Newborn Screening Long-term Follow-Up Assessment

Since the early 1960s newborn screening has been a vital public health service, enabling early identification and treatment of heritable disorders and genetic diseases. Each year the United States screens approximately four million infants for metabolic and other heritable disorders.

Newborn screening, however, is more than just a laboratory test. Public health authorities recognize that it comprises a complex system beginning with laboratory screening and continuing through confirmatory testing and diagnosis to medical management and care coordination for those with confirmed disorders. It must also include evaluation for the continuous quality improvement of all system components.

In the wake of the April 2005 release of the first guidelines defining a core panel of conditions for state newborn screening, there is a compelling need to examine the parts of the system required to support an expanded testing panel and the associated increase in the number of infants referred and diagnosed with rare and potentially life-threatening disorders. Activities occurring after screening and after diagnosis which limit the health consequences of confirmed disorders should be examined to strengthen the overall newborn screening infrastructure. Such activities collectively comprise newborn screening long-term follow-up (LTFU) and have long been an under-funded and comparatively neglected component of the newborn screening system. Nonetheless, LTFU activities are essential to both realize the full public health benefits of newborn screening and document them.

Background

Historically, newborn screening has developed as a state-managed activity, with little federal guidance or oversight. Consequently, state and territorial newborn screening programs vary in terms of their disease panels, administrative structure and funding mechanisms.

Recent federal attention to newborn screening has focused primarily on the development of a recommended uniform testing panel for states. The Health Resources and Services Administration’s (HRSA’s) Maternal and Child Health Bureau commissioned the American College of Medical Genetics (ACMG) to develop this panel based on the best scientific evidence available. That panel and associated recommendations were endorsed by the Department of Health and Human Services’ (DHHS) Secretary’s Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children, known as the Secretary’s Advisory Committee, in July 2005. Although the ACMG report has not yet received an official DHHS endorsement, it has already prompted most states to expand their newborn screening panels, raising complex issues related to broader newborn screening systems.

Compared to the process of screening and diagnosis, far less attention has been paid to LTFU, including: a) medical management, care coordination and periodic assessment of medical outcomes for those with confirmed disorders; and, b) systematic data collection to guide continuous quality improvement of all newborn screening systems.

A recent study found that about half of state and territorial newborn screening programs conduct LTFU activities, as they define them, for newborns with confirmed disorders. Of the programs that engage in LTFU, almost half report that they follow no standardized policies or procedures.

Without systems in place to ensure effective disease management after diagnosis, the full promise of newborn screening—the prevention of illness, short- and long-term disability, and premature death—cannot be achieved. Moreover, as states begin to screen for disorders that are extremely rare and less well understood—as the ACMG report recommends—disease management and treatment become more complex, while the need for long-term medical management and outcome data becomes more critical.

In the absence of comprehensive follow-up systems to address these needs across diagnosed populations, some authorities have questioned whether an expanded screening panel offers sufficient value from a public health perspective. As far back as 1999, a newborn screening task force convened by the American Academy of Pediatrics and HRSA endorsed the view of the United Kingdom’s David Hall that “if it is important enough to screen for, it is important enough to follow-up.” That task force, co-sponsored by seven other public health organizations, set forth a lengthy agenda to integrate, standardize and otherwise improve all aspects of the newborn screening system from heelstick blood collection to LTFU.

The Secretary’s Advisory Committee—through its Subcommittee on Follow-up and Treatment—is now actively discussing the need for a framework for LTFU and treatment of individuals identified by newborn screening.
Defining LTFU

There are at least two well-considered definitions of newborn screening LTFU, formulated by expert working groups: the definition included in the ACMG report and the definition developed by the Clinical and Laboratory Standards Institute (CLSI), a non-profit organization that promotes the development and use of voluntary consensus standards and guidelines within the healthcare community.

As shown in Textbox 2, both definitions consider LTFU to begin at the point of initiation of treatment and to continue for at least a substantial period. The CLSI definition extends the period of LTFU throughout the lives of affected individuals. Similarly, both definitions list a range of LTFU activities, including monitoring and/or facilitating access to necessary treatment interventions and collecting data to evaluate the newborn screening program. The ACMG definition extends the scope of data collection to “assess efficacy, sustainability and safety of early treatment intervention and uncover new disease/treatment outcomes.”

The National Newborn Screening and Genetics Resource Center’s Program Evaluation and Assessment Scheme (PEAS), a tool devised to help states evaluate and improve the components of their newborn screening programs, is another consensus-based document that addresses LTFU. Although the tool does not have a definition of LTFU per se, it states that short-term follow-up “ends with resolution of the screening results (i.e., newborn diagnosed and accessing appropriate intervention activities, newborn not affected or newborn lost to follow-up)” and goes on to delineate several performance measures for long-term program evaluation and medical management. These measures encompass:

• Development and periodic review of long-term outcome and medical management indicators;
• Periodic assessment of patient progress through defined outcome indicators; and,
• Periodic evaluation of the accumulated data as the basis for subsequent program improvements.

Additional PEAS indicators address computerized information systems and follow-up support activities, including patient education, counseling and medical management.

Finally, a 2005 survey of state newborn screening programs found some consistency in the activities state newborn screening coordinators consider to be part of LTFU. More than 80 percent of the 48 survey respondents indicated that LTFU included ensuring that management and treatment services are provided to patients and that needed changes in management and treatment plans are identified and made in a timely manner. About two-thirds identified ensuring patient access to a medical home over their lifespans and ensuring the availability of support services, such as transportation and information, as part of LTFU.

A Framework: Components of LTFU

Drawing from the definition of LTFU in the ACMG report, the Association of Maternal and Child Health Programs (AMCHP) proposes the following framework to encourage discussion, planning and implementation of comprehensive LTFU systems. The proposed components of LTFU include:

• Assuring that ongoing, high-quality, medical management—including specialty care and care coordination when needed—are provided within the context of a medical home to children, adults and families affected by heritable disorders;
• Assuring transition of young adults to appropriate adult medical care;
• Periodically assessing patient progress through review of defined outcome indicators;
• Collecting and analyzing state and national LTFU data; and,
• Engaging in continuous quality improvement at the local, state and national levels.

LTFU begins after short-term follow-up ends; that is, with the initiation of treatment. For the purposes of maternal and child health (MCH) program responsibility, LTFU ends upon transition to the adult service delivery system at 21 years of age. Concurrent with such a transition, public health agencies should assure the formal transfer of LTFU responsibility from MCH to an appropriate public health program to continue LTFU throughout affected individuals’ lifespans.

Current State LTFU Activities

Given a dearth of published information on the content of state LTFU activities, the AMCHP Newborn Screening and Genetics Advisory Group surveyed a sample of state newborn screening and MCH programs. (see Textbox 3, p. 4) Based on 21 states’ responses to a July 2006 e-mail survey to all state and territorial MCH directors, and in consultation with state and national newborn screening authorities, the advisory group identified six states—Louisiana, Michigan, New Jersey, Pennsylvania, Oregon and Washington—thought to be actively engaged in planning

Textbox 1: The Secretary’s Advisory Committee
The Secretary’s Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children was authorized under Title XXVI of The Children’s Health Act of 2000 to advise the Secretary of the U.S. Department of Health and Human Services regarding the most appropriate application of universal newborn screening tests, technologies, policies, guidelines and programs to effectively reduce morbidity and mortality in newborns and children having or at risk for heritable disorders. Committee members were appointed in February 2004 and the committee convened for the first time in June 2004. Unless it is renewed, the committee charter expires in February 2007. For more information, including minutes of past meetings, visit the committee Web site at mchb.hrsa.gov/programs/genetics/committee/.
A plan exists for periodically assessing patient progress through review of the defined outcome indicators. Long-term outcome data are periodically solicited, compiled and evaluated, from families, primary care providers and subspecialists. Program improvements are initiated on the basis of long-term program evaluation data.

Long-term outcome indicators have been developed in consultation with appropriate subspecialty expertise for each screened medical management indicators are periodically reviewed for suitability by subspecialty consultants and the advisory committee from state to state. The Newborn Screening Advisory Group found the following trends.

**Trend:** Typically LTFU activities are divided among several state programs, with the specific division of responsibilities varying from state to state. In addition to the state newborn screening program, other programs commonly involved include the public health laboratory, the state MCH program, encompassing the children with special health care needs (CSHCN) program, the genetics program and the epidemiology program.

- In Michigan, the newborn screening program resides administratively within the state Bureau of Epidemiology. It is tasked with assuring the availability of specialty care for children diagnosed with newborn screening disorders—which has entailed funding some specialty clinics—and conducting a range of quality assurance and provider training activities. The CSHCN program, within the Bureau of Family, Maternal and Child Health, subsidizes genetic counseling and medical care for a number of newborn screening disorders; provides case management to high-needs, technology-dependent children receiving home care; and, provides limited care for state newborn screening programs’ voluntary use.

**Textbox 2: Existing Definitions & Performance Indicators for LTFU**

**American College of Medical Genetics**

*Short-term follow-up* includes those activities that ensure all infants are screened, abnormal results are appropriately and expeditiously handled, and affected infants are promptly identified, appropriately referred and treatment initiated where applicable.

*Long-term follow-up* extends the period of follow-up substantially to monitor continuously the medical management and care coordination of those affected who require such; assesses efficacy, sustainability and safety of early treatment intervention; uncovers new disease and treatment outcomes; and, is valuable for demonstrating utility or limitation of testing.

**Clinical and Laboratory Standards Institute**

*Follow-up*—Actions taken to ensure that a newborn whose screening test results are “out-of-range” or “invalid” receives appropriate further tests and evaluation in a timely fashion; and, actions taken to ensure that the newborn screening system can evaluate the effectiveness of screening.

*Short-term Follow-up*—Actions conducted to ensure a valid screening test has been performed in cases of invalid initial test results, and appropriate and timely repeat or confirmatory testing and intervention in response to out-of-range screening test results. Short-term follow-up ends with diagnosis and documentation of treatment or intervention, if applicable, and referral information.

*Long-term follow-up*—Actions commencing after confirmed diagnosis in an affected individual to ensure the screening program can evaluate the effectiveness of their follow up program that may include the process of ensuring availability of ongoing intervention services and support to affected individuals throughout their lives.

**National Newborn Screening and Genetics Resource Center (Program Evaluation and Assessment Scheme)**

*Long-Term Program Evaluation and Medical Management Performance Indicators:*

- A plan exists for periodically assessing patient progress through review of the defined outcome indicators.
- Long-term outcome indicators have been developed in consultation with appropriate subspecialty expertise for each screened condition.
- Long-term outcome indicators are periodically reviewed for suitability by appropriate subspecialty consultants.
- Long-term outcome data are periodically solicited, compiled and evaluated, from families, primary care providers and subspecialists.
- Long-term outcome data are compared with expected state and national goals, and the information shared in the program’s annual report.
- Program improvements are initiated on the basis of long-term program evaluation data.
- Appropriate medical management indicators, developed by subspecialty consultants, exist for each condition.
- Medical management indicators are periodically reviewed for suitability by subspecialty consultants and the advisory committee and updated as appropriate.
- Medical management outcome data are periodically collected, evaluated and reported to the newborn screening program’s advisory committee.

*Developed as part of a cooperative agreement with the Health Resources and Services Administration, Maternal and Child Health Bureau, for state newborn screening programs’ voluntary use.*

or implementing newborn screening LTFU activities. Through a site visit to the Michigan newborn screening program and telephone interviews with newborn screening and MCH staff in the other five states, detailed information on the six states’ LTFU activities was collected. Information from other states—obtained via the email survey—is also included.

Overall, the advisory group found that even in these relatively active states, LTFU activities are limited. Moreover, even relatively longstanding activities have generally not progressed beyond the early stages of development. The Newborn Screening and Genetic Advisory Group found the following trends.
coordination assistance to any enrolled family that requests it. The state genetics program, affiliated with the newborn screening program, has been instrumental in the development of a state genetics needs assessment and plan that includes goals for improving newborn screening LTFU. Finally, although the public health laboratory is not directly involved in LTFU, laboratory staff are included on the state’s newborn screening committee and have input into LTFU policies. All of these programs collaborate closely on a range of issues.

**Trend:** States are most actively engaged in the first component of LTFU listed in AMCHP’s framework: assuring that high-quality medical management and care coordination are provided to children, adults and families affected by heritable disorders.

This finding is perhaps unsurprising, given that care coordination, the identification and linkage of support structures, health services and funding resources, falls within the traditional mandate of state MCH programs as in the Michigan example above. CSHCN programs typically have connections to pediatric specialists, early intervention programs, family support services and financing systems, such as Medicaid and the state Children’s Health Insurance Program. CSHCN programs also serve a gap-filling role, often directly funding services not covered by other programs.

It should be noted, however, that CSHCN services are not uniformly available to all children diagnosed with disorders through newborn screening, but are restricted to those who meet state-defined eligibility requirements and who opt to enroll. Moreover, there is often no systematic tracking of health outcomes for CSHCN enrollees and states may not consider these activities to be part of newborn screening LTFU per se.

Data on services provided under the auspices of the CSHCN program may be maintained by specialty clinics, such as in Oregon and Washington, that issue periodic reports to the state or may be collected by the state as part of the billing process and integrated into an existing genetics or newborn screening database, as in Louisiana.

- **Oregon** state government uses about a third of its MCH Block Grant funds to subsidize services for eligible children with metabolic disorders who are seen at the Oregon Health & Science University Child Development and Rehabilitation Center (CDRC), the only metabolic clinic in the state. In an atypical arrangement, the state CSHCN program is administratively located within the CDRC. This program conducts some community-based case management for eligible children until age 21. The only other state assistance provided post-diagnosis to infants with newborn screening disorders is a food and formula service that is operated at CDRC on a sliding fee scale.

- **New Jersey** uses a combination of financial resources from the MCH Block Grant and state and county tax revenue to ensure that case management is available in each of the state’s 21 counties for eligible children from birth to 21 years of age. Services are provided by nursing and social work professionals employed by health service grantees such as local health departments or hospitals. These local agencies recognize their communities’ unique needs and resources. More than 90 percent of the program’s caseload, approximately 12,000 children annually, comes from direct referrals from the New Jersey Special Child Health Services Registry. Registration is mandated by New Jersey statute for children born with birth defects, including all conditions in the newborn screening panel. Registration forms are submitted by various health professionals, the majority being birthing facilities within the state. Case managers, within seven days of receipt of referrals, attempt a telephone contact with each family referred from the registry. Participation in case management is voluntary. Case managers offer information and referral resources and conduct home visits as needed. They may also develop an individualized service plan with the family focusing on medical, dental, developmental, educational, rehabilitative, social, emotional or economic needs. Case managers also provide periodic monitoring as needed.

- **Pennsylvania**'s newborn screening and follow-up program contracts with four treatment centers to provide services for uninsured children with metabolic disorders using a combination of state and MCH Block Grant funds. The centers submit monthly, electronic invoices to the state Department of Health via a web-based electronic billing system. Invoice

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**Textbox 3: Maternal and Child Health Programs: Natural LTFU Partners**

Title V programs are funded through the Maternal and Child Health Services Block Grant (MCHBG), a discretionary federal grant program permanently authorized through Title V of the Social Security Act. Most block grant funds are allocated to states, with a smaller proportion set aside at the federal level for special projects of regional and national significance (SPRANS), encompassing everything from genetics research to university-affiliated service and training. A second set of grants, known as Community Integrated Service Systems, funds home visiting, rural programs and projects for children with special health care needs and others. States must match $3 for every $4 in federal funds provided. Most provide significantly more. In addition, states must spend 30 percent of MCHBG funds on preventive and primary care for children and youth and 30 percent on services for children with special health care needs. Finally, as part of the block grant requirements, states must report annually on 18 national and several state-specific performance measures consistent with the Government Performance and Results Act. One of these relates to bloodspot screening: “Performance Measure #01: The percent of newborns who are screened and confirmed with condition(s) mandated by their state-sponsored newborn screening program (e.g., phenylketonuria and hemoglobinopathies) who receive appropriate follow-up as defined by their state.” Another measure relates to newborn hearing screening. For more information visit www.mchb.hrsa.gov.
data—consisting of patient name, diagnosis, eligibility status for state-funded services and services provided—are maintained in the electronic billing system.

- **Texas** follows the diagnosed cases of sickle cell hemoglobinopathies and congenital adrenal hyperplasia (CAH) for 18 years with annual surveys sent to the child's physician asking about treatment, hospitalizations and complications. The state follows children with hypothyroidism, phenylketonuria (PKU) and galactosemia for four years, ensuring they are in care and receiving appropriate treatment.

- **Washington** allocates a portion of collected newborn screening fees and MCH Block Grant funds to the PKU and Biochemical Genetics Clinic at the University of Washington to support diagnosis and treatment services for children born with PKU, biotinidase deficiency, galactosemia, homocystinuria, maple syrup urine disease and MCAD deficiency. The clinic sends quarterly reports to the state that include data regarding diagnostic confirmation, services provided and ongoing clinical status. Follow-up for sickle cell disease and the other severe hemoglobinopathies is also subsidized by newborn screening fees. The state receives long-term medical and developmental data from comprehensive sickle cell clinics at Odessa Brown Clinic, a satellite of Children's Hospital in Seattle, and Mary Bridge Children's Center in Tacoma.

**Trend: The level of clinical tracking varies greatly for each disorder category.** Because metabolic services tend to be offered by few providers and typically centralized in a few clinics within the state or region, data are fairly easily captured for individuals with these disorders. However, few states have devised their own data elements for systematic tracking. Moreover, states assign few or no resources to locate children who are not receiving care or not receiving care at a designated, in-state specialty clinic.

It is much more challenging for states to capture data on individuals who have a broader network of providers to choose from—such as those with hemoglobinopathies or endocrine disorders—and from those whose conditions require little or no specialty care. Tracking these children tends to be much more inconsistent and opportunistic.

- **New Jersey** Newborn Screening and Genetic Services provides families of infants with a positive newborn screen access to confirmatory testing, diagnosis and treatment through ten specialty care centers and private sub-specialist practitioners, partially supported by state funds. Newborn screening follow-up activities for children identified through the newborn screening program include, but are not limited to, services for children with cystic fibrosis, inherited endocrine defects, inherited metabolic defects, and sickle cell anemia and other hemoglobinopathies. Funding also partially supports four metabolic, five endocrine, three cystic fibrosis and five sickle cell programs as well as two biochemical genetics laboratories. However, the newborn screening program stops all follow-up and patient contact once a diagnosis is made. Any post-diagnosis data appears on quarterly grant progress reports, which do not identify patients as newborn screening referrals versus other types of referrals and serve only as a snapshot for grant activities.

- **Louisiana**'s state genetics program contracts with metabolic centers at Tulane University in New Orleans and Louisiana State University in Baton Rouge. Infants with out-of-range tests results are referred to these centers for diagnosis, formula provision, dietary management and support services, such as parent support groups. While the genetics program maintains a database of all out-of-range screening results among Louisiana infants, tracking protocols differ based on the disorder category. The two metabolic centers report data on services provided to patients for as long as patients remain in care. Children with sickle cell hemoglobinopathies remain in the system for five years. Those with genetic hypothyroidism are followed only until confirmation of treatment initiation.

- **Oregon** infants' LTFU is not the responsibility of any state agency. While all the infants and children with metabolic disorders are seen in one clinic, only half of the children with hemoglobinopathies and endocrinopathies are followed routinely by pediatric subspecialists. The fate and quality of care for the other half is unknown and even the specialty clinics do not collect routine outcome data.

- **Michigan**'s newborn screening program contracts with three outside agencies to provide follow-up and medical management services: the Children’s Hospital of Michigan Metabolic Program in Detroit, the Michigan Chapter of the Sickle Cell Disease Association of America in Detroit, and the University of Michigan Medical Center in Ann Arbor for endocrine disorders. The level of follow-up varies by disease category. The metabolic program treats virtually all of the children with metabolic disorders in the state and reports results of confirmatory testing and date of treatment initiation. Other data are maintained on-site with the possibility of state reporting. The Sickle Cell Disease Association collects and reports data on: (a) confirmation of diagnosis and initiation of penicillin prophylaxis; (b) penicillin compliance; (c) hospitalizations; (d) provision of counseling and education for parents; and, (e) annual psychosocial assessment. The data system, however, is currently only partially computerized, although the state has received a three-year HRSA grant to make it fully computerized and web-based. The University of Michigan Pediatric Endocrine Follow-up Program maintains clinical and laboratory protocols for the diagnosis and management of congenital hypothyroidism (CH) and CAH; conducts short- and long-term follow-up for CH and CAH in collaboration with the Pediatric Endocrine Advisory Council, a group of board certified pediatric endocrinologists that was organized and receives ongoing funding through a state contract; maintains a data-base of all Michigan newborns diag-
nosed with these two disorders; and, maintains a center of excellence for the management of CAH. The state is in the early stages of an effort to centralize treatment of CAH. Funding for all of these efforts comes primarily from newborn screening fees, which are allocated to a restricted account and divided equally between laboratory services and follow-up and medical management.

- **Washington**’s treatment network for the endocrine disorders—CH and CAH—is less centralized than for metabolic disorders. Follow-up for endocrine disorders usually ends at several months of age once diagnosis, treatment and continuity of care have been established.

### Trend: States have experimented with innovative approaches to LTFU, particularly when dedicated federal funding has been available.

- **The HRSA Region II Genetics Collaborative** has provided twelve contracts to specialty care centers throughout the mid-Atlantic region to develop and implement case management database systems to track children with special health care needs.

- **The HRSA Region IV Genetics Collaborative**’s LTFU working group is refining a set of data elements for long-term tracking of infants and children with MCAD deficiency, owing to a substantial number of cases in the region. All 32 of the specialists in Region IV seeing children diagnosed with MCAD deficiency have agreed to report data to a registry with no financial reimbursement. Fifteen of these specialists have met in person to develop a preliminary list of data elements, and the working group is now refining these elements and purchasing software to develop the registry. The Great Lakes states involved in the project hope to document medical outcomes, treatment efficacy and continuity of care. Once the MCAD deficiency project is complete, the working group plans to select an amino acid disorder and another fatty acid disorder for further registry development.

- **The HRSA Region VII Genetics Collaborative** is piloting a telemedicine program in Oregon and Idaho to make it easier for families to access clinical genetics specialty services—such as genetics and metabolic nutrition counseling—in non-metropolitan areas. The genetics collaborative is also working with newborn screening coordinators in Alaska, Idaho, Hawaii and Nevada to assess regional short- and long-term follow-up needs.

- **New Jersey** has six hospitals providing prenatal and general genetics services through six genetics grants. These facilities evaluate, diagnose, manage and treat a wide variety of genetic conditions and provide a range of pre-conceptual, prenatal and postnatal genetic counseling. Newborn screening and genetics grants ensure provision of services to individuals who are uninsured or under-insured, with billing done on a sliding fee scale and charity care available when needed.

- **Oregon Health and Science University** recently concluded a three-year, CDC-funded project to develop and pilot a database to collect LTFU data on children with metabolic disorders to evaluate the efficacy of tandem mass spectrometry screening. Data are abstracted from clinic chart notes in an ad hoc arrangement that works in a small clinic environment where the MS/MS children are readily identified when they return for treatment. Data are de-identified and pooled with data from affected infants in Iowa and Idaho, demonstrating the value of shared data analysis. Because the program has not solicited parents’ informed consent, only data from clinic charts can be collected—a limitation that is acceptable for immediate research needs, but that renders the database less valuable as a research tool for LTFU. After CDC funding ends in October 2006, the program’s future is uncertain. It is likely that LTFU efforts will continue in Oregon at least for the next year as participants search for more permanent funding, possibly from newborn screening fees.

- **Michigan** is conducting a range of innovative activities including a HRSA-funded effort to develop a minimum LTFU dataset for children with sickle cell hemoglobinopathies, a comprehensive evaluation of the state treatment program for metabolic disorders and CAH, and investigating the feasibility of a medical home pilot project that would provide designated, trained physician practices a monthly per-child fee for primary care services delivered to qualified special needs children. The question the state hopes to answer through this last project is: Can we spend money differently, rather than spending more, to achieve better health outcomes? Finally, the Michigan Department of Community Health (MDCH) is in the third year of a five-year CDC cooperative agreement to integrate genomics into public health. The MDCH has conducted a comprehensive genetics assessment, identified six long-term goals and associated action steps, and begun to implement the plan. To date, the state has identified a biochemical genetics laboratory to do confirmation testing, instituted expanded newborn screening for more than 40 disorders, hired a newborn screening nurse consultant to do educational and quality assurance work with hospital staff throughout Michigan, and begun funding several genetic counseling clinics.

- **Nevada** has a birth defects registry tied to the state newborn screening database. All families in the database are proactively contacted at least once a year to ascertain whether they are still receiving services, either through the metabolic specialists or endocrinologists who practice in the state. Those who are not in care are offered assistance to ensure ongoing treatment.

- **Virginia**, with the expansion of its newborn screening panel, has implemented an automatic referral of all infants identified with disorders to Care Connection for Children (CCC), the existing statewide network of centers of excellence for CSHCN. CCC staff provide leadership to enhance specialty medical services, care coordination, evaluation of medical in-
surance benefits, referral to CSHCN resources, family-to-family support, and training and consultation with community providers on CSHCN issues. CCC care coordinators work closely with contracted genetic and metabolic treatment centers, which assure ongoing nutritional evaluation and management of infants and children. Inter-program agreements allow those eligible for either Medicaid or the Special Supplemental Nutrition Program for Women, Infants and Children (WIC) to receive their metabolic formulas seamlessly via WIC clinics.

Washington's newborn screening program funds voluntary, periodic neuropsychological testing of a cohort of children with congenital hypothyroidism seen at the Congenital Hypothyroid Developmental Evaluation Clinic at the University of Washington. Test results are used to evaluate developmental progress and the overall effectiveness of the newborn screening program.

Challenges and Opportunities

Challenges
By far the biggest challenges facing those who wish to strengthen LTFU systems are the low priority accorded to LTFU compared to other newborn screening activities and an associated scarcity of resources.

A 2003 federal study found that of the more than $120 million states spend on newborn screening each year, roughly $89 million is dedicated to laboratory activities and $31 million to administrative and follow-up activities carried out up to the point of confirmation of diagnosis and referral for treatment. Of note, the study did not inquire about state expenditures incurred post-diagnosis for disease management and related activities.12

A 2005 survey of state newborn screening coordinators documented that among the respondents that reported conducting LTFU activities, an average of just one to two full time employees were assigned to carry out these activities—significantly fewer than respondents indicated needing.13

One state-level official who provided input into this report commented that particularly with the expansion of the newborn screening test panel, his agency has insufficient staff to conduct meaningful LTFU. His solution is to try to include limited LTFU activities in the contracts of the specialty centers treating children with metabolic disorders. It will, however, be much more difficult to motivate providers and institutions to carry out LTFU on behalf of the state in the absence of such financial arrangements.

Opportunities
Timeliness: The release of the ACMG report in April 2005 has prompted states to examine their newborn screening programs anew. Although much of that effort has been directed to the screening panel and short-term follow-up, LTFU proponents may be able to capitalize on policymakers' renewed attention by emphasizing the necessity of a comprehensive newborn screening system that includes LTFU. Moreover, some long-term tracking will be necessary to document the value of expanded newborn screening.

Ongoing Projects: Federally supported projects, such as the HRSA Regional Genetics Collaboratives, have stimulated efforts to develop LTFU datasets, medical home pilot projects and the like. As these efforts are further developed, sample datasets, model policies and other products can be shared and adapted for use by additional states. At the programmatic level, state officials seem genuinely interested in implementing LTFU activities even when constrained by limited resources. Summary data such as that routinely reported to the National Newborn Screening Information System (NNSIS) at the HRSA-funded NNSGRC (www2.uthscsa.edu/nnsis) also provide useful comparative and denominator data for reviewing national incidences and disease trends.

Uniform Core Datasets: The rarity of most newborn screening disorders means that there is added statistical value in pooling data across states. Uniform core datasets would both promote such pooling and be more cost-effective to develop than multiple state-specific datasets for each newborn screening disorder. They would also facilitate LTFU as patients and their families move within and between states.

Building on Existing Data Systems: Many states already have vital registration databases, birth defects registries, immunization registries, newborn screening short-term follow-up files or genetics databases. With appropriate privacy safeguards, these existing information systems might usefully be integrated, eliminating duplication of data collection, promoting greater collaboration across health programs, facilitating research and ultimately enhancing continuity-of-care for infants and families. Some states have already made significant progress in this area.

• In Michigan virtually all resident physicians submit information to the state immunization registry online at www.mcir.org, which also captures data from affiliated programs, including hearing screening, newborn bloodspot screening, Medicaid, genetics, avian influenza and lead screening. Children who are temporarily lost to follow-up by one program are often “rediscovered” through the immunization registry.

• New Jersey has consolidated two statewide surveillance systems to streamline the data collection process. The Special Child Health Services (SCHS) registry includes birth defects and special needs components. Over 8,000 new entries are added annually. SCHS registry data is used for surveillance, needs assessments, research, collaborative projects and linkage to services. For example, data have been used by county-based case management units to determine the number of children who might need services. Research projects utilizing data from the registry include the National Birth Defects Study, the National Down Syndrome Study and special studies on: Accutane and birth defects; infant mortality and the coding
and contribution of birth defects; the accuracy of birth defects reporting on the electronic birth certificate; the need for pulse oximetry screening; the effects of the collapse of the World Trade Center buildings on the incidence of birth defects; the relationship between water contaminants and neural tube defects; and, geographic patterns of selected birth defects and environmental factors.

- Rhode Island’s confidential, computerized child health information system, KIDSNET, contains: immunization records; results from metabolic, hearing and developmental risk assessments for newborns; results from lead tests; and, other information such as home visiting and participation in the Early Intervention Program and WIC. KIDSNET is available online at www.health.ri.gov/family/kidsnet/index.php.

Next Steps

The five recommendations listed below are based on the collective input of the more than three dozen newborn screening experts who contributed to this report—including members of the AMCHP Newborn Screening and Genetics Advisory Group and all those who participated in the e-mail survey, site visit and telephone interviews.

1. **Publicize and advocate that LTFU is an essential part of a quality newborn screening program and a public health responsibility.**

Newborn screening advocates within the private community and at all levels of government must champion stronger LTFU systems. The CLSI newborn screening follow-up guidelines, the NNSGRC’s PEAS checklist and the work of the Secretary’s Advisory Committee to address LTFU are all important contributions that will hopefully prompt further activity.

A potential avenue to focus attention on LTFU is via the MCH Block Grant performance measures. Performance Measure #1, which deals with newborn screening, could be strengthened by developing national standards for newborn screening follow-up. The 1999 American Academy of Pediatrics/HRSA newborn screening task force suggested that additional state and local measures for newborn screening systems focus on outcomes such as survival, health and functional status, and quality-related factors such as parental involvement and satisfaction and number lost to follow-up in the course of specialty care.14

Without strong advocates to articulate the need for comprehensive LTFU systems—and to document the benefits of those systems—LTFU will remain the most under-developed component of state newborn screening programs.

2. **Develop an implementation plan for the LTFU components outlined in this report.**

States must begin now to plan for the implementation of LTFU systems. Needs assessment, identification of funding sources and exploration of existing LTFU models are all necessary parts of this process. The sampling of state LTFU activities listed earlier in this report documents some successful implementation strategies. In addition, the LTFU framework presented in this report should help states develop an implementation plan with federal guidance.

3. **Secure funding for LTFU.**

It is critical to recognize that LTFU has not received appropriate financial support. Development of a robust LTFU system will require significant investment of federal and state funds. State MCH and newborn screening professionals who provided input for this report cited a need for the federal and state governments to "specify" funds and develop "funding models" to assure resources for LTFU.

A 2003 federal study found that more than $120 million of state funding was spent in newborn screening. However, this study did not inquire about state expenditures for the LTFU activities.15 Current resources committed to LTFU are limited. Significant new funding is needed to develop and maintain LTFU.

Federal support for demonstration projects to develop various aspects of LTFU systems, as discussed in steps 4 and 5 below, will also be essential to jumpstart significant activity in this area.

4. **Develop standards for data collection related to newborn screening LTFU.**

In order for states to collect and analyze their LTFU data, there is a critical need for standardizing data collection, which could be part of a broader effort to develop integrated child health profiles. Federal agencies can provide leadership, encouragement and resources to spur this developmental work. CDC has already funded projects to help develop measures for LTFU for metabolic disorders and hemoglobinopathies. The Maternal and Child Health Bureau has encouraged this work through its NNSGRC and the Regional Genetics Collaboratives. However, more concerted federal involvement is needed.

5. **Provide resources and technical assistance to states as they develop LTFU activities.**

Newborn screening has long been recognized as a shared federal-state responsibility. The convening of the Secretary’s Advisory Committee and funding the development of the ACMG report on expanded newborn screening are perhaps the most prominent recent federal activities to provide guidance and assistance to state newborn screening programs. Other examples include the establishment of the NNSGRC and its program assistance reviews and national information database; HRSA-funded Regional Genetics Collaboratives; the medical home learning collaborative; and, at least two CDC-funded projects related to LTFU data collection, one in Colorado and another involving Oregon, Iowa and Idaho. These and other efforts have helped enormously to advance the critical assessment of
the nation’s newborn screening systems and to encourage the adoption of evidence-based practices.

Precisely because these federal efforts have been so successful—and in an era of increasing fiscal pressures on states—expanded federal assistance is vital to ramp up the investigation and eventual adoption of effective LTFU systems. In addition to the activities cited in step 4 above, areas needing further federal attention include:

- Workforce development to assure an adequate, well-trained pool of specialty care providers;
- Models for utilizing satellite clinics, telemedicine and other innovative mechanisms to assure access to care in rural areas;
- Continued development of operational guidelines and policies for state-subsidized medical homes;
- Models to evaluate quality assurance and health outcomes; and,
- Integration of new treatment technologies and protocols.

Conclusion

The expansion of newborn screening test panels across the country presents both an opportunity and an obligation for newborn screening professionals, advocates and policymakers to strengthen those components of the newborn screening system needed to support children and families of children who are diagnosed with heritable disorders. LTFU activities, in particular, have been comparatively neglected system components. They include medical management, care coordination and periodic assessment of progress through defined outcome indicators for those with confirmed diagnoses; data collection and analysis; and, continuous quality improvement of all newborn screening systems. Federal agencies responsible for newborn screening—most notably HRSA’s Maternal and Child Health Bureau and the CDC—have provided valuable leadership in this area through special projects and learning collaboratives that are beginning to yield results. These efforts must continue and multiply with a significant commitment of new resources. At the same time, states must begin to plan for implementation of comprehensive, coordinated LTFU programs. Without such work, the full public health benefit of newborn screening will not be achieved.

Endnotes

1 Although hearing screening is an essential part of newborn screening, it is not considered in this paper since hearing screening programs were developed and are often administered separately from bloodspot-based screening programs.
5 As of Aug. 15, 2006, 46 states were offering some form of expanded newborn screening using tandem mass spectrometry, according to data collected by the National Newborn Screening and Genetics Resource Center. Current information is available at genes-r-us.uthscsa.edu/nbdisorders.htm.
8 Ibid Hoff.
9 Ibid ACMG.
13 Ibid Hoff.
14 Ibid AAP.
15 Ibid Dodd.

This report was prepared by AMCHP’s Newborn Screening and Genetics Advisory Group. For more information about the key resources and partners highlighted in this report, please refer to the AMCHP website: www.amchp.org.