CLINICAL AND LABORATORY STANDARDS INSTITUTE®

5th Edition

CLSI GP40™

Preparation and Testing of Reagent Water in the Medical Laboratory

CLSI GP40 provides guidelines on water purified for medical 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.

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Preparation and Testing of Reagent Water in the Medical Laboratory

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Abstract

Clinical and Laboratory Standards Institute GP40—*Preparation and Testing of Reagent Water in the Medical Laboratory* provides information on water purity requirements for medical 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 CLSI GP40 includes updated information regarding the preparation and testing of reagent and other purified water in medical 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. Guidelines for water purification system validation, ongoing maintenance, and revalidation on a recurring schedule are provided.

The Type I, II, and III designations for types of purified laboratory water, used in the 3rd edition of CLSI GP40, have been replaced with purity types that provide more meaningful specifications for medical laboratory testing in this edition and the 4th edition of CLSI GP40. Clinical laboratory reagent water (CLRW) can be used 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 (SRW).

Resistivity measurement has been retained to monitor inorganic impurities. The 3rd edition recommended that water purification systems include a stage to reduce organic contamination but required no control. This edition and the 4th edition recognize 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 is included. 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.

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 are now included 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 3rd edition. Resistivity is more sensitive than pH to H^+ and OH^- contamination. Resistivity is not a sensitive indicator of weakly ionized contaminants, which can elute as concentrated pulses from ion-exchange beds when they approach depletion. Release of weakly ionized contaminants (eg, silica) can be avoided by appropriate design and regular maintenance of ion-exchange components.

Overview of Changes

CLSI GP40 was revised in 2024 under the Limited Revision Process and replaces the 4th edition of the guideline, which was published in 2012. Several changes were made in this edition, including:

- Adding information for SRW for molecular biology measurement procedures
- Providing additional details regarding verification of commercially available bottled purified water
- Updating water monitoring to include electronic monitoring of water and records as well as electronic warnings to alert for water purification equipment maintenance before failure
- Providing additional information on testing water for microbial contamination
- Adding as Appendix A a comparison of specifications in CLSI GP40 with ASTM International specifications

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- Relocating to Appendix B technical details for sparging to remove dissolved CO_2 when necessary to measure resistivity
- Relocating to Appendix D technical details for epifluorescence assessment of microbial contamination
- Relocating to Appendix E technical details for endotoxin testing

NOTE: The content of CLSI GP40 is supported by the CLSI consensus process and does not necessarily reflect the views of any single individual or organization.

KEY WORDS

autoclave and wash water

clinical laboratory reagent water

high-purity water

instrument feed water

molecular biology water

purified water

reagent water

special reagent water

water purification

Chapter 1

Introduction

Preparation and Testing of Reagent Water in the Medical Laboratory

1 Introduction

1.1 Scope

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

- Clinical laboratory reagent water (CLRW)
- Special reagent water (SRW)
- Molecular biology water, a type of SRW
- Instrument feed water
- Water supplied by a method manufacturer
- Autoclave and wash water
- 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. CLSI GP40 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 CLSI GP40 to recommend specific types of water purification systems. Instead, CLSI GP40 provides information about discrete purification technologies and monitoring strategies that can be applied in various combinations to achieve and maintain the necessary water purity.

1.2 Introduction

The goal of every medical laboratory is to produce accurate results. Purified water constitutes the major component of many reagents, buffers, and diluents used in medical 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.

CLSI GP40 recommends measuring certain parameters of purified water used in medical laboratory applications as a means of QC for purification systems. The parameters are resistivity, an indicator of ionic contamination; total organic carbon (TOC), 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. CLSI GP40 is not intended to ensure 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.

Appendix A. Comparison of Clinical Laboratory Reagent Water Specifications in CLSI GP40 to Reagent Water Specifications from ASTM International

Abbreviations for Appendix A

ASTM ASTM International

CLRW clinical laboratory reagent water

EU endotoxin units

Table A1 illustrates the similarities and differences between the four water purity levels outlined by ASTM International (ASTM) and clinical laboratory reagent water (CLRW). CLRW is intended to be a general use purified water for many medical laboratory measurement procedures.

Because medical laboratory testing includes a wide diversity of measurement technologies, CLSI GP40 recommends that a medical laboratory develops specifications for a special reagent water when specifications different than those for CLRW are required for a particular type of measurement procedure.

Table A1. Comparison of ASTM Water Types and CLRW. (Reprinted with permission from ASTM International, *Standard Specification for Reagent Water.*)

Property (ASTM)	ASTM Definitions				CLSI GP40
	Type I	Type II	Type III	Type IV	CLRW
Electrical conductivity, max, µS/cm at 298 K (25°C)	0.056	1.0	0.25	5.0	0.1 (reciprocal of resistivity)
Electrical resistivity, min, MΩ·cm at 298 K (25°C)	18	1.0	4.0	0.2	10
pH at 298 K (25°C)	[a]	[a]	[a]	5.0 to 8.0	N/A[b]
Total organic carbon, max, µg/L	50	50	200	No limit	500 ng/g (500 µg/L)
Sodium, max, µg/L	1	5	10	50	8.27[c]
Chlorides, max, µg/L	1	5	10	50	12.76[c]
Total silica, max, µg/L	3	3	500	No limit	N/A[b]
Particulate and colloid content	0.2-µm filter	Not specified	0.45-µm filter	Not specified	0.22-µm filter

Abbreviations: ASTM, ASTM International; CLRW, clinical laboratory reagent water; max, maximum; min, minimum; N/A, not applicable; pH, negative logarithm of hydrogen ion concentration.

[a] The measurement of pH in Type I, II, and III reagent waters has been eliminated from the ASTM specification because these grades of water do not contain constituents in sufficient quantity to significantly alter the pH.

[b] Specifications and methods for measuring pH and silicates, as SiO_2, have not been included in the 4th or current editions of CLSI GP40. Resistivity is more sensitive than pH to H^+ and OH^- contamination. Resistivity is not a sensitive indicator of weakly ionized contaminants, which can elute as concentrated pulses from ion-exchange beds when they approach depletion. Release of weakly ionized contaminants (eg, silica) can be avoided by appropriate design and regular maintenance of ion-exchange components.

[c] Based on the resistivity of 10 MΩ·cm at 298 K (25°C) for 0.36 µmol/L NaCl.

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