Fiscal Note for Permanent Amendment of 10A NCAC .0102 and 10A NCAC 43H .0314 and Permanent Adoption of 10A NCAC 42B .0108

Agency:	North Carolina Commission for Public Health Department of Health and Human Services State Laboratory of Public Health Newborn Screening Program
Rule Citations:	10A NCAC 42B .0102 Newborn Screening 10A NCAC 42B .0108 Fees 10A NCAC 43H .0314 Submission of Blood Specimens for Screening of Newborns
Agency Contacts:	Dee Pettit Assistant Director, Science and Technology State Laboratory of Public Health dee.pettit@dhhs.nc.gov Virginia Niehaus Rulemaking Coordinator, Commission for Public Health Director of Regulatory and Legal Affairs, Division of Public Health virginia.niehaus@dhhs.nc.gov
Rulemaking Authority:	GS 130A-125
Impact Summary:	State Government: Yes Local Government: No Private Sector: Yes Substantial Impact: Yes[1]

Introduction and Purpose

North Carolina General Statute (GS) 130A-125, as amended by SL 2018-5, Section 11E.1., directs the Commission for Public Health to adopt rules necessary to implement the Newborn Screening Program (NBSP) described in the statute. Specifically, the statute instructs the Commission to "amend the rules as necessary to ensure that each condition listed on the Recommended Uniform Screening Panel developed by the Secretary of the United States Department of Health and Human Services and the Advisory Committee on Heritable Disorders of Newborns and Children (the RUSP) is included in the Newborn Screening Program, except that the Commission is exempt from rule making with respect to adding screening tests for Pompe disease, Mucopolysaccharidosis Type I (MPS I), and X-Linked Adrenoleukodystrophy (X-ALD)."

In compliance with the statute, the proposed Rules would align the State's NBSP with the core conditions listed on the RUSP. The NBSP panel already involves screening for many of the conditions included on the RUSP, and per statute, three conditions/diseases listed on the RUSP- Pompe disease, MPS I, and X-ALD- are exempt from rulemaking.[2] Therefore, the effect of aligning

[1] "Substantial economic impact" is defined at GS 150B-21.4(b1) as "an aggregate financial impact on all persons affected of at least one million dollars ($1,000,000) in a 12-month period."

[2] Although these three diseases/conditions are exempt from rulemaking pursuant to GS 130A-125 they were added to the NBSP screening panel under 10A NCAC 42B .0107, effective September 1, 2018.

the NBSP panel with the RUSP through rulemaking is the addition of one condition- spinal muscular atrophy (SMA)- to the NBSP's screening panel. Although there is currently no cure for SMA, the addition of SMA to the NBSP panel will allow for earlier diagnosis of SMA in babies born in North Carolina, which could reduce the devastating consequences of progressive muscle weakness and severe physical disability due to degeneration of motor neurons cells.

Newborn screening for SMA will be included in the routine newborn screening that is conducted by the NBSP at the North Carolina State Laboratory of Public Health (NCSLPH). Screening is usually conducted during the first few days of a baby's life. The process begins when a doctor or nurse collects a few drops of blood from a baby's heel and dries the drops onto a filter paper card. The hospital sends these dried blood spots to NCSLPH, where the blood spots are used for screening to detect over 30 core conditions on the RUSP.

SMA, specifically, is screened for by the detection of changes in the Survival Motor Neuron 1 (SMN1) gene that are associated with an elevated risk for SMA. SMA is group of genetic neuromuscular disorders that result in the progressive destruction of lower motor neurons found in the brain stem and spinal cord that weakens the muscles that are associated with essential functions such as breathing, swallowing, speaking, and walking. SMA has a broad phenotypic spectrum that is classified across five clinical groups based on age of onset, motor milestones attained, and age at death. Most children have SMA Type I, which is associated with weakness that can become severe and lead to death if treatment is not initiated.[3] SMA is the most common genetic cause of death in infants.[4] Newborn screening cannot distinguish between the SMA types but can identify an elevated risk for SMA due to gene mutation.

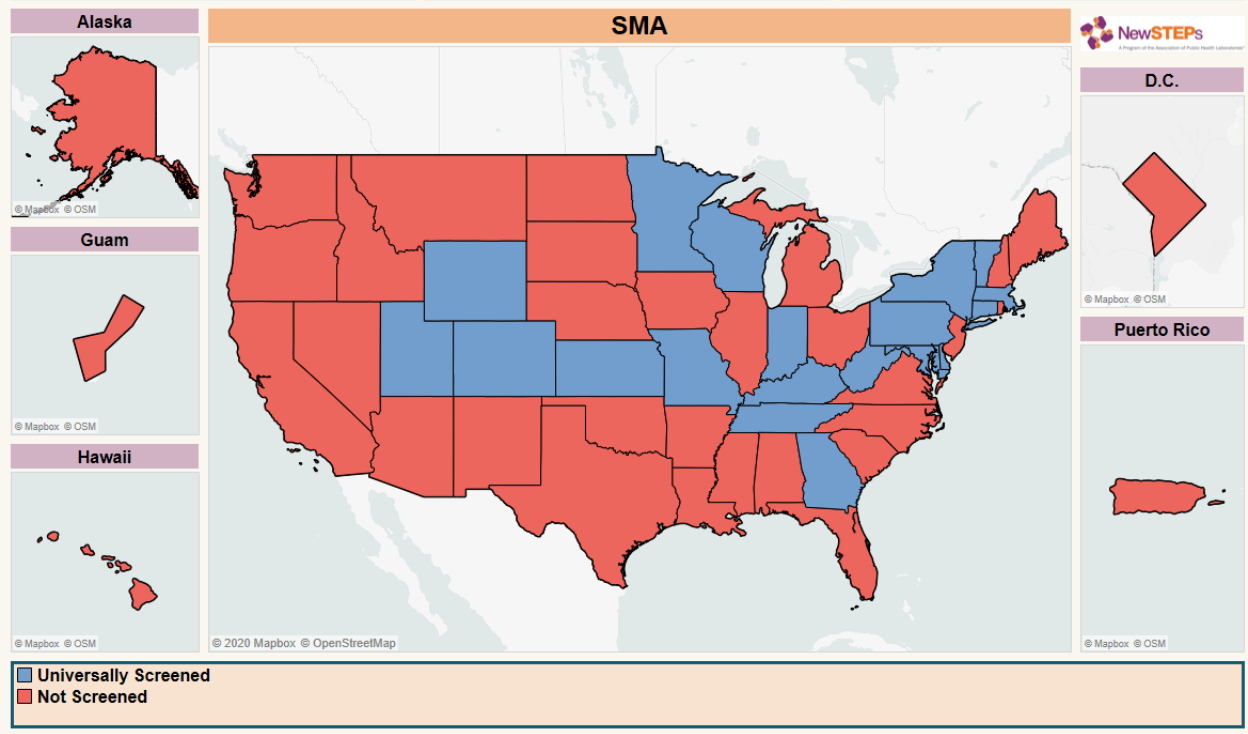
Babies who are identified through the NBSP screening process as having an elevated risk of SMA would be examined by a physician that specializes in the treatment of genetic and metabolic conditions. Further testing of the baby would be done to help predict when symptoms may begin, if the baby does not already have symptoms. The specialist would be able to prescribe treatment, such as nusinersen (tradename "Spinraza"), a drug that is injected into the fluid surrounding the spinal cord, which may improve the baby's motor function and survival.[5] In addition to pharmaceutical-based treatment, parents or guardians of children with SMA can also pursue a recently-developed, one-time gene therapy treatment that has been approved by the FDA since May 2019.[6] Early diagnosis and referral to a specialist also allows for the family to become more engaged with health counseling and enables future family planning.

Public health agencies across the United States screen approximately four million newborns for at least 30 diseases/conditions every year, but not all newborn screening programs currently screen for SMA. The United States Department of Health and Human Services (HHS) Secretary's Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC) recommends disorders to be included on the RUSP, but ultimately each state determines which disorders to include in its screening. Most states screen for the majority of core disorders included in the RUSP, although some of the more recent additions- such as SMA, which was added to the RUSP in July 2018- are still in

[3] United States National Institutes of Health, National Library of Medicine, "Spinal muscular atrophy," March 31, 2020, https://ghr.nlm.nih.gov/condition/spinal-muscular-atrophy#genes, accessed April 8, 2020.
[4] United States Food and Drug Administration, "FDA approves first drug for spinal muscular atrophy," December 23, 2016, https://www.fda.gov/news-events/press-announcements/fda-approves-first-drug-spinal-muscular-atrophy, accessed April 8, 2020.
[5] Id.
[6] Owen Dyer, "Health ministers condemn Novartis lottery for Zolgensma, the world's most expensive drug," *The BMJ*, February 12, 2020, https://www.bmj.com/content/368/bmj.m580.full, accessed April 10, 2020.

the process of being adopted and onboarded.[7] Currently, 19 states are conducting newborn screening to detect SMA (see *Figure 1*, below).

Figure 1: SMA Screening Status Map[8]



Researchers have recently used a population-based carrier screening study to determine the incidence of SMA in the United States as 1 in 11,000.[9] While stable incidences based on newborn screening in the United States are too early to determine, approximately 0.008% to 0.015% of babies screened in the last two years had abnormal results. Given that there are approximately 120,000 births per year in North Carolina, we estimate that approximately 11 babies born in North Carolina each year have SMA. This is generally consistent with the estimated birth prevalence in other countries of 8.5 to 10.7 individuals with SMA per 100,000. [10]

Newborn screening for SMA and the laboratory processes for conducting the screening are both very recent developments in the field of newborn screening. Unfortunately, this means that there is limited

[7] In July of 2018, the Secretary for the United States Department of Health and Human Services gave notice of his acceptance of the recommendation made by the Advisory Committee on Heritable Disorders in Newborns and Children to include SMA on the RUSP. A copy of that notice is available at: https://www.hrsa.gov/sites/default/files/hrsa/advisory-committees/heritable-disorders/reports-recommendations/final-sign-azar-response-sma.pdf.

[8] NewSTEPS, "Newborn Screening Status for All Disorders," 2020, https://www.newsteps.org/resources/newborn-screening-status-all-disorders, accessed April 7, 2020.

[9] Sugarman EA, Nagan N, Zhu H, et al, "Pan-ethnic carrier screening and prenatal diagnosis for spinal muscular atrophy: clinical laboratory analysis of >72,400 specimens," *European Journal of Human Genetics,* Vol. 20, August 3, 2011, https://www.nature.com/articles/ejhg2011134, accessed April 12, 2020..

[10] Jedrzejowska M, Milewski M, Zimowski J, et al, "Incidence of spinal muscular atrophy in Poland--more frequent than predicted?," *Neuroepidemiology,* Vol. 34, Issue 3, January 15, 2010, https://www.ncbi.nlm.nih.gov/pubmed/20090376, accessed April 11, 2020; Arkblad E, Tulinius M, Kroksmark AK, Henricsson M, Darin N, "A population-based study of genotypic and phenotypic variability in children with spinal muscular atrophy," *Acta paediatrica* (Oslo, Norway : 1992), Vol. 98, Issue 5, January 20, 2009, https://www.ncbi.nlm.nih.gov/pubmed/19154529, accessed April 11, 2020.

information available to assess whether the implementation of SMA newborn screening can be expected to identify cases of children with SMA who would otherwise never receive a diagnosis (and, as a result, would never receive potentially life-saving care). We have consulted on this topic with medical experts in the State who currently diagnose and manage the care of individuals with SMA, all of whom have been diagnosed prior to the implementation of newborn screening for SMA in the State. Based on the expected prevalence of SMA in North Carolina and the number of cases that have been identified, experts have advised that the 11 children with SMA who are born each year in North Carolina would be expected to receive a diagnosis at some point in their lives. Although we anticipate that all or most of these 11 children would receive a diagnosis of (and likely treatment for) SMA at some point in their lives, identification of SMA through newborn screening will allow for earlier detection and diagnosis across the board as well as substantially improved health outcomes.

Without screening, diagnosing SMA can take time because most babies with SMA do not immediately display symptoms. Newborn screening for SMA allows diagnosis in the first weeks of life and is especially advantageous when a baby has no symptoms at birth. This is the time in the child's life when treatment has its best chance for success. Some research suggests that early treatment (i.e., when treatment begins before symptoms develop) improves motor outcomes and lowers the risk of death or the eventual need for a ventilator in people with SMA. For children who do develop symptoms, management of SMA requires a comprehensive, multidisciplinary approach. Although treatment is often provided at neurology centers, the entire care team for a patient with SMA can include primary care physicians; neurology, physiatry, pulmonary, cardiology, orthopedics, and developmental specialists; nurses; physical, occupational, and speech therapists; nutritionists; and genetic counselors.[11]

Description of Proposed Rules

Alignment with the RUSP

The proposed Rules 10A NCAC 42B .0102 and 10A NCAC 43H .0314 have been amended to comply with the directive issued in GS 130A-125 to align the conditions/diseases that the NBSP screens for with the RUSP. Specifically, 42B .0102 was amended by replacing the list of individual diseases/conditions with a reference to the core conditions that are included on the RUSP. Similarly, 43H .0314 was amended by removing reference to specific conditions/diseases and adding a reference back to the information provided in 42B .0102.

Fees

10A NCAC 42B .0108 is a new rule that is proposed for permanent adoption and that addresses fees charged by NCSLPH in relation to newborn screening. In subsection (b), the Rule references the language in GS 130A-125(c) that sets the fee for newborn screening at $128.00 and specifically authorizes the Commission for Public Health to increase this fee when the increase is "necessary to offset the cost of incorporating a condition listed on the RUSP into the Newborn Screening Program." In accordance with statute, we have proposed increasing the fee by $4.00, for a total fee of $132.00, in order to cover the programmatic costs of aligning the NBSP with the RUSP.

Timeline for Implementation

[11] R.S. Finkel, et al, "Diagnosis and management of spinal muscular atrophy: Part 2: Pulmonary and acute care; medications, supplements and immunizations; other organ systems; and ethics," *Neuromuscular Disorders*, Vol 3, Issue 3, 2018; E. Mercuri, et al, "Diagnosis and management of spinal muscular atrophy: Part 1: Recommendations for diagnosis, rehabilitation, orthopedic and nutritional care," *Neuromuscular Disorders,* Vol. 28, Issue 2, 2018.

10A NCAC 42B .0102(b) has been amended to mirror existing language pertaining to the NBSP in 10A NCAC 42B .0107. This language sets out conditions to be met in onboarding a new condition added to the RUSP to the State's NBSP.

Please see the Appendix for the full text of the proposed rules.

Impact Analysis

State Government

We anticipate an economic impact to State government that will affect two agencies within the North Carolina Department of Health and Human Services: the Division of Public Health (DPH) and the Division of Health Benefits (DHB/NC Medicaid). DPH is home to NCSLPH and the Women's and Children's Health Section, Children and Youth Branch, Genetics and Newborn Screening Unit, which together operate the State's Newborn Screening Program. The economic impact to NCSLPH will involve programmatic costs associated with implementing the Rules, including hiring two additional staff members and the costs of reagents, which are chemical substances that are needed to conduct the screenings, and other consumable supplies. The economic impact to the Genetics and Newborn Screening Unit will include opportunity costs associated with staff time spent conducting follow up for the children with SMA who are identified through the screening process. DHB operates the State's Medicaid program, and the economic impact to DHB is expected to stem from a small increase in the screening fee, for which hospitals will request Medicaid reimbursement.

Economic Impact to the Division of Public Health

NCSLPH must have the necessary staff, equipment, and supplies in place to begin screening for a new disorder. We anticipate needing to hire two additional staff members in laboratory medical specialist positions in order to begin including SMA in our screening panel. These individuals must meet Clinical Laboratory Improvement Amendments (CLIA) regulations for a General Supervisor with a subspecialty in Molecular Detection and Characterization, have a bachelor's degree in medical technology, microbiology, chemistry or a closely related biological science field, and have over three years of experience in a medical laboratory or related area of work. The midpoint salary for a staff person in this position is $63,552, or an hourly rate of $41.21 when benefits are also taken into consideration.[12] This translates to $87,803.44 per staff member per year, or a total annual cost to State government of $175,606.88 for personnel expenses. These staff members' time will be dedicated entirely to carrying out SMA screening and will be broken up as follows: 10% of time for prenalytical processing, 60% of time spent on analytical processing, and 30% of time dedicated to post analytical processing.

Table 1: NBSP SMA Staff Members Salary and Benefits

Salary and Fringe Benefits per Staff Member[13]		
Salary/Benefit	% of Salary	Total Value

[12] These are GN12 positions. The information regarding midpoint salary for GN12 was obtained from the North Carolina Office of State Human Resources GN Salary Schedule, which is available at: https://oshr.nc.gov/state-employee-resources/classification-compensation/compensation/salary-schedule-gn.

[13] The benefits listed were identified using the North Carolina Office of State Human Resources "Total Compensation Calculator," which is available at https://oshr.nc.gov/state-employee-resources/classification-compensation/total-compensation-calculator. In using this tool, we did not account for years of service, which may increase an employee's annual paid sick and vacation days, which are capped at 12 and 26 days, respectively, after 20 years of qualifying service to the State.

Salary	100	$63,552.00
FICA	7.65	$4,861.73
Retirement, Death, and Disability Benefit	19.70	$12,519.74
Health Insurance	10.81	$6,869.97
Hourly Rate Calculation		
Total Salary + Fringe	Hours Worked / Year	Hourly Rate
$87,803.44	2080	$42.21

TOTAL ANNUAL COST FOR TWO (2) NBSP SMA STAFF MEMBERS ….. $175,606.88

To reduce long-term programmatic costs NCSLPH will implement a strategy to detect SMA at the same time as screening for Severe Combined Immunodeficiency (SCID). The approach of analyzing multiple biomarkers for disorder identification in one chemical reaction, called multiplexing, reduces the costs associated with chemical reagents and consumable supplies (e.g., micropipette tips, microtiter plates, etc.). However, despite this strategy, NCSLPH anticipates a slight increased cost associated with reagents and consumables, as well as one-time equipment costs, to conduct screening for SMA.

With regard to equipment, NCSLPH has recently procured new real-time polymerase chain reaction (PCR) instrumentation and will procure new automated liquid handling instrumentation, and other small laboratory equipment to support multiplex testing. This equipment is paid for through the Newborn Screening Equipment Replacement and Acquisition Fund established under GS 130A-125(d). Since implemented, $31 of each newborn screening fee collected has been allocated towards this Fund. In State Fiscal Year (SFY) 2020, the Fund was used to purchase new PCR instrumentation ($152,971) and small laboratory equipment ($430). In SFY 2021, we anticipate that the Fund will be used to purchase new automated liquid handling instrumentation ($350,000). These purchases are supported in full by the Fund and are not part of the programmatic expenses that are offset by the $4 NBSP fee increase (discussed below). For this reason, these expenses were not taken into consideration in calculating the necessary fee increase amount.

In recognition of the likely increase in programmatic expenses related to implementing the inclusion of SMA in North Carolina's NBSP, GS 130A-125 authorizes the Commission for Public Health to increase the fee for newborn screening "no more than the amount necessary to offset the cost of incorporating a condition listed on the RUSP into the Newborn Screening Program."[14] As discussed earlier, NCSLPH anticipates that new programmatic expenses related to SMA screening will include the hiring of two staff members, but it will also necessitate the purchase of reagents and consumables (e.g., micropipette tips, microtiter plates, etc.). These consumables are necessary to conduct SMA screenings and will not be paid for through the Newborn Screening Equipment Replacement and Acquisition Fund.

Based on our experience conducting similar screening tests and our familiarity with SMA screening protocols and current vendor prices for laboratory materials, we determined that the reagents and consumables needed would cost approximately $2.29 per screening test. Although there are approximately 120,000 babies born in North Carolina each year, the actual tests run are not on a 1:1 basis with births, due to validation tests and re-tests (conducted on an as-needed basis). The number of tests is anticipated to be approximately 134,000 per year. Therefore, the approximate total cost of regents and consumables is expected to be $307,200 in total per year. To factor this total annual

[14] NCGS 130A-125(c).

expense into the fee increase, we divided $307,200 by the 120,000 anticipated births in North Carolina per year, which amounts to an increase of $2.56 per screening, as set out in Table 2.

Table 2: NBSP SMA Costs of Reagents and Consumables

Fee Increase Needed to Offset Programmatic Cost of Reagents and Consumables		
Total Cost of Additional Reagents and Consumables Needed Per Year	Approximate Number of Births in North Carolina Per Year	Fee Increase Needed to Offset SMA Reagent and Consumable Costs
$307,200.00	120,000	$2.56

The additional costs associated with purchasing reagents and consumables, as well as cost of hiring two new laboratory medical specialists, represent the total increase in programmatic expenses that NCSLPH expects to incur in order to begin screening for SMA. These costs, which were used calculate the fee increase necessary to offset them, are reflected in the calculations in Table 3 below.

Table 3: NBSP SMA Programmatic Expenses and Fee Calculation

Annual NBSP Programmatic Expenses Related to SMA		
Cost for Two SMA Staff	Cost for Reagents and Consumables	Total Annual Cost to State Government
$175,606.88	$307,200.00	$482,806.88
Fee Increase Calculation		
Total Annual Programmatic Costs Related to SMA	Approximate Number of Births in North Carolina per Year	Fee Increase Needed per Screening to Offset SMA Programmatic Costs
$482,806.88	120,000	$4.02

As Table 3 above shows, we anticipate that it will cost NCSLPH approximately $482,806.88 in programmatic expenses to implement the inclusion of SMA in the State's newborn screening panel. This value and the approximate annual number of births in North Carolina were used to determine that it would be necessary to increase the newborn screening fee by $4.02 (rounded down to $4 to account for the use of approximate figures in the calculations, such as births per year, which are expected to fluctuate annually). This fee increase will offset the increase in programmatic expenses associated with incorporating SMA into the NBSP.

NCSLPH charges the fee associated with newborn screening to the party submitting the specimen-most often, a birthing hospital. The hospital may seek reimbursement for the screening fees from the patient (if self-pay), from the health insurance company, or from Medicaid. An overwhelming majority of births in North Carolina occur in a hospital setting.[15] The costs to private health insurance, self-pay families, and the Medicaid program that are expected to stem from the $4 fee increase are addressed in later sections.

[15] In 2017, it was estimated that only 1.53% of births in North Carolina occurred outside of a hospital. Marian MacDorman and Eugene Declercq, "Trends and State Variations in Out-of-Hospital Births in the United States, 2004-2017," *Birth Issues in Prenatal Care*, Vol. 46, Issue 2, June 2019, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6642827/, accessed April 8, 2020.

Once a child has been identified through newborn screening as having an increased risk of SMA, the laboratory result is provided to staff in the Division of Public Health's Genetics and Newborn Screening Unit, which is housed in the Women and Children's Health Section, Children and Youth Branch. The staff person in the Genetics and Newborn Screening Unit is responsible for conducting follow-up activities, which include reporting the result and making recommendations to the physician of record; checking in with the physician of record to track the result of confirmatory testing; monitoring whether an appointment with a genetics specialist is made and attended by the family; recording information about the final diagnosis (if there is one) in two data systems, NewSTEPS and STARLIMS; and, as needed, communicating with local health departments, social workers, and WIC program staff to coordinate other support for the family.

Genetics and Newborn Screening Unit staff already do follow-up work for other conditions and diseases currently included in the newborn screening panel. Based on that experience, we estimate that additional follow-up work for children with SMA will require 34 hours of staff time per year, or approximately 3.1 hours per child who is identified as having SMA. The midpoint salary for staff members who conduct follow up work is 58,845, or an hourly rate of $39.09, when benefits are also taken into consideration.[16] This translates to an annual opportunity cost to the Division of Public Health of $1,329.06. The time spent conducting SMA follow-up will be an opportunity cost, as we do not plan to hire any additional staff to assist with this work.

Table 4: Genetics and Newborn Screening (GNS) Unit Staff Member Salary and Benefits

Salary and Fringe Benefits per Staff Member[17]		
Salary/Benefit	% of Salary	Total Value
Salary	100	$58,845.00
FICA	7.65	$4,501.64
Retirement, Death, and Disability Benefit	19.70	$11,592.47
Health Insurance	10.81	$6,361.14
Hourly Rate Calculation		
Total Salary + Fringe	Hours Worked / Year	Hourly Rate
$81,300.25	2080	$39.09

TOTAL ANNUAL OPPORTUNITY COST FOR GNS STAFF TIME …….. $1,329.06

Economic Impact to the Division of Health Benefits

As noted in the previous section, the fee for newborn screening is charged to the provider who submits the blood spot specimen for screening and is most often a birthing hospital. To our

[16] This is a GN11 position. The information regarding midpoint salary for GN11 was obtained from the North Carolina Office of State Human Resources GN Salary Schedule, which is available at: https://oshr.nc.gov/state-employee-resources/classification-compensation/compensation/salary-schedule-gn.

[17] The benefits listed were identified using the North Carolina Office of State Human Resources "Total Compensation Calculator," which is available at https://oshr.nc.gov/state-employee-resources/classification-compensation/total-compensation-calculator. In using this tool, we did not account for years of service, which may increase an employee's annual paid sick and vacation days, which are capped at 12 and 26 days, respectively, after 20 years of qualifying service to the State.

knowledge, hospitals pass the expense on to patients who self-pay and by seeking reimbursement from private health insurance or Medicaid. In the short term, if a hospital cannot pass along the fee cost to insurers due to previously-negotiated reimbursement contracts, then the hospitals may temporarily be responsible for the fee increases until those contracts can be revisited.

The $4.00 fee increase proposed in the Rule 42B .0108 is expected to impact North Carolina's Medicaid program, which provides insurance coverage for many of North Carolina's newborns. We estimate an increased annual cost of $66,504 to the State for its share of the increased costs for newborn screening for babies born eligible for Medicaid. In our calculations, we assume that Medicaid will cover approximately 51,000 (42.5%) of 120,000 total births in the State. These values are proxies based on the most recently available data on the number of births in North Carolina per year and the percentage of those births that were covered by Medicaid. Specifically, 42.5% was generated as the average percent of births covered by Medicaid in North Carolina in the last three years for which data is available (42.14% in 2018, 43.03% in 2017, and 42.35% in 2016, the average of which is 42.5%).[18] We also chose to use an estimate of 120,000 total births in North Carolina per year, which is the value used by NCSLPH to calculate the NBSP fee increase and which is within the range of total births in North Carolina from recent years, including 2018 (118,954 births), 2017 (120,125 births), and 2016 (120,779 births).[19]

The costs to the Medicaid program are shared between the State of North Carolina and the federal government according to the Federal Medical Assistance Percentage (FMAP), which is a formula that takes into account the average per capita income for each state relative to the national average. NCSLPH expects to begin screening for SMA in the first quarter of 2021; therefore, the FMAP rate for the federal fiscal year that runs from October 1, 2020 through September 30, 2021 was used in determining the State's share of the total increased costs to Medicaid stemming from the $4 fee increase.[20] The FMAP rate, which is representative of the federal government's share of costs, is set at 67.4% for North Carolina for 2021.[21] This means that North Carolina will be responsible for 32.6% of the State's Medicaid costs in that fiscal year.

Table 5: State Share of NBSP Fee Costs to NC Medicaid Program

Annual Total Cost to Medicaid Program for NBSP Fee Increase		
Increase in Fee Amount as Proposed in the Rules	Number of Medicaid-Covered Births in North Carolina Per Year	Total Cost to Medicaid Program per Year
$4.00	51,000	$204,000.00
State Share of the Total Annual Cost to Medicaid for the NBSP Fee Increase		

[18] These values were identified using the CDC's WONDER database and querying live births by state by payer by year for North Carolina within the Natality Information- Live Births, 2016-2018 (expanded) data set. 2018 is the most recent year for which data is available. The system can be accessed at: https://wonder.cdc.gov/natality.html.

[19] The North Carolina State Center for Health Statistics has published final vital statistics data on its website for the years 2016, 2017, and 2018 (the most recent year for which final data is available). Those reports are available at: https://schs.dph.ncdhhs.gov/data/provisional/.

[20] Agencies are not required to calculate economic impact to the federal government; therefore, we have not calculated the federal government's share of the total increased costs to Medicaid.

[21] United States Federal Register, Vol. 84, No. 232, December 3, 2019, https://www.govinfo.gov/content/pkg/FR-2019-12-03/pdf/2019-26207.pdf, accessed April 12, 2020; *see also* Medicaid.gov, "Financial Management," https://www.medicaid.gov/medicaid/financial-management/index.html, accessed April 12, 2020. Note that if the public health emergency related to COVID-19 is still in effect during the first quarter of 2021 then a 6.2% FMAP increase, authorized under the Families First Coronavirus Response Act, will also apply.

Total Cost to Medicaid Program per Year	State Responsibility for Percent of Total Medicaid Costs	Total Annual Cost to State Government
$204,000.00	32.6%	$66,504.00

We expect that DHB also already incurs costs related to the provision of treatment and care for Medicaid-eligible children who are identified as having SMA. These costs are discussed below, but are not included in the total estimated costs to State government because we do not anticipate that newborn screening for SMA, as proposed under the Rules, will identify children with SMA who would otherwise go entirely unidentified and thereby generate new expenses for the Medicaid program. Experts in the field believe that without newborn screening, children with SMA will still be identified, diagnosed, and treated at some point in their lives.

With newborn screening for SMA in place, however, those children can be identified, diagnosed, and begin receiving treatment much earlier in life, which may have an effect on disease burden and potentially increase the benefits of therapeutic management.[22] For example, it is estimated that if newborn screening for SMA were implemented in all states and all four million children born in the United States each year were screened, the effect of early diagnosis and treatment would prevent death or the need for mechanical ventilation in 48 babies before their first birthdays.[23] Note that there is a high degree of uncertainty in these estimates due to the limited data currently available on pre-symptomatic vs post-symptomatic treatment outcomes. In addition to improving survival rates, longevity, and quality of life, these effects of early detection and treatment for SMA are also expected to lead to reduced overall healthcare expenditures during a child's lifetime that would be a benefit to Medicaid. Unfortunately, newborn screening for SMA has only been in place for a few years and there is very limited research on the exact costs and savings associated with earlier detection and care, which makes the economic impact challenging to quantify and compare against current costs related to diagnosis, treatment, and other non-treatment medical care.

We anticipate that the North Carolina Medicaid program may be responsible for the costs of treatment for Medicaid-eligible children under the Early and Periodic Screening, Diagnostic, and Treatment (EPSDT) Medicaid benefit. Under EPSDT, states are required to "provide any additional health care services that are coverable under the Federal Medicaid program and found to be medically necessary to treat, correct or reduce illnesses and conditions discovered regardless of whether the service is covered in a state's Medicaid plan" and to make available the necessary health care services for "treatment of all physical and mental illnesses or conditions discovered by any screening and diagnostic procedures."[24]

[22] Droege, M., Sproule, D., Arjunji, R., Gauthier-Loiselle, M., Cloutier, M., & Dabbous, O., "Economic burden of spinal muscular atrophy in the United States: a contemporary assessment," *Journal of Medical Economics,* Vol. 23, Issue 1, August 4, 2019, https://www.ncbi.nlm.nih.gov/pubmed/31322019, accessed April 11, 2020.

[23] In March of 2018, the Evidence-based Review Group prepared and submitted a report titled "Evidence-based Review of Newborn Screening for Spinal Muscular Atrophy (SMA): Final Report" for the Maternal and Child Health Bureau, Health Resources and Services Administration (HRSA), U.S. Department of Health and Human Services. That report is available at: https://www.hrsa.gov/sites/default/files/hrsa/advisory-committees/heritable-disorders/reports-recommendations/sma-final-report.pdf.

[24] Medicaid.gov, "Early and Periodic Screening, Diagnostic, and Treatment," https://www.medicaid.gov/medicaid/benefits/early-and-periodic-screening-diagnostic-and-treatment/index.html, accessed April 8, 2020.

Currently, there is no cure for SMA and the only FDA-approved pharmaceutical-based treatment for SMA is nusinersen (tradename "Spinraza").[25] According to a July 2, 2018 media release, the North Carolina Medicaid program does cover Spinraza and will provide reimbursement for Spinraza (when the drug is medically indicated) at a maximum reimbursement rate of $135,000.00 per dose, which is the approximate actual cost of one dose of the drug.[26] Six doses of Spinraza are required in the first year, and three doses per year for each following year, for a total cost of $810,000 in year one and $405,000 each year thereafter, for the remainder of the child's life. These costs include the pharmacological treatment and do not include costs to administer the drug via intrathecal injection, which are expected to vary by provider and/or clinical facility. It is also likely the patients will require substantial additional medical care to complement treatment with Spinraza, but no studies have yet examined these costs. Estimates of medical costs before the availability of Spinraza were between $104,197 and $385,914 annually.[27]

Under the assumptions that Medicaid will cover 42.5% of approximately 120,000 births in North Carolina and that there are approximately 11 babies with SMA born in North Carolina every year, we estimate that there are approximately 4.68 children born every year in North Carolina who have SMA *and* are Medicaid-eligible at birth. With the further assumption that these babies remain continuously eligible for Medicaid, under the 2021 FMAP rate, North Carolina could expect to pay approximately $264,060 of the total costs to Medicaid for treatment on Spinraza in the first year of a child's life and approximately $132,030 for Spinraza treatment every year thereafter until the child is no longer covered by Medicaid.

In addition to Spinraza, children with SMA may also receive treatment in the form of a recentlydeveloped gene therapy. Onasemnogene abeparvovec-xioi, also known as Zolgensma, is a gene replacement therapy for SMA that was FDA approved in May 2019 to treat children under the age of 2 two who have genetically confirmed SMA. This one-time dose therapy sells in the United States for $2.1 million dollars.[28] This therapy is very new, and it is not yet clear if the Medicaid program will provide coverage for this treatment. If Medicaid were to cover Zolgensma, it is likely that Medicaid would negotiate the price of the therapy.

Total Cost to State Government

Based on the above analyses, with numbers memorialized in Table 6, we anticipate that total annual impact to the State government will be an increased cost of $70,639.94.

[25] United States Food and Drug Administration, "FDA approves first drug for spinal muscular atrophy," December 23, 2016, https://www.fda.gov/news-events/press-announcements/fda-approves-first-drug-spinal-muscular-atrophy, accessed April 8, 2020.

[26] North Carolina Department of Health and Human Services, Division of Health Benefits, "Nusinersen injection, for intrathecal use (Spinraza) HCPCS code J2326 - Unclassified Drugs: Billing Guidelines and Change in Coverage," July 2, 2018, https://medicaid.ncdhhs.gov/blog/2018/07/02/nusinersen-injection-intrathecal-use-spinraza-hcpcs-code-j2326-unclassified-drugs, accessed April 8, 2020.

[27] Michael Lee, Urbano Franca, Robert Graham, Michael McManus, "Pre-Nusinersen Hospitalization Costs of Children With Spinal Muscular Atrophy," *Perspectives in Pediatric Neurology,* Vol. 92, March 2, 2019, https://www.pedneur.com/article/S0887-8994(18)31158-5/fulltext, accessed April 8, 2020.

[28] Owen Dyer, "Health ministers condemn Novartis lottery for Zolgensma, the world's most expensive drug," *The BMJ*, February 12, 2020, https://www.bmj.com/content/368/bmj.m580.full, accessed April 10, 2020.

Table 6: Net Impact to State Government	
Cost and Benefits to DPH Per Year	
Total Costs	
Costs for NCSLPH Staff	$175,606.88
Costs for Additional NCSLPH Supplies	$307,200.00
Opportunity Costs for GNS Staff	$1,329.06
Total Costs to DPH	$484,135.94
Total Benefit	
State Share of Medicaid Costs Related to NBSP Fee Increase (DHB)	$66,504.00
Private Sector and Federal Share of Costs Related to NBSP Fee Increase	$389,544.00
"Other/Unknown/Not Stated" Share of Costs Related to NBSP Fee Increase[29]	$23,952.00
Total Estimated Fee Income Per Year	$480,000.00
DPH NET COST	$4,135.94
Cost to DHB Per Year	
Total Costs	
State Share of Medicaid Costs Related to NBSP Fee Increase	$66,504.00
TOTAL COST	$66,504.00
Net Cost to State Government Per Year	
Net Cost to DPH	(-) $4,135.94
Cost to DHB	(-) $66,504.00
TOTAL COST TO STATE GOVERNMENT PER YEAR	$70,639.94

Local Government

The Rules as they currently exist and as they are proposed for amendment and adoption do not involve local government and they are therefore not expected to have an economic impact at the local government level.

Private Sector

Economic Impact to Private Insurance Companies

As noted in the previous section, the fee for newborn screening is charged to the provider who submits the blood spot specimen for screening and is most often a birthing hospital. To our

[29] Based on an average calculated using the most recently available data, the payment source for approximately 4.99% of all births in North Carolina each year is classified as "other/unknown/not stated" (4.99% in 2018, 4.97% in 2017, and 5.02% in 2016). Although the source of payment for the birth is unknown, NCSLPH expects to receive a fee for these births. 4.99% of 120,000 expected births per year is 5,988 births. These values were identified using the CDC's WONDER database and querying live births by state by payer for 2018 within the Natality Information-Live Births, 2016-2018 (expanded) data set. The system can be accessed at: https://wonder.cdc.gov/natality.html.

knowledge, hospitals pass the expense on to insurers and self-pay patients. If part of a bundled payment, hospitals may be temporarily responsible for the fee increase while insurance contracts are revisited (discussed further below). The $4.00 fee increase is expected to impact private health insurance programs operating in North Carolina, which covers an average of 45.6% of all births in the state, based on the most recently available data (46.05% in 2018, 45.1% in 2017, and 45.64% in 2016).[30] This amounts to approximately 54,720 children born in North Carolina per year being covered by private insurance. Assuming all of those newborns covered by private insurance receive newborn screening, we anticipate an annual increased cost to private health insurance companies of $218,880. It is possible that some portion of this expense will be passed on to the private health insurance companies' beneficiaries through co-payments, coinsurance, premiums, or pre-deductible out-of-pocket costs.

Table 7: Increased Fee Costs to Private Health Insurance Companies

Expenses to Private Insurance for Fee Increase Per Year		
Increase in Fee Amount as Proposed in the Rules	Number of Private Insurance Covered Births in North Carolina Per Year	Cost to Private Insurance Industry Per Year
$4.00	54,720	$218,880.00

Given the estimated prevalence of SMA in North Carolina and the portion of births in the state covered by private insurance, we estimate that there will be 5.02 children born each year in North Carolina who have SMA *and* will be eligible for private insurance coverage. As with Medicaid, we expect that private insurance companies already encounter costs related to providing children with SMA with treatment and other care. These costs are discussed below, but are not included in the total estimated costs to the private sector because the information we have at this time suggests that newborn screening for SMA, as proposed under the Rules, will not identify children with SMA who would otherwise go unidentified or untreated. Therefore, screening is not expected to generate new expenses for the private insurance companies.

Additionally, in contrast to the Medicaid program, it is difficult to know to what degree various private insurance companies will cover Spinraza treatment or gene therapy (if either treatment will be covered at all). For example, BlueCross BlueShield of North Carolina appears to provide coverage only when specific criteria are met, including the onset of SMA symptoms before 20 months of age.[31] There are also many factors that inform whether a child will continue to be covered by private insurance as they grow up. Finally, and as discussed in the previous section on impact to the Division of Health Benefits, the earlier detection of SMA through newborn screening is expected to enable children to receive treatment earlier, thereby improving their overall health outcomes and survival and reducing health care expenditures for care later on in their lives. Unfortunately, newborn screening for SMA has only been in place for a few years and there is very limited research on the exact costs and savings associated with earlier detection and care, which makes the economic impact

[30] These values were identified using the CDC's WONDER database and querying live births by state by payer for 2018 within the Natality Information- Live Births, 2016-2018 (expanded) data set. The system can be accessed at: https://wonder.cdc.gov/natality.html.

[31] BlueCross BlueShield of North Carolina, "Corporate Medical Policy: Nusinersen (Spinraza)," October 2019, https://www.bluecrossnc.com/sites/default/files/document/attachment/services/public/pdfs/medicalpolicy/nusinersin_spinraza.pdf, accessed April 9, 2020.

challenging to quantify and compare against current costs related to diagnosis, treatment, and other non-treatment medical care.

Economic Impact to "Self-Pay" Families

In addition to private insurance and Medicaid, there are a small number of births in North Carolina each year that are paid for out of pocket by families. "Self-pay" is used to pay for an average of 6.91% of all births in the state based on the most recently available data (6.82% in 2018, 6.93% in 2017, and 6.99% in 2016).[32] If each of these families were to pay for newborn screening then we would expect the proposed Rules to impact approximately 8,292 families who would each see an increased expense of $4.00 per newborn screening. The overall fee increase for families using self-pay, collectively, is estimated to be $33,168.

Table 8: Increased Fee Costs to All "Self-Pay" Families

Expenses to "Self-Pay" Families for Fee Increase Per Year		
Increase in Fee Amount as Proposed in the Rules	Number of "Self-Pay" Covered Births in North Carolina Per Year	Cost to "Self-Pay" Families Per Year
$4.00	8,292	$33,168.00

Given that we anticipate SMA screening to identify a total of 11 children per year with SMA, we could expect that 0.76 (less than one) of those births would be to "self-pay" families *and* to a child identified as having SMA. As with private insurance companies and Medicaid, we expect that self-pay families may already encounter expenses related to treatment and other forms of care for a child with SMA. These potential costs are discussed throughout this fiscal note, but are not included in the total estimated costs to private sector because there is currently no research to suggest that newborn screening for SMA, as proposed under the Rules, will identify children with SMA who would otherwise go unidentified and thereby generate new expenses for the individual families.

Given the high costs of treatment for SMA over a child's lifetime, we anticipate that many families of children identified with SMA who are "self-pay" at the time of the child's birth and who choose to pursue treatment may ultimately try to obtain some type of private insurance coverage. Alternatively, families who begin paying for treatment out of pocket might also spend down their assets and resources to the point of becoming eligible for Medicaid coverage for their child with SMA. Children whose families who do not pursue treatment early- because of the prohibitive cost or for other reasons- and who later develop severe muscle weakness may qualify for Medicaid later in life if their symptoms allow them to qualify for the program on the basis of disability. Finally, the prohibitively high cost of treatment; the costs of premiums and potential for partial coverage or non-coverage of treatment under private insurance; and ineligibility for Medicaid may deter some families of children with SMA from pursuing treatment altogether. These families may still encounter expenses for medical care outside of treatment. Researchers have previously estimated that the cost of medical

[32] These values were identified using the CDC's WONDER database and querying live births by state by payer for 2018 within the Natality Information- Live Births, 2016-2018 (expanded) data set. The system can be accessed at: https://wonder.cdc.gov/natality.html.

care for a child with SMA before Spinraza or gene therapy became available ranged from $104,197 to $385,914 annually.[33]

Experts in the field believe that without newborn screening, children with SMA will still be identified, diagnosed, and treated at some point in their lives. With newborn screening for SMA in place, however, those children can be identified, diagnosed, and begin receiving treatment much earlier in life. This is expected to have significant implications for each child's health outcomes and length of life, as well as overall health care expenditures. Unfortunately, newborn screening for SMA has only been in place for a few years and there is very limited research on the exact costs and savings associated with earlier detection and care, which makes the economic impact challenging to quantify and compare against current costs that "self-pay" families may incur related to diagnosis, treatment, and other non-treatment medical care.

Economic Impact to Birthing Hospitals

As noted in the section above on impacts to the Division of Health Benefits, birthing hospitals that are charged the fee for newborn screening generally pass that cost on by seeking reimbursement from the self-paying patient, private insurance, or Medicaid. We recognize, however, that if a hospital cannot pass along the fee cost to insurers due to previouslynegotiated reimbursement contracts then the hospitals may temporarily be responsible for the fee increases until those contracts can be revisited. Without information on how many newborn screenings every birthing hospital orders each year; the portion of their patients per year that are "self-pay," privately insured, or Medicaid-eligible; the existing terms of the hospitals' contracts with each private insurance provider and the Medicaid program; and the expiration date of those contracts, it is difficult to determine the costs that private hospitals may encounter if their current contracts preclude them from seeking reimbursement for the increased $4 fee and during the period before their contracts can be renegotiated. However, it would be a subset of the costs currently discussed under this private sector analysis.

Summary

In compliance with GS 130A-125, the proposed Rules would align the State's NBSP screening panel with the core conditions listed on the RUSP and would establish a fee increase to cover the programmatic costs of implementing the screenings on the RUSP. The effect of aligning the NBSP with the RUSP through rulemaking is the addition of one condition, SMA, to the NBSP's screening panel.

Although there is currently no cure for SMA, the addition of SMA to the NBSP panel will allow for earlier diagnosis of SMA in babies born in North Carolina, which could reduce the devastating consequences of progressive muscle weakness and severe physical disability due to degeneration of motor neurons cells. Experts in the field believe that, without newborn screening, children with SMA will still be identified, diagnosed, and treated at some point in their lives. With newborn screening for SMA in place, however, those children can be identified, diagnosed, and begin receiving treatment much earlier in life. Some research suggests that early treatment (i.e., when treatment begins before symptoms develop) improves motor outcomes and lowers the risk of death or the eventual need for a ventilator in people with SMA. In addition to improving survival rates, longevity, and quality of life, these effects of early detection and treatment for SMA are also expected to lead to reduced overall healthcare expenditures during a child's lifetime.

[33] Michael Lee, Urbano Franca, Robert Graham, Michael McManus, "Pre-Nusinersen Hospitalization Costs of Children With Spinal Muscular Atrophy," *Perspectives in Pediatric Neurology,* Vol. 92, March 2, 2019, https://www.pedneur.com/article/S0887-8994(18)31158-5/fulltext, accessed April 8, 2020.

Table 9 describes the economic impact of including SMA in the NBSP screening panel over one year. This impact would be expected to continue during subsequent years. As demonstrated by the calculations in Table 9, we anticipate that the proposed Rules, which reflect the specific requirements set forth in GS 130A-125, will have a substantial economic impact due to costs and benefits incurred by State government and the private sector.

Table 9: Economic Impact on All Persons Affected by the Proposed Rules Per Year

Total Impact to State Government	
Income to DPH from $4 Fee Increase	$480,000.00
Programmatic Expenses to DPH	($484,135.94)
Impact to DHB for $4 Fee Increase	($66,504.00)
Total Impact to Local Government	$0 (no impact)
Fee Impact to Private Sector	
Impact to Private Insurance Companies from $4 Fee Increase	($218,880.00)
Impact to "Self-Pay" Families for $4 Fee Increase	($33,168.00)
Quantified Net Cost to North Carolina	($322,687.94)
Unquantified Benefits to Children and Families	Improved survival rates, longevity, and quality of life, reduced total medical care costs for approximately 11 babies each year

Alternatives

Pursuant to GS 150B-21.4(b2)(5), when an agency concludes its analysis and determines that the proposed rules will have a substantial economic impact, the agency shall include in its fiscal note a description of at least two alternatives to the proposed rules that were considered by the agency and rejected.

One alternative option would have been to delay the implementation of screening for SMA; however, this would have resulted in more babies born with SMA who are unable to receive the benefit of early detection and the chance to begin treatment in the first months of each child's life. As we explained in earlier sections, the benefits of early treatment are thought to be potentially significant for increased chance of survival and longevity, improved health outcomes, and reduced overall health care expenditures across the child's life. Considering the benefits of screening, early detection, and early treatment to the public, we did not pursue the alternative option of delaying implementation of SMA screening for North Carolina's newborns.

A second alternative option would have been to implement newborn screening for SMA, but not increase the screening fee or increase the fee by a lower amount. As documented in earlier sections, we have proposed to increase the newborn screening fee by no more than the amount necessary to offset the increase in programmatic costs. If we did not increase the newborn screening fee, the Division of Public Health would have to reorient the workload of current staff and make tradeoffs for the use of equipment, reagents, and consumables, which would impact the NCSLPH's ability to do other critical work, such as testing for private well, child blood lead levels, and communicable diseases and conditions. These other testing services are essential to protecting public health in North Carolina and, for that reason, we chose not to pursue that option.

Appendix: Proposed Rule Text

10A NCAC 42B .0102 is proposed for amendment as follows:

10A NCAC 42B .0102 ~~CLINICAL CHEMISTRY/NEWBORN~~ NEWBORN SCREENING

(a) This laboratory will conduct screening for ~~examine specimens for evidence of certain inborn errors of metabolism, for the detection of chronic diseases, diabetes, renal diseases, hypertension, certain clinical chemistry and hematology tests when requested by authorized senders of specimens within the guidelines of the Division of Maternal and Child Health and the Division of Public Health.~~ the core conditions listed on the Recommended Uniform Screening Panel developed by the Secretary of the United States Department of Health and Human Services and the Advisory Committee on Heritable Disorders of Newborns and Children (the "RUSP"), which is hereby incorporated by reference, including any subsequent editions and amendments, and available free of charge at https://www.hrsa.gov/advisory-committees/heritable-disorders/rusp/index.html. Specimens shall be submitted to this laboratory for screening in accordance with the procedures set forth in 10A NCAC 43H .0314.

(b) ~~This laboratory performs tests for hemoglobinopathies such as sickle cell trait and disease.~~ The process to develop and implement new screening for the conditions described in Paragraph (a) of this Rule shall begin after the screening fee is established and adequate funds exist to acquire instrumentation, equipment, Program supplies, Program personnel, perform assay validations, implement preventative follow-up interventions, secure necessary infrastructure, and with the assurance that the laboratory has met all federal, State, and local requirements.

History Note: *Authority G.S. 130A-88; 130A-125;*
Eff. October 1, 1985;
Amended Eff. September 1, 1990;
Pursuant to G.S. 150B-21.3A, rule is necessary without substantive public interest Eff. December 23, 2017.

10A NCAC 42B .0108 is proposed for adoption as follows:

10A NCAC 42B .0108 FEES

(a) The State Laboratory of Public Health shall charge a fee of one hundred thirty-two dollars ($132.00) to cover the programmatic costs of the newborn screening performed by the State Laboratory of Public Health under 10A NCAC 42B .0102(a).

(b) In accordance with G.S. 130A-125, the Commission for Public Health, in consultation with the Secretary of the North Carolina Department of Health and Human Services, has determined that the fee listed in Paragraph (a) of this Rule is necessary to offset the cost of incorporating the conditions identified in 10A NCAC 42B .0102(a) in the Newborn Screening Program.

Authority G.S. 130A-125;

10A NCAC 43H .0314 is proposed for amendment as follows:

10A NCAC 43H .0314 SUBMISSION OF BLOOD SPECIMENS FOR SCREENING OF NEWBORNS

(a) The attending physician shall ~~draw~~ collect a blood specimen for each infant born in North Carolina and shall submit such specimens to the North Carolina State Laboratory of ~~for~~ Public Health for testing as set forth in 10A NCAC 42B .0102. ~~for the following metabolic and other hereditary and congenital disorders:~~

~~(1) phenylketonuria (PKU);~~

~~(2) galactosemia;~~

~~(3) congenital primary hypothyroidism;~~

~~(4) congenital adrenal hyperplasia (21-hydroxylase deficiency); and~~

~~(5) sickle cell disease.~~

(b) Notwithstanding Paragraph (a) of this Rule, parents or guardians may object to screening in accordance with G.S. 130A-125(b).

(c) The hearing screening component of the Department's Newborn Screening Program is found in 10A NCAC 43F .1200.

History Note: *Authority G.S. 130A-125;*
Eff. April 1, 1992;
Transferred and Recodified from 15A NCAC 21E .0501 Eff. February 10, 1993;
Amended Eff. April 1, 1994;
Temporary Amendment Eff. October 1, 1999;
Amended Eff. August 1, 2000;
Pursuant to G.S. 150B-21.3A, rule is necessary without substantive public interest Eff. December 6, 2016.