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

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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

6 September 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 the Clinical and Laboratory Standards Institute Executive Offices, 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 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.

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

CLINICAL AND LABORATORY STANDARDS INSTITUTE

(Formerly NCCLS)
Providing NCCLS standards and guidelines,
ISO/TC 212 standards, and ISO/TC 76 standards

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

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 C3-P4, *Preparation and Testing of Reagent Water in the Clinical Laboratory; Proposed 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.

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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 water, as well as the importance of validating that a grade of reagent water is fit for its intended purpose in clinical laboratory testing. 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 grades of purified water, used in the previous edition, have been replaced with purity grades 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. Autoclave and wash water will generally be satisfactory replacement for Type III water. The definitions of the new grades of water include a number of parameters that were not used in previous editions and do not use 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 issues 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, SiO_2, and sterility 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 has not been included in this edition of the guideline, because most laboratory applications do not require sterile water. When necessary, water can be sterilized; however, the method of sterilization must not degrade the purity of the water.

Key Words

Clinical laboratory water, high-purity water, purified water, reagent water, water purification

Invitation for Participation in the Consensus Process

An important aspect of the development of this and all 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 Clinical Chemistry and Toxicology 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.

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

1 Scope

Purified water requirements are specified for clinical laboratory testing procedures. The following purity grades are described:

- clinical laboratory reagent water (CLRW);
- special reagent water (SRW);
- instrument feed water;
- autoclave and wash water; and
- commercially available bottled water.

Procedures are provided for measuring and trending parameters to control ionic, organic, and microbial contamination in purified laboratory water. Recommendations are provided to control particulate and colloidal contamination. The guideline requires the laboratory to validate a selected grade of water as fit for its intended purpose in laboratory tests. 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

A key element of success in the clinical laboratory is the constancy of test result quality. The physician or caregiver counts on results that represent only patient analyte measurement, not the measurement of microbial or chemical contaminants that may be extraneously introduced during a laboratory procedure.

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. Purified water is a 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; *viable plate counts*, an indicator of microorganism contamination; and *total organic carbon*, an indicator of organic 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 grade of purified water, or to monitor the performance of a purification system, should be measured frequently enough to detect potential changes in the system, and the measurements should be trended to detect drift and anticipate maintenance.

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 grades 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.

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; plans for quality control procedures; and guidance for quality control applications.

EP7-A **Interference Testing in Clinical Chemistry; Approved Guideline (2002).** This guideline provides background information guidance, and experimental procedures for investigating, identifying, and characterizing the effects of interfering substances on clinical chemistry test results.

GP2-A4 **Clinical Laboratory Technical Procedure Manuals; Approved Guideline—Fourth Edition (2002).** GP2-A4 addresses the design, preparation, maintenance, and use of technical procedure manuals in the clinical laboratory.

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