CLINICAL AND LABORATORY STANDARDS INSTITUTE®

2nd Edition

POCT05

Performance Metrics for Continuous Interstitial Glucose Monitoring

This guideline provides consensus guidelines for health care professionals, *in vitro* diagnostic and medical device manufacturers, and regulatory agencies regarding the use of continuous glucose monitoring (CGM) systems and data obtained from CGM systems. This guideline covers how CGM data should be assessed for accuracy, how CGM systems should be assessed for factors that can decrease accuracy, and how CGMs should be operated for optimal performance.

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

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Performance Metrics for Continuous Interstitial Glucose Monitoring

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Abstract

Clinical and Laboratory Standards Institute guideline POCT05—*Performance Metrics for Continuous Interstitial Glucose Monitoring* provides consensus information for health care professionals, *in vitro* diagnostic and medical device manufacturers, and regulatory agencies regarding how continuous glucose monitoring (CGM) data should be assessed for accuracy, how CGM systems should be assessed for factors that can decrease accuracy, and how CGMs should be operated for optimal performance. This guideline defines and explores multiple aspects of CGM performance, including use cases, point and trend accuracy, evaluation of threshold alerts, system stability and reliability, clinical studies for assessing CGM performance, calibration, measurement traceability, and special considerations such as shelf life, cybersecurity, and product labeling.

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Foreword

Continuous glucose monitoring (CGM) systems are medical devices that measure glucose in the interstitial fluid just under the skin and use algorithms to predict blood glucose values from the measurement. This guideline applies to such devices; however, similar concepts might be applicable to noninvasive or minimally invasive devices. This guideline covers how CGM data should be assessed for accuracy, how CGM systems should be assessed for factors that can decrease accuracy, and how CGM systems should be operated for optimal performance.

The CGM market is experiencing strong growth as accuracy, convenience, sensor duration, and data management capabilities improve and as patients, health care professionals, and payers see the benefits that these devices can provide in the management of glucose levels. Many clinical trials comparing CGM with other blood glucose monitoring methods have demonstrated decreases in mean glycemia, glycemic variability, and the incidence of hypoglycemia. Optimal CGM system performance, as well as practical data comparisons between sensors, can be obtained by following the technical specifications presented in this guideline.

NOTE: To facilitate the readability of this guideline, mg/dL is used as the unit of measure. This preference does not constitute a recommendation for mg/dL over mmol/L. If needed, the following formula can be used to convert mg/dL to mmol/L:

$$\text{mmol/L} = \frac{\text{mg/dL}}{18} \quad (1)$$

Overview of Changes

This guideline replaces the previous edition of the approved guideline, POCT05-A, published in 2008. Several changes were made in this edition, including:

- Extensively revising every chapter
- Adding new chapters that discuss:
  - CGM device use cases
  - Cybersecurity for CGM devices
  - CGM device labeling
- Rearranging subchapters and appendixes, including:
  - Changing stand-alone chapter on lag time to become part of Chapter 8
  - Including text describing establishing measurement traceability in Chapter 4
  - Replacing appendix on clinical studies with Chapter 9
  - Replacing appendix on rate deviation with Subchapters 6.3.1, 6.3.2, and 6.4
- Eliminating appendix covering continuous glucose-error grid analysis

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

Key Words

Accuracy, bias, calibration, continuous, diabetes, glucose, lag, metrics, monitoring, sensor, stability, trueness

Performance Metrics for Continuous Interstitial Glucose Monitoring

Chapter 1: Introduction

This chapter includes:

- Guideline's scope and applicable exclusions
- Background information pertinent to the guideline's content
- Standard precautions information
- Terminology information, including:
  - Terms and definitions used in the guideline
  - Abbreviations and acronyms used in the guideline

1.1 Scope

This guideline provides recommendations for methods used to determine analytical and clinical metrics of continuous glucose monitoring (CGM) as an indicator of blood glucose values. It discusses use cases, point accuracy, trend accuracy, evaluation of threshold alerts, system stability and reliability, clinical studies for assessing CGM performance, calibration, traceability of measurement, cybersecurity, and device labeling.

The intended users of this guideline are *in vitro* diagnostic and medical device manufacturers, regulatory agencies, and health care professionals. This guideline is not intended for use by patients and does not discuss devices that do not meet the definitions of continuous, interstitial, and glucose monitoring.

1.2 Background

The use of self-monitoring of blood glucose (SMBG) devices or glucose meters has led to more normal glucose levels and lower risk of cardiovascular and long-term complications in both type 1 and type 2 diabetes. Patients typically use SMBG devices to test blood glucose levels several times a day to plan diet and/or exercise, to manage diabetes medications, including insulin dosages, and to correct abnormal blood glucose values. Although these devices are easier to use than in the past, many diabetes patients do not comply with SMBG testing at the frequency recommended by their physician because of the cost of testing supplies, the pain of repeated SMBG measurements, the environmental drawbacks of blood and sharps waste, and the overall inconvenience of monitoring.

CGM devices are typically attached to the skin by an adhesive patch or implanted under the skin. Unlike SMBG devices that measure glucose levels in blood (capillary), CGM devices sample interstitial fluid (ISF) from under the skin. Circulating blood glucose distributes into ISF, where it is eventually absorbed by cells. ISF glucose levels are related to although not necessarily the same as blood glucose levels. Depending on physiological circumstances, compared with blood glucose levels, ISF levels may be higher or lower at different times.

CGM devices offer patients the potential to monitor glucose without repeated skin punctures, which are required for SMBG measurements. Although CGM is "continuous," CGM devices may actually only report ISF glucose intermittently, varying from every few seconds to several minutes between measurements. Software inside CGM devices can combine current levels with previous results to predict a future direction of glucose change. CGM instruments can thus display not only a single glucose result but also the direction of glucose change (up, down, or stable), as well as the magnitude of change (amount of glucose change per minute). CGM devices thus offer the potential to predict hypoglycemic or hyperglycemic events before they occur, alert when they do occur, monitor for glucose variations that may not be detectable with SMBG monitoring only a few times a day, and predict future glucose values for determining therapy adjustments. Furthermore, glucose measurements from CGM devices can be combined with insulin pump dosing information to deliver both up-to-date glucose levels and insulin dosing information on the same screen or incorporated into a closed-loop artificial pancreas system that delivers insulin automatically, based on the continuous measurements.

Currently, true glucose traceability in ISF cannot be established, because reference measurement procedures for glucose are available only for the sample types (matrixes) plasma, serum, and whole blood but not for ISF. For accuracy evaluations, it is important to specify the sampling method and sample type and to use a reference glucose measurement method that is accurate and traceable to a primary standard (eg, an internationally recognized reference material and/or method) (as defined by the *Vocabulaire International de Métrologie [International Vocabulary of Metrology – Basic and General Concepts and Associated Terms] [VIM]*).[1]

CGM data can be classified with a two-dimensional grid for CGM-enabled systems that presents both the types of use cases and the types of device control that a CGM-enabled system can support. Personalized therapies enabled by CGM include insulin therapy management with real-time CGM and automated insulin dosing systems.

Point accuracy of a CGM can be defined as the numerical agreement of a test result between the CGM and a glucose reference method. There is no single metric accepted for evaluating the performance of a CGM. Several metrics are frequently used to describe sensor accuracy in different ways. These metrics include:

- Agreement rates (ie, the percentage of CGM values falling within a specified distance from the reference measurement)

- Agreement when the CGM reading is outside the display range (ie, the concordance of measurements that are specified as "low" or "high" with reference values in these extreme ranges)

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