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# NBS02-A2

## Newborn Screening Follow-up; Approved Guideline—Second Edition

SAMPLE

This guideline describes the basic principles, scope, and range of follow-up activities within the newborn screening system.

A guideline for global application developed through the Clinical and Laboratory Standards Institute consensus process.

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Clinical and Laboratory Standards Institute  
950 West Valley Road, Suite 2500  
Wayne, PA 19087 USA  
P: 610.688.0100  
F: 610.688.0700  
[www.clsi.org](http://www.clsi.org)  
[standard@clsi.org](mailto:standard@clsi.org)

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## Newborn Screening Follow-up; Approved Guideline—Second Edition

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Judith Tuerck, RN, MS  
Bridget Wilcken, MD, FRACP, FRCPA  
Dianne R. Webster, PhD, FHGSA  
Irene Forsman, MS, RN  
Alex R. Kemper, MD, MPH, MS  
David Millington, PhD  
Jan Ostrup  
Brad L. Therrell, PhD  
Toni Torresani, PhD  
Jerry Vockley, MD, PhD

### Abstract

Newborn screening for congenital conditions is a public health system composed of testing, follow-up, diagnosis, management, evaluation, and education. As part of the system, follow-up activities play an essential role in facilitating early detection, diagnosis, and intervention for affected newborns. Clinical and Laboratory Standards Institute document NBS02-A2—*Newborn Screening Follow-up; Approved Guideline—Second Edition* describes the basic principles, scope, and range of follow-up activities within the newborn screening system. It is intended for use by those involved in any aspect of follow-up, including health care providers, parents, and others concerned with the health and welfare of newborns.

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## Contents

Abstract.....	i
Committee Membership.....	iii
Foreword.....	vii
1 Scope.....	1
2 Standard Precautions.....	1
3 Terminology.....	1
3.1 A Note on Terminology.....	1
3.2 Definitions.....	2
3.3 Abbreviations and Acronyms.....	3
4 General Considerations for Follow-up in Newborn Screening Programs.....	4
5 Condition Definitions.....	4
6 Short-term Follow-up.....	4
6.1 Definition.....	4
6.2 Participants/Responsibilities.....	4
6.3 Condition-specific Algorithms.....	6
6.4 Follow-up Paradigms.....	6
6.5 Short-term Follow-up Issues.....	7
6.6 Reporting, Documentation, and Communications.....	8
7 Long-term Follow-up Cases.....	10
7.1 Special Considerations for Improvement.....	11
7.2 Challenges.....	11
8 Education.....	11
8.1 Parents.....	11
8.2 Health Care Providers.....	12
8.3 Newborn Screening Personnel.....	12
9 Evaluation and Quality Assurance of Follow-up.....	12
10 Funding.....	13
11 Advisory Committee.....	13
12 Laws and Rules.....	13
References.....	15
Additional References.....	16
Appendix. Newborn Screening Follow-up Process.....	19
The Quality Management System Approach.....	20

**Contents (Continued)**

Related CLSI Reference Materials .....21

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## Foreword

Newborn screening is an essential public health activity focused on testing every newborn for certain congenital conditions which, without early management, can result in significant morbidity and mortality. Screening tests separate newborns at higher risk of having a condition from those who are at low risk. Screening is not diagnostic, and newborns identified with presumptive findings require further testing and clinical evaluation to confirm their status as affected or unaffected. Newborn screening for many congenital conditions is now routine throughout much of the world and traditionally uses a dried blood specimen—blood applied to purpose-manufactured collection paper sent to specialized screening laboratories. In addition, birthing facility point-of-care screening for newborn hearing loss has been performed for several years, and birthing facility screening for critical congenital heart defects and various other conditions has recently been introduced into newborn care.

Effective newborn screening systems (NSS) provide the infrastructure for universal access and rapid follow-up for affected newborns whose lives and health may be at risk. A complete system for screening comprises six parts: testing, follow-up, diagnosis, intervention and/or management, evaluation, and education.<sup>1</sup> Parents/legal guardians, all health care providers, and the newborn screening program (NSP) involved in the care of the newborn should collaborate to ensure that the NSS functions effectively to provide maximum benefit.

It is estimated that approximately one newborn in 600 will be affected with a congenital condition detectable by dried blood spot screening, and three newborns in 1000 will be affected with hearing loss.<sup>2</sup> Birth incidences of conditions may vary greatly among different populations, but if congenital heart defects are included, then in most parts of the world around 1% of newborns will be identified as being at risk for physical and/or developmental disabilities, or even death, as a result of a condition that can currently be identified by a newborn screening test. Technological advances will, in the future, enable programs to screen for increasing numbers of conditions.

Follow-up activities can be divided into two broad categories: short-term follow-up (STFU) and long-term follow-up (LTFU). Within newborn screening, simply reporting “screen positive,” “out-of-range,” or “invalid” results does not ensure appropriate or timely treatment for affected newborns.<sup>3-5</sup> Rapid, efficient, and effective *short-term follow-up* is critical to ensure that newborns needing further testing are evaluated quickly, and receive the testing indicated and prompt and appropriate referral for subspecialty care and support services.<sup>6-8</sup> Active STFU responsibility ends when the infant is proven either not to be affected or has been verified to be under appropriate care, including treatment.

The primary aim of newborn screening is to provide intervention to affected babies. LTFU is the means by which accountability of NSS and NSPs can be ensured. It determines if they are sustaining their primary aims of preventing mortality and mitigating morbidity. Such follow-up is vital to the evaluation of newborn screening benefits throughout the life of an individual, as well as to the family and society.<sup>9</sup> NSPs may not be directly involved in long-term outcome assessment, but if they do not play a central coordinating role, then they need to facilitate LTFU and be aware of the results.

The quality of follow-up services directly affects the lives of families with babies. This document outlines the role of follow-up services within an NSS, and provides guidance for developing, ensuring, and maintaining effective follow-up services. NBS02 has been updated, and sections dealing with LTFU have been expanded to include discussion of assessment of health outcomes from newborn screening. Additions include a section about the development of condition definitions, which are essential for assessing health outcomes, and expansion of the section on education. Also, the terms “in-range” and “out-of-range” have been updated to be consistent with other CLSI documents and global usage. Efforts have been made to reach consensus among an internationally representative group of newborn screening stakeholders to describe best practices for newborn screening follow-up.

**Key Words**

Community/public health resources, congenital heart defects, dried blood spot screening, endocrinology, hearing loss, long-term follow-up, metabolic disorders, newborn hearing screening, newborn screening, point-of-care test, population screening, quality assurance, short-term follow-up

SAMPLE

## Newborn Screening Follow-up; Approved Guideline—Second Edition

### 1 Scope

The primary goal of this guideline is to enhance the quality of follow-up services for newborns screened through public health or other newborn screening programs (NSPs). The quality of these services has a direct impact on the health of newborns and families, and on the effectiveness of newborn screening as a system.

*Short-term follow-up* (STFU), in the first days and weeks of life, is essential to ensure that all newborns receive a valid screening test, and that those with screen positive results receive a definitive diagnosis, in the most expedient manner possible, and appropriate clinical management if confirmed.

*Long-term follow-up* (LTFU) comprises all of the activities that should occur after a patient is diagnosed and subsequently confirmed with a condition. It includes care coordination, assuring the availability of evidence-based treatment, continuous quality improvement, new knowledge discovery, and, importantly, periodic assessment of the clinical outcomes in affected individuals without which there can be no assurance that newborn screening goals are being met. It should also include efforts to document cases diagnosed clinically or outside the newborn screening system (NSS).

This guideline outlines STFU and LTFU activities that should be included in an NSS. It does not address other components of the overall NSS, such as laboratory methods, intervention protocols, or administrative organization. It is intended for global use by public health officials, policy makers, and all involved in any aspect of follow-up within NSS, including confirmatory laboratory personnel, health care providers, parents, and families.

### 2 Standard Precautions

Because it is often impossible to know what isolates or specimens might be infectious, all patient and laboratory specimens should be treated as infectious and handled according to “standard precautions.” Standard precautions are guidelines that combine the major features of “universal precautions and body substance isolation” practices. Standard precautions cover the transmission of all known infectious agents and thus are more comprehensive than universal precautions, which are intended to apply only to transmission of blood-borne pathogens. The Centers for Disease Control and Prevention address this topic in published guidelines that focus on the daily operations of diagnostic medicine while encouraging a culture of safety in the laboratory.<sup>10</sup> For specific precautions for preventing the laboratory transmission of all known infectious agents from laboratory instruments and materials and for recommendations for the management of exposure to all known infectious diseases, refer to CLSI document M29.<sup>11</sup>

### 3 Terminology

#### 3.1 A Note on Terminology

CLSI, as a global leader in standardization, is firmly committed to achieving global harmonization wherever possible. Harmonization is a process of recognizing, understanding, and explaining differences while taking steps to achieve worldwide uniformity. CLSI recognizes that medical conventions in the global metrological community have evolved differently in the United States, Europe, and elsewhere; that these differences are reflected in CLSI, International Organization for Standardization, and European Committee for Standardization (CEN) documents; and that legally required use of terms, regional usage, and different consensus timelines are all important considerations in the harmonization process. In light of

this, CLSI's consensus process for development and revision of standards and guidelines focuses on harmonization of terms to facilitate the global application of standards and guidelines.

In CLSI newborn screening documents, the terms *newborn* and *infant* have distinct meanings. *Newborn* indicates a person from birth to 30 days old, and *infant* indicates a person from 1 month to 1 year old. In situations that could apply to both (or either) age groups, the term *baby* is used.

## 3.2 Definitions

**confirmatory/diagnostic test** – test to prove or disprove the presence of a specific condition suggested by screening tests; **NOTE:** For dried blood spot screening, this testing is from a specimen other than the original screening specimen.

**follow-up** – actions taken to ensure that a person whose test results are screen positive or invalid receives appropriate further tests and evaluation in a timely fashion; and actions taken that ensure the newborn screening system evaluates the effectiveness of screening.

**intervention** – specific follow-up activities (eg, clinical assessment, medical management) targeted at improving health and/or developmental outcomes of an affected newborn.

**invalid screen** – inability to complete the screening algorithm according to established criteria, due to problems such as unsuitable specimen, no specimen, inconsistent or ambiguous results, or incomplete patient information.

**long-term follow-up (LTFU)** – all of the activities that should occur after a patient is diagnosed and subsequently confirmed with a condition. It may include care coordination, assuring the availability of evidence-based treatment, continuous quality improvement, and new knowledge discovery, as well as periodic assessment of the clinical outcomes in affected individuals.

**lost to follow-up** – status assigned to an individual unable to be located for completion of follow-up despite all prescribed protocols being followed.

**newborn dried blood spot (DBS) screening** – process of collecting blood onto a filter paper collection device, testing defined analytes by approved laboratory methods, and reporting results as appropriate.

**newborn hearing screening** – the process of using a physiological measure of auditory function to detect potential hearing loss present at birth that may interfere with the development of speech and language.

**newborn screening program (NSP)** – public health or other administrative entity responsible for development, implementation, and oversight of newborn screening laws, policies, and procedures for a given newborn screening system, including education, screening, follow-up, diagnosis, management, and evaluation.

**newborn screening system (NSS)** – a collaboration of newborn screening stakeholders including public and private agencies, institutions, parents, policy makers, health care providers, and caregivers working together to ensure that all newborns within a defined geographical area have access to newborn screening and those found affected are able to access appropriate care.

**point-of-care screening** – encompasses screening tests that are administered and interpreted close to the site of direct delivery of medical care (ie, birthing hospital/nursery).<sup>12</sup>

**primary care provider** – health care professional who provides routine health care and coordinates and collaborates with specialty care; **NOTE:** In some jurisdictions, the term “medical home” is used.

## The Quality Management System Approach

Clinical and Laboratory Standards Institute (CLSI) subscribes to a quality management system approach in the development of standards and guidelines, which facilitates project management; defines a document structure via a template; and provides a process to identify needed documents. The quality management system approach applies a core set of “quality system essentials” (QSEs), basic to any organization, to all operations in any health care service’s path of workflow (ie, operational aspects that define how a particular product or service is provided). The QSEs provide the framework for delivery of any type of product or service, serving as a manager’s guide. The QSEs are as follows:

Organization	Personnel	Process Management	Nonconforming Event Management
Customer Focus	Purchasing and Inventory	Documents and Records	Assessments
Facilities and Safety	Equipment	Information Management	Continual Improvement

NBS02-A2 addresses the QSE indicated by an “X.” For a description of the other documents listed in the grid, please refer to the Related CLSI Reference Materials section on the following page.

Organization	Customer Focus	Facilities and Safety	Personnel	Purchasing and Inventory	Equipment	Process Management	Documents and Records	Information Management	Nonconforming Event Management	Assessments	Continual Improvement
		M29			NBS04	X NBS01 NBS03 NBS04 NBS05					

### Path of Workflow

A path of workflow is the description of the necessary steps to deliver the particular product or service that the organization or entity provides. A laboratory path of workflow consists of the sequential processes: preexamination, examination, and postexamination and their respective sequential subprocesses. All laboratories follow these processes to deliver the laboratory’s services, namely quality laboratory information.

NBS02-A2 addresses the clinical laboratory path of workflow processes indicated by an “X.” For a description of the other documents listed in the grid, please refer to the Related CLSI Reference Materials section on the following page.

Examination ordering	Preexamination			Examination			Postexamination	
	Sample collection	Sample transport	Sample receipt/processing	Examination	Results review and follow-up	Interpretation	Results reporting and archiving	Sample management
NBS01	NBS01	NBS01	X NBS01 NBS04	X NBS01 NBS04 NBS05	NBS04 NBS05	NBS04	X	NBS01

## Related CLSI Reference Materials\*

- M29-A3**      **Protection of Laboratory Workers From Occupationally Acquired Infections; Approved Guideline—Third Edition (2005).** Based on US regulations, this document provides guidance on the risk of transmission of infectious agents by aerosols, droplets, blood, and body substances in a laboratory setting; specific precautions for preventing the laboratory transmission of microbial infection from laboratory instruments and materials; and recommendations for the management of exposure to infectious agents.
- NBS01-A5**      **Blood Collection on Filter Paper for Newborn Screening Programs; Approved Standard—Fifth Edition (2007).** This document addresses the issues associated with specimen collection, the filter paper collection device, and the application of blood to filter paper, and provides uniform techniques for collecting the best possible specimen for use in newborn screening programs.
- NBS03-A**      **Newborn Screening for Preterm, Low Birth Weight, and Sick Newborns; Approved Guideline (2009).** This guideline outlines the recommended protocols for screening preterm, sick, or low birth weight infants for hearing loss and disorders detectable through dried blood spot testing.
- NBS04-A**      **Newborn Screening by Tandem Mass Spectrometry; Approved Guideline (2010).** This guideline serves as a reference source for the numerous activities related to operating a tandem mass spectrometry laboratory as part of public and private newborn screening programs with the goal of creating greater test accuracy, performance, and consistency among laboratories, thereby ensuring data quality that will ultimately benefit all newborns worldwide.
- NBS05-A**      **Newborn Screening for Cystic Fibrosis; Approved Guideline (2011).** This document describes the use of newborn screening laboratory tests for detecting risk for cystic fibrosis from newborn dried blood spots (DBS) and addresses both the primary screening tests and the reflex tests performed on DBS.

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\* CLSI documents are continually reviewed and revised through the CLSI consensus process; therefore, readers should refer to the most current editions.



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