP. [1]

Once recommended by the ACHDNC, it is up to each individual state to determine if they have the capacity and resources to add new conditions. In Louisiana, proposed new conditions are brought before the GDPAC. There are preliminary discussions regarding whether there is a FDA approved testing method and a safe and effective treatment protocol. Additional research is performed to evaluate the costs associated with OPH Laboratory and Genetics Program staffing, required instrumentation, pilot guidelines and other readiness factors. This information is used to work with Louisiana Medicaid to determine a Current Procedural Terminology (CPT) Code for test billing and payment. Once these factors are determined, the advisory committee votes on whether or not to add the condition and forwards the recommendation to the OPH Assistant Secretary. With the Assistant Secretary's approval, the OPH Laboratory conducts a pilot project to evaluate the efficacy of the methodology used for testing. Concurrently, the OPH Genetics Diseases Program works with the OPH Laboratory and agency leadership to initiate rulemaking. After the Notice of Intent is announced in the Louisiana Register, the updated rule is promulgated. Physicians, the public and other stakeholders are notified of this change through website updates and notification through partners such as the Louisiana Chapter of the American Academy of Pediatrics and the March of Dimes.

Historically, LDH has added conditions to the state Newborn Screening Panel as state funds become available to support the cost of testing and treatment. This includes funding for the laboratory testing and required instrumentation, as well as adequate follow-up staffing and resources for proper training and education of public health professionals and medical providers. From the time the Louisiana

[1] https://www.hrsa.gov/advisory-committees/heritable-disorders/rusp/nominate.html

Genetics Disease Program Advisory Committee recommends that a new condition be added to the state's panel, it can take up to two years before testing all newborns can begin.

Potential Inclusion of MPS I, Pompe, and SMA in Louisiana's Newborn Screening Panel

In October 2019, the OPH Genetics Diseases Program convened the advisory committee to review the current evidence and feasibility of adopting MPS I, Pompe, and SMA as conditions in the state's Newborn Screening Panel. Below is an overview of each condition, when it was added to the RUSP, incidence, anticipated number of cases in Louisiana each year, cost to test each child, treatment options, and the GDPAC recommendation for each condition. The costs noted in the information below are the costs associated with testing all infants born in Louisiana. Additional information on treatment costs compared to the costs incurred by not treating the conditions will need to be provided by Medicaid.

Mucopolysaccharidosis Type I (MPS I) – added to RUSP February 2016

MPS I is a rare genetic disorder caused by a change in a single human gene. Studies of patients with symptoms suggest that about 1 out of every 100,000 people has MPS I. People with MPS I do not have enough of the Iduronidase enzyme that helps to break down certain waste products in cells. Babies with MPS I appear normal. There are 2 types of MPS I: the severe type and the attenuated type. Most children with MPS I have the severe type. In this type, MPS I can cause problems with the heart, airways, eyes and ears, muscles, bones, joints, and brain. These problems can worsen quickly and cause early death.[2] Presently, MPS I has been added to the newborn screening panel in 19 states.

Incidence: Based on screening data and the risk of being born with MPS I, contributing experts to the ACHDNC'S External Evidence Review Report on MPS1 expect that screening all newborns in the United States for MPS I would detect approximately 44 babies with the condition each year (about 1.1 out of every 100,000 children born). It would prevent up to two deaths before age 5 years due to the disease each year.[3] The anticipated prevalence in Louisiana is about one case every two years.

Cost of Testing and Follow-Up: Based on a population of about 63,000 infants born in the state each year, the cost of testing would be $14 per test or $882,000 per year. This cost includes equipment, administrative costs and additional staffing.

Treatment: There is no cure for MPS I. Early diagnosis allows early monitoring and treatment for babies with MPS I. Treatments that can stop MPS I problems from getting worse include enzyme replacement therapy and human stem cell transplantation, also called a "bone marrow transplant." The treatment a patient receives depends on many factors, including the type of MPS I.

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[2] https://www.ninds.nih.gov/disorders/patient-caregiver-education/fact-sheets/mucopolysaccharidoses-fact-sheet

[3] U.S. Department of Health and Human Services, Advisory Committee on Heritable Disorders in Newborns and Children (2019). Newborn Screening for Mucopolysacchardosis Typle 1 {MPS1): A systematic review of evidence report of findings: United States, 2015. (Report No. 1.1) Retrieved from: https://www.hrsa.gov/sites/default/files/hrsa/advisory-committees/heritable-disorders/rusp/previous-nominations/mps1-external-evidence-review-report.pdf

Other considerations:

- GDPAC Recommendations: Although the Committee agrees that this condition should be added to Louisiana's newborn screening panel, the consensus is that more information is needed from subject matter experts to determine OPH's readiness to implement testing.
- OPH Laboratory: Two separate lab methods can be used to test for MPS1, Tandem Mass Spectrometry (TMS) and Digital Microfluidics Enzymatic Activity. Both methods would be used to also detect Pompe. However, if the TMS method is used, other conditions that are not on the Recommended Uniform Screening Panel will be detected including Gaucher Disease, Niemann-Pick A/B Disease, Krabbe Disease, and Fabry. There is a medical duty to report the incidental finding of a test. While the testing method would generate these additional results in the course of testing, there are added costs to formally reporting them that are not included in the $14 calculated. These costs include: added staffing review, proficiency, competency and quality control costs for each added condition tested. Decisions regarding the reporting and follow up on these conditions not on the panel would need to be further evaluated for follow up resources and cost. However, no additional reimbursements would be made by Medicaid since the same testing method is used.

Glycogen Storage Disorders Type II (Pompe) – added to the RUSP March 2015

Pompe Disease is a rare disease caused by a change in a single gene. Studies of patients with symptoms suggest that between 1 and 2.5 out of every 100,000 people have Pompe Disease. People with Pompe Disease do not have enough of a certain enzyme that helps the body break down stored sugar. Babies with the disease appear normal. There are two types of Pompe Disease: infantile- and late-onset. The first type can cause muscle problems that begin in early infancy. Most children with Pompe Disease have the late-onset type. Problems from the disease can worsen quickly and cause death within the first year. Today, Pompe Disease has been adopted to the newborn screening panel in 21 states.

Incidence: Based on what is known about screening and the risk of being born with Pompe Disease, experts expect that screening all newborns in the United States for Pompe Disease would detect approximately 144 babies with the disease each year (about 3.6 out of every 100,000 children born). It would prevent up to 28 people with the disease from needing a breathing machine and up to 19 deaths due to the disease each year.[4] The anticipated prevalence in Louisiana is about 2-3 cases per year.

Cost of Testing and Follow-Up: This test can be performed using the same methodology as MPSI and would not incur a cost for test the test itself. However, additional costs will be incurred for follow-up and other administrative costs totaling $182,610 or $2.90 per infant.

Treatment: There is no cure for Pompe Disease, but Enzyme Replacement Therapy can reduce progression of the disease.

Other considerations:

- GDPAC Recommendations: Although the Committee agrees that this condition should be added to Louisiana's newborn screening panel, the consensus is that more information is needed from subject matter experts to determine OPH's readiness to implement testing.

[4] U.S. Department of Health and Human Services, Advisory Committee on Heritable Disorders in Newborns and Children (2019). *Evidence Report: Newborn screening for Pompe disease:* United States, 2013. (Retrieved from: https://www.hrsa.gov/sites/default/files/hrsa/advisory-committees/heritable-disorders/rusp/previous-nominations/pompe-external-evidence-review-report-2013.pdf

- OPH Laboratory: As with MPSI, two separate lab methods can be used to test for MPS1, Tandem Mass Spectrometry (TMS) and Digital Microfluidics Enzymatic Activity. See MPSI Other Considerations.

Spinal Muscular Atrophy (SMA) – added to the RUSP July 2018

SMA is a rare genetic disorder. Studies of patients with symptoms suggest that about 1 out of every 11,000 people has SMA. People with SMA have a change in the SMN1 gene that prevents it from making adequate amounts of the protein that nerve cells need to survive. Some individuals can compensate for this change by making enough of the protein with a related gene called SMN2. There are different types of SMA. Most children have SMA Type 1, which causes weakness and, without treatment, can worsen quickly and lead to death. Currently, 11 states have added SMA to their newborn screening panel.

Incidence: Based on what is known about screening and the risk of being born with SMA, experts expect that screening all newborns in the United States for SMA would detect approximately 364 babies with the disorder each year. Each year, screening could prevent about 50 infants from needing a ventilator (breathing machine) and about 30 deaths due to SMA Type 1.[5] The anticipated prevalence in Louisiana is about 5-6 cases per year.

Cost of Testing and Follow-Up: Based on a population of about 63,000 infants born in the state each year, the cost of testing would be $5.54 per test or $349,020 per year. This cost includes equipment, administrative costs, additional staffing and consulting costs.

Treatment: There is no cure for SMA yet, but early diagnosis allows early monitoring and treatment. Nusinersen is a recently approved medicine that reduces the progression of SMA symptoms. When used early in the disease process, it can sometimes prevent damage to nerve cells. Zolgensma is another approved therapy for patients with all forms and types of SMA who are under two years of age at the time of dosing. It is an SMN-enhancing therapy, via intravenous infusion, that replaces the missing or mutated SMN1 gene. Other treatments can also help with certain symptoms, at least for a while. The timing and type of treatment for SMA depends on the disease type.

Other considerations:

- GDPAC recommendations: Although the Committee agrees that this condition should be added to Louisiana's newborn screening panel, the consensus is that more information is needed from a neurology subject matter expert to determine OPH's readiness to implement testing. The Genetic Diseases Program will be recruiting neurologists to speak to the committee and will schedule a follow-up meeting.

[5] U.S. Department of Health and Human Services, Advisory Committee on Heritable Disorders in Newborns and Children (2019). *Evidence-based Review of Newborn Screening for Spinal Muscular Atrophy (SMA): Final Report:* United States, 2018. (Version 5.2) (Retrieved from: https://www.hrsa.gov/sites/default/files/hrsa/advisory-committees/heritable-disorders/reports-recommendations/sma-final-report.pdf

Proposed Timeline for Adding SMA

January-February 2020	The GDPAC discusses any concerns that potentially need addressing to ensure that they are resolved and votes on nominated conditions. Negotiations between Medicaid and OPH being to address the cost of testing and treatment for new conditions. Medicaid proposes the new cost in the next fiscal year.
March-May 2020 *(please note this is a best case estimate)*	The OPH Laboratory begins verification and establishment of testing for SMA. At this time, X-linked adrenoleukodystrophy (X-ALD) will also be included as it uses the same laboratory protocol as SMA. This is a method used to evaluate the accuracy and reliability of the testing and then must establish procedures and protocols. • This process can take several months for each unique methodology, and it is estimated that the laboratory may require between six months to one year. • The laboratory timeframe will be dependent on which tests are adopted and the required personnel and equipment. The Genetics Program begins the rulemaking process to add the new conditions to the Newborn Screening administrative code.
June-September 2020	The rulemaking process continues with the following processes: • Presentation to the weekly LDH Leadership Huddle for approval • Fiscal and Economic Impact Statement • Family Impact Statement • Poverty Impact Statement • Small Business Impact Statement • Provider Impact • Public Hearing/Comments • Notice of Intent/Promulgation in the Louisiana Register
October-December 2020	Providers, parents and other stakeholders are notified and testing for added and validated conditions begins.

The timeline for adding Pompe and MSP I to the screening panel will be dependent on readiness to implement and the ability for the GDPAC to address any testing-related concerns.

Conclusion and Next Steps

The cost of testing and the potential impact of adding the remaining conditions on the RUSP to the Louisiana Newborn Screening Panel have been outlined in the response. The Genetic Diseases Program Advisory Committee will continue to meet quarterly, or as needed, to ensure all resources are in place to begin testing, have a robust follow-up system and a system to refer patients for treatment that will be covered by Medicaid.

A summary of the response to the legislation is included below:

- **HCR 34 of the 2019 Regular Session:** This response has provided the costs of potentially adding MPSI and Pompe disease to the Louisiana newborn screening panel and the number of infants per year that might be affected. Next steps for these conditions include:
    - Further work with the GDPAC is needed to determine LDH's readiness to begin testing and to address concerns related to testing results for other conditions.
    - A mechanism for funding this activity needs to be determined.

- **SCR 16 of the 2019 Regular Session:** This response has provided the cost to add SMA to the newborn screening panel. Next steps for this condition includes:
    - Additional information on availability of treatment is needed from a neurology subject matter expert before a vote from the GDPAC can take place.
    - In addition, a funding mechanism needs to be provided. OPH is working with Medicaid to ensure reimbursement for testing and coverage for treatment.

- The GDPAC will continue to convene quarterly, or as needed, to make expert recommendations for implementing recommended newborn screenings in Louisiana. In addition, the committee plans to develop an annual report for the legislature on the activities of the Genetics Program, including annual review of the RUSP, implementation plans for remaining conditions, and any progress made on implementation.

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