Development of a State Condition-Readiness Tool for Disorders Not on the Recommended Uniform Screening Panel

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How Michigan adds conditions

- Michigan historically has followed the recommendations of the Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC)
  - “The [NBS QAAC] shall also include in the report recommendations to revise the list to include additional newborn screening tests that are nationally recognized in the scientific literature or national standards for conditions that can be ameliorated or treated if identified by a newborn screening test...”
Michigan Newborn Screening Program is occasionally approached by families, state legislators, or clinicians to consider adding other disorders not included on the ACHDNC Recommended Uniform Screening Panel (RUSP)

Needed a systematic approach to review requests
Tool Development

- Review of ACHDNC resources
- Current ACHDNC evaluation process
- Other resources
  - Washington State’s 2016 APHL presentation
  - Ontario’s process
Tool Development

- Collaboration from
  - NBS follow-up program staff
  - NBS laboratory staff
  - NBS Coordinating Center staff
  - NBS Technical Advisory Committee
  - NBS Quality Assurance Advisory Committee
How does Michigan use the tool?

- Guidelines used for non-RUSP conditions
- Tool assists in drafting response to stakeholders requesting addition of a new condition to Michigan’s NBS panel
- If the condition has never been brought to ACHDNC attention, draft response but no further action
- If the condition has been brought to ACHDNC and not recommended for RUSP, guidelines can be used to assess Michigan’s readiness to add
- Conditions added prior to development of tool are grandfathered in
- Tool will be reviewed every 3 years
How does Michigan use the tool?

• Utilize committee structure
  – Subcommittee reviews, discusses, formulates recommendation and presents to TAC
  – TAC recommends approval to QAAC
  – QAAC makes final recommendation
  – Legislature process follows
Readiness Table

• Total for each section determines status of condition

• Conditions meeting ready or developmental stages can go through Michigan’s approval process
Criteria sub-sections

- Required criteria
- Supporting factors
  - Condition characteristics
  - Laboratory/Screening
  - Follow-up/Diagnosis
  - Clinic/Treatment availability

![Condition Readiness Criteria Table](chart.png)

Conditions that meet the *ready* or *developmental* stages can begin Michigan's approval process.
Required Criteria

- All 7 criteria must be met to pass
- Criteria include:
  - Support from NBS lab, follow-up and Michigan clinical specialists
  - Condition is identifiable in newborn period
  - Sensitive, specific, screening test with high-throughput capability
  - Established benefits of early intervention and treatment
  - Condition does not have a known late-onset form (additional caveats must be met if late-onset forms are known)

<table>
<thead>
<tr>
<th>Required criteria</th>
<th>Met</th>
<th>Not Met</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Support from appropriate screening facility and condition is considered feasible to add (NBS lab for blood spot screening hospital for point of care screen).</td>
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<tr>
<td>2. Support from Bureau of Epidemiology and Population Health and condition is considered feasible to add (NBS follow-up and/or other relevant maternal child health programs).</td>
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<tr>
<td>3. Support from Michigan clinical specialists and condition is considered feasible to add (clinicians identified who support screening and are ready to accept referrals and treat patients who are identified with this condition through newborn screening).</td>
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<td>4. Condition can be identified in the newborn period when it would not ordinarily be detected clinically.</td>
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<tr>
<td>5. A screening test with appropriate sensitivity, specificity and high-throughput capability is or is projected to be available within 12 months.</td>
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<tr>
<td>6. Established benefits of early detection, timely intervention and safe, efficacious treatment that provide a significant improvement in quality of life for identified newborns.</td>
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<tr>
<td>7. Condition does not have a known late onset form. If the condition does not meet this requirement, four additional criteria must be fulfilled.</td>
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<tr>
<td>a) More newborns are projected to be at risk of early childhood onset than identified with late/unknown onset or other variants of the disease based on the proposed screening protocol.</td>
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<tr>
<td>b) Effective therapeutic intervention is known for the majority of individuals identified through newborn screening.</td>
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<tr>
<td>i) Surveillance for possibility of disease onset alone does not constitute therapeutic intervention.</td>
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<tr>
<td>c) The treatment for the patient is considered low risk.</td>
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Supporting Factors: Condition characteristics

- Natural history is well understood
- Expected incidence in Michigan
- Profound burden to those affected
- Latent state of disease
- Onset of symptoms in first year of life
Supporting Factors: Laboratory/Screening

- False positive rate
- Positive predictive value
- Sensitivity
- Cost of screening
- Screening is best done in newborn period
- Targets severest form of condition
- Discriminates states of onset for condition

### Ready

| B. Lab/Screening: screening methodology is currently available in lab and >70% criteria met (at least 5) |

### Developmental

| B. Lab/Screening: screening methodology will be available but is not currently in lab and >50% criteria met (at least 4) |

### Unprepared

| B. Lab/Screening: screening methodology is not yet available and <50% criteria met (less than 4) |
Supporting Factors: Follow-up/Diagnosis

- Cost of follow-up
- Available, accessible and accurate diagnostic tests
- Diagnostic process is minimally invasive
- Minimal harm from follow-up for those diagnosed with carrier/variant/late onset/mild disease
- Early diagnosis prevents severe developmental delay, morbidity, mortality

### C. Follow-up/Diagnosis

<table>
<thead>
<tr>
<th>Met</th>
<th>Not Met</th>
<th>Unknown</th>
</tr>
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<tr>
<td>20. The NBS Program can reasonably take on the cost of follow-up for the condition (cost including personnel, follow-up coordinating center, etc. needed to implement screening is less than $100,000).</td>
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<tr>
<td>21. Diagnostic tests are available, accessible and accurate (if applicable, can discriminate early vs. late onset disease states or can discriminate between mild and severe forms of the condition).</td>
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<td>22. Diagnostic process is minimally invasive (can be completed with blood or urine samples).</td>
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<td>23. There is minimal harm in long-term follow-up for patients whose testing leads to a diagnosis of carrier/variant/uncertain/late onset/mild disease status.</td>
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<td>24. Early diagnosis prevents severe developmental delay, morbidity or mortality.</td>
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<td>C. Follow-up/Diagnosis: ≥80% criteria met (at least 4)</td>
<td>C. Follow-up/Diagnosis: ≥60% criteria met (at least 3)</td>
<td>C. Follow-up/Diagnosis: &lt;60% criteria met (less than 3)</td>
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Supporting Factors: Clinic/Treatment availability

- Treatment is well-established
- Treatment is non-invasive (minimal harm)
- Treatment is available and effective
- Treatment improves quality of life
- Caregivers choose to treat
- Facilities and specialists available and accessible
- CSHCS eligibility

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First use of tool: Guanidinoacetate methyltransferase deficiency (GAMT)

- June 2017 – MetQIC meeting to review GAMT deficiency with condition readiness tool

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<th>Condition Readiness Criteria for Addition to Michigan’s Newborn Screening Panel</th>
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<td>Required criteria: all 7 are met AND supporting factors A-D meet the below criteria</td>
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<td>A. Condition: ≥80% criteria met (at least 4)</td>
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- Detailed notes from MetQIC discussion
- Caveats and comments from discussion listed in meeting minutes
- Developmental result

Unanimous yes vote by all voting members in attendance to forward their findings to TAC
Conclusions

• Criteria were viewed as useful by staff and advisory committees
• Provides a standardized and systematic structure for condition review
• Clarifies factors that need to be considered prior to adding disorders
• Reinforces the importance of a systematic process to evaluate conditions
• Helps direct discussions with professionals
Acknowledgments

• Co-authors
  o Mary Kleyn, Manager, Newborn Screening Follow-up Program
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  o Dr. Robert Conway, CHMMC Clinic Director
  o Dr. Mary Seeterlin, NBS Laboratory Scientist
  o Newborn Screening Committees: MetQIC, TAC and QAAC

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