The Centers for Disease Control NSMBB Molecular Assessment Program (MAP): Evaluation of Newborn Screening Molecular Testing

Newborn screening (NBS) is the process of testing infants for serious developmental, metabolic, and genetic disorders. The Health and Human Services (HHS) Secretary's Advisory Committee on Heritable Disorders in Newborns and Children (SACHDNC) lists 31 core disorders that are recommended to be included in every NBS program in the United States. These core conditions share criteria including that they are prevalent in the U.S. population; can be screened for using a simple, robust test; and a treatment or intervention exists if the disorder is detected early. The majority of screening for these disorders is through a biochemical test. The recommended inclusion of cystic fibrosis (CF) to the core panel of disorders in the mid-2000s resulted in the first wide-spread use of a molecular test in NBS to increase the sensitivity and specificity of biochemical screening results. In addition to CF, several programs adopted second-tier molecular tests for disorders including galactosemia, MCAD, PKU, and CAH. In 2010, the SACHDNC added Severe Combined Immunodeficiency (SCID) to the core screening panel. This disorder signified the first time a molecular assay was used as a primary screening test. The inclusion of SCID will require the expansion of molecular testing activities in NBS programs. Despite the increased use of molecular testing, there are still several public health programs that have yet to introduce molecular testing into their NBS programs.

As NBS laboratories introduce molecular assays into their routine testing, it is imperative that the specific concerns related to molecular testing are addressed to ensure the quality of test performance and laboratory practice. Molecular testing requires specific guidelines that are not covered by CLIA. In response to this, the Newborn Screening and Molecular Biology Branch (NSMBB), in the U.S. Centers for Disease Control and Prevention, developed a pilot initiative, the Molecular Assessment Program (MAP). MAP will involve the public health laboratory personnel working together with the NSMBB molecular quality improvement program to provide quality management guidance for molecular testing in NBS laboratories. The framework for MAP was modeled after the Newborn Screening System Performance Evaluation Assessment Scheme (PEAS), developed by the National Newborn Screening and Genetics Resource Center and NBS partners as an evaluation tool for quality improvement.

MAP is focused on the NBS program components that have specific concerns for molecular testing. The evaluation criteria can be sub-divided into pre-analytic, analytic, and post-analytic phases of the testing process and are derived from multiple sources including the:

- Newborn Screening Performance Enhancement Assessment Scheme (PEAS)
- CLIA Guidelines for Moderate and High Complexity Tests
- ACMG Standards and Guidelines for Clinical Genetics Laboratories
- CAP Molecular Pathology Checklist
- NYSDOH Clinical Laboratory Evaluation Program
- Good Laboratory Practices for Molecular Genetic Testing for Heritable Diseases and Conditions, MMWR (2009) 58(RR06)

These evaluation criteria have been arranged into the following checklists for the components of the testing process.

MAP will be a broad assessment of categories that have specific molecular testing concerns The proposed components for review include:

Pre-Analytic
- Standard Operating Procedures
- QA/QM Manual
- Assay Validation
- Personnel

Analytic
- Performance of Test Methods
- Proficiency Testing Procedures and Results

Post-Analytic
- Procedures for Results Reporting

These standards and guidelines do not necessarily assure a successful outcome and should not be considered inclusive of all proper procedures and tests or exclusive of other procedures and tests that are reasonably directed to obtaining the same results.