



GP40-A4-AMD

Preparation and Testing of Reagent Water in the Clinical Laboratory; Approved Guideline—Fourth Edition

This document provides guidelines on water purified for clinical laboratory use; methods for monitoring water quality and testing for specific contaminants; and water system design considerations.

Clinical and Laboratory Standards Institute

Setting the standard for quality in clinical 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 clinical 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 addressed according to the consensus process by a committee of experts.

Appeals Process

If it is believed that an objection has not been adequately addressed, the process for appeals is documented in the CLSI Standards Development Policies and Process document.

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 further 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: 610.688.0100
F: 610.688.0700
www.clsi.org
standard@clsi.org

ISBN 1-56238-610-7
ISSN 0273-3099

GP40-A4-AMD
Vol. 26 No. 22
Formerly C03-A4-AMD
Vol. 26 No. 22

Preparation and Testing of Reagent Water in the Clinical Laboratory; Approved Guideline—Fourth Edition

Volume 26 Number 22

W. Gregory Miller, PhD, DABCC, FACB
Erich L. Gibbs, PhD
Dennis W. Jay, PhD, DABCC, FACB
Kenneth W. Pratt, PhD
Bruno Rossi, MS
Christine M. Vojt, MT(ASCP), MS
Paul Whitehead, PhD, CChem, FRSC

Abstract

CLSI document GP40-A4-AMD—*Preparation and Testing of Reagent Water in the Clinical Laboratory; Approved Guideline—Fourth Edition* provides information on water purity requirements for clinical laboratory testing, validation of specifications, technology available for water purification, and test procedures to monitor and trend water purity parameters.

Clinical and Laboratory Standards Institute (CLSI). *Preparation and Testing of Reagent Water in the Clinical Laboratory; Approved Guideline—Fourth Edition*. CLSI document GP40-A4-AMD (ISBN 1-56238-610-7). Clinical and Laboratory Standards Institute, 950 West Valley Road, Suite 2500, Wayne, Pennsylvania 19087 USA, 2006.

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.



CLINICAL AND
LABORATORY
STANDARDS
INSTITUTE®

Copyright ©2006 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. *Preparation and Testing of Reagent Water in the Clinical Laboratory; Approved Guideline—Fourth Edition*. CLSI document GP40-A4-AMD. Wayne, PA: Clinical and Laboratory Standards Institute; 2012.

Proposed Standard—First Edition
January 1976

Approved Guideline—Second Edition
August 1991

Tentative Standard—First Edition
January 1978

Approved Guideline—Third Edition
October 1997

Approved Standard—First Edition
February 1980

Proposed Guideline—Fourth Edition
June 2005

Proposed Guideline—Second Edition
June 1985

Approved Guideline—Fourth Edition
June 2006

Tentative Guideline—Second Edition
December 1988

Amended Fourth Edition
June 2012

ISBN 1-56238-610-7

ISSN 0273-3099

Contents

Abstract.....	i
Committee Membership.....	iii
Summary of Changes in GP40 Amendment.....	ix
Foreword.....	xi
1 Scope.....	1
2 Introduction.....	1
3 Definitions	2
4 Specifications.....	5
4.1 Frequency of Monitoring Water Purity Parameters.....	5
4.2 Organization of Water Purity Specifications	6
4.3 Clinical Laboratory Reagent Water (CLRW).....	7
4.4 Special Reagent Water (SRW).....	8
4.5 Instrument Feed Water.....	9
4.6 Water Supplied by a Method Manufacturer for Use as a Diluent or Reagent	9
4.7 Commercially Bottled, Purified Water	9
4.8 Autoclave and Wash Water Applications	10
5 Validation and Trend Monitoring	10
5.1 Validation of Purified Water as Fit for Its Intended Purpose in Laboratory Procedures.....	10
5.2 Trend Monitoring of Water Purity Specifications	11
5.3 Water Purification System Validation	12
6 Design Considerations	13
6.1 Filters	14
6.2 Reverse Osmosis (RO) Membranes.....	15
6.3 Contactor Membranes.....	16
6.4 Ion-Exchange Resins	16
6.5 Activated Carbon	18
6.6 Distillation	19
6.7 Ultraviolet Light	21
6.8 Storage and Distribution	22
7 Testing	24
7.1 Resistivity	24
7.2 Microbial Content by Colony Count.....	29
7.3 Microbial Content by Epifluorescence Microscopy	31
7.4 Endotoxins	34
7.5 Determination of Oxidizable Organic Substances, Expressed as Total Organic Carbon (TOC).....	36
References.....	41
Additional References.....	43

Contents (Continued)

Appendix A. Resistivity Measurement in a Sparged Water Sample.....44

Appendix B. Methods for Correction or Compensation of Resistivity Measurements46

The Quality System Approach.....48

Related CLSI/NCCLS Publications49

SAMPLE

Foreword

This edition of the guideline includes updated information regarding the preparation and testing of reagent water in clinical laboratories. Specifications are based on measuring parameters that serve as indicators for the total ionic, organic, and microbial contamination. Emphasis is placed on the value of trending these parameters as an effective way to control the quality and consistency of purified laboratory water, as well as the importance of validating that a given type of laboratory water is fit for its intended purpose. A new section provides guidelines for water purification system validation, ongoing maintenance, and revalidation on a recurring schedule.

The Type I, II, III designations for types of purified laboratory water, used in the previous edition, have been replaced with purity types that provide more meaningful specifications for clinical laboratory testing. Clinical laboratory reagent water (CLRW) can be used in place of Type I and Type II water for most applications. In situations in which the CLRW purity may not be satisfactory, or may not be required, a specified type of purified water can be validated as fit-for-purpose and used by a laboratory as a special reagent water. Autoclave and wash water will generally be a satisfactory replacement for Type III water. The definitions of the new types of water include parameters that were not used in previous editions and some of the parameters that were used in previous editions.

Resistivity measurement has been retained to monitor inorganic impurities. The previous edition recommended that water purification systems include a stage to reduce organic contamination, but required no control. This edition recognizes that organic contamination can be difficult to remove from feed water, can be introduced by components of water purification systems or biofilms, and must be controlled. Therefore, a total organic carbon (TOC) parameter has been added. Note that on-line or in-house measurements of TOC are not required. It is acceptable to send CLRW samples to a referral laboratory for TOC measurement. (See Section 7.5 for additional information on contamination risks when TOC is at low levels.)

Plate counting of colonies is a widely used method for monitoring the level of microorganisms in purified laboratory water, and this edition continues to specify this approach. However, epifluorescence and endotoxin testing have been added as optional tests, because they provide additional information and results can be determined quickly.

Specifications and methods for measuring pH and silicates, as SiO_2 , have not been carried forward from the previous edition. Resistivity is more sensitive than pH to H^+ and OH^- contamination. Resistivity is not a sensitive indicator of weakly ionized contaminants, which may elute as concentrated pulses from ion-exchange beds when they approach depletion. However, the release of weakly ionized contaminants (silica being but one example) can be avoided by appropriate design and regular maintenance of ion-exchange components.

A parameter for sterility of general-purpose purified laboratory water has not been included in this edition of the guideline, because most clinical laboratory applications do not require sterile water. Water can be sterilized as necessary for some applications; however, the method of sterilization may degrade the purity of the water.

Key Words

Autoclave and wash water, bottled water, clinical laboratory reagent water, high-purity water, instrument feed water, purified water, reagent water, special reagent water, water purification

Preparation and Testing of Reagent Water in the Clinical Laboratory; Approved Guideline—Fourth Edition

1 Scope

A number of types of purified water for use in clinical laboratory testing procedures are specified:

- clinical laboratory reagent water (CLRW);
- special reagent water (SRW);
- instrument feed water;
- water supplied by a method manufacturer;
- autoclave and wash water; and
- commercially bottled, purified water.

Procedures are provided for measuring parameters that monitor ionic, organic, and microbial contamination in purified laboratory water. These parameters should be monitored over time to identify trends in performance so corrective action can be taken before a parameter exceeds specified limits. Recommendations are provided to control particulate and colloidal contamination. The guideline includes validation by the laboratory that a selected type of water is fit for its intended purpose. Suggested approaches for validation of water purification systems are included.

It is beyond the scope of this guideline to recommend specific types of water purification systems. Instead, the guideline provides information about discrete purification technologies and monitoring strategies that can be applied in various combinations to achieve and maintain the required water purity.

2 Introduction

The goal of every clinical laboratory is to produce accurate results. Purified water constitutes the major component of many reagents, buffers, and diluents used in clinical laboratory testing. It can also become an indirect component of tests when it is used for washing and sanitizing instruments and laboratory ware, generating autoclave steam, etc. Inadequate control of contamination in purified water is an important potential cause of laboratory error.

This guideline recommends measuring certain parameters of purified water used in clinical laboratory applications as a means of quality control for purification systems. The parameters are: *resistivity*, an indicator of ionic contamination; *total organic carbon*, an indicator of organic contamination; and *viable plate counts*, an indicator of microorganism contamination. Epifluorescence and endotoxin testing are included as optional approaches for measuring contamination from microbial sources. Particulate contamination is controlled by including appropriate filtration, or distillation, in the purification system. The guideline is not intended to assure the adequacy of purified water for a given laboratory application; rather, water of a specified purity must be validated as fit for use in a particular laboratory application. Any parameters used to specify a type of purified water, or to monitor the performance of a purification system, must be measured frequently enough to detect potential changes in the system, and the measurement results should be monitored for trends to anticipate maintenance before the water quality degrades to a point that will cause problems with laboratory testing.

Other organizations have published guidelines and specifications for purified water intended for various applications. Water conforming to the guidelines and specifications of these organizations may or may not be equivalent to the types of purified water described in this CLSI guideline. Any type of purified water should be validated as fit for purpose before being used in clinical laboratory testing.

3 Definitions

absorption – a process by which a substance is taken up chemically or physically in bulk by a material (absorbent) and held in pores or interstices in the interior; **NOTE:** See also **adsorption, sorption**.

accuracy – closeness of agreement between a test result and the accepted reference value (ISO 3534-1)¹; **NOTE: Accuracy of a measurement** is defined as the closeness of the agreement between the result of a measurement and a true value of the measurand (VIM93).²

activated carbon – porous carbon material used for removal of impurities; **NOTE:** See Section 6.5 for details.

adsorption – adherence of molecules, atoms, and ionized species of gas or liquid to the surface of another substance (solid or liquid) as the result of a variety of weak attractions that involve ionic, Van der Waals, and surface-active (hydrophobic/hydrophilic) forces; **NOTE:** See also **absorption, sorption**.

anion exchange resin – an ion-exchange resin with immobilized positively charged exchange sites, which can bind negatively charged ionized species.

azeotrope – a blend of two or more components with equilibrium vapor phase and liquid phase compositions that are the same at a given temperature and pressure.

bactericide – a chemical or physical agent that kills bacteria.

biocide – a chemical or physical agent that kills microorganisms (as used in this document).

biofilm – microorganisms, enclosed in a glycoprotein/polysaccharide matrix, that adhere to each other and/or to surfaces and may form macroscopic layers.³

CA membrane – a reverse osmosis membrane constructed of cellulose diacetate/triacetate.

calibration – the set of operations that establish, under specified conditions, the relationship between values of quantities indicated by a measuring instrument or measuring system, or values represented by a material measure or a reference material, and the corresponding values realized by standards (VIM93).²

catalyst – a substance that increases the kinetics of a chemical reaction without being consumed in the reaction.

cation exchange resin – an ion-exchange resin with immobilized negatively charged exchange sites, which can bind positively charged ionized species.

colloid – small, solid particles that will not settle out of a solution.

concentrate – the liquid containing dissolved and suspended matter that concentrates on one side of a membrane.

condenser – the stage of a distillation system that removes sufficient heat from a vaporized liquid to cause the vapor to change to a liquid phase.

conductivity – conductivity is the reciprocal of **resistivity**; **NOTE:** For water purification systems, conductivity is usually reported in microsiemens per centimeter ($\mu\text{S}/\text{cm}$).

contactor membrane – a hydrophobic membrane used in removing dissolved gases from water.

The Quality System Approach

Clinical and Laboratory Standards Institute (CLSI) subscribes to a quality 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 HS1—*A Quality Management System Model for Health Care*. The quality system approach applies a core set of “quality system essentials” (QSEs), basic to any organization, to all operations in any healthcare service’s path of workflow (i.e., 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 quality system essentials (QSEs) are:

Documents & Records Organization Personnel	Equipment Purchasing & Inventory Process Control	Information Management Occurrence Management Assessment	Process Improvement Service & Satisfaction Facilities & Safety
--	--	---	--

GP40-A4-AMD addresses the quality system essentials (QSEs) indicated by an “X.” For a description of the other documents listed in the grid, please refer to the Related CLSI/NCCLS Publications section on the following page.

Documents & Records	Organization	Personnel	Equipment	Purchasing & Inventory	Process Control	Information Management	Occurrence Management	Assessment	Process Improvement	Service & Satisfaction	Facilities & Safety
				X	X						

Adapted from CLSI/NCCLS document HS1—*A Quality Management System Model for Health Care*.

Related CLSI/NCCLS Publications*

- C24-A2** **Statistical Quality Control for Quantitative Measurements: Principles and Definitions; Approved Guideline—Second Edition (1999).** This guideline provides definitions of analytical intervals, planning of quality control procedures, and guidance for quality control applications.
- EP7-A2** **Interference Testing in Clinical Chemistry; Approved Guideline—Second Edition (2005).** This document provides background information, guidance, and experimental procedures for investigating, identifying, and characterizing the effects of interfering substances on clinical chemistry test results.
- GP2-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.

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.



Explore the Latest Offerings from CLSI!

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



Power Forward with this Official Interactive Guide

Fundamentals for implementing a quality management system in the clinical laboratory.



Find Membership Opportunities

See the options that make it even easier for your organization to take full advantage of CLSI benefits and our unique membership value.



Visit the CLSI U Education Center

Where we provide the convenient and cost-effective education resources that laboratories need to put CLSI standards into practice, including webinars, workshops, and more.



Shop Our Online Products

Including eCLIPSE Ultimate Access™, CLSI's cloud-based, online portal that makes it easy to access our standards and guidelines—*anytime, anywhere.*

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

SAMPLE



CLINICAL AND
LABORATORY
STANDARDS
INSTITUTE®

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

P: 610.688.0100 Toll Free (US): 877.447.1888 F: 610.688.0700

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

ISBN 1-56238-610-7