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New Guideline Supports the Development and Evaluation of Continuous Interstitial Glucose Monitoring Devices

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Abstract

For the millions of patients who are managing diabetes, daily self-monitoring of blood glucose is a fact of life. However, the cost and inconvenience of self-monitoring have led to noncompliance by many patients. Continuous interstitial glucose monitoring (CGM) has emerged as a promising and welcome alternative to traditional glucose monitoring, which requires the patient to endure repeated finger sticks. The Clinical and Laboratory Standards Institute (CLSI) (Wayne, PA) has been working cooperatively with the Diabetes Technology Society on the development of a consensus guideline for CGM. CLSI has recently released document POCT5-P—*Performance Metrics for Continuous Interstitial Glucose Monitoring; Proposed Guideline*. This document specifies requirements and recommendations for methods determining analytical and clinical metrics of CGM. This guideline will support and streamline the further development and evaluation of CGM devices.

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For the millions of patients who are managing diabetes, daily self-monitoring of blood glucose (SMBG) is a fact of life. However, the cost and inconvenience of self-monitoring have led to noncompliance by many patients. Continuous interstitial glucose monitoring (CGM) has emerged as a promising and welcome alternative to traditional glucose monitoring, which requires the patient to endure repeated finger sticks. In addition, CGM has the added benefit of providing information about the direction and magnitude of glucose change; therefore, alerting the patient to the danger of a hypoglycemic event. Although a relatively new technology, CGM offers the potential of better and more efficient management of diabetes, especially for patients whose diabetes requires intensive monitoring.

Because CGM offers the ability to report trends in glucose levels over time, a capability not available in traditional finger-stick monitoring methods, the development of new evaluation methods for determining the accuracy of CGM devices is necessary. As more manufacturers develop CGM devices, consistent evaluation protocols become more important.

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Abbreviations: (CGM) continuous interstitial glucose monitoring, (CLSI) Clinical and Laboratory Standards Institute, (FDA) Food and Drug Administration, (SMBG) self-monitoring of blood glucose

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The Clinical and Laboratory Standards Institute (CLSI) (Wayne, PA) has been working cooperatively with the Diabetes Technology Society on the development of a consensus guideline for CGM. CLSI has recently released document POCT5-P—*Performance Metrics for Continuous Interstitial Glucose Monitoring; Proposed Guideline*. This document specifies requirements and recommendations for methods determining analytical and clinical metrics of CGM.[1] This guideline will support and streamline the further development and evaluation of CGM devices.

"The POCT5-P document presents the use of CGM—how to present the data, how to compare the data between different continuous interstitial glucose monitors, and how to compare the data with spot blood testing. It deals with point accuracy, trend accuracy, physiology of interstitial fluid, lag time, and other ways to describe and present the data," explains David Klonoff, M.D., FACP, of the Diabetes Technology Society in Foster City, California, and chair holder of the CLSI subcommittee that developed the guideline. "These guidelines should help save time and effort in developing new products by establishing for the manufacturers how the products must perform," he adds.

Continuous Interstitial Glucose Monitoring: An Exciting New Technology

Continuous interstitial glucose monitoring devices are relative newcomers in the field of glucose monitoring. The impact of the technology has been extraordinary for patients looking for freedom from the burden of more conventional SMBG devices and methodologies and for doctors who appreciate the additional information CGM provides.

"The current methods of glucose monitoring provide an infrequent and incomplete picture of what is going on with a patient's physiology. The power of CGM is that it measures the level of interstitial fluid glucose continuously, and provides the patient with real-time glucose trend information; that includes the concentration (mg/dl, mmol/liter), direction (stable, increasing, or decreasing), and rate of change (<1 mg/dl/min, 1 to 2 mg/dl/min, >2 mg/dl/min). The trend information will help the patient with diabetes manage their meals, activity, and medications more effectively. CGM is especially useful in the detection and prediction of hypoglycemia, where there are only a few minutes to act before the onset of serious symptoms," says Jeffrey Joseph, DO, director of the Artificial Pancreas Center at Thomas Jefferson University in Philadelphia, Pennsylvania, and a member of the subcommittee that produced POCT5-P.

"CGM allows people to keep diabetes under better control. There have been many studies published in the past several years, which demonstrate that if blood sugar is kept in tighter control over time, the risk of all diabetes complications—including heart disease, kidney disease, nerve disease, and eye disease—decrease dramatically," adds John Mastrototaro, Ph.D., of Medtronic MiniMed in Northridge, California, and also a member of the subcommittee that produced the guideline.

A Guideline for Evaluation and Resource for Regulatory Requirements

The new POCT5-P guideline helps researchers and manufacturers developing CGM devices to develop metrics for performance evaluation of the monitors. Until this guideline, each company was responsible for developing and designing its own clinical trials. The guideline will streamline this process and also provide a valuable resource to clinicians interpreting data from CGM devices.

"The document is a guideline that will help companies developing CGM systems better understand how to evaluate the system. POCT5-P outlines some of the appropriate metrics for assessing the performance of the CGM device, and also provides guidance on the types of clinical trials necessary to evaluate the metrics appropriately," says Mastrototaro.

Based on the Food and Drug Administration (FDA) Modernization Act of 1997, the FDA is authorized to recognize consensus standards, such as those developed by CLSI, other American National Standards Institute-accredited standards development organizations, and international standards development organizations. A declaration of conformity to FDA-recognized consensus standards by a manufacturer seeking FDA approval for an *in vitro* diagnostic assay (e.g., a new CGM assay) helps streamline the regulatory process. The FDA involvement in the development of POCT5-P ensures that the regulatory perspective is included in this consensus document, along with those of representatives from the industry and professions sectors.

"For anyone developing a CGM system, this guidance will aid in designing the right kinds of clinical trials to evaluate the right metrics, in order to streamline the process by which they seek and gain FDA approval, and ultimately market the product," notes Mastrototaro.

Klonoff adds, "This document informs scientists of the guidelines that are needed to present data and perform

the experiments the FDA wants to see. We are hopeful that the FDA will adopt the CLSI guideline, and we believe they will, since participants from the FDA were involved in the development of the consensus document."

Additional Reference for Glucose Monitoring

As new technologies in the field of glucose monitoring emerge, there is a need to assist clinicians in interpreting and comparing patient results. In order to make appropriate patient care decisions, medical professionals need to determine whether differences in results are because of test methodologies or patient condition.

The Clinical and Laboratory Standards Institute has recently released the document POCT6-P—*Guidelines for Comparison of Glucose Methodologies That Use Different Sample Types; Proposed Guideline*. This document provides information to assist the clinical and point-of-care staff in result comparisons of glucose tests. The information will include preanalytical, analytical, and physiological considerations. Use of this guideline will help clinicians design evaluation protocols for technology or devices under consideration and will help ensure that even early adopters of new technologies will do so with the knowledge that ensures patient safety. For manufacturers, the guideline will help ensure that they can meet and understand customer requirements in their product design for glucose testing systems. The impacts to be reviewed include sample type, test methodology, calibration, sample transportation, or delay in testing, as well as test frequency.[2]

"On a daily basis, clinicians look at a chart that contains point-of-care glucose device results and main laboratory results. In some cases, they also have other specific glucose devices in specialty areas like surgery and ICU. To provide a continuum of care and make correct intervention decisions, the clinician needs to understand why different technologies and sample types could give different results. Without this type of information, the clinician could assume that any detectable difference is only related to the patient condition. This document will help educate clinicians on technology-related causes for differences in results from different technologies," explains Mary C. Coyle, M.S., MT(ASCP), of Roche Diagnostics Corporation in Indianapolis, Indiana, and chair holder of the CLSI subcommittee that developed POCT6-P.

Both POCT5-P and POCT6-P support the philosophy of CLSI to continually produce consensus documents, balancing viewpoints of industry, government, and the health care professions, which represent the gold standard of best practices and guidelines. Coyle describes the documents as "consolidated reference material that has been reviewed by a team of experts representing industry, government, and professions."

For more information on these and other CLSI documents and resources, visit www.clsi.org. CLSI welcomes comments and questions about the documents; this feedback serves as the basis for updated document editions. All comments and responses are formally addressed and published in the next edition of the document. For more information about CLSI references and best practices, visit www.clsi.org or call 610-688-0100.

References:

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2. CLSI. *Guidelines for Comparison of Glucose Methodologies That Use Different Sample Types; Proposed Guideline*. CLSI document POCT6-P. Wayne, PA: Clinical and Laboratory Standards Institute; 2008.