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.

Clinical and Laboratory Standards Institute

Setting the standard for quality in medical laboratory testing around the world.

The Clinical and Laboratory Standards Institute (CLSI) is a not-for-profit membership organization that brings together the varied perspectives and expertise of the worldwide laboratory community for the advancement of a common cause: to foster excellence in laboratory medicine by developing and implementing medical laboratory standards and guidelines that help laboratories fulfill their responsibilities with efficiency, effectiveness, and global applicability.

Consensus Process

Consensus—the substantial agreement by materially affected, competent, and interested parties—is core to the development of all CLSI documents. It does not always connote unanimous agreement but does mean that the participants in the development of a consensus document have considered and resolved all relevant objections and accept the resulting agreement.

Commenting on Documents

CLSI documents undergo periodic evaluation and modification to keep pace with advances in technologies, procedures, methods, and protocols affecting the laboratory or health care.

CLSI's consensus process depends on experts who volunteer to serve as contributing authors and/or as participants in the reviewing and commenting process. At the end of each comment period, the committee that developed the document is obligated to review all comments, respond in writing to all substantive comments, and revise the draft document as appropriate.

Comments on published CLSI documents are equally essential and may be submitted by anyone, at any time, on any document. All comments are managed according to the consensus process by a committee of experts.

Appeal Process

When it is believed that an objection has not been adequately considered and responded to, the process for appeal, documented in the CLSI *Standards Development Policies and Processes,* is followed.

All comments and responses submitted on draft and published documents are retained on file at CLSI and are available upon request.

Get Involved—Volunteer!

Do you use CLSI documents in your workplace? Do you see room for improvement? Would you like to get involved in the revision process? Or maybe you see a need to develop a new document for an emerging technology? CLSI wants to hear from you. We are always looking for volunteers. By donating your time and talents to improve the standards that affect your own work, you will play an active role in improving public health across the globe.

For additional information on committee participation or to submit comments, contact CLSI.

Clinical and Laboratory Standards Institute
P: +1.610.688.0100
F: +1.610.688.0700
www.clsi.org
standard@clsi.org

CLSI C40-Ed3
April 2024
Replaces CLSI C40-A2

Measurement Procedures for the Determination of Lead in Whole Blood

Patrick J. Parsons, PhD, CChem, FRSC
Carl E. Wolf, PhD, MS, F-ABFT
Mahesheema Ali, MSc, PhD, NRCC, FAACC
Sanjib Bhattacharyya, PhD
Mary Jean Brown, ScD, RN
Saswati Das, MD, MBBS
Trivikram Dasu, PhD, D(ABMLI)
Adrienne S. Ettinger, ScD, MPH, MS, FACE
Montserrat Gonzalez-Estecha, MD, PhD
Guray Guven, PhD
Jeffery M. Jarrett, MS
Deanna M.R. Jones, PhD
Robert L. Jones, PhD
Juliane Lessard, PhD
Nelly Mañay, PhD
Fred Leland McClure, MSci, PhD, F-ABFT
Michelle McLean, MS, MLS(ASCP), BS
Karen E. Murphy, BS
Emily J. Pacer, MS
Christopher D. Palmer, PhD
Noel V. Stanton, MS
Daniel Zhou, MHA, MLS(ASCP)^{CM}, SC^{CM}

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.

Clinical and Laboratory Standards Institute (CLSI). *Measurement Procedures for the Determination of Lead in Whole Blood.* 3rd ed. CLSI guideline C40 (ISBN 978-1-68440-218-2 [Print]; ISBN 978-1-68440-219-9 [Electronic]). Clinical and Laboratory Standards Institute, USA, 2024.

CLINICAL AND LABORATORY STANDARDS INSTITUTE®

Suggested Citation

CLSI. *Measurement Procedures for the Determination of Lead in Whole Blood.* 3rd ed. CLSI guideline C40. Clinical and Laboratory Standards Institute; 2024.

Previous Editions:
June 2001, October 2013

CLSI C40-Ed3

ISBN 978-1-68440-218-2 (Print)

ISBN 978-1-68440-219-9 (Electronic)

ISSN 1558-6502 (Print)

ISSN 2162-2914 (Electronic)

Volume 44, Number 12

Committee Membership

Consensus Council

The Consensus Council sets priorities for CLSI standards development and votes on Final Draft documents to confirm that process requirements have been met. Consensus Council members are listed on the CLSI website: https://clsi.org/standards-development/consensus-council/

Document Development Committee on Lead Determination in Whole Blood

Patrick J. Parsons, PhD, CChem, FRSC
Chairholder
New York State Department of Health
USA

Carl E. Wolf, PhD, MS, F-ABFT
Vice-Chairholder
VCU Health
USA

Mary Jean Brown, ScN, RN
Committee Secretary
Harvard Chan School of Public Health
USA

Montserrat Gonzalez-Estecha, MD, PhD
Hospital General Universitario Gregorio Marañón; Sociedad Española de Medicina de Laboratorio SEQC-ML
Spain

Guray Guven, PhD
Meridian Bioscience Inc.
USA

Robert L. Jones, PhD
Centers for Disease Control and Prevention
USA

Jennifer Lowry, MD
The Children's Mercy Hospital
USA

Nelly Mañay, PhD
University of the Republic of Uruguay, Faculty of Chemistry
Uruguay

Michelle McLean, MS, MLS(ASCP), BS
Roche Diagnostics
USA

Karen E. Murphy, BS
National Institute of Standards and Technology
USA

Noel V. Stanton, MS
Wisconsin State Laboratory of Hygiene
USA

Expert Panel on Clinical Chemistry and Toxicology

Expert panel volunteers support the development of CLSI documents by providing technical expertise in specialty areas. Expert panel members are listed by area of expertise on the CLSI website: https://clsi.org/standards-development/expert-panels/

Staff

Clinical and Laboratory Standards Institute
USA

Emily J. Gomez, MS, MLS(ASCP)^{CM}MB^{CM}
Program Manager

Laura Martin
Editorial Manager

Catherine E.M. Jenkins, ELS
Editor

Kristy L. Leirer, MS
Editor

Lisa M.W. Walker, MS, ELS
Editor

Acknowledgment

CLSI, the Consensus Council, and the Document Development Committee on Lead Determination in Whole Blood gratefully acknowledge the following volunteers for their important contributions to the revision of this guideline:

Mahesheema Ali, MSc, PhD, NRCC, FAACC
The MetroHealth System; Case Western Reserve University School of Medicine
USA

Sanjib Bhattacharyya, PhD
City of Milwaukee Health Department
USA

Saswati Das, MD, MBBS
Ram Manohar Lohia Hospital
India

Trivikram Dasu, PhD, D(ABMLI)
Amazon Diagnostics
USA

Adrienne S. Ettinger, ScD, MPH, MS, FACE
Centers for Disease Control and Prevention
USA

Jeffery M. Jarrett, MS
Centers for Disease Control and Prevention
USA

Deanna M.R. Jones, PhD
Centers for Disease Control and Prevention
USA

Juliane Lessard, PhD
FDA Center for Devices and Radiological Health
USA

Fred Leland McClure, MSci, PhD, F-ABFT
USA

Emily J. Pacer, MS
New York State Department of Health
USA

Christopher D. Palmer, PhD
New York State Department of Health
USA

Charles Thornton, PhD
Meridian Bioscience Inc.
USA

Daniel Zhou, MHA, MLS(ASCP)^{CM}, SC^{CM}
UCSF Health
USA

Contents

Contents (Continued)

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.

Use of Triton™ X-100 (alkyl polyglucoside) in this guideline is not an endorsement on the part of CLSI. With each use of the trade name, "or the equivalent" is added to indicate that this guideline also applies to any equivalent products.

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