CLINICAL AND LABORATORY STANDARDS INSTITUTE®

3rd Edition

CLSI C40™

Measurement Procedures for the Determination of Lead in Whole Blood

CLSI C40 provides recommendations on the measurement of lead (Pb) in whole blood, including specimen collection procedures and determination of Pb by graphite furnace atomic absorption spectrometry, anodic stripping voltammetry (based on disposable screen-printed electrode technologies), and inductively coupled plasma mass spectrometry. It also includes quality assurance and quality control guidance and information on proficiency testing programs and laboratory certification.

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

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Measurement Procedures for the Determination of Lead in Whole Blood

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Abstract

Clinical and Laboratory Standards Institute C40—*Measurement Procedures for the Determination of Lead in Whole Blood* is intended for use by members of the medical laboratory community involved in the determination of lead (Pb) in blood, as well as by personnel involved in specimen collection. This guideline discusses the clinical significance of blood lead (BPb) measurements; specimen collection; and Pb determination by graphite furnace atomic absorption spectrometry, anodic stripping voltammetry (based on disposable screen-printed electrode technologies), and inductively coupled plasma mass spectrometry. It also discusses reference materials, QC procedures, and laboratory policies for BPb testing.

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Foreword

Lead (Pb) is a naturally occurring heavy metal, long known for its toxic effects on human health, especially in children. The determination of Pb in whole blood (ie, the blood lead [BPb] test) is considered the reference standard for assessing human exposure. Current methods of analysis are capable of measuring BPb at historically low concentrations and in very small sample volumes. Over the last 40 years, the blood lead level (BLL) deemed harmful to children has been lowered many times. In 2012, a blood lead reference value (BLRV) of 5 µg/dL (0.24 µmol/L) was adopted to identify children with BLLs that are higher than most children's levels.[1] Globally, population BLLs continue to decline as Pb is removed from products and thus from the environment. In 2019, updated data from the United States showed that the geometric mean for BPb had fallen to 0.820 µg/dL for the period 2015 to 2016. For children ages 1 to 5 years, the geometric mean BPb was 0.758 µg/dL for the same period, and the 95th percentile was 2.76 µg/dL. In 2021, a US public health organization lowered the BLRV from 5 µg/dL (0.24 µmol/L) to 3.5 µg/dL (0.17 µmol/L). This trend toward decreasing population BLLs has also been noted in other countries. Given that no safe BLL has been established, the importance of reporting results below 5 µg/dL (0.24 µmol/L) has only increased, along with a renewed interest in the accuracy, precision, and reliability of laboratory measurements. Better-quality BPb measurements are expected to support public health decision-making and mitigation efforts.

Overview of Changes

This guideline replaces CLSI C40-A2, published in 2013. Several changes were made in this edition, including:

- Adding detailed analytical procedures for BPb measurements based on inductively coupled plasma mass spectrometry
- Updating:
  - Information on the clinical and public health significance of BLLs < 5 µg/dL (0.24 µmol/L)
  - Guidance on anodic stripping voltammetry (ASV) devices that use disposable screen-printed electrode technologies
  - Guidance for laboratories on quality assurance practices at BLLs of 3.5 µg/dL
  - Current information on laboratory certification and proficiency testing programs (or external quality assessment) in the United States, Canada, and Europe, provided in Appendix A
  - The protocol for checking materials and specimen collection supplies for Pb contamination, provided in Appendix B
- Deleting:
  - The classic ASV procedure for older benchtop instrumentation
  - A procedure for urine Pb measurement, which is now considered redundant for clinical purposes

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.

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KEY WORDS

analysis

anodic stripping voltammetry

blood

electrothermal atomic absorption spectrometry

graphite furnace atomic absorption spectrometry

inductively coupled plasma mass spectrometry

lead poisoning

quality control

reference materials

Chapter 1

Introduction

Measurement Procedures for the Determination of Lead in Whole Blood

1 Introduction

1.1 Scope

The goal of this guideline is to provide up-to-date information on the determination of lead (Pb) in whole blood (BPb). Preexamination considerations, such as specimen collection for screening and diagnosis, the role of capillary compared with venous blood specimens, anticoagulant selection, collection containers, and contamination monitoring and control, are included.

Examination considerations are focused on the three major instrumental methods used to determine BPb: **(1)** electrothermal atomic absorption spectrometry (ETAAS), also known as graphite furnace atomic absorption spectrometry (GFAAS); **(2)** inductively coupled plasma mass spectrometry (ICP-MS); and **(3)** anodic stripping voltammetry (ASV) based on disposable electrochemical technologies. CLSI C40 does not include considerations for classic ASV based on benchtop devices that use a carbon-based electrode with a thin film of mercury (Hg) because commercial instrumentation is no longer available and analytical performance is no longer considered fit for purpose. Other considerations include internal and external QA and QC and guidance on troubleshooting common problems with BPb testing.

Postexamination considerations, such as criteria for repeat testing of the original clinical specimen, reporting test results, and guidance on requesting an additional blood specimen, are also included. Information on proficiency testing (PT) programs is provided, along with guidance on acceptable performance across the various schemes.

CLSI C40 also provides a brief review of the background and clinical significance of BPb measurements, as well as recommendations for evaluating test results within the context of method uncertainty, contamination errors, and other laboratory limitations.

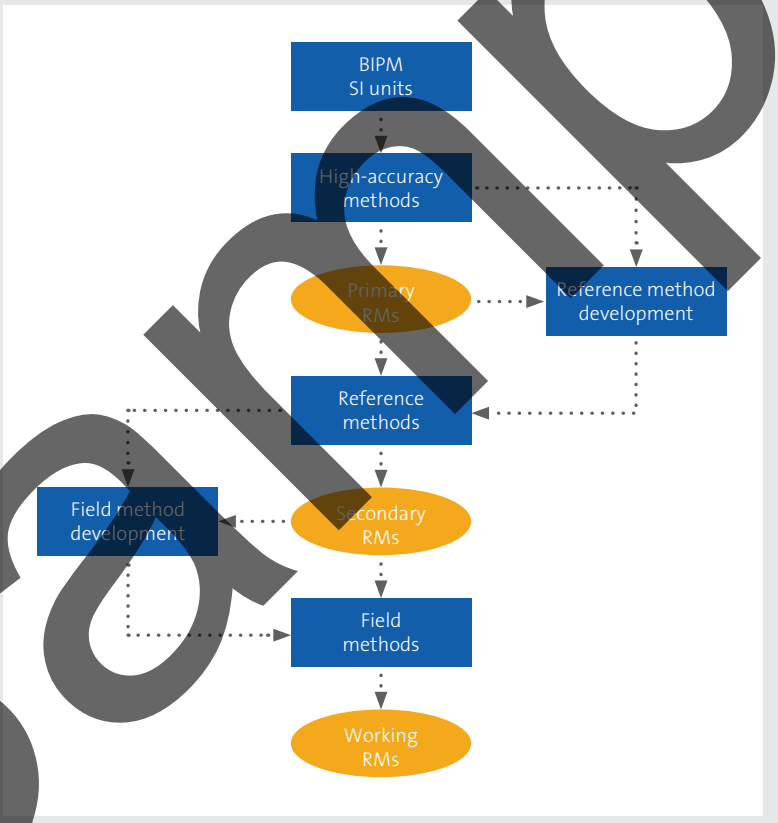
This guideline is intended for use by members of the medical laboratory community worldwide (and by point-of-care [POC] testing facilities) involved in the measurement of BPb using well-established methods, as well as by personnel involved in specimen collection. The determination of Pb in urine is no longer included because this test is now considered redundant for clinical purposes.

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.[2] 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 M29.[3]

methods, which should agree within the limits of the methods' uncertainties. In the medical laboratory community, high-trueness methods are called primary reference (measurement) procedures, which are reference measurement procedures used to obtain a measurement result without relation to a measurement standard for a quantity of the same kind.[4] Primary reference procedures include gravimetric, volumetric, and coulometric analyses, as well as ID-MS, all of which can be connected directly to the mole.

Primary reference procedures have a valid and well-understood theoretical basis and yield results that are precise and have negligible systematic error.[106] The magnitude of the primary reference procedure's final imprecision and bias, expressed in the uncertainty statement, is compatible with the primary reference procedure's stated end purpose. The mean primary reference procedure value is considered the "true" value. The process of developing and maintaining a primary reference procedure is costly and time consuming and is usually undertaken by national metrological laboratories. Laboratories such as NIST (United States), the Laboratory of the Government Chemist (United Kingdom), the Joint Research Centre (European Commission), Bundesanstalt für Materialforschung (Germany), the National Research Council (Canada), and the National Institute for Metrology (People's Republic of China) have produced CRMs as primary standards using primary reference procedures (see Figure 5).



Abbreviations: BIPM, International Bureau of Weights and Measures; CRM, certified reference material; RM, reference material; SI, Système International d'Unités (International System of Units).
[a] The fundamental units of measurement, Système International d'Unités (International System of Units), appear at the apex of this system. They are linked through high-accuracy measurement procedures to primary RMs. A primary RM is an RM that has the highest metrological qualities and whose value is determined by a primary reference measurement procedure.[16] In effect, primary RMs are CRMs whose values can be accepted without additional verification by the user. Thus, primary RMs represent an accurate realization of the matrix and measurands. The system then cascades through methods and materials of decreasing accuracy and characterization.

Figure 4. Hierarchy of RMs Providing the Traceability Links for Clinical Measurements[a]

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