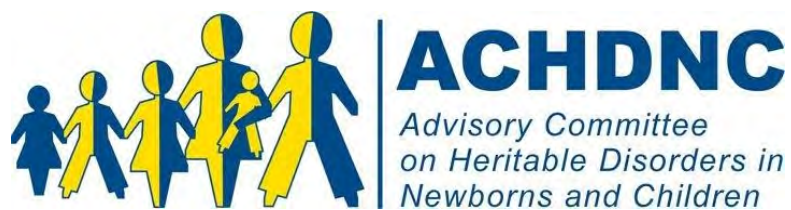


**THE ADVISORY COMMITTEE ON HERITABLE  
DISORDERS IN NEWBORNS AND CHILDREN**

**REPORT TO CONGRESS (2019)**



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# 1. EXECUTIVE SUMMARY

The Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC or Committee) was established to advise and provide evidence-based recommendations to the Secretary of the United States (U.S.) Department of Health and Human Services (HHS) regarding the most appropriate application of universal newborn screening tests, technologies, policies, guidelines, and standards. The Committee also makes systematic evidence-based and peer-reviewed recommendations regarding conditions for inclusion on the Recommended Uniform Screening Panel (RUSP): a list of conditions recommended by the Secretary of HHS, for states to screen for at birth as part of their state universal newborn screening programs. The Committee's advice and recommendations are intended for use by the Secretary to develop priorities and policies that enhance states' ability to reduce morbidity and mortality in newborns and children who have or are at risk of developing genetic disorders. Such disorders may be present at birth and can cause irreparable harm—including disability or even death—if left undetected. Newborn and childhood screening saves lives and improves quality of life throughout the life span. The Health Resources and Services Administration (HRSA) provides coordination, management, and operational services to the Committee.

In 2019, the Committee focused its efforts on analyzing its condition review process for evaluating conditions nominated to the RUSP, with the overarching goal of strengthening the Committee's decision-making processes. In addition, during 2019, the Committee reviewed and discussed:

- Condition Nomination and Review Process: Nomination; systematic evidence-based review; decision modeling and decision making; cost and public health system impact (PHSI) assessments; stakeholder values; and review of current conditions on the RUSP;
- Implementation of RUSP Conditions: Evaluation of screening implementation and outcomes after addition to the RUSP;
- Expansion of Interoperability: Database connection; matching vital records with specimens to provide a better understanding of screenings; identification of infants that did not receive a screen; and use of electronic orders to support quality and timeliness; and
- Rare Diseases: Registries and their purposes; centralized data collection; creating opportunities for collaboration; and data ownership.

## 2. LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

<b>Term</b>	<b>Definition</b>
<b>ACHDNC</b>	Advisory Committee on Heritable Disorders in Newborns and Children. Also referred to as the Committee.
<b>APHL</b>	Association of Public Health Laboratories
<b>CAH</b>	Congenital Adrenal Hyperplasia
<b>CCHD</b>	Critical Congenital Heart Disease
<b>CDC</b>	Centers for Disease Control and Prevention
<b>CF</b>	Cystic Fibrosis
<b>CMV</b>	Cytomegalovirus
<b>FDA</b>	Food and Drug Administration
<b>GRADE</b>	Grading of Recommendations, Assessment, Development and Evaluation
<b>HCY</b>	Homocystinuria
<b>Heritable disorders</b>	A group of genetically inherited conditions present at birth that, undetected, can cause intellectual/physical disabilities and life-threatening illnesses
<b>HHS</b>	Department of Health and Human Services
<b>HRSA</b>	Health Resources and Services Administration
<b>MPS I</b>	Mucopolysaccharidosis I
<b>NBS</b>	Newborn screening, or the practice of testing babies for disorders and conditions that can hinder their normal development, enabling early detection/treatment and preventing intellectual/physical disabilities and life-threatening illnesses
<b>NewSTEPS</b>	Newborn Screening Technical Assistance and Evaluation Program
<b>NIH</b>	National Institutes of Health
<b>NORD</b>	National Organization for Rare Diseases
<b>ORDR</b>	Office of Rare Diseases Research
<b>PHSI</b>	Public Health System Impact
<b>RUSP</b>	Recommended Uniform Screening Panel. Standard guideline for the newborn screening of genetic conditions, consisting of a list of conditions referred to as a screening panel. This panel provides guidance to the states regarding the latest evidence-based medical recommendations for newborn screening. It includes all conditions approved by the Secretary.
<b>SCID</b>	Severe Combined Immunodeficiency
<b>US</b>	United States
<b>X-ALD</b>	X-linked adrenoleukodystrophy

### **3. REPORT**

The Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC or Committee) was formed to advise the Secretary of the United States (U.S.) Department of Health and Human Services regarding the best applications of newborn screening tests, technologies, policies, guidelines, and standards ([ACHDNC 2018](#); [Appendix A](#)). As part of its mission, the Committee provides the following to the Secretary:

- Recommendations and advice regarding grants and projects funded, awarded, or authorized for the screening of genetic disorders in newborns and children
- Technical information required to develop policies and priorities for the Heritable Disorders Program meant to enhance the screening, counseling, and health care services provided at the state and local levels for newborns and children who either have or are at risk for genetic disorders
- Advice, recommendations, and information designed to enhance, expand, or improve the Secretary's ability to reduce mortality and morbidity from genetic disorders in newborns and children

The purpose of this report is to summarize the Committee's activities for the 2019 calendar year to fulfill the legislative requirement for the submission of an annual report to Congress, the Secretary, the Interagency Coordinating Committee on Newborn and Child Screening, and state health departments ([US Code 2014](#)).

The discussion of the Committee's activities in this report is subdivided into sections aligned with the Committee's legislatively mandated duties. For ease of reference, the specific legislation relating to each activity is presented alongside the activity descriptions in the subsections that follow.

#### **3.1 Advice, Technical Information, and Systematic Evidence-Based and Peer-Reviewed Recommendations**

The Advisory Committee shall

- (1) provide advice and recommendations to the Secretary concerning grants and projects awarded or funded under section 300b-8 of this title
- (2) provide technical information to the Secretary for the development of policies and priorities for the administration of grants under section 300b-8 of this title
- (3) make systematic evidence-based and peer-reviewed recommendations that include the heritable disorders that have the potential to significantly impact public health for which all newborns should be screened, including secondary conditions that may be identified as a result of the laboratory methods used for screening

##### **3.1.1 Nominated and Recommended Conditions**

*No recommendations in 2019*

### **3.1.2 RUSP Condition Nomination and Evidence Review Process**

The Committee heard a presentation on the systematic evidence-based process used to inform the Committee about conditions nominated for addition to the RUSP. The presentation included an overview of the decision-making process, population-level decision modeling, the Public Health System Impact (PHSI) Assessment, and cost analysis.

#### **Population-Level Decision Modeling**

To ensure sufficient evidence to move nominated conditions forward, the Committee evaluated additional methodologies for incorporation into the evidence review process. This evaluation process prompted the decision to incorporate a systematic approach to decision-making under conditions of uncertainty known as decision analytic modeling (also referred to as decision modeling or simulation modeling). Because conditions nominated for the RUSP have often had a lower evidence base at the time of nomination, the Committee discussed the criteria it would use to determine whether the evidence available is sufficient to conduct modeling.

#### **Public Health System Impact Assessment**

The purpose of the Public Health System Impact (PHSI) Assessment is to inform the Committee, stakeholders, and advocacy groups about implementation barriers that states face when adding new conditions as well as describing the overall feasibility and costs of adding a new condition. The PHSI data collection process includes: 1) gathering all the available information from state newborn screening programs for a given condition; 2) performing an in-depth review of early adopters' processes; and 3) anonymously disseminating the information gathered in the analysis to every state newborn screening program. A new resource to support this process is the Newborn Screening Technical Assistance and Evaluation Program (NewSTEPs) Readiness Tool, which captures information about states' overall readiness to expand newborn screening. The goal of this tool is to understand the challenges and opportunities that state newborn screening programs face when adding a new conditions to their state screening panel.

#### **Cost Assessments**

One approach to cost assessment in the context of newborn screening is asking states that have started, or are about to start, screening a nominated condition to calculate real or projected costs for implementing the new condition; this information is then analyzed with a focus on the direct costs of screening and confirmatory testing. Using projected costs presents challenges to generalizing and standardizing estimates across states. Potential solutions include creating a consistent cost assessment tool; recommending that pilot studies funded by HHS report costs using common data elements; collecting all data from screening programs; and analyzing those data to create a cost function that varies based on annual number of births in the state, number of screenings per infant, and the number of tests by screening laboratories.

#### **Stakeholder Values in Newborn Screening Decision-Making**

The Committee heard about the assessment of stakeholder values in the evidence review and decision-making processes. Factors to consider include:

1. Competing options include adding a condition to the RUSP, testing for a particular condition, and deciding to not include the condition.

2. Characterization of the various outcomes of newborn screenings. For example: the immediate number of positives or negatives and how many turn out to be false positives, the individual level of health impact, and the impact on newborn screening systems.
3. Uncertainty stemming from ranges of accuracy within screenings and gaps within pilot studies. Significant challenges often arise due to the fast pace of advances in screening and treatment, paired with insufficient evidence on their benefits or harms.

#### Examples of Methods for Assessing Stakeholder Values:

- Grading of Recommendations, Assessment, Development and Evaluation (GRADE) guidelines focus on patients' perspectives and individual clinical decision-making as opposed to public health recommendations. GRADE is a systematic approach to examining the magnitude of estimates on important health outcomes and the confidence in those estimates. It also considers estimates of typical values and preferences and the confidence in those estimates, the variability of values and preferences, and resource use.
- A Quality-Adjusted Life Year (equated to living one year in perfect health and calculated as a function of time and utility) is a standardized measurement of health outcomes that can facilitate comparisons across health conditions and populations. To accurately apply this model, a full understanding of the health condition, awareness of the perspective, and consideration of any contextual factors are needed.
- The goal of a Citizen's Jury is to reach a diverse group of individuals to ensure a holistic assessment of values and preferences on a particular public health issue. For this method to be effective, it would require the Committee to educate the Citizens' Jury on all of the available information on a nominated condition. If done well, a Citizen's Jury can result in a complex assessment of diverse stakeholder values and preferences that can be communicated in lay terms to the public.

### **3.1.3 ACHDNC's Evaluation of the Condition Nomination and Evidence Review Process**

The ACHDNC continued its evaluation of the Condition Nomination and Evidence Review Process, with the goal of better synthesizing the evidence used to make recommendations for additions to the RUSP. The Committee formed an expert advisory panel that included subject matter experts from state newborn screening programs and the field of evidence-based decision-making from the United States and Canada that provided information on ways to strengthen the Committee's review process.

The Committee examined the potential application of GRADE to rare diseases; assessment of published and unpublished evidence; a "scoping" review of available literature before full evidence review; controlled data collection; data resources, such as registries; panels focusing on conditions covering multiple disorders; long-term follow-up methods; and the need for defined, consistent, and harmonized terminology. Identifying critical outcomes would help the Committee to evaluate the strength of the evidence, which in turn would help to standardize the decision-making approach for additions to the RUSP.



The Committee also discussed strategies related to the Public Health System Impact Assessment; determination of various stakeholder values; assessment of the decision matrix; reconsideration of conditions already on the RUSP; the nominations process; weights of survey data during the decision-making process; and internal validity and generalizability across states of cost measurement, including follow-up costs such as quality control, contractual issues, support levels from NIH or sponsors, and staff and monitoring. Limitations concerning hypothetical survey questions, the OMB survey approval process and funding pose challenges to addressing potential issues.

Refer to [Section 3.5.9](#) for cost and effectiveness of newborn screening.

Refer to [Section 3.5.10](#) for causes, public health impacts, and risk of newborn screening.

Refer to [Section 3.4.1](#) and [Section 3.5.6](#) for information on Newborn Screening Pilot Studies.

## **3.2 Technical Assistance and Nomination Review**

The Advisory Committee shall

- (4) provide technical assistance, as appropriate, to individuals and organizations regarding the submission of nominations to the uniform screening panel, including prior to the submission of such nominations
- (5) take appropriate steps, at its discretion, to prepare for the review of nominations prior to their submission, including for conditions for which a screening method has been validated but other nomination criteria are not yet met, in order to facilitate timely action by the Advisory Committee once such submission has been received by the Committee

In 2019, the Committee received a nomination for Congenital Cytomegalovirus (CMV). The Committee Chair requested the nominators provide required information not found in the nomination package and awaits submission of a complete nomination package.

The Committee provided ongoing technical assistance by responding to questions from groups regarding the RUSP nomination process and about the type of data and information needed for nominating a condition.

## **3.3 Decision Matrix**

The Advisory Committee shall

- (6) develop a model decision-matrix for newborn screening expansion, including an evaluation of the potential public health impact, including the cost of such expansion, and periodically update the recommended uniform screening panel, as appropriate, based on such decision matrix

Refer to [Section 3.1.2](#) for information on the RUSP Condition Nomination and Evidence Review Process, including potential public health impact, population-level decision modeling, and cost assessment. The Committee's review of the evidence review process used to evaluate conditions for the RUSP will inform the revision of the decision matrix.

## 3.4 State Capacity to Screen

The Advisory Committee shall

(7) consider ways to ensure that all States attain the capacity to screen for the conditions described in paragraph (3), and include in such consideration the results of grant funding under section 300b-8 of this title

### 3.4.1 Analysis: Impact of Adding Conditions to the RUSP

The Committee performed a retrospective analysis of the process of implementing screening for five conditions added to the RUSP from 2010 through 2017—Severe Combined Immunodeficiency (SCID), Critical Congenital Heart Disease (CCHD), Pompe Disease, Mucopolysaccharidosis I (MPS I) and X-linked adrenoleukodystrophy (X-ALD)— and the impact on state newborn screening programs and the newborn screening system. This review covered state implementation, public health implications and clinical outcomes, and the system impacts of adding conditions to the RUSP. This provided an opportunity to develop standard review methods to address screening implementation and outcomes after a condition is added to the RUSP. It concluded that longitudinal data and a clear and standard definition of “pursuing implementation” are needed. (Pursuing implementation involves both enabling state-level legislation and public- and private-sector proponents advocating for state-mandated screening.) The Committee also noted the barriers newborn screening programs face in adopting and implementing new screening methods.

Challenges of implementing screenings have included: different screening targets; high retest rates for preterm infants compared to full-term infants; variation in incidence by race/ethnicity; variability in approach to requiring the screening; decentralization in hospitals, birthing centers, and homes; variability in reporting requirements and screening algorithms; special settings, such as high altitudes and Neonatal Intensive Care Units; labor- and time-intensive commercial testing kits; difficulty in obtaining reference testing samples; pseudodeficiency; diagnostic uncertainty; false positives and negatives; and late-onset conditions. The Committee hopes that its upcoming newborn screening interviews yield more specific knowledge about the challenges and what support it can provide to states.

Refer to [Section 3.5.2](#) for information on common challenges to new disorder implementation.

Implementation has been facilitated by: collaborations and partnerships established among the Federal Government, states, and nonprofit organizations; national technical assistance activities; newborn screening pilots; relatively straightforward commercially available kits that ensured uniformity; development of educational material, use of birth defect registries, telemedicine; reduction of false positives by use of second-tier biochemical tests and post-analytical tools; pilot studies to determine cut-offs; registry databases with mutations and expected clinical characters; adjustments to the follow-up algorithm; potential for multiplexing with other diseases, and registry databases. Common facilitators are peer research networks; pilot and/or implementation funding; working groups for newborn screening; clinical follow-up and management, particularly for disorders with later-onset forms; next-generation sequencing for second-tier testing; and common legislative approaches.

Average implementation time for state programs to begin screening for new conditions ranged from less than one year to 2.6 years.

Future steps in the review process are interviewing newborn screening programs at the state level regarding issues of implementation specifically looking at early adopters and late adopters to understand barriers and facilitators to implementing screening for new conditions and the impact on public health programs. It is important to understand the challenges and opportunities that state newborn screening programs face as well as the length of time a state may take to add new conditions.

### **New Disorders Readiness Tool**

The Committee received an update on NewSTEPs work to support states in implementing three disorders added to the RUSP: Pompe, MPS-1, and X-ALD. Through HRSA funding, NewSTEPs developed and administered its New Disorders Readiness Tool to track newborn screening programs' overall readiness for screening for new disorders. Many of the states that are leading on implementation efforts did not provide data; therefore, some lessons learned regarding implementation facilitation are limited.

### **3.4.2 Interoperability in Newborn Screening**

The Committee heard a presentation from representatives of two state newborn screening programs who shared their experiences implementing electronic test ordering and automatic daily electronic data transfers between vital records and newborn screening. States experience differences between data exchange, data interfacing, and data interoperability, and some aspects of newborn screening could benefit from the use of interoperability through databases. Process examples from Minnesota and Texas were shared. Program efficiencies and inefficiencies, barriers, and variation were discussed. State-level program work to facilitate data interoperability has the potential to improve individual-level outcomes and impact the population level by informing an understanding of disease by shaping the clinical guidelines and affecting public policy.

Refer to [Section 3.5.6](#) for information on linking data resources.

## **3.5 Recommendations, Advice, or Information (Morbidity and Mortality)**

The Advisory Committee shall

- (7) provide such recommendations, advice or information as may be necessary to enhance, expand or improve the ability of the Secretary to reduce the mortality or morbidity from heritable disorders, which may include recommendations, advice, or information dealing with the following

The Committee provides the Secretary with recommendations, advice, and information on a broad range of topics relating to newborn screening in order to reduce newborn and child mortality or morbidity from genetic disorders. The subsections below describe activities falling under this charge that were undertaken or overseen by the Committee in the 2019 calendar year.

### **3.5.1 Follow-Up Activities**

(A) follow-up activities, including those necessary to achieve best practices in rapid diagnosis and appropriate treatment in the short-term, and those that ascertain long-term case management outcomes and appropriate access to related services

In 2019, under the Committee’s charge to provide the Secretary with guidance and information on health care services for newborns and children who have or are at risk for heritable and other life-threatening disorders, the Committee developed and submitted to the Secretary *Medical Foods for Inborn Errors of Metabolism: The Critical Need to Improve Patient Access*. This white paper highlights the urgent need to address the discrepancies in medical insurance medical food reimbursement that exist from state to state in the United States (U.S.). Thomas J. Engels, Acting Administrator for HRSA, thanked the Committee “for providing an informative summary of the current landscape of medical foods in the U.S. and outlining the challenges faced by individuals living with inborn errors of metabolism (IEM)”.

The paper is included in Appendix C of this report.

### **3.5.2 Implementation, Monitoring, and Evaluation**

(B) implementation, monitoring, and evaluation of newborn screening activities, including diagnosis, screening, follow-up, and treatment activities

The Committee learned that common challenges to new disorder implementation are hiring and training personnel, delays in procurement and installation of equipment, updating laboratory information management systems, lack of shared genomic variant databases, and developing follow-up programs and clinical management plans for infants with late-onset or unknown disease risk. The Committee hopes that upcoming newborn screening interviews yield more specific knowledge about the challenges and what support it can provide to states.

### **3.5.3 Diagnostic and Other Technology**

(C) diagnostic and other technology used in screening

In 2019, the Committee supported the development of the following diagnostic and other technology:

#### **New Disorders Readiness Tool**

Refer to [Section 3.4.1](#) for information on the New Disorders Readiness Tool.

#### **Longitudinal Pediatric Data Resource Tool**

The Committee heard a presentation on screening methodologies for congenital adrenal hyperplasia (CAH) and homocystinuria (HCY). The Centers for Disease Control and Prevention’s (CDC) Newborn Screening and Molecular Biology Branch (NSMBB) is currently developing four different approaches to enhance detection of HCY and CAH in newborns. One of the goals of this initiative is to provide vendors with testing method options. NSMBB also

provides financial and technical support to state newborn screening programs to enhance existing screening methods and implement screening methods for conditions added to the RUSP.

### **3.5.4 Availability and Report of Testing**

(D) the availability and reporting of testing for conditions for which there is no existing treatment, including information on cost and incidence

The Committee did not undertake activities relating to the availability or reporting of testing for conditions for which there is no existing treatment during the 2019 calendar year.

### **3.5.5 Conditions Not Included in the RUSP**

(E) conditions not included in the recommended uniform screening panel that are treatable with Food and Drug Administration-approved products or other safe and effective treatments, as determined by scientific evidence and peer review

The Committee did not undertake activities relating to conditions not included on the RUSP during the 2019 calendar year.

### **3.5.6 Minimum Standards and Related Policies and Procedures**

(F) minimum standards and related policies and procedures used by State newborn screening programs, such as language and terminology used by State newborn screening programs to include standardization of case definitions and names of disorders for which newborn screening tests are performed

The Committee is working on resources that may help states with risk assessment, terminology, interpretation of test results, and communicating test results; in the case of normal (within-range) results, it is understanding the limitations of screening results; in the case of abnormal (out-of-range) results, it is communicating the importance of diagnostic testing and possible interventions.

### **3.5.7 Quality Assurance, Oversight, and Evaluation**

(G) quality assurance, oversight, and evaluation of State newborn screening programs, including ensuring that tests and technologies used by each State meet established standards for detecting and reporting positive screening results

Refer to [Section 3.5.3](#) for information on the CDC NSMBB's work to enhance detection of HCY and CAH in newborns.

### **3.5.8 Public and Provider Awareness and Education**

(H) public and provider awareness and education

The Committee worked to address opportunities and challenges related to interpretation of newborn screening results, including how to communicate the strengths and limitations of these results.

Refer to [Section 3.5.6](#) for information on the Committee’s work on a report for potential publication in a peer-reviewed journal about interpreting newborn screening results.

The Committee discussed potentially developing an educational slide deck and/or other tools for clinicians to promote provider awareness around fully conveying newborn screening results (positive, abnormal, negative and normal) to families, and to be able to clearly explain the difference between screening and diagnostic testing.

### **3.5.9 Cost and Effectiveness**

(I) the cost and effectiveness of newborn screening and medical evaluation systems and intervention programs conducted by state-based programs

Refer to [Section 3.1.2](#) for a review of RUSP Condition Nomination and Evidence Review Process Cost Assessment.

### **3.5.10 Causes, Public Health Impacts, and Risk Factors**

*Legislative language*

(J) identification of the causes of, public health impacts of, and risk factors for heritable disorders

### **Benefits of Program Interoperability**

The Committee heard a presentation on newborn screening program interoperability that included definitions and comparisons of the terms interoperability and interfacing. Some areas that could benefit from the use of interoperability through databases include specimen tracking, electronic order and reporting (ETOR), hearing and critical congenital heart disease (CCHD) screenings, record and birth defect registries, long-term follow-up, pediatric specialists, and immunizations. These databases can then be accessed by doctors, laboratorians, and other providers in order to obtain the best outcomes for patients. For example, by linking vital records and birth records, states could identify babies that have been missed and provide them with screening. This will provide a more accurate denominator of the babies born within program statistics, analysis for quality improvement, and an understanding of a state’s success rate. Expanded interoperability allows newborn screening to gain efficiency, use staff more effectively, increase testing accuracy, improve patient outcomes, and potentially provide an audit of the newborn screening system.

Refer to [Section 3.5.6](#) for further information on the benefits of program interoperability for newborn screening and [Section 3.4.2](#) to learn about state experiences with this.

Refer to [Section 3.5.11](#) to learn about condition-specific efforts from the Cystic Fibrosis Registry, Primary Immune Deficiency Treatment Consortium Severe Combined Immunodeficiencies Data Collection, and Homocystinuria and Congenital Adrenal Hyperplasia..

## **Resources for Facilitating Rare Disease Research**

The Committee is aware of the need to support research of rare diseases, and one goal is to analyze the value of additional data resources and to identify ways to increase synergy between existing resources that include data, internal and external expertise, and information and technology platforms. Registries are decentralized and tend to be disease or institution specific. Thousands of existing registries focus on different aspects of disease tracking from clinical to health care outcomes; it can be difficult to build broadly useful tools. Multiple entities, including the Society for Inherited Metabolic Disorders (SIMD), some NIH institutes including the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), and the Food and Drug Administration (FDA) are developing or implementing initiatives to coordinate data sharing between existing resources. The Committee will begin to examine individual registries with an emphasis on utilization to conduct long-term follow-up.

Refer to [Section 3.5.11](#) for information on the Office of Rare Diseases Research (ORDR) and the National Organization for Rare Diseases (NORD) IAMRARE Registry.

### **3.5.11 Coordination of Surveillance Activities**

(K) coordination of surveillance activities, including standardized data collection and reporting, harmonization of laboratory definitions for heritable disorders and testing results, and confirmatory testing and verification of positive results, in order to assess and enhance monitoring of newborn diseases

## **National Efforts**

The Committee heard a panel presentation on available, potentially useful data resources for considering conditions nominated to the RUSP and for assessing long-term outcomes.

### Office of Rare Diseases Research (ORDR)

The Office of Rare Diseases Research (ORDR), part of the National Institutes of Health's (NIH) National Center for Advancing Translational Sciences (NCATS), facilitates coordination between multiple stakeholders in the rare diseases community, including scientists, clinicians, patients, and patient groups. The office's online Genetics and Rare Diseases (GARD) Information Center provides comprehensive plain language information on rare diseases to the public. GARD maintains a database containing information on rare and genetic diseases which can include newborn screening information.

ORDR developed a Toolkit for Patient-Focused Therapy Development that includes the new rare diseases registry (RaDaR), designed to provide an easy-to-use educational tool to help new patient advocacy groups adopt quality practices early in the development of disease registries. ORDR has also developed the Rare Diseases Clinical Research Network, which supports the establishment of rare disease clinical research consortia of excellence and has more than 40,000 participants.



*Therapeutics for Rare and Neglected Diseases and Bridging Interventional Development Gaps*  
ORDR also has created the Therapeutics for Rare and Neglected Diseases program and the Bridging Interventional Development Gaps program, both of which work with outside laboratories with disease-area expertise to help move drugs from the laboratory to clinical trial.

#### National Organization for Rare Diseases (NORD)

The National Organization for Rare Diseases (NORD) IAMRARE Registry and its Patient Centered Research Program partners with stakeholders including NIH and FDA, to develop patient natural history studies; provide research grants; publish original research; and support efforts of disease-specific communities to maintain ownership of their data. Through a cooperative agreement with FDA, NORD funds 34 partners that use the organization's registry platform to store data collected from surveys on a variety of rare diseases. NORD also provides training, user and instruction guides, best practices, recommendations and guidelines. NORD and FDA also support patient-listening sessions. NORD's platform tracks participants by assigning them a globally unique identifier (GUID), which allows individuals to be tracked across registries.

#### Best Practices and Models: International Rare Disease Consortium (IRDiRC)

The Committee heard a presentation from the NIH National Center for Advancing Translational Sciences Office of Rare Diseases Research on International Rare Disease Consortium (IRDiRC), which was convened to promote international collaboration and advance rare diseases research worldwide. IRDiRC does not have regulatory authority but provides guidance and recommendations that can be adopted by individual member organizations for their own research programs or priorities. It developed a website of resources for the purposes of encouraging collaboration and leveraging best practices; high-quality, widely applicable models; and, data collected by members and regional authorities. The IRDiRC diagnostic committee has been analyzing cross-border health data and research including registries.

### **Condition-Specific Efforts**

#### Cystic Fibrosis Registry

The Committee heard a presentation from the Cystic Fibrosis (CF) Foundation on its Cystic Fibrosis Registry, an Institutional Review Board (IRB)-approved, patient-consented, observational database. The registry collects data on diagnosis, demographics, treatment, and other types of care; measurements in screening tests; and other conditions and events. Registry data are used to track CF's natural history and the impact of delivered therapies. The CF Smart Report involves vendor collection of patient summary reports and graphical trends on key metrics, and it contains a tool to identify patients who may be eligible for clinical trials. The registry accepts outside requests for data.

#### Primary Immune Deficiency Treatment Consortium (PIDTC): Severe Combined Immunodeficiencies (SCID) Data Collection

Part of the NIH-funded Rare Diseases Clinical Research Network (RDCRN), the PIDTC gathers data on severe combined immunodeficiency (SCID) through a variety of pilot studies as well as a quality of life study. It operates with a central IRB).



## Improving Detection of Newborns at Risk for Homocystinuria and Congenital Adrenal Hyperplasia

Refer to [Section 3.5.3](#) for information on the Centers for Disease Control & Prevention (CDC) Newborn Screening and Molecular Biology Branch, Division of Laboratory Sciences (NSMBB) Longitudinal Pediatric Data Resource Tool.

### **3.5.12 Timeliness of Collection, Delivery, Receipt, and Screening**

(L) the timeliness of collection, delivery, receipt, and screening of specimens to be tested for heritable disorders in newborns in order to ensure rapid diagnosis and follow-up

The Committee began working on a report that assessed current timeliness activities across the U.S. The report will be completed in 2020.

## **4. FUTURE DIRECTIONS**

### **RUSP Evidence Review Process**

The Committee will use what it has learned through its analysis of the evidence review process and update the decision matrix to reflect that new knowledge. It will explore grouping conditions for review purposes and will work to increase the transparency of its process.

### **Roadmap for Moving Forward**

In 2020 and beyond, the Committee expects to:

- Explore testing platforms and methodologies that potentially increase accuracy and precision of results;
- Review the RUSP nomination form to determine potential revision;
- Explore potential applications of whole genome sequencing;
- Explore resources available for rare disease research;
- Explore communication between prenatal and post-natal providers; and
- Analyze challenges that impact the identification and treatment of individuals living with a heritable disorder; these include health care costs, impact of screening, ethical issues, funding for research, tracking long-term outcomes, and time and labor involved in conducting evidence reviews.

## **5. CONCLUSIONS**

This report was prepared to summarize the Committee's activities and outcomes for the 2019 calendar year and to fulfill the legislative requirement for the submission of an annual report on the Committee's activities to Congress, the Secretary, the Interagency Coordinating Committee on Newborn and Child Screening, and state health departments. The mission of the Committee is to reduce morbidity and mortality in newborns and children who have, or who are at risk for, genetic disorders. It accomplishes this mission by providing advice, recommendations, and technical information to the Secretary of the Department of Health and Human Services and helping to develop policies and priorities meant to enhance services at the state and local levels. In addition, it invites public comments as an important way to identify issues and concerns relating to newborn screening.

In 2019, the Committee initiated a review of its evidence review processes. This includes identification of challenges, methodologies, resources, and potential solutions. Through this analysis, it has formed a strong basis for developing a more transparent, thorough, and meaningful process to guide Committee decision-making.

The Committee also continued to serve in a leadership role in the field of newborn screening and genetic disorders by supporting efforts to improve data quality and follow-up and treatment. In 2019, it issued a formal report highlighting the urgent need to address the discrepancies in medical insurance medical food reimbursement.

The coordinated efforts of the Committee and stakeholders—including policymakers, state public health agencies, providers, and the public—will continue to ensure that newborns and children have universal access to high-quality screening, diagnosis, follow-up, disease management and treatment, evaluation, and education. Together, these efforts will support state newborn screening programs and continue to reduce or prevent the potentially devastating consequences of disabilities, life-threatening diseases, or death.

## **6. REFERENCES**

Advisory Committee on Heritable Disorders in Newborns and Children website.  
<https://www.hrsa.gov/advisory-committees/heritable-disorders/index.html>.  
Accessed August 28, 2020.

## **7. APPENDICES**

### **Appendix A. Membership of the Advisory Committee on Heritable Disorders in Newborns and Children**

The Secretary of Health and Human Services (or his/her designee) appoints members to the Committee. The Committee may include up to 15 voting members, including the Chair and federal ex-officio members, as well as up to 15 nonvoting organizational representatives, as the Secretary determines necessary. In addition, a Designated Federal Official (DFO) from the Health Resources and Services Administration’s Maternal and Child Health Bureau serves as the government’s agent for matters related to the management of the Committee’s activities. This individual ensures that all procedures are within applicable statutory, regulatory, and Health and Human Services General Administration Manual directives. The following is a list of the Committee members who served in 2019.

#### **Members**

- **Mei Wang Baker, MD**  
Professor of Pediatrics  
University of Wisconsin School of Medicine and Public Health  
Co-Director, Newborn Screening Laboratory at Wisconsin State Laboratory of Hygiene

- **Susan A. Berry, MD**  
Professor and Director  
Division of Genetics and Metabolism  
Departments of Pediatrics and Genetics, Cell Biology & Development  
University of Minnesota
- **Joseph A. Bocchini, Jr., MD (Chairperson until April 24, 2019)**  
Professor and Chairman  
Department of Pediatrics Louisiana State University
- **Jeffrey P. Brosco, MD, PhD**  
Professor of Clinical Pediatrics  
University of Miami School of Medicine Department of Pediatrics  
Deputy Secretary, Children's Medical Services Florida State Department of Health
- **Kyle Brothers, MD, PhD**  
Endowed Chair of Pediatric Clinical and Translational Research  
Associate Professor of Pediatrics  
University of Louisville School of Medicine
- **Jane M. DeLuca, PhD, RN**  
Associate Professor  
Clemson University School of Nursing
- **Cynthia M. Powell, MD, FACMG, FAAP (Chairperson starting on April 25, 2019)**  
Professor of Pediatrics and Genetics  
Director, Medical Genetics Residency Program  
Pediatric Genetics and Metabolism  
The University of North Carolina at Chapel Hill
- **Annamarie Saarinen**  
Co-founder, CEO Newborn Foundation
- **Scott M. Shone, PhD, HCLD(ABB)**  
Director  
North Carolina State Laboratory of Public Health
- **Beth Tarini, MD, MS, FAAP**  
Associate Director  
Center for Translational Research  
Children's National Health System

#### **Ex-Officio Members**

- **Agency for Healthcare Research and Quality**  
**Kamila B. Mistry, PhD, MPH**  
Senior Advisor  
Child Health and Quality Improvement
- **Centers for Disease Control and Prevention**  
**Carla Cuthbert, PhD**  
Chief, Newborn Screening and Molecular Biology Branch  
National Center for Environmental Health

- **Food and Drug Administration**  
**Kellie B. Kelm, PhD**  
Deputy Director  
Division of Chemistry and Toxicology Devices Office of In Vitro Diagnostics and Radiological Health
- **Health Resources and Services Administration**  
**Michael D. Warren, MD, MPH, FAAP**  
Associate Administrator  
Maternal and Child Health Bureau
- **National Institutes of Health**  
**Diana W. Bianchi, MD**  
Director  
Eunice Kennedy Shriver National Institute of Child Health and Human Development

**Designated Federal Official**

- **Catharine Riley, PhD, MPH**  
Genetic Services Branch  
Division of Services for Children with Special Health Needs  
Maternal and Child Health Bureau  
Health Resources and Services Administration

**Appendix B. Recommended Uniform Screening Panel (as of July 2018)**

The Recommended Uniform Screening Panel (RUSP) can be accessed [here](#).

**Appendix C. List of Publications By the Committee During 2019**

- *Report to Congress 2018*. Advisory Committee on Heritable Disorders in Newborns and Children. March 2019. [Read the report](#).
- *Medical Foods for Inborn Errors of Metabolism: The Critical Need to Improve Patient Access*. Advisory Committee on Heritable Disorders in Newborns and Children. Access information about the report [here](#).