CLINICAL AND LABORATORY STANDARDS INSTITUTE®

February 2009

C46-A2

Blood Gas and pH Analysis and Related Measurements; Approved Guideline—Second Edition

SAMPLE

This document provides clear definitions of the quantities in current use, and provides a single source of information on appropriate specimen collection, preanalytical variables, calibration, and quality control for blood pH and gas analysis and related measurements.

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 advancements 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.

Appeals Process

When it is believed that an objection has not been adequately considered and responded to, the process for appeals, 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
950 West Valley Road, Suite 2500
Wayne, PA 19087 USA
P: +1.610.688.0100
F: +1.610.688.0700
www.clsi.org
standard@clsi.org

SAMPLE

C46-A2
Vol. 29 No. 8
ISBN 1-56238-694-8 Replaces C46-A
ISSN 0273-3099 Vol. 21 No. 14

Blood Gas and pH Analysis and Related Measurements; Approved Guideline—Second Edition

Volume 29 Number 8

Paul D'Orazio, PhD
Sharon S. Ehrmeyer, PhD
Ellis Jacobs, PhD, DABCC, FACB
John G. Toffaletti, PhD
Jesper H. Wandrup, DrMed, Cand Scient

SAMPLE

Abstract

This guideline is a consolidation of six CLSI documents and projects. The Area Committee on Clinical Chemistry and Toxicology concluded that CLSI's constituencies (professions, government, and industry) would be better served with the production of a single document that retains the essential information from the six original documents, while making it even more relevant and useful. It addresses blood gas, pH, and related measurements (eg, hemoglobin and hemoglobin fractions, oxygen content, hemoglobin-oxygen saturation, electrolytes, and selected metabolites) as measured in blood. It defines terminology and discusses performance characteristics as well as preanalytical variables and analytical considerations. It also addresses quality control issues.

This guideline consolidates and updates previously published CLSI/NCCLS documents C12-A—*Definitions of Quantities and Conventions Related to Blood pH and Gas Analysis*; *Approved Standard;* C21-A—*Performance Characteristics for Devices Measuring pO_2 and pCO_2 in Blood Samples*; *Approved Standard;* C25-A—*Fractional Oxyhemoglobin, Oxygen Content and Saturation, and Related Quantities in Blood: Terminology, Measurement, and Reporting*; *Approved Guideline;* C27-A—*Blood Gas Preanalytical Considerations: Specimen Collection and Controls*; *Approved Guideline;* and C32-P—*Considerations in the Simultaneous Measurement of Blood Gases, Electrolytes, and Related Analytes in Whole Blood; Proposed Guideline;* and unpublished CLSI document C33—*Practical Blood Gas and pH Quality Control.*

Sections of another CLSI document H11 also are included; however, H11 will remain a separate document, because its content is of interest to a broader audience.

Clinical and Laboratory Standards Institute (CLSI). *Blood Gas and pH Analysis and Related Measurements; Approved Guideline—Second Edition*. CLSI document C46-A2 (ISBN 1-56238-694-8). Clinical and Laboratory Standards Institute, 950 West Valley Road, Suite 2500, Wayne, Pennsylvania 19087 USA, 2009.

The Clinical and Laboratory Standards Institute consensus process, which is the mechanism for moving a document through two or more levels of review by the health care community, is an ongoing process. Users should expect revised editions of any given document. Because rapid changes in technology may affect the procedures, methods, and protocols in a standard or guideline, users should replace outdated editions with the current editions of CLSI documents. Current editions are listed in the CLSI catalog and posted on our website at www.clsi.org. If your organization is not a member and would like to become one, and to request a copy of the catalog, contact us at: Telephone: 610.688.0100; Fax: 610.688.0700; E-Mail: customerservice@clsi.org; Website: www.clsi.org.

Copyright ©2009 Clinical and Laboratory Standards Institute. Except as stated below, any reproduction of content from a CLSI copyrighted standard, guideline, companion product, or other material requires express written consent from CLSI. All rights reserved. Interested parties may send permission requests to permissions@clsi.org.

CLSI hereby grants permission to each individual member or purchaser to make a single reproduction of this publication for use in its laboratory procedure manual at a single site. To request permission to use this publication in any other manner, e-mail permissions@clsi.org.

Suggested Citation

CLSI. *Blood Gas and pH Analysis and Related Measurements; Approved Guideline—Second Edition.* CLSI document C46-A2. Wayne, PA: Clinical and Laboratory Standards Institute; 2009.

Previous Editions:
March 2000, September 2001

Reaffirmed:
March 2014

SAMPLE

ISBN 1-56238-694-8
ISSN 0273-3099

Contents

Abstract i

Committee Membership iii

Foreword vii

1 Scope 1

2 Introduction 1

3 Standard Precautions 1

4 Terminology 1

4.1 Concepts and Definitions 1
4.2 Abbreviations/Acronyms 10

5 Preanalytical Considerations 10

5.1 Patient Preparation 10
5.2 Sample Device and Collection Procedures 11
5.3 Transport of Specimens 14
5.4 *In Vivo* Effects on Measurements 15
5.5 Specimen Handling 17

6 Analytical Interferences 18

6.1 Interferences With Measurement of pH and Blood Gases 18
6.2 Interferences With Measurement of Electrolytes (Na^+, K^+, Ca^{++}, Mg^{++}, and Cl^-) 19
6.3 Interference With Measurement of Glucose and Lactate 19
6.4 Interference With Measurement of Hematocrit 19
6.5 Interference With Cooximetry Measurements 20
6.6 Other Interferences 20

7 Blood Gas Analyzer Calibration 21

7.1 Principles of Calibration 21
7.2 Blood Gas Analyzer Calibration 21
7.3 Calibration Traceability 21
7.4 Internal Electronic Barometer 23
7.5 Calibration of pO_2 and pCO_2 in Systems for Point-of-Care Testing 24

8 Blood Gas Quality Control 24

8.1 Types of Quality Control 24

References 28

Appendix A. Instrument Performance Characteristics to Be Specified by the Manufacturer 33

Appendix B. Recommendations for Measurement and Reporting of Hemoglobin Fractions and Related Quantities 36

Appendix C. Measurement Technologies Used in Instruments for Analysis of Blood Gases, pH, and Related Analytes 38

Summary of Consensus Comments and Working Group Responses 41

SAMPLE

Contents (Continued)

Summary of Delegate Comments and Working Group Responses 44

The Quality Management System Approach 48

Related CLSI Reference Materials 49

SAMPLE

Foreword

The previous edition of this document, C46-A, was the result of the decision of the Area Committee on Clinical Chemistry and Toxicology to combine and update four approved-level documents, one proposed-level document, and one unpublished document. The intent was for this document to serve more effectively the three major constituents (professions, government, and industry) of CLSI.

C46-A consolidated the following documents:

- C12-A—*Definitions of Quantities and Conventions Related to Blood pH and Gas Analysis*; *Approved Standard;*
- C21-A—*Performance Characteristics for Devices Measuring pO_2 and pCO_2 in Blood Samples*; *Approved Standard;*
- C25-A—*Fractional Oxyhemoglobin, Oxygen Content and Saturation, and Related Quantities in Blood: Terminology, Measurement, and Reporting*; *Approved Guideline;*
- C27-A—*Blood Gas Preanalytical Considerations: Specimen Collection and Controls*; *Approved Guideline;*
- C32-P—*Considerations in the Simultaneous Measurement of Blood Gases, Electrolytes, and Related Analytes in Whole Blood; Proposed Guideline;* and
- C33—*Practical Blood Gas and pH Quality Control* (unpublished).

Sections of CLSI/NCCLS document H11[1] were also included; however, H11[1] remained a separate document, because its content includes greater detail and is of interest to a broader audience.

The current revision of the document, C46-A2, includes the following updates:

- Section 5, *Preanalytical Considerations,* was expanded to include a discussion specific to transport of specimens (see Section 5.3). Section 5.4, In Vivo *Effects on Measurements*, replaces the former section, *Patient Condition,* and was expanded.
- Section 6, *Analytical Interferences*, was expanded significantly, including references to recent literature.
- Section 7, *Blood Gas Analyzer Calibration*, was expanded significantly, including current requirements for calibration traceability.
- Section 8, *Blood Gas Quality Control,* includes newer approaches for "alternative" quality control.
- Appendix B, *Recommendations for Measurement and Reporting of Hemoglobin Fractions and Related Quantities*, was added.
- Appendix C, *Measurement Technologies Used in Instruments for Analysis of Blood Gases, pH, and Related Analytes*, was added.

SAMPLE

Key Words

Electrolytes, fractional hemoglobins, hemoglobin-oxygen saturation, metabolites, oxygen content, partial pressure of carbon dioxide, partial pressure of oxygen, pH

SAMPLE

Blood Gas and pH Analysis and Related Measurements; Approved Guideline—Second Edition

1 Scope

This guideline addresses blood gas, pH, and related measurements (eg, hemoglobin and hemoglobin fractions, oxygen content, hemoglobin-oxygen saturation, electrolytes, hematocrit, glucose, and lactate) as measured in blood. The guideline is limited to devices for measurement of these quantities *in vitro*. Devices for *in vivo* monitoring and patient-attached, *ex vivo* monitors for blood gas, pH, and related measurements, although common in many respects to devices for *in vitro* measurements, are not specifically addressed.

This document defines terminology and discusses performance characteristics as well as preanalytical variables, analytical considerations, and quality control (QC) issues.

This guideline is primarily intended for laboratory technologists, respiratory therapists, critical care practitioners, and others responsible for obtaining and analyzing blood for pH, oxygen, carbon dioxide, and related measurements. It will also be useful to manufacturers and those responsible for teaching this subject to medical students, residents, and allied health personnel.

2 Introduction

Several aspects of blood pH and gas analysis are unique among clinical laboratory determinations, and, at the same time, no other test results have more immediate impact on patient care. This area of laboratory medicine also has the reputation of being somewhat confusing, partly because of the many different measured and derived quantities that have been used over the years. This document provides clear definitions of the several quantities in current use and includes information on appropriate specimen collection, preanalytical variables, and QC. There is also a section containing a list of performance characteristics pertinent to blood gas analyzers, which can be used by manufacturers to provide operational specifications in a uniform way to facilitate comparison by potential customers of different instruments.

3 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 infectious agents and thus are more comprehensive than universal precautions, which are intended to apply only to transmission of blood-borne pathogens. Standard and universal precaution guidelines are available from the US Centers for Disease Control and Prevention.[2] For specific precautions for preventing the laboratory transmission of all infectious agents from laboratory instruments and materials and for recommendations for the management of exposure to all infectious disease, refer to CLSI document M29.[3]

4 Terminology

4.1 Concepts and Definitions

This section contains terms and definitions in standard CLSI format integrated with related information and concepts. The formal definitions are accompanied by supplementary information necessary to

SAMPLE

©Clinical and Laboratory Standards Institute. All rights reserved.

understand and apply the concepts of blood gases and related quantities. The definitions and supplemental information contained in this section were developed with the intent of providing maximum clarity for the typical reader of this document.

The reader is referred to the definitions and explanatory notes found in the CLSI Harmonized Terminology Database, both for related terms and definitions not contained in this document and for a more precise understanding of a term's concept.

4.1.1 pH

pH – the symbol for the negative common logarithm of the relative molal hydrogen ion activity (aH^+), which is a measure of the effective concentration of hydrogen ions in solution; **NOTE:** Historically, pH arose as a symbol for the "power of hydrogen."

$$pH = -\log aH^+ \quad (1)$$

pH is commonly used as both the symbol and the name of the quantity. The concept of pH is unique among physicochemical quantities in that it involves a single-ion activity that is experimentally immeasurable. Because the activity of a single ionic species is a thermodynamically inexact quantity, the International Union of Pure and Applied Chemistry (IUPAC) adopted a conventional scale of pH. It is defined by reference buffer solutions with pH values assigned using a special electrochemical cell without liquid junction and containing a hydrogen-gas working electrode and a silver/silver chloride reference electrode.[4-6]

4.1.2 Partial Pressure of CO_2 and O_2

partial pressure//tension – *of a gas in a solution*, pressure that would exist in a gas phase, in equilibrium with the solution.[7,8]

For carbon dioxide and oxygen, the partial pressures are symbolized as pCO_2 and pO_2, respectively. "Partial" indicates that it is one part of the total ambient pressure.

The customary unit for pCO_2 and pO_2 is millimeter of mercury, represented by the symbol mmHg, and is used throughout this document. The kilopascal (kPa) is the unit of measure for pressure (partial) in the International System of Units (SI).[9] The relationship between these two units is 1 mmHg = 0.133 kPa. Kilopascal units are reported in the text as (kPa).

4.1.2.1 Symbols

The symbols chosen for use in this document are all compatible with International Federation of Clinical Chemistry and Laboratory Medicine (IFCC)/IUPAC recommendations.

Quantity Symbols: In this document, each quantity designation, including partial pressure (*p*), saturation (*s*), substance fraction (*F*), and substance concentration (*c*), shall be designated as shown.

Specimen Type and Source Symbols: If necessary, characterize the type of sample (eg, in blood) and its source (eg, arterial). **NOTE:** Blood = B; extracellular fluid = ecf; arterial = a; alveolar = A; venous = v; mixed venous = $\bar{v}$; capillary = c.

Composite Symbol: A composite symbol, based on the aforementioned principles, for an arterial blood CO_2 tension would thus be: pCO_2 (a).

SAMPLE

 ©Clinical and Laboratory Standards Institute. All rights reserved.

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 approach is based on the model presented in the most current edition of CLSI/NCCLS document HS01—*A Quality Management System Model for Health Care.* 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:

Documents & Records	Equipment	Information Management	Process Improvement
Organization	Purchasing & Inventory	Occurrence Management	Customer Service
Personnel	Process Control	Assessments—External & Internal	Facilities & Safety

C46-A2 addresses the QSEs 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.

Documents & Records	Organization	Personnel	Equipment	Purchasing & Inventory	Process Control	Information Management	Occurrence Management	Assessments—External & Internal	Process Improvement	Customer Service	Facilities & Safety
GP02 H11		H11	H11	H03	X C24 C29 EP17 H03 H04 H11 H18 HS03 M29	GP02			H11		H03 H11 M29

Adapted from CLSI/NCCLS document HS01—*A Quality Management System Model for Health Care*.

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. For example, CLSI/NCCLS document GP26—*Application of a Quality Management System Model for Laboratory Services* defines a clinical laboratory path of workflow, which consists of three sequential processes: preexamination, examination, and postexamination. All clinical laboratories follow these processes to deliver the laboratory's services, namely quality laboratory information.

C46-A2 addresses the clinical laboratory path of workflow steps 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.

Preexamination				**Examination**			**Postexamination**	
Examination ordering	Sample collection	Sample transport	Sample receipt/processing	Examination	Results review and follow-up	Interpretation	Results reporting and archiving	Sample management
X H03 H11	X C31 H03 H04 H11 H15	X C31 H03 H11 H18	X C31 H03 H11 H15 H18	X H03 H15 H18	X H03 H15	X	X	

Adapted from CLSI/NCCLS document HS01—*A Quality Management System Model for Health Care*.

SAMPLE

©*Clinical and Laboratory Standards Institute. All rights reserved.*

Related CLSI Reference Materials*

C24-A3 **Statistical Quality Control for Quantitative Measurement Procedures: Principles and Definitions; Approved Guideline—Third Edition (2006).** This guideline provides definitions of analytical intervals; planning of quality control procedures; and guidance for quality control applications.

C29-A2 **Standardization of Sodium and Potassium Ion-Selective Electrode Systems to the Flame Photometric Reference Method; Approved Standard—Second Edition (2000).** This standard contains recommendations on the expression of the results of ion-selective electrode measurement of sodium and potassium ion activities in undiluted serum, plasma, or whole-blood in clinical practice.

C31-A2 **Ionized Calcium Determinations: Precollection Variables, Specimen Choice, Collection, and Handling; Approved Guideline—Second Edition (2001).** This document addresses preanalytical considerations, such as patient condition, specimen choice, collection, and handling—that can influence the accuracy and clinical utility of ionized calcium measurements.

EP17-A **Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline (2004).** This document provides guidance for determining the lower limit of detection of clinical laboratory methods, for verifying claimed limits, and for the proper use and interpretation of the limits.

GP02-A5 **Laboratory Documents: Development and Control; Approved Guideline—Fifth Edition (2006).** This document provides guidance on development, review, approval, management, and use of policy, process, and procedure documents in the medical laboratory community.

H03-A6 **Procedures for the Collection of Diagnostic Blood Specimens by Venipuncture; Approved Standard—Sixth Edition (2007).** This document provides procedures for the collection of diagnostic specimens by venipuncture, including line draws, blood culture collection, and venipuncture in children.

H04-A6 **Procedures and Devices for the Collection of Diagnostic Capillary Blood Specimens; Approved Standard—Sixth Edition (2008).** This document provides a technique for the collection of diagnostic capillary blood specimens, including recommendations for collection sites and specimen handling and identification. Specifications for disposable devices used to collect, process, and transfer diagnostic capillary blood specimens are also included.

H11-A4 **Procedures for the Collection of Arterial Blood Specimens; Approved Standard—Fourth Edition (2004).** This document provides principles for collecting, handling, and transporting arterial blood specimens to assist with reducing collection hazards and ensuring the integrity of the arterial specimen.

H15-A3 **Reference and Selected Procedures for the Quantitative Determination of Hemoglobin in Blood; Approved Standard—Third Edition (2000).** This document describes the principle, materials, and procedure for reference and standardized hemoglobin determinations. It includes specifications for secondary hemiglobincyanide (HiCN) standards.

H18-A3 **Procedures for the Handling and Processing of Blood Specimens; Approved Guideline—Third Edition (2004).** This document includes criteria for preparing an optimal serum or plasma sample and for the devices used to process blood specimens.

HS03-A **Pulse Oximetry; Approved Guideline (2005).** Pulse oximetry is a widely used device for the clinical assessment of arterial oxygenation and pulse rate. The clinical applications, quality assessment, and limitations are discussed in this guideline.

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.

SAMPLE

* Proposed-level documents are being advanced through the Clinical and Laboratory Standards Institute consensus process; therefore, readers should refer to the most current editions.

©*Clinical and Laboratory Standards Institute. All rights reserved.*

CLINICAL AND LABORATORY STANDARDS INSTITUTE®

Explore the Latest Offerings From CLSI!

As we continue to set the global standard for quality in laboratory testing, we are adding products and programs to bring even more value to our members and customers.

By becoming a CLSI member, your laboratory will join 1,600+ other influential organizations all working together to further CLSI's efforts to improve health care outcomes. You can play an active role in raising global laboratory testing standards—in your laboratory, and around the world.

Find out which membership option is best for you at **www.clsi.org/membership.**

Find what your laboratory needs to succeed! CLSI U provides convenient, cost-effective continuing education and training resources to help you advance your professional development. We have a variety of easy-to-use, online educational resources that make *e*Learning stress-free and convenient for you and your staff.

See our current educational offerings at **www.clsi.org/education.**

When laboratory testing quality is critical, standards are needed and there is no time to waste. eCLIPSE™ Ultimate Access, our cloud-based online portal of the complete library of CLSI standards, makes it easy to quickly find the CLSI resources you need.

Learn more and purchase eCLIPSE at **clsi.org/eCLIPSE.**

For more information, visit www.clsi.org today.

SAMPLE

SAMPLE

CLINICAL AND
LABORATORY
STANDARDS
INSTITUTE®

950 West Valley Road, Suite 2500, Wayne, PA 19087 USA

P: +1.610.688.0100 **Toll Free (US):** 877.447.1888 **F:** +1.610.688.0700

E: customerservice@clsi.org **www.clsi.org**

ISBN 1-56238-694-8