



# GENETICS BRIEF

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## Tandem Mass Spectrometry

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*“Currently, as a result of scientific and technological advances, and because of increased consumer interest, state governments are experiencing increased attention to expanding state mandated newborn screening for certain rare metabolic disorders detectable through tandem mass spectrometry testing.” (Therrell, 2001)*

### Overview of Current NBS System

Newborn screening is “a public health program aimed at the early identification of conditions for which early and timely interventions can lead to the elimination or reduction of associated mortality, morbidity, and disabilities...and involves the following components: screening, short-term follow-up, diagnosis, treatment/management, and evaluation” (Newborn Screening Task Force, 1999). In the United States, approximately 4 million babies are screened each year resulting in the identification of approximately 3,000 infants with disorders requiring follow-up care (National Newborn Screening Report, 1998). The number of disorders screened varies by state and ranges from four to almost thirty (NNSGRC, 2002). State programs also vary in the laws and regulations governing their program, oversight responsibilities, and storage and use of residual specimens. Consensus guidelines or federal national standards could assist the states in determining the appropriate tests to include in their newborn screening panel.

### Tandem Mass Spectrometry—The Technology

A tandem mass spectrometer is able to detect the presence of certain diseases by separating out molecules in a specimen by their weight. The speed of tandem mass spectrometry (MS/MS) makes it well equipped to “handle the large number of samples that are processed in newborn screening programs,” and is considered to be more precise for the diagnosis of certain conditions than the technology currently used. Its use in newborn screening is still new and “scientific data are limited regarding incorporating this technology into newborn screening” (CDC MMWR, 2001). It also should be noted that MS/MS cannot detect some disorders currently screened for, including hypothyroidism (ACMG, 2000).

### Current Use of MS/MS in State Newborn Screening Programs

MS/MS allows for the screening of a large number of disorders; however, it is unclear whether some of the disorders that can be screened for meet various criteria for inclusion in a newborn screening program. Various organizations, including the World Health Organization (WHO), have published a range of screening criteria. For example, the WHO’s criteria suggest that a test “lead to a clear diagnosis in the majority of cases” for a common or “serious but less common” disease for which there is effective treatment and/or prevention (WHO, 1999). Given the lack of data on whether some metabolic abnormalities screened for using MS/MS meet such criteria, as well as the lack of data surrounding the use of MS/MS in newborn screening, some states have implemented pilot programs or deferred any action (see table for details).

### Issues in the Use of MS/MS for Newborn Screening

There are several issues when considering the integration of MS/MS into state newborn screening programs. Data is needed to demonstrate the effectiveness of the technology when applied to newborn screening, including the incidence and prevalence of each disease being screened for, as well as the sensitivity, specificity, and validity of the test. The natural history and the impact of available interventions for identified metabolic aberrations must be described. Due to the nature of the technology, it is also possible to screen for a number of disorders for which

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there is no cure, leading to debate over what disorders should be included in the panel, and what criteria should be used in making that decision. The availability of MS/MS, pressure from consumer advocacy groups, and for-profit companies which offer the testing, have put pressure on state governments to expand their newborn screening programs.

State	Number of Disorders Screened for Using MS/MS	Status of Program
California	24	A
Hawaii	24	A
Iowa	28	B, R
Maine	19	A, R
Massachusetts	18	A, R
Minnesota	19	B
Montana	14	A
North Dakota	1	B
Nebraska	26	A
New Jersey *	6	R
North Carolina **	20	R
Ohio	6	R
Rhode Island	19	A, R
South Carolina	1	R
South Dakota	26	A
Wisconsin	17	B, R

\* testing mandated for 1/1/02 but not yet in place  
 \*\* full screening with MS/MS mandated with disorders to be added as they are identified  
 A For select populations, limited pilot programs, or by request  
 B Universal pilot program  
 R Requirement of the state  
 Source: *The National Newborn Screening and Genetics Resource Center*

The integration of MS/MS into state newborn screening programs is inextricably tied to the issue of funding. In addition to funding the purchase of MS/MS equipment, states must consider infrastructure investments that will be necessary to support the technology. If states decide to screen for incurable disorders, which is possible using MS/MS, the question remains as to the financial responsibility for providing follow-up care and treatment, including medical foods and medications, potentially for a lifetime. Additional cost considerations include the training of laboratory personnel to operate and maintain the equipment and the increase in the number of patients identified annually—estimated increase is 50% to 100% (ACMG 2000)—requiring follow-up, treatment and other services.

### Conclusion

As more states begin to examine the use of MS/MS in their own programs, it is clear that there are both advantages and disadvantages to the technology. MS/MS highlights questions surrounding newborn screening that existed before its advent, including selection of diseases to include in a newborn screening panel and financing of programs. It also raises several issues based on the technology itself, including the sensitivity and validity of the technology, and the investments needed to fully integrate MS/MS into state newborn screening programs.

MS/MS will continue to make newborn screening an important issue for state health agencies and governments.

### Selected References and Resources

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