CLINICAL AND LABORATORY STANDARDS INSTITUTE®

1st Edition

# EP37

## Supplemental Tables for Interference Testing in Clinical Chemistry



This document includes recommended testing concentrations for analytes and endogenous substances that may interfere in clinical chemistry measurement procedures and is intended for use with the evaluation procedures in the Clinical and Laboratory Standards Institute guideline EP07.

A CLSI supplement for global application.

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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

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# Supplemental Tables for Interference Testing in Clinical Chemistry

Robert J. McEnroe, PhD
Goce Dimeski, PhD, FFSc (RCPA)
W. Greg Miller, PhD
Oswald Sonntag, PhD



## Abstract

The supplemental tables presented in this document are intended for use with the evaluation procedures presented in CLSI document EP07—*Interference Testing in Clinical Chemistry.* EP07 describes protocols for manufacturers of *in vitro* diagnostic measurement procedures to screen potentially interfering substances, quantify interference effects, and confirm interference in patient samples. It also describes procedures for medical laboratories to verify interference claims and investigate discrepant results caused by unsuspected interfering substances. The supplemental tables in EP37 provide recommended test concentrations for analytes and endogenous substances that may interfere in clinical chemistry measurement procedures.

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## Contents

## Foreword

The interference testing process has remained relatively stable for many years. Recent updates were made to CLSI document EP07 to clarify the procedures and provide simpler options for data analysis. Because the interference testing process is stable, EP07 is unlikely to be updated frequently. However, medical therapies are constantly evolving. Therefore, to more frequently update the tables of possible interferents and their recommended testing concentrations, EP07's former Appendixes C and D have been removed from that guideline and placed into this supplement as Tables 1 and 2. Several changes were made to the information, including:

- Adding international units and the conversion factor
- For drugs, including the drug structure, molecular formula, and molar mass
- Including more drugs

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

### Key Words

Interference, interference testing, interferents, test concentrations

### Abbreviations and Acronyms

| | |
|---|---|
| AIDS | acquired immunodeficiency syndrome |
| ATP | adenosine triphosphate |
| CNS | central nervous system |
| DNA | deoxyribonucleic acid |
| EDTA | ethylenediaminetetraacetic acid |
| GABA | gamma-aminobutyric acid |
| GI | gastrointestinal |
| HIV | human immunodeficiency virus |
| ID-MS | isotope dilution mass spectrometry |
| INN | International Nonproprietary Name |
| LDL | low-density lipoprotein |
| MRSA | methicillin-resistant *Staphylococcus aureus* |
| pH | negative logarithm of hydrogen ion concentration |
| RNA | ribonucleic acid |
| SI | Système International d'Unités (International System of Units) |

# Supplemental Tables for Interference Testing in Clinical Chemistry

## Instructions for Use of Table 1

Table 1 provides recommended test concentrations for many common drugs and some drug metabolites and anticoagulant agents. These concentrations are provided in both mg/dL and µmol/L units (except where indicated differently, eg, heparin in units/dL). The recommended test concentrations are typically three times the highest drug concentrations expected during treatment, except when such a high concentration is not achievable.

**NOTE:** Recommended test concentrations may be rounded for ease of preparation.

The conversion factor for converting from mass units to molar units is provided. In addition, the molecular formula and chemical structure are provided for most of the drugs. In some cases, the molecular formula or chemical structure is too complex to include.

**NOTE 1:** The numbers in Table 1 are reported differently than in previous editions of EP07. Concentrations are shown in exponential notation of base 10 to display values uniformly across the very wide range of concentrations.

**NOTE 2:** The compounds listed in Table 1 are listed using the International Nonproprietary Name (INN) and, when different, the name used by the United States Adopted Names (USAN) Council is also given. When the names are different, the USAN name is listed first, with the INN listed in parentheses.

### Conversion of Exponential Notation Units

- **Positive exponent:** Move the decimal point to the right by the number of places specified by the exponent (ie, number after E). For example, to convert 5-aminosalicylic acid to the highest drug concentration under therapeutic treatment in µmol/L:

  1. Locate the value under the heading **Highest Drug Concentration Under Therapeutic Treatment, µmol/L:** 4.44E+01.

  2. As indicated by "01" after "+," move the decimal point in "4.44" one place to the right, ie, multiply by 10: 4.44 • 10 = 44.4 µmol/L.

- **Negative exponent:** Move the decimal point to the left by the number of places specified by the exponent (ie, number after E).

  For example, to convert abiraterone to the highest drug concentration under therapeutic treatment in mg/dL:

  1. Locate the value under the heading **Highest Drug Concentration Under Therapeutic Treatment, mg/dL:** 2.26E−02.

  2. As indicated by "02" after "−," move the decimal point two places to the left, ie, divide by 100: 2.26/ 100 = 0.0226 mg/dL.

- **00 exponent:** Use the stated value with no adjustment.

  For example, to find the abacavir test concentration in mg/dL:

  1. Locate the value under the heading **Recommended Test Concentration, mg/dL:** 1.27E+00.

  2. As indicated by "00" after "+," the decimal point does not move and the value is used as shown: 1.27 mg/dL.

## Conversion of Mass Concentration to Molar Concentration

To convert from mass concentration (eg, mg/dL) to molar concentration (eg, µmol/L), multiply the mass concentration by the conversion factor listed in Table 1. For example, the mass to molar concentration conversion for 5-aminosalicylic acid is: 6.80E−01 mg/dL • 6.54E+01 = 44.4E+01 µmol/L.

When a factor is not available, convert the units as shown in the following example:

millimoles = mmol/L

**EXAMPLE:** Convert 110 mg/dL glucose to molar units, then to millimoles, as follows:

The chemical formula for glucose is $C_6H_{12}O_6$.

1. Determine the gram molecular weight of $C_6H_{12}O_6$.
   The molecular weight is the sum of the atomic weights of carbon, hydrogen, and oxygen:
   C (carbon) = 12.01 g/mol • 6 = 72.06 g/mol
   H (hydrogen) = 1.01 g/mol • 12 = 12.12 g/mol
   O (oxygen) = 15.99 g/mol • 6 = 95.94 g/mol
   The sum of C + H + O = 72.06 + 12.12 + 95.94 = 180.12 g/mol.
   The gram molecular weight of glucose is 180.12 g/mol.

2. Determine the molar units for 110 mg/dL glucose.
   a) Use the gram molecular weight to convert the units:

$$\frac{110\,\text{mg}}{\text{dL}} \bullet \frac{10\,\text{dL}}{\text{L}} = \frac{1100\,\text{mg}}{\text{L}} \bullet \frac{1\,\text{g}}{1000\,\text{mg}} = \frac{1.10\,\text{g}}{\text{L}} \bullet \frac{1\,\text{mol}}{180.12\,\text{g}} = \frac{0.0061\,\text{mol}}{\text{L}}$$

   b) Convert to millimoles:

$$\frac{0.0061\,\text{mol}}{\text{L}} \bullet \frac{1000\,\text{mmol}}{\text{mol}} = \frac{6.105\,\text{mmol}}{\text{L}}$$

110 mg/dL glucose converted to molar units is 6.105 mmol/L.

## Conversion of Molar Concentration to Mass Concentration

**EXAMPLE:** Convert 66.49 nmol/L of dopamine to mg/dL:

The chemical formula for dopamine is $C_8H_{11}NO_2$.

1. Determine the gram molecular weight of $C_8H_{11}NO_2$.
   The molecular weight is the sum of the atomic weights of carbon, hydrogen, nitrogen, and oxygen:

## The Quality Management System Approach

Clinical and Laboratory Standards Institute (CLSI) subscribes to a quality management system (QMS) approach in the development of standards and guidelines that facilitates project management, defines a document structure via a template, and provides a process to identify needed documents. The QMS 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:

| | | | |
|---|---|---|---|
| Organization | Personnel | Process Management | Nonconforming Event Management |
| Customer Focus | Purchasing and Inventory | Documents and Records | Assessments |
| Facilities and Safety | Equipment | Information Management | Continual Improvement |

EP37 covers the QSE indicated by an "X." For a description of the other documents listed in the grid, please refer to the Related CLSI Reference Materials.

| Organization | Customer Focus | Facilities and Safety | Personnel | Purchasing and Inventory | Equipment | Process Management | Documents and Records | Information Management | Nonconforming Event Management | Assessments | Continual Improvement |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | X<br>C56<br>EP07 | | | | | |

### Path of Workflow

A path of workflow is the description of the necessary processes to deliver the particular product or service that the organization or entity provides. A laboratory path of workflow consists of the sequential processes: preexamination, examination, and postexamination and their respective sequential subprocesses. All laboratories follow these processes to deliver their services, namely quality laboratory information.

EP37 covers the medical laboratory path of workflow processes indicated by an "X." For a description of the other documents listed in the grid, please refer to the Related CLSI Reference Materials section.

| Preexamination | | | | Examination | | | Postexamination | |
|---|---|---|---|---|---|---|---|---|
| Examination ordering | Sample collection | Sample transport | Sample receipt and processing | Examination | Results review and follow-up | Interpretation | Results reporting and archiving | Sample management |
| | | | C56 | X<br>EP07 | X<br>C56 | X | C56 | |

## Related CLSI Reference Materials*

**C56** **Hemolysis, Icterus, and Lipemia/Turbidity Indices as Indicators of Interference in Clinical Laboratory Analysis. 1st ed., 2012.** This document provides background information on mechanisms of hemolysis, icterus, lipemia/turbidity (HIL) interference; intended usefulness of HIL indices; establishment of HIL alert indices; availability of automated HIL detection systems; and interpretation, strengths, limitations, and verification of HIL indices in the clinical laboratory.

**EP07** **Interference Testing in Clinical Chemistry. 3rd ed., 2018.** This guideline provides background information, guidance, and experimental procedures for investigating, identifying, and characterizing the effects of interfering substances on clinical chemistry test results.



* CLSI documents are continually reviewed and revised through the CLSI consensus process; therefore, readers should refer to the most current editions.

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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**

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