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SECRETARY

State of Louisiana

Louisiana Department of Health
Office of Public Health

July 5, 2016

The Honorable Fred H. Mills, Jr., Chairman
Senate Health and Welfare Committee
P.O. Box 94183, Capitol Station
Baton Rouge, LA 70804

The Honorable Frank A. Hoffmann, Chairman
House Health and Welfare Committee
P.O. Box 94062, Capitol Station
Baton Rouge, LA 70804

Subject: Louisiana Department of Health (LDH) response to SCR 17 of the 2015 Legislative Session

Dear Honorable Chairs:

During the 2015 Legislative Session, the Louisiana Department of Health (LDH), formerly the Department of Health and Hospitals (DHH), was directed to evaluate and report on the health benefits and costs of adding Krabbe disease to the list of mandatory screenings performed on newborns when it is recommended by the United States Department of Health and Human Services Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC), the American College of Medical Genetics (ACMG) and the Louisiana Newborn Screening Advisory Committee (LANSAC). At this time, Krabbe disease screening is not recommended. However, this letter is being submitted to educate legislators on Krabbe disease and the limited research on testing and treating this condition.

Krabbe disease, formally known as globoid cell leukodystrophy, is an inherited disorder that destroys the protective coating (myelin) of nerve cells in the brain and throughout the nervous system. It is an inborn error of lipid (fat) metabolism associated with mutations of the galactosylceramidase (GALC) gene. Symptom onset has been documented at a broad range of ages since the original description of Krabbe disease, leading to four main clinical sub-types distinguished by age of symptom onset: early infantile, late infantile, juvenile and adult. Patients with early infantile Krabbe disease (EIKD) present with

extreme irritability, spasticity, and developmental delay before six months of age, followed by progressive neurologic deterioration and death.

The incidence for Krabbe is 1 in 100,000 newborns. In Louisiana, the birth rate is approximately 63,000 births per year. The Office of Public Health (OPH) Laboratory screens about 52,000 newborns annually. The remaining 11,000 newborns born at eight hospitals across the state are tested through an out of state lab, PerkinElmer Genetics.

(Source: External Review Report of the Advisory Committee on Heritable Disorders in Newborns and Children, December 2009)

Health Benefits of Adding Krabbe Disease to the Newborn Screening Panel

In order for a new condition to be added to the panel for screening, an interested group must submit a nomination form to the ACHDNC. This form undergoes federal administrative review and then an evidenced based review by an external body to essentially determine if the proposed test has; a) clear definition, b) if a clear test result can be established and c) if there is an effective treatment for the condition. Based on information obtained by the review, the ACHDNC has decided to not recommend universal screening for Krabbe Disease.

The purpose of newborn screening is to test for conditions that have a clear treatment method. Krabbe Disease does not have a clear treatment method. In a letter from the ACHDNC external review committee dated February 17, 2010, the committee found that "substantial harm is possible (either from testing and/or identification; from treatment/other interventions, or both)". The ACHDNC has not reviewed Krabbe disease since then.

New York is the only state that has implemented testing for Krabbe disease. Out of over 1.9 million infants screened between 2006 and 2014, 620 babies were referred for further testing which included head imaging, DNA mutation analysis and frequent specialist visits. These evaluations resulted in five babies with Krabbe disease who were referred for a bone marrow transplant, the only treatment for this condition. Bone marrow transplant is most effective if done before 1 month of age. Of the five cases:

- Case 1: had a bone marrow transplant at 1 month of age and is doing well, although with gross motor delays (standing/walking issues)
- Case 2: was delayed in getting the transplant which occurred at 2 months of age, and has severe developmental delay and spasticity
- Case 3: died as complication of bone marrow transplant
- Case 4: died as complication of bone marrow transplant
- Case 5: family decided against bone marrow transplant

Presently, there is no FDA-approved test for this condition. Any testing through the Office of Public Health's laboratory would not be supported by the company through which testing supplies are purchased nor by the Centers for Disease Control and Prevention. Establishing such a laboratory developed test is beyond the current capacity of the OPH Laboratory and would require a large investment to acquire the needed equipment and staff. Human positive control materials for validating this assay would be difficult to obtain due to the rarity of this condition; it could take several years to obtain sufficient material to validate the assay.

Healthcare Costs of Adding Krabbe Disease to the Newborn Screening Panel

It is estimated that start up testing for Krabbe disease would cost the state at least $1,311,141 for year 1, which includes the cost of lab start up equipment, genetics equipment, staff, and contracts. For subsequent years, testing would cost approximately $607,941 annually. The cost per test per infant is expected to be $25 for the first year of testing and will decrease to $12 per infant for the subsequent 4 years.

- Lab Costs
  - Equipment:
    - 1 Sequencer, year 1 only ($100,000)
    - Reagents, controls, PT testing for validation, and patient samples, year 1, at $75,000 (Cost for subsequent years would be $70,000 annually)
    - 2 Tandem Mass Spectrometers, year 1 only, at $350,000 each ($700,000)
    - Rainin Liquidator, year 1 only ($20,000)
    - Plates, tips, and solvents, approximately $0.20 per infant, 0.2*52,000 ($10,400 annually)
    - Reagent from Perkin Elmer approximately $1.00 per sample, 1*52,000 ($52,000 annually)
  - Staff:
    - 2 Lab Scientists, $61,709 salary plus fringe ($169,700 annually)
  - Maintenance:
    - Sequencer annual service contract cost beginning in Year 2 ($15,000)
    - 2 Tandem Mass Spectrometers annual service contract cost beginning in Year 2 ($105,000)
    - Rainin Liquidator Maintenance cost beginning in Year 2 ($3,000)
  - Cost per year:
    - Year 1 – $1,127,100
    - Years 2 through 5 – $425,100 annually

- Genetics Program Costs
  - Equipment:
    - Computer and printer, year 1 only ($1200)
  - Staff:
    - 1 Program Monitor to contact physician and family to ensure reporting and treatment, $60,248 salary plus fringe ($82,841)
  - Professional Services:
    - Contracts with specialists (neurologist, endocrinologist, and hematology oncologist) from Tulane and LSU to hold clinics in regional health units ($100,000)
  - Cost per year
    - Year 1: $184,041
    - Years 2 through 5: $182,841
- Total Costs:
  - Year 1, $1,311,141 (approximately $25 per test)
  - Years 2 through 5, $607,941 (approximately $12 per test)

Based on the evidence presented in this letter, LDH does not have the capacity to add Krabbe disease to the newborn screening panel. Furthermore, treatment would have to occur out of state as stem cell transplant in newborns is not done in Louisiana; it is unlikely that insurance will pay for treatment, which is still experimental.

If you have further questions or concerns regarding this report or any public health matter, please contact Beth Scalco at (225) 342-8093 or Beth.Scalco@la.gov.

Sincerely,

M. Beth Scalco

Beth Scalco
Assistant Secretary
Office of Public Health

cc: David R. Poynter, Legislative Research Library