Progress Toward Stakeholder Support of Universal Newborn CMV Screening: State and National Experiences

September 25, 2018

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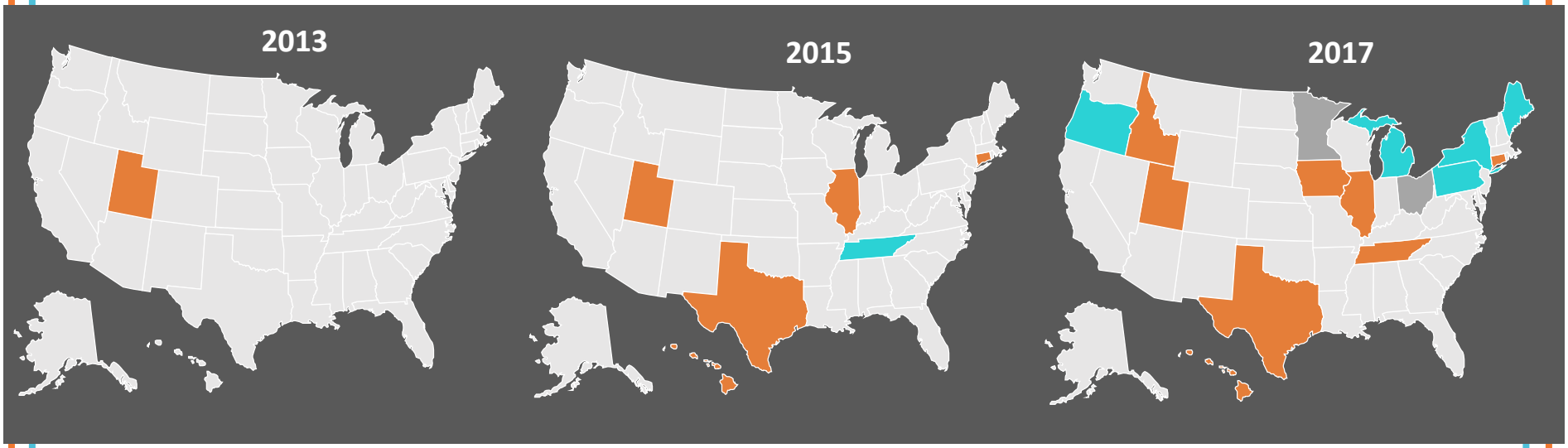

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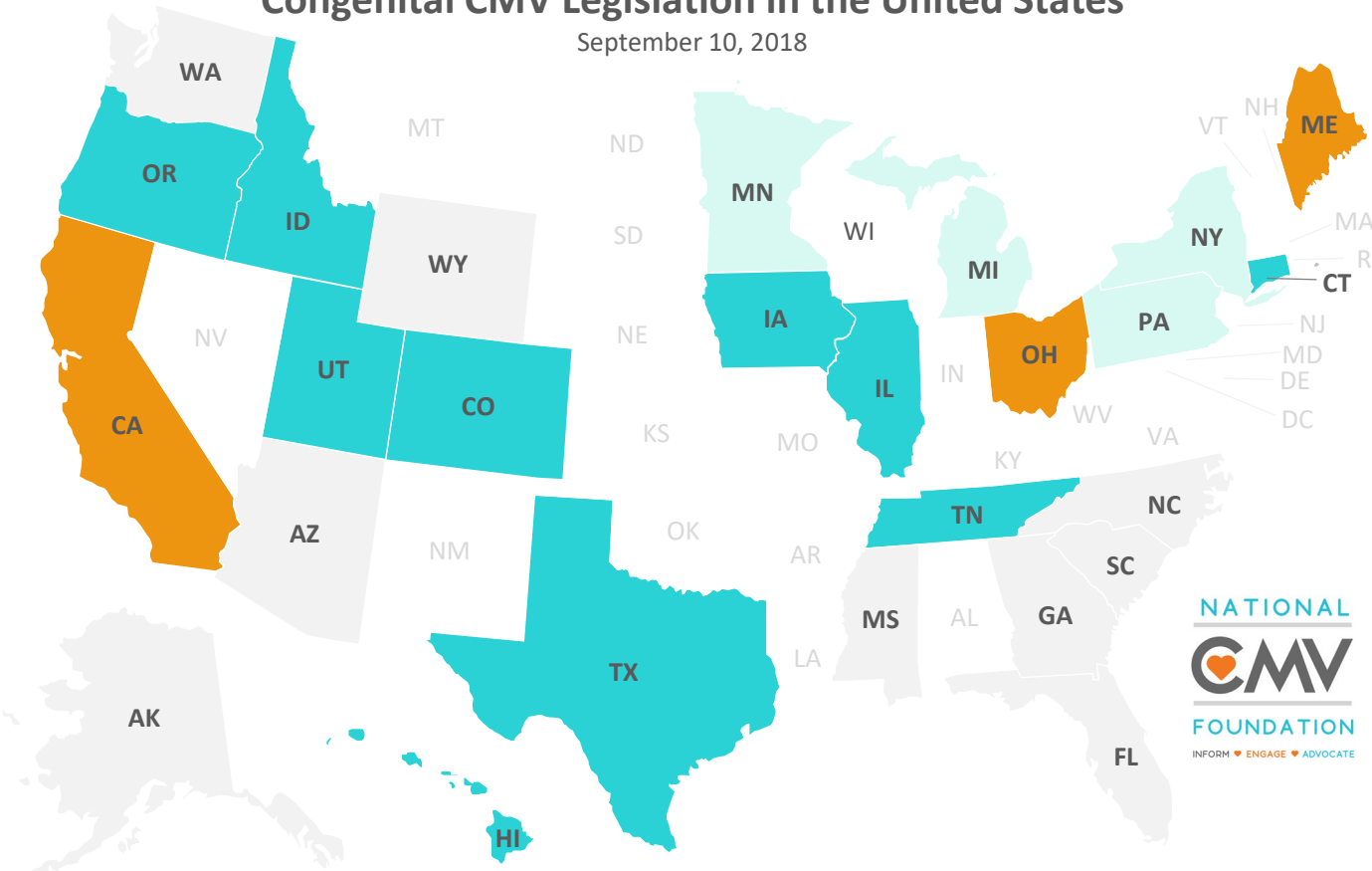
Congenital CMV Legislation in the United States

September 10, 2018



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■ Other Law Enacted ■ Screening or Education Law Enacted ■ Law Proposed ■ Law Drafted ■ Stakeholder Interest in Legislation

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CA DHCS Opposition - 2018

Dear Senator Portantino:

ASSEMBLY BILL 1801 (AS AMENDED JUNE 7, 2018) - OPPOSE

The Department of Health Care Services (DHCS) must inform you of its opposition to Assembly Bill (AB) 1801.

AB 1801 would require DHCS to establish a Commission on Cytomegalovirus (CMV) Public Education and Testing (Commission) in order to examine data and develop recommendations regarding congenital CMV. AB 1801 would require the Commission to submit a report to the Legislature no later than December 31, 2019, and an additional report to the Legislature on or before December 31, 2022, that includes its findings.

Although DHCS supports raising awareness around CMV transmission, DHCS must oppose AB 1801 because it would undermine the California Department of Public Health's universal newborn screening program, which follows the guidance of the federal Recommended Uniform Screening Panel. This is California's existing process and program for which universal testing for specified diseases in newborns occurs.

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CA RUSP Legislation - 2017

- 2010 - Severe combined immunodeficiency and critical congenital heart disease adopted by the RUSP
- Average of 3-4 years to adopt these conditions into state newborn screening panels

- Prior to CA SB 1095 (Pan), California had to introduce new legislation with each RUSP addition
- "This bill would require the department to expand statewide screening of newborns to include screening for any disease that is detectable in blood samples as soon as practicable, but **no later than 2 years after the disease is adopted by the federal Recommended Uniform Screening Panel (RUSP),** or enrollment of this bill, whichever is later."

…does **YOUR** state have a barrier to RUSP implementation??

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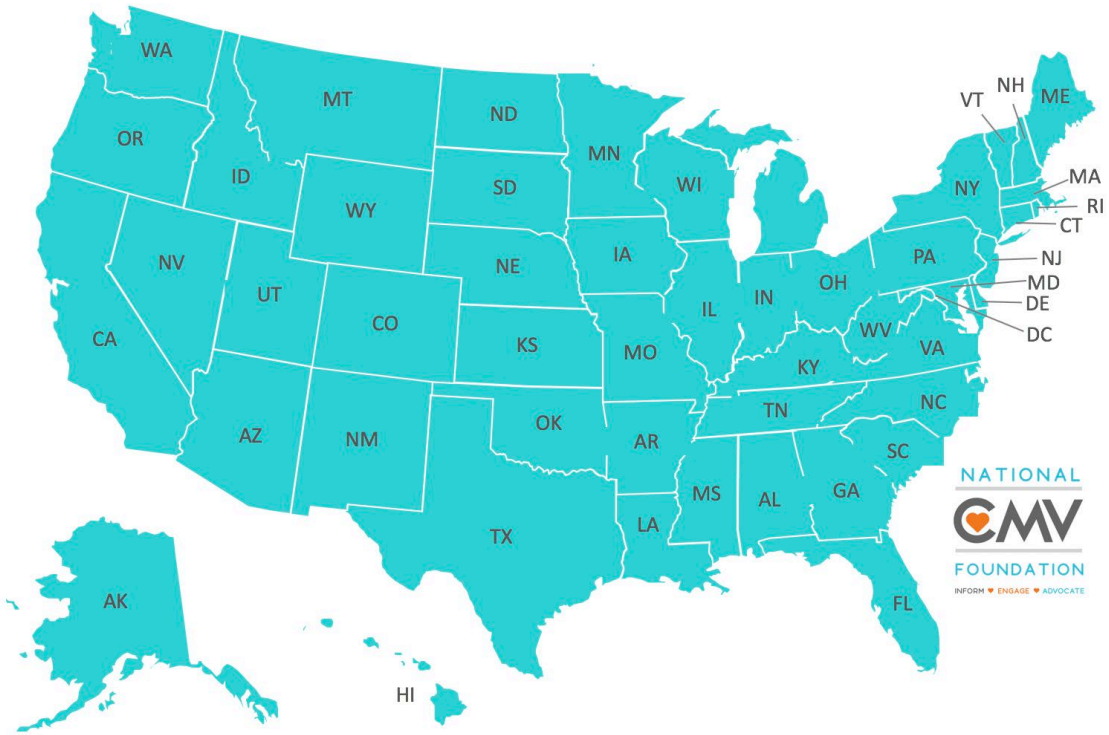

Nomination to the Recommended Universal Screening Panel (RUSP)

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Baylor College of Medicine

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN®

STANLEY A PLOTKIN, MD
Consultant in Vaccinology

Pfizer

Texas Children's Hospital

MERCK

UAB MEDICINE
PEDIATRICS

Children's of Alabama

NATIONWIDE CHILDREN'S
When your child needs a hospital, everything matters.℠

THE OHIO STATE UNIVERSITY
COLLEGE OF MEDICINE

UNIVERSITY OF MINNESOTA
Driven to Discover℠

NCHAM
National Center for Hearing Assessment and Management
Utah State University™
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Why the RUSP?
Why now?

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International Consensus - 2015

- Consensus group convened at international CMV conference in Brisbane, Australia in 2015

- "…consideration should be given to universal neonatal cytomegalovirus screening to **enable early detection of congenital cytomegalovirus-infected infants, facilitating early detection and intervention for sensorineural hearing loss and developmental delay** where appropriate (level 2b evidence)."

- Congenital cytomegalovirus infection in pregnancy and the neonate: consensus recommendations for prevention, diagnosis, and therapy. Lancet Infectious Disease 2017. William D Rawlinson, Suresh B Boppana, Karen B Fowler, David W Kimberlin, Tiziana Lazzarotto, Sophie Alain, Kate Daly, Sara Doutré, Laura Gibson, Michelle L Giles, Janelle Greenlee, Stuart T Hamilton, Gail J Harrison, Lisa Hui, Cheryl A Jones, Pamela Palasanthiran, Mark R Schleiss, Antonia W Shand, Wendy J van Zuylen

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International Consensus - 2015

- "The consensus recommendations from the group were that the diagnosis of congenital cytomegalovirus infection in neonates should include **real-time PCR of saliva, urine, or both, as soon as possible after birth** but within the first 3 weeks of life, with **saliva as the preferred sample** (level 2b evidence)."

- Congenital cytomegalovirus infection in pregnancy and the neonate: consensus recommendations for prevention, diagnosis, and therapy. Lancet Infectious Disease 2017. William D Rawlinson, Suresh B Boppana, Karen B Fowler, David W Kimberlin, Tiziana Lazzarotto, Sophie Alain, Kate Daly, Sara Doutré, Laura Gibson, Michelle L Giles, Janelle Greenlee, Stuart T Hamilton, Gail J Harrison, Lisa Hui, Cheryl A Jones, Pamela Palasanthiran, Mark R Schleiss, Antonia W Shand, Wendy J van Zuylen

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Pediatrics - 2017

- "A targeted CMV screening approach does identify the majority of infants with CMV-related SNHL in the newborn period. However, **this method fails to identify a significant number of infants** with CMV-related SNHL during infancy highlighting the need to develop approaches to improve detection of CMV-related hearing loss at birth. **Strategies to identify all infants with cCMV who remain at risk for late onset and progressive hearing losses are needed**."

- A Targeted Approach for Congenital Cytomegalovirus Screening Within Newborn Hearing Screening. Pediatrics Volume 139 , number 2 , February 2017. Karen B. Fowler, DrPH, a Faye P. McCollister, EdD, b Diane L. Sabo, PhD, c Angela G. Shoup, PhD, d Kris E. Owen, AuD, d Julie L. Woodruff, AuD, e Edith Cox, AuD, f Lisa S. Mohamed, AuD, f Daniel I. Choo, MD, g Suresh B. Boppana, MD, h on behalf of the CHIMES Study

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Maine Study Group - 2017

- Recommendation #3: “Require a targeted screening approach with the long-term goal of universal screening - The workgroup recommends that providers be required to screen newborn babies for cCMV at the time of birth. **The group supports the long-term goal of universal saliva/urine screening because it is currently thought to be the most reliable means of early detection.** However, given the practicality and potential cost of universal saliva/urine screening, the group urges the legislature to require targeted screening for newborn babies after two failed hearing tests, or the presence of other risk factors, before hospital discharge.”

- Maine CDC CMV Report. Submitted to the Joint Standing Committee on Health and Human Services. 2017.

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AAP Newsletter - 2014

Volume 17, Issue 1 THE SECTION ON INFECTIOUS DISEASES Page 13

Beware Well-Intended Cytomegalovirus Legislation

William M. McDonnell, MD, JD
Chair, AAP Committee on Medical Liability and Risk Management

New Cytomegalovirus Law

There is an oft-cited aphorism that "the road to hell is paved with good intentions," which comes to mind after recent legislation regarding congenital cytomegalovirus syndrome. Traditionally, regulation of the practice of medicine in the United States has been left to members of the profession itself. In the dynamic field of medicine, clinicians, researchers, and other scientists are best-positioned to determine what medical practice standards are appropriate, and when those standards should change in light of evolving scientific knowledge. When clinicians fail to provide care consistent with these practice standards, medical malpractice liability may be imposed.

A recent law enacted by the Utah Legislature (H.B. 81, now codified at U.C.A. §26-10-10) took a different approach, and if duplicated in other states, may threaten physicians' abilities to practice medicine in a manner consistent with the best available science.

CMV Laws in Other States

Discussion about the CMV law has now extended to other states. For example, similar bills are pending in Illinois and Connecticut. There is no question that children should be protected by good science and good clinical care. However, delegating medical practice standards to legislatures, no matter how well-intentioned, presents significant problems. Not only must pediatricians be aware of the legal restrictions on their practices, but they should also proactively lend their voices and their expertise to legislative debates before these laws are enacted.

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AAP Editorial - 2015

- "During the 2015 state legislative sessions, lawmakers again delved into the contentious issue of cytomegalovirus (CMV) screening for newborns who fail an infant hearing test. In their response to the proposed legislation, AAP chapters sought to balance the concerns of families about infant hearing loss and the need to ensure **evidence-based practices** — which **do not support screening of newborns for CMV who fail an infant hearing test but are otherwise asymptomatic** — are reflected in state law."

- Chapters Views and News: Chapters respond to state bills seeking mandatory CMV screening from the AAP Department of Practice and Division of Quality. 2015.

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AAP Quotes - 2015

- *"With no proof of benefit and with the potential for harm from antiviral treatment,* ***we should be very careful in considering universal treatment of these babies.*** *These kinds of laws may indirectly result in or drive such treatment, though, because we all know that when a baby is identified through the law's mandated screening following a failed hearing test, then the parents and doctor often will feel they must 'do something.' In doing so, we could be hurting the very children we are trying to help."*

- *"I think it's important to ask legislators considering similar kinds of legislative mandates on clinical practice,* ***'What is the scientific evidence that supports this mandate?' …codifying diagnosis and treatment modalities into state law is fraught with peril*** *and may ultimately lead to worse outcomes for kids that need our help the most."*

- Chapters Views and News: Chapters respond to state bills seeking mandatory CMV screening from the AAP Department of Practice and Division of Quality. 2015.

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AAP Position - 2017

- "According to current AAP Red Book recommendations, antiviral therapy should be limited to patients with symptomatic congenital CMV disease within the first month of life. Infants with asymptomatic congenital CMV infection should not receive antiviral treatment, as antivirals for the treatment of CMV can be potentially toxic. For this reason, the AAP does not support state laws mandating targeted screening for CMV infection as defined above. The AAP **encourages continued assessment of the potential benefits and risks of universal screening of infants for CMV, as this approach would better identify all babies who are at risk of CMV-associated hearing loss.** Mandatory universal screening for CMV infections is not ready for implementation through state laws, but is being debated actively among state legislators and advocacy groups at this time."

- State Advocacy Engagement on Congenital Cytomegalovirus (CMV) Detection Guidance for AAP Chapters. 2017.

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RUSP Nomination

- https://www.hrsa.gov/advisory-committees/heritable-disorders/rusp/nominate.html
- The Committee encourages individuals and organizations to form multi-disciplinary teams to submit nominations for conditions to be considered for inclusion on the RUSP. Teams should include researchers and/or clinicians with expertise on the condition being nominated, advocacy and/or professional organizations with knowledge of issues relevant to newborn screening, and interested consumers/individuals.

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RUSP Nomination

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.

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ACHDNC Form for Nomination of a Condition for Inclusion in the Uniform Screening Panel	
DATE	
NAME OF NOMINATOR AND ORGANIZATION (include professional degrees)	INDICATE AFFILIATION (i.e., Health Professional, Subject Matter Expert, Researcher, Clinician, Advocate, etc.)
CO-SPONSORING ORGANIZATIONS (include professional degrees)	INDICATE AFFILIATION (i.e., Health Professional, Subject Matter Expert, Researcher, Clinician, Advocate, etc.)

Note: Please reference each statement/answer with the corresponding reference number listed in Section III – Key References.

SECTION I – CONDITION INFORMATION AND TREATMENT

SECTION I, PART A

CONDITION	STATEMENT
Nominated Condition	
Type of Disorder	
Screening Method	
Gene	
Locus	Include ClinVar link if applicable.
OMIM or other names for condition	Include Genetics Home Reference link if applicable.
Case Definition	
Incidence	Determined by what method(s): pilot screening or clinical identification?
Timing of Clinical Onset	Relevance of the timing of newborn screening to onset of clinical manifestations.
Severity of Disease	Morbidity, disability, mortality, spectrum of severity.

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SECTION I, PART B

TREATMENT	STATEMENT
Modality	Drug(s), diet, replacement therapy, transplant, other. Include information re regulatory status of treatment.
Urgency	How soon after birth must treatment be initiated to be effective?
Efficacy (Benefits)	Extent of prevention of mortality, morbidity, disability. Treatment limitations, such as difficulty with acceptance or adherence.
Availability	Limits of availability?
Potential Harms of Treatment	Potential medical or other ill effects from treatment

SECTION II – EVIDENCE-BASED INFORMATION

For a nominated condition to be considered there are 3 core requirements:

1. Validation of the laboratory test (see Section II, Part A)
2. Widely available confirmatory testing with a sensitive and specific diagnostic test (see Section II, Part B)
3. A prospective population based pilot study (see Section II, Part C)

SECTION II, PART A

TEST	STATEMENT
Screening test(s) to be used	Description of the high volume method, instrumentation and if available as part of multi-analyte platform.
Modality of Screening	(Dried blood spot, physical or physiologic assessment, other)
Does the screening algorithm include a second tier test? If so, what type of test and availability?	(Dried blood spot, physical or physiologic assessment, other)

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TEST	STATEMENT
Clinical Validation	Location, duration, size, preliminary results of past/ongoing pilot study for clinical validation, positive predictive value, false positive rate, analytical specificity, sensitivity.
Analytical Validation	Limit of detection/quantitation, detection rate, reportable range of test results, reference range. Include regulatory status of test, information about reference samples and controls required for testing and availability of or potential for external quality assurance system, e.g., QC and PT for both screening and confirmatory tests.
Considerations of Screening and Diagnostic Testing	False positives, carrier detection, invasiveness of method, other.
Potential Secondary Findings	Detection or suggestion of other disorders.

SECTION II, PART B

CONFIRMATORY TESTING	STATEMENT
Clinical and Analytical Validity	Quantitative or qualitative? Include sensitivity, specificity, etc.
Type of test and/or sample matrix (blood, radiology, urine, tissue sample, biophysical test)	
Is test FDA cleared/approved	Include availability information, sole source manufacturer, etc.
List all CLIA certified labs offering testing in the US	Link to GeneTests and Genetic Test Reference if applicable.

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SECTION II, PART C

POPULATION-BASED PILOT STUDY	STATEMENT
Location of Prospective Pilot	
Number of Newborns Screened	
Number of Screen Positive Results	Positive by primary test vs. 2nd tier test if applicable.
False Positive Rate; False Negative Rate (if known)	False positive by primary test vs. 2nd tier test if applicable.
Number of Infants Confirmed with Diagnosis	How is diagnosis confirmed [clinical, biochemical, molecular]?

SECTION III – KEY REFERENCES

LIST OF REFERENCES **Limited to 20 references from scientific journals to support statements in Sections I-IV. For sources based on un/non-published data, references may be written statements from clinicians, researchers, and/or investigators.**	
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SUBMISSION CHECK LIST		SUBMIT NOMINATIONS ELECTRONICALLY TO:
☐	Cover letter by Nominator	Catharine Riley, PhD, MPH Email: CRiley@hrsa.gov Genetic Services Branch Division of Services for Children with Special Health Needs Maternal and Child Health Bureau Health Resources and Services Administation 5600 Fishers Lane, Room 18W-68 Rockville, MD 20857
☐	Nomination form	
☐	Conflict of Interest Forms filled out by Nominator and all Co-Sponsoring Organizations	
☐	Copies of publications/articles used as references	
CONTACT INFORMATION FOR NOMINATOR:		

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Hearing

Strong evidence shows that newborn hearing screening leads to earlier identification and treatment of babies with hearing loss. The AAP supports the 1994 statement of the Joint Committee on Infant Hearing, which endorses the goal of universal detection of hearing loss in babies before 3 months of age, with appropriate intervention no later than 6 months of age.[13] Universal detection of infant hearing loss requires universal screening of all infants. Newborn hearing screening is mandated in most states.

No high-quality studies were found on hearing screening for older children or adolescents. In spite of the rising incidence of hearing loss, presumably related to environmental or headphone and earbud acoustic trauma, hearing screening questions used in the primary care setting do not identify adolescents at risk of hearing loss. For these reasons, universal hearing screening is recommended once during the Early Adolescence, the Middle Adolescence, and the Late Adolescence Visits. Screening in these age groups may be enhanced by including 6,000 and 8,000 Hz high frequencies in the screening audiogram. In addition to screening, counseling on the risk of hearing loss caused by environmental exposures may be considered.

Hearing: Universal	
Bright Futures Visits	**Newborn, First Week; 1, 2 Month**
Citation	American Academy of Pediatrics Task Force on Newborn and Infant Hearing. Newborn and infant hearing loss: detection and intervention. *Pediatrics.* 1999;103(2):527-530
Bright Futures Visits	**4, 5, 6, 8, 10 Year**
Citation	Harlor AD Jr, Bower C. Hearing assessment in infants and children: recommendations beyond neonatal screening. *Pediatrics.* 2009;124(4):1252-1263
Bright Futures Visits	**Once During the Early, the Middle, and the Late Adolescence Visits**
Citation	Sekhar DL, Zalewski TR, Beiler JS, et al. The sensitivity of adolescent hearing screens significantly improves by adding high frequencies. *J Adolesc Health.* 2016;59(3):362-364

Hearing: Selective	
Bright Futures Visits	**4, 6, 9, 12, 15, 18 Month; 2, 2½ Year**
Risk assessment	• Caregiver concern[a] regarding hearing, speech, language or developmental delay. • Family history[a] of permanent childhood hearing loss. • Neonatal intensive care of >5 days or any of the following regardless of length of stay: extracorporeal membrane oxygenation, assisted ventilation, exposure to ototoxic medications (gentamycin and tobramycin) or loop diuretics (furosemide/Lasix), and hyperbilirubinemia that requires exchange transfusion. • In utero infections such as cytomegalovirus,[a] herpes, rubella, syphilis, and toxoplasmosis. • Craniofacial anomalies, including those involving the pinna, ear canal, ear tags, ear pits, and temporal bone anomalies.

continued

How can you help the RUSP?

- Watch National CMV Foundation for requests for calls and letters of support.

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