CLINICAL AND LABORATORY STANDARDS INSTITUTE®

3rd Edition

NBS02

Newborn Screening Follow-up and Education

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

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

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Newborn Screening Follow-up and Education

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Abstract

Clinical and Laboratory Standards Institute guideline NBS02—*Newborn Screening Follow-up and Education* describes the basic principles, scope, and range of follow-up and education activities within a newborn screening (NBS) program and system. NBS systems are responsible for education, screening, follow-up, diagnosis, intervention, and evaluation. Follow-up and education activities are part of the NBS system and play an essential role in facilitating early detection, diagnosis, and intervention for affected babies. This guideline is intended for those involved in any aspect of follow-up and/or education, including health care providers, parents, and others concerned with the health and welfare of newborns.

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Foreword

Newborn screening (NBS) is an essential public health service focused on testing every newborn for certain congenital diseases, groups of diseases, and/or phenotypic differences, including hearing differences, that can result in significant morbidity and/or mortality without early intervention.[1] Screening tests are not diagnostic. Rather, they separate newborns at higher risk of having a disease, group of diseases, or phenotypic difference from newborns at low risk. Therefore, newborns who have screen-positive results, indicating higher risk, must undergo additional diagnostic testing and clinical evaluation to confirm their status as affected or unaffected.

A complete NBS system comprises six parts: education, screening, follow-up, diagnosis, intervention and/or management, and evaluation.[2] Although the NBS system historically focused primarily on the screening tests performed within the public health laboratory, it is now understood that education, follow-up, diagnosis, intervention and/or management, and evaluation are equally important. An effective NBS system provides the infrastructure for universal access, education, and rapid follow-up for at-risk newborns. Parents and/or legal guardians; hospital, birthing facility, and midwifery personnel; health care providers (HCPs); and the NBS program should collaborate to ensure that the NBS system functions effectively and efficiently, providing maximum benefit to the family.

The primary aim of the NBS system is to provide early intervention for affected babies. Pre- and postdiagnostic follow-up helps ensure the accountability of NBS programs and systems. Follow-up, which determines whether NBS systems are achieving and sustaining their primary aims of preventing or minimizing morbidity and mortality, is vital to evaluating the benefits of NBS to an individual throughout his or her life, as well as to the family and society.[3] The quality of follow-up services directly affects the lives of families with at-risk and affected babies. This guideline outlines the role of follow-up services within an NBS system and provides guidance on developing and maintaining effective follow-up services, as well as on educating parents and legal guardians; hospital, birthing facility, and midwifery personnel; and HCPs on their roles in ensuring the success of NBS systems.

Overview of Changes

This guideline replaces the previous edition of the approved guideline, NBS02-A2, published in 2013. Several changes were made in this edition, including:

- Explaining general and NBS-specific terminology, including recent changes:
  - Describing use of the term *special care baby unit and/or neonatal intensive care unit*
  - Clarifying use of the terms *disease*, *disorder*, and *condition*
  - Clarifying definitions for *short-term follow-up* and *long-term follow-up*
- Expanding discussion of the role of communication and education in the prenatal and postnatal periods and throughout NBS systems
- Discussing timeliness initiatives related to follow-up
- Expanding discussion of postdiagnostic follow-up needs for affected individuals and families
- Outlining considerations for use of advanced screening technologies and their effect on education and follow-up needs
- Describing follow-up considerations for new diseases or groups of diseases added to screening panels

NOTE: The content of this guideline is supported by the CLSI consensus process and does not necessarily reflect the views of any single individual or organization.

KEY WORDS

congenital heart disease
dried blood spot screening
long-term follow-up
newborn hearing screening
newborn screening
quality assurance
short-term follow-up

Chapter 1

Introduction

Newborn Screening Follow-up and Education

1 Introduction

1.1 Scope

The primary goal of this guideline is to enhance the overall quality and continuity of newborn screening (NBS) follow-up and education services offered through public health or other NBS programs. The timeliness, quality, and effectiveness of these services directly affect the health and well-being of babies and their families, as well as the effectiveness of the NBS system.

This guideline discusses both the follow-up and education components of the NBS system. Awareness, education, training, and engagement in NBS programs are pivotal to the ongoing success of NBS as a public health initiative. To ensure efficient coordination and informed decision-making, it is important that these efforts span the entire NBS system, including the preanalytical, analytical, and postanalytical phases. As NBS continues to expand and become more complex, NBS programs increasingly need to invest resources in information dissemination and evaluate the success of those efforts in achieving NBS-related communication goals.

Likewise, post-NBS follow-up services have evolved and might now span from the first days after birth to many years after a patient is diagnosed with a disease or trait or found to have hearing differences. Follow-up services include ensuring that all newborns have received a valid screen; establishing vigorous processes to ensure appropriate follow-up for babies with actionable results; and assessing care coordination, family needs, and health outcomes after diagnosis. In general, robust follow-up is an essential part of the screening pathway, contributing to the NBS goals of quickly detecting at-risk newborns and improving health outcomes for affected babies.

The NBS program should assess the resources available in its geographic location for disease diagnosis, treatment and other interventions, and follow-up. A lack of resources can limit the value of screening. Detecting newborns at increased risk for a disease might not be advisable if sufficient resources for care are not available.

This guideline outlines the wide range of follow-up and education activities that should be included in an NBS system. It is intended for global use by public health officials, policy makers, health care providers (HCPs), and anyone involved in any aspect of follow-up or education within NBS systems, including NBS program personnel, confirmatory laboratory personnel, parents, families, and other caregivers. It does not cover other components of the NBS system, such as laboratory methods, disease-specific monitoring, treatment and other intervention protocols, or specific follow-up considerations for point-of-care (POC) screening (eg, newborn hearing screening, critical congenital heart disease [CCHD] screening by pulse oximetry).

Although funding, laws, regulations, and external advisory committees certainly apply to and affect follow-up and education activities within NBS programs, the details of these components are not included in this guideline. However, it is important for NBS programs to ensure that follow-up and education activities are accounted for within funding, regulatory, and advisory structures by including program elements such as health education, short-term follow-up (STFU) and long-term follow-up (LTFU) staffing needs, materials development and dissemination, contracts with specialty centers, and coverage of medical foods and formulas.

1.2 Standard Precautions

Because it is often impossible to know what isolates or specimens might be infectious, all patient and laboratory specimens are 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 bloodborne pathogens. Published guidelines are available that discuss the daily operations of diagnostic medicine in humans and animals while encouraging a culture of safety in the laboratory.[4] 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.[5]

1.3 Terminology

CLSI, as a global leader in standardization, is firmly committed to achieving global harmonization whenever 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 different countries and regions and that legally required use of terms, regional usage, and different consensus timelines are all important considerations in the harmonization process. CLSI recognizes its important role in these efforts, and its consensus process focuses on harmonization of terms to facilitate the global application of standards and guidelines. Table 1 is provided to clarify the intended interpretations of the following terms.

Table 1. Common Terms or Phrases With Intended Interpretations

Term or Phrase	Intended Interpretation
"Needs to" or "must"	Explains an action directly related to fulfilling a regulatory and/or accreditation requirement or is indicative of a necessary step to ensure patient safety or proper fulfillment of a procedure
"Require"	Represents a statement that directly reflects a regulatory, accreditation, performance, product, or organizational requirement or a requirement or specification identified in an approved documentary standard
"Should"	Describes a recommendation provided in laboratory literature, a statement of good laboratory practice, or a suggestion for how to meet a requirement

CLSI uses the globally applicable terms *preexamination, examination,* and *postexamination* in its documents. However, in the NBS laboratory, dried blood spot (DBS) specimens are "examined" to ensure they are satisfactory before they are "analyzed." Hence, for the purposes of CLSI NBS documents, the terms *preanalytical, analytical,* and *postanalytical* are used in place of *preexamination, examination,* and *postexamination*. Additionally, the term *analysis* is used in place of *examination*. However, the terms *preanalytical, analytical,* and *postanalytical* are not typically used for the POC components of NBS. For POC NBS, in alignment with CLSI documents that cover POC testing, the terms *preexamination, examination,* and *postexamination* remain more appropriate. Although contradictions among these terms might exist between new CLSI NBS documents and already published NBS documents, these contradictions will be reconciled as documents go through the routine revision process.

In CLSI NBS documents, the terms *newborn* and *infant* have distinct meanings. *Newborn* indicates a person from birth to 28 days old, while *infant* indicates a person from 29 days to 1 year old. In situations that could apply to both (or either) age groups, the term *baby* is used.

In this guideline, *special care baby unit and/or neonatal intensive care unit* (SCBU/NICU) is used to identify facilities providing care above the level provided for newborns rooming with the mother or in well-baby nurseries, acknowledging that SCBUs generally provide less intensive care than some higher-level NICUs.

Use of the terms *disease, disorder,* and *condition* varies among NBS programs, systems, and stakeholders when they are referring to newborns with confirmed positive NBS test results. NBS tests are performed to detect newborns at an increased risk for a *disease* that has a known, underlying cause and that necessitates treatment, so the term *disease* is used for consistency throughout this guideline, with a few exceptions. The term *disorder* is used only when the term is part of a disease name (eg, lysosomal storage disorders, fatty acid oxidation disorders). The term *condition* is used only to generally describe a newborn and/or maternal circumstance or state of being (eg, the *condition* of prematurity, effects of maternal and newborn *conditions* and treatments on screening results). To refer to newborn hearing screening outcomes, the term *hearing differences* is used, rather than the term *disease*, to indicate that this finding is not typically considered a disease, but a phenotypic difference.[6,7] Additionally, although the term *disease* is used throughout this guideline, it is important to acknowledge that phenotypic differences not typically considered a disease (eg, hearing differences, sickle cell trait) are also detected through NBS.

Many terms are used to describe professionals who provide health care for a baby (eg, primary care provider, neonatologist, pediatrician, disease specialist). For the purposes of this guideline, the term *health care provider* is defined and used to refer generally to nonspecified health care professionals. The terms *primary health care provider* and *specialty care provider* are defined and used specifically to describe personnel or roles typically involved in NBS follow-up processes. In situations that do not apply specifically to either a *primary health care provider* or a *specialty care provider,* the generic term *health care provider* is used.

The terminology used to report NBS results varies from program to program. *In-range* results might be reported as *screen negative, normal, low disease probability, disease unlikely,* or similar terminology. Reporting of *out-of-range* results might depend on whether the program uses a single cutoff (ie, action limit) or whether it also uses a secondary cutoff to determine follow-up actions in the event of *screen-positive* results for a particular disease. When a single cutoff is used (see Figure 1), *out-of-range* results might be reported as *screen positive, disease probable,* or similar terminology. If a second-level cutoff is used (see Figure 2), results that fall within the borderline range (ie, results are *out of range*, but not to the level of a referral for diagnostic testing and clinical evaluation) might be reported as *borderline positive, disease possible,* or similar terminology. When a borderline result is obtained a second time (on a separate specimen), the newborn is usually referred for diagnostic testing and clinical evaluation. The use of borderline classifications and actions are usually limited to diseases, or specific clinical phenotypes within a disease spectrum, for which delaying final results while obtaining an additional screening specimen poses minimal harm. The laboratory's specimen submitters, HCPs, and follow-up personnel should consult their jurisdiction's program for clarification on preferred terminology.

The Quality Management System Approach

Clinical and Laboratory Standards Institute (CLSI) subscribes to a quality management system (QMS) approach in the development of standards and guidelines that facilitates project management, defines a document structure using a template, and provides a process to identify needed documents. The QMS 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:

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

The QSEs covered by NBS02 and its related CLSI documents are available on the CLSI website: https://clsi.org/qse

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