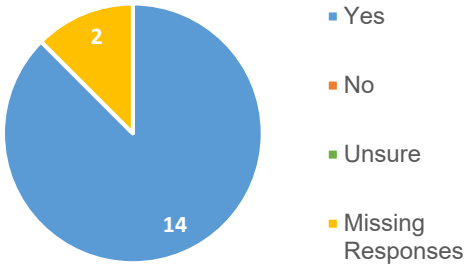
WASHINGTON STATE BOARD OF HEALTH

Newborn Screening Technical Advisory Committee: Guanidinoacetate methyltransferase (GAMT) and Arginase 1 Deficiency (ARG1-D)

GAMT Deficiency Voting Summaries and Comments

The following is a compilation of comments from technical advisory committee (TAC) members provided when voting on each individual criteria, and an overall recommendation for GAMT Deficiency. Comments have been summarized and are organized by each criterion, and then overall comments are provided.

Criteria Evaluation

Criteria	Comments and Major Themes
1. Available Screening Technology 	• GAMT testing has high sensitivity and specificity. • Screening technology is already in place at the Department of Health NBS lab to support screening for the condition. • "This is life-changing screening" – the testing will benefit affected children, their families, and communities.

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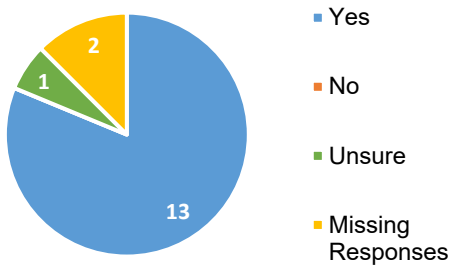
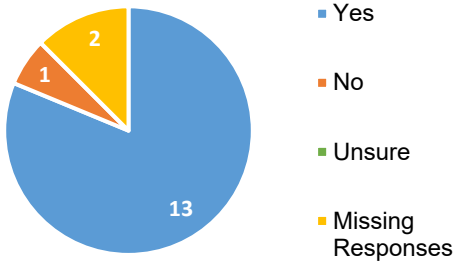
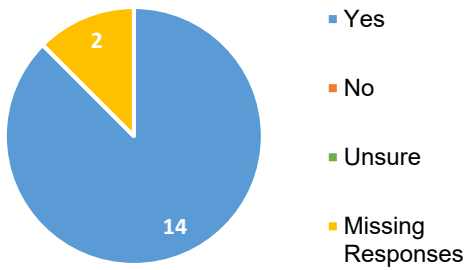
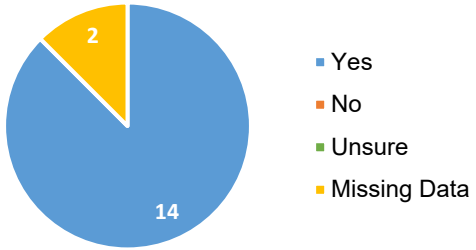
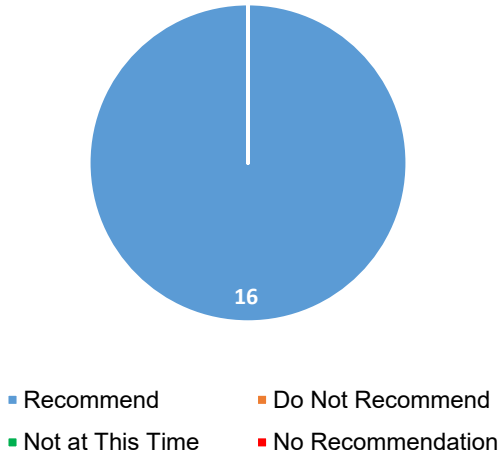
2. Diagnostic Testing and Treatment Available 	• If diagnosed early, treatment options are available with proven positive impact and efficacy. • Biochemical and genetic testing is available for confirmation of diagnosis, and there are specialists in areas of Washington to manage this condition. • Initial treatment options include starting over-the-counter creatine supplements after a post-positive result screen while waiting for diagnostic results. Treatment is also reasonable in terms of cost and is low risk to a child until the confirmatory test is back. • Treatment is available but concerns around a delay in timely intervention. • The utility and effectiveness of screening tests are also dependent on the plan for positive tests. Without a clinically relevant and timely action plan, criterion 2 is not met.
3. Prevention Potential and Medical Rationale 	• Most infants will become symptomatic and clinically identified after 3 months of age. The best outcomes were for babies who were treated at birth. Therefore, the preventative potential and rationale require an expedited follow-up plan. • Early detection mitigates or prevents severe long-term consequences of the disease. • Clinical decision-making can occur for initiating treatment while waiting for diagnosis between care teams. • Not sure if this is met. However, the harms may be moderate versus severe, and so this still meets the criterion.

4. Public Health Rationale 	• The at-risk population will likely not be known unless the family already has one affected child. • Screening based on symptoms alone delays diagnosis and is associated with worse outcomes because long-term consequences may persist even with treatment. • Early universal screening minimizes risk for life-long disabilities and is equitable. • Even though GAMT is a rare disease, population-based screening is important to prevent late-onset clinical diagnosis, associated with severe/moderate developmental delays and increased healthcare costs.
5. Cost Benefit / Cost Effectiveness 	• Is the loss of productivity from the parents/family members/caretakers considered? Family members also have additional costs and losses. Family members often lose days of work and have additional therapy and medical needs. • The emotional impact of false positives can be daunting. • Cheap test. Highly sensitive and specific. No new technology required. Positive cost/benefit ratio. • Cost-benefit analysis supports universal testing

Overall Recommendation



Recommendation Options	Comments and Major Themes
1. I recommend the Board add GAMT Deficiency to the list of conditions for which all Washington-born newborns must be screened.	• Screening is available and cost-effective, and there's treatment available. • Early universal screening identifies patients before the onset of symptoms, optimizes outcomes, and minimizes long-term disabilities. • Recommend adding GAMT, if there are concrete plans that will be clearly communicated to families and healthcare providers for the next steps and timelines before this test goes live. The primary care clinic's experience with Pompe Disease being added to the NBS and false positive results was traumatic. Families can never have that experience back when the joy of a healthy newborn birth is derailed by potentially serious medical diagnosis with long wait times for confirmatory results. • This has been thoroughly reviewed and recommended by the ACHDNC for the RUSP. Since so many children with GAMT fly under the radar without consistent early symptoms, many are diagnosed with Autism or Cerebral Palsy. They could

	have been treated. Time is of the essence. The later a diagnosis is given, the more severe impact on the quality of life.
2. I do not recommend the Board add GAMT Deficiency to the list of conditions for which all Washington-born newborns must be screened.	*No comments.*
3. At this time, I do not recommend the Board add GAMT Deficiency to the list of conditions for which all Washington-born newborns must be screened; I recommend the Board revisit GAMT Deficiency at a future date.	*No comments.*