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# Newborn Screening Follow-up; Proposed Guideline

*PLEASE*

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This proposed document is published for wide and thorough review in the new, accelerated Clinical and Laboratory Standards Institute (CLSI) consensus-review process. The document will undergo concurrent consensus review, Board review, and delegate voting (i.e., candidate for advancement) for 90 days.

Please send your comments on scope, approach, and technical and editorial content to CLSI.

Comment period ends

13 December 2005

The subcommittee responsible for this document will assess all comments received by the end of the comment period. Based on this assessment, a new version of the document will be issued. Readers are encouraged to send their comments to Clinical and Laboratory Standards Institute, 940 West Valley Road, Suite 1400, Wayne, PA 19087-1898 USA; Fax: +610.688.0700, or to the following e-mail address: customerservice@clsi.org

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*COMMENT*

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.

CLINICAL AND LABORATORY STANDARDS INSTITUTE

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**Guideline** A document developed through the consensus process describing criteria for a general operating practice, procedure, or material for voluntary use. A guideline may be used as written or modified by the user to fit specific needs.

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**CONSENSUS PROCESS**

The CLSI voluntary consensus process is a protocol establishing formal criteria for:

- the authorization of a project
- the development and open review of documents
- the revision of documents in response to comments by users
- the acceptance of a document as a consensus standard or guideline.

Most documents are subject to two levels of consensus—"proposed" and "approved." Depending on the need for field evaluation or data collection, documents may also be made available for review at an intermediate consensus level.

**Proposed** A consensus document undergoes the first stage of review by the healthcare community as a proposed standard or guideline. The document should receive a wide and thorough technical review, including an overall review of its scope, approach, and utility, and a line-by-line review of its technical and editorial content.

**Approved** An approved standard or guideline has achieved consensus within the healthcare community. It should be reviewed to assess the utility of the final document, to ensure attainment of consensus (i.e., that comments on earlier versions have been satisfactorily addressed), and to identify the need for additional consensus documents.

Our standards and guidelines represent a consensus opinion on good practices and reflect the substantial agreement by materially affected, competent, and interested parties obtained by following CLSI's established consensus procedures. Provisions in CLSI standards and guidelines may be more or less stringent than applicable regulations. Consequently, conformance to this voluntary consensus document does not relieve the user of responsibility for compliance with applicable regulations.

**COMMENTS**

The comments of users are essential to the consensus process. Anyone may submit a comment, and all comments are addressed, according to the consensus process, by the committee that wrote the document. All comments, including those that result in a change to the document when published at the next consensus level and those that do not result in a change, are responded to by the committee in an appendix to the document. Readers are strongly encouraged to comment in any form and at any time on any document. Address comments to Clinical and Laboratory Standards Institute, 940 West Valley Road, Suite 1400, Wayne, PA 19087, USA.

**VOLUNTEER PARTICIPATION**

Healthcare professionals in all specialties are urged to volunteer for participation in CLSI projects. Please contact us at customerservice@clsi.org or +610.688.0100 for additional information on committee participation.

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# Newborn Screening Follow-up; Proposed Guideline

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## Abstract

Newborn screening for congenital conditions is a public health system composed of screening, follow-up, diagnosis management, evaluation, and education. As part of the system, follow-up activities play an essential role in facilitating early diagnosis and intervention for affected newborns. Clinical and Laboratory Standards Institute document I/LA27-P—*Newborn Screening Follow-up; Proposed Guideline* 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 healthcare providers, parents, and others concerned with the health and welfare of newborns.

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## Proposed Guideline

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## Contents

## Foreword

Newborn screening is an essential public health activity that strives to screen every newborn for a variety of congenital conditions, which if not detected and managed early, can result in significant morbidity and mortality. It is one of the most successful population-based screening programs ever implemented. Screening tests separate newborns who probably have a condition from those who probably do not. Screening is not intended to be diagnostic and newborns identified with suspicious findings must undergo further testing and clinical evaluation.

Effective newborn screening systems provide the infrastructure for universal access and rapid follow-up. Properly constructed, they facilitate timely intervention for affected newborns whose life and health may be at risk. Systems for newborn hearing screening (NHS) and dried blood spot (DBS) screening are comprised of six parts: screening, follow-up, diagnosis, management, evaluation, and education.[1] Parents/legal guardians and families, obstetric and pediatric health professionals, audiologists, birthing facilities, public health newborn screening programs, laboratories, and other providers involved in the care of newborns should partner to ensure that the system functions effectively. The public health newborn screening program refers to the administrative entity responsible for development, implementation, and oversight of policy and procedures within the screening system, where this exists.

These guidelines provide a reference for developing and providing follow-up services within a newborn screening system. They are specifically focused on NHS and DBS screening, but applicable to other types of universal newborn screening. The primary function of follow-up services within the newborn screening system is to locate newborns with screening results that are “out-of-range” or “invalid,” in order to determine if a newborn has a screened condition, and for affected newborns, to facilitate prompt treatment and referral for subspecialty care and support services.

It is estimated that three newborns in 1000 will be affected with hearing loss and approximately one newborn in 800 will be affected with a metabolic, endocrine, or hematologic disorder detectable by DBS screening.[2,3] This equates to an estimate of one newborn per 250 births who are at serious risk of physical and/or developmental disabilities, or even death, as a result of their condition. Because there are genetic components to most of the conditions included in newborn screening, birth prevalence rates may vary depending on the screened population. Technological advances will continue to enable programs to screen for increasing numbers of conditions in the future. This guideline provides reference information to ensure that appropriate follow-up occurs.

The need to include follow-up services in the newborn screening system originated with the realization that simply reporting “out-of-range” or “invalid’ screen results did not ensure appropriate or timely treatment for affected newborns.[4-6] Rapid, efficient, and effective follow-up is critical to ensure that newborns needing further testing are evaluated quickly. Within newborn screening systems, effective follow-up, often provided by nurses or genetic counselors, facilitates actions to ensure that the newborn is located and receives timely confirmatory testing that leads to a rapid diagnosis (not affected or affected). Further, it ensures that affected newborns receive prompt and appropriate referral for subspecialty care and support services.

Follow-up activities can be divided into two broad categories, short-term and long-term follow-up. Successful follow-up requires coordinated efforts of dedicated follow-up personnel within the newborn screening program working with system partners, including: parents, birthing facilities, primary care providers, appropriate subspecialty care providers, early intervention programs, and laboratory professionals.

The aim of short-term follow-up (STFU) is to locate newborns with screening results that are “out-of-range” or “invalid,” in order to determine if a newborn has a screened condition, and for affected

newborns, to facilitate prompt treatment and referral for subspecialty care and support services. STFU ends with diagnosis and documentation of treatment (if applicable) and referral information.

Long-term follow-up (LTFU) allows for the evaluation of the benefits resulting from newborn screening throughout the life of an individual. These benefits may impact the individual, the family, and/or society. Evaluation requires periodic assessment of indicators that are measurable, functional, and appropriate to the condition detected. LTFU may include facilitation of care coordination services to ensure that the needs of the affected newborn/individual and family are met.

The quality of follow-up services directly impacts the lives of families with newborns. This document outlines the role of follow-up services within a newborn screening system, and provides guidance for developing and maintaining effective follow-up services. Efforts have been made to reach consensus among a representative group of newborn screening stakeholders, and they seek to describe best practices for newborn screening follow-up. It is anticipated that these guidelines will require periodic review and update, as screening expands and follow-up activities are required to meet increased needs.

**Invitation for Participation in the Consensus Process**

An important aspect of the development of this and all Clinical and Laboratory Standards Institute (CLSI) documents should be emphasized, and that is the consensus process. Within the context and operation of CLSI, the term “consensus” means more than agreement. In the context of document development, “consensus” is a process by which CLSI, its members, and interested parties (1) have the opportunity to review and to comment on any CLSI publication; and (2) are assured that their comments will be given serious, competent consideration. Any CLSI document will evolve as will technology affecting laboratory or healthcare procedures, methods, and protocols; and therefore, is expected to undergo cycles of evaluation and modification.

The Area Committee on Immunology and Ligand Assay has attempted to engage the broadest possible worldwide representation in committee deliberations. Consequently, it is reasonable to expect that issues remain unresolved at the time of publication at the proposed level. The review and comment process is the mechanism for resolving such issues.

The CLSI voluntary consensus process is dependent upon the expertise of worldwide reviewers whose comments add value to the effort. At the end of a 90-day comment period, each subcommittee is obligated to review all comments and to respond in writing to all which are substantive. Where appropriate, modifications will be made to the document, and all comments along with the subcommittee’s responses will be included as an appendix to the document when it is published at the next consensus level.

**Key Words**

Dried blood spot screening, long-term follow-up, newborn hearing screening, newborn screening, population screening, quality assurance, short-term follow-up

# Newborn Screening Follow-up; Proposed Guideline

## 1 Scope

Newborn screening is a system comprised of screening, follow-up, diagnosis, management, evaluation, and education. Follow-up is essential to ensure valid screening results are known for every eligible newborn, that all out-of-range results are followed to definitive diagnosis and appropriate clinical management, and that long-term outcome data are collected for program assessment and quality assurance. The primary goal of this guideline is to improve the quality of follow-up services for newborns screened through public health newborn screening programs. The quality of follow-up services directly impacts the health of newborns and families. This provides guidance for effective follow-up to ensure timely identification and treatment of affected newborns.

This guideline is limited to follow-up activities associated with invalid and out-of-range test results within a newborn screening system. It is not intended to address other components of the overall newborn screening system, such as screening, confirmatory testing, education, treatment, or system evaluation practices outside of follow-up.

This guideline is intended to be used globally by public health officials and those who are involved in any aspect of follow-up within newborn screening systems, including: maternity healthcare providers, hospital personnel, newborn healthcare providers, pediatric subspecialty providers (e.g., hematology, endocrinology, metabolism, pulmonology, genetics, and audiology), parents and families, other providers involved with the care of newborns, confirmatory clinical laboratories, and newborn screening program personnel.

## 2 Definitions

**confirmatory/diagnostic test** – test to prove or disprove the presence of a specific condition identified by screening tests (for DBS screening, this testing is from a specimen other than the screening specimen).

**false negative** – “in-range” result in an affected newborn. This may occur because the test result was normal, there was a laboratory procedure/testing error, failure to obtain or test a specimen, an inadequate specimen, communication, or other issues; **NOTE:** For more information, refer to Section 4.2.2.5.

**false positive** – “out-of-range” result in an unaffected newborn.

**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.

**in-range result** – screening result that is within the expected range of testing results established for a particular condition.

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

**invalid screen** – inability to complete the screening process according to established criteria, such as unsuitable specimen or test, no specimen or test, or incomplete information.

**long-term follow-up (LTFU)** – actions commencing after confirmed diagnosis in an affected individual to ensure the screening program can evaluate the effectiveness of the program and may include the