FDA LABELING CHANGE ON POINT OF CARE (POC) GLUCOSE DEVICES (GLUCOSE METERS)

BACKGROUND: The Food and Drug Administration (FDA) has enacted labeling changes specific to the use of multi-patient waived whole blood glucose devices. Under the section of “Intended Use” in the 510(k) Summary the limitation clause “The performance of this system has not been evaluated on the critically ill” has been added. The labeling change is specifically intended to alert the end-user that these devices have limitations and are not applicable in some healthcare settings. The Clinical Laboratory Improvement Amendments (CLIA) regulations specify, in order to maintain the classification as waived testing, the user must strictly adhere to all of the instructions in the product insert from “intended use” to “limitations of the procedure.” Any modifications to the assay as set forth in the manufacturer’s labeling and instructions, including specimen type, instrumentation, or procedure, that could affect its performance specifications for sensitivity, specificity, accuracy, or precision or any change to the stated purpose of the test, its approved test population, or any claims related to interpretation of the results would result in the change in complexity from waived to high complexity. Consequently, the use of such devices on critically ill patients constitutes an off-label use in which the laboratory must, with the current regulatory guidance, develop any off-label application as a laboratory developed test (LDT.)

DISCUSSION: As defined in the CLIA regulations, a modified FDA cleared/approved test (off-label application) becomes a high complexity test requiring extensive validation, correlation, and adherence to strict testing personnel qualifications.

- CLIA defines waived tests as “simple laboratory examinations and procedures that have an insignificant risk of an erroneous result.”
- The FDA determines the criteria for tests being simple with a low risk of error and approves manufacturer’s applications for a test system waiver as defined by the accompanying package insert. Recently the FDA has required that all labeling for blood glucose monitoring systems include a statement in their device labeling indicating the clause, “The performance of this system has not been evaluated on the critically ill.”
- The Centers for Medicare & Medicaid Services (CMS) specify that to meet waived requirements all of the instructions in the product insert from “intended use” to “limitations of the procedure” must be followed and “ensuring that any test system limitations are observed.” (CLIA Brochure: How to Obtain a CLIA Certificate of Waiver)
- The College of American Pathologists (CAP) All Common Checklist requirement, COM.40250 (July 2013), requires that for FDA approved/cleared tests: the laboratory follows manufacturer instructions or provides documentation of validation study(ies) if the test has been modified. If the laboratory modifies manufacturer instructions, the test is categorized as a non-FDA approved/cleared test, and the modification must be validated by the laboratory. For example, the laboratory must verify the established performance specifications of FDA-approved assays (accuracy, precision, analytic sensitivity, interferences, reference range, and reportable range, as applicable).
For waived tests, if manufacturer instructions are modified, the test is no longer considered waived and requirements for high complexity testing apply.

**CONSIDERATIONS FOR MANAGEMENT:** The Laboratory Director, in conjunction with the medical staff, must consider the following:

1. The facility must define “critically ill” for their given institution for the POC glucose testing. Examples of definitions used by some VA Laboratories include:
   - A patient on mechanical ventilation with a mean arterial pressure less than 60 mmHg despite the use of pressors.
   - Any patient with decreased peripheral blood flow; examples might be an individual with severe dehydration, hypotension, shock, decompensated heart failure, or peripheral arterial occlusive disease.
   - Some facilities may attempt to identify critically ill patients on the basis of their location, such as ICU patients, Emergency Room (ER) patients, and Operating Room (OR) patients. The VA National Enforcement Office does not recommend the identification of critically ill patients solely by location. **NOTE:** If the facility chooses to identify critically ill patients by location, the facility must perform a risk assessment to ensure all areas are evaluated.

2. POC glucose meter testing performed on patients that do not meet the defined criteria for critically ill may continue to be tested via the glucose meter in accordance with waived testing regulations.

3. POC glucose meter testing performed on patients defined as critically ill:
   a. VA National Enforcement Office does not recommend using glucose meters to monitor critically ill patients. The best practice is to test critically ill patients using a venous specimen tested on a traditional laboratory methodology that is approved for use on critically ill patients.
   b. If the facility intends to use the glucose meter for testing in the defined critically ill population then this will be considered as a modification of the manufacturer instructions.
      (1) To comply with CLIA and accreditation requirements, the test complexity converts from waived to high complexity and all requirements for high complexity testing apply. This includes:
         (a) Establishment of method performance specifications for the meter(s)
         (b) Performance of a complete validation on each instrument used to test critically ill patients including validation of the accuracy, precision, and analytic sensitivity on each instrument. **NOTE:** Because this is high complexity testing, the validation process must be completed on each instrument (including backup instruments); validations on meters used to test critically ill patients cannot be performed on a subset of meters.
         (c) Evaluation for analytic interferences may be accomplished through the review of the manufacturer interference studies or other studies performed. When studies that assess inferences that may be unique to critically ill patients are not available, additional studies to assess interferences for critically ill patients are required.
(d) Verification of the Analytic Measurement Range (AMR)

(e) Establishment of reference interval

(2) The Quality Control process must follow non-waived requirements.

(3) Calibration and reagent requirements for non-waived testing must be followed including:

(a) AMR validation every 6 months for all devices used for critically ill patients.

(b) Correlation between each POC instrument and the main laboratory instrument every 6 months.

(4) Personnel

(a) Only personnel that meet requirements of high complexity testing can perform the POC glucose testing on glucose meters for critically ill patients.

(b) The CLIA High Complexity personnel standards (CFR 493.1489) must be used to assess personnel for the minimum educational requirements. i.e. An RN with a Bachelor of Science degree could meet the CLIA high complexity personnel standards, but generally an RN with an Associate degree would not meet the minimum CLIA personnel standards.

(c) For CAP laboratories, individuals performing POC glucose meter testing on critically ill patients must be included in the laboratory’s CAP Personnel Roster. Evidence of educational requirements consistent with the CLIA High Complexity personnel requirements would be required.

(d) Competency assessment would include all 6 elements defined by CLIA for staff performing high complexity testing.

4. Facilities utilizing whole blood glucose meters must provide physicians (providers) and testing personnel education to include:

a. Awareness of FDA labeling change.

b. Information on all the limitations of the POC glucose meter. Consider including description of test limitations for all glucose meter protocols in VistA Test Description Information.

c. Awareness of the limitations of the POC glucose testing using a glucose meter. Whenever POC glucose meter results are deemed questionable, i.e. inconsistent with the condition of the patient, the provider should order an intravascular glucose level to be performed in the main lab. The glucose meter results must agree within +/-12 mg/dL of the laboratory analyzer values at glucose concentrations below 100 mg/dL and within +/-12.5% of the laboratory analyzer values at glucose concentration at or above 100 mg/dL.


d. Provide a protocol for moderate complexity venous or arterial determinations for critically ill patients.

**EVALUATION OF POC GLUCOSE METER PROTOCOLS:** A risk assessment to determine when main laboratory venipuncture glucose testing is necessary must be performed.
POC glucose meter protocols should include the requirement for a moderate complexity venous or arterial glucose determination in certain situations. The following are suggested:

1. Correlate results obtained on the glucose meter with the clinical laboratory when insulin is being administered but the POC glucose meter level is not responding.
2. Correlate results obtained on the glucose meter with the clinical laboratory in any situation where the POC glucose meter level is inconsistent with the clinical presentation.
3. Periodically correlate results obtained on the glucose meter with the clinical laboratory.
4. Thoroughly review the POC glucose meter product insert and ensure protocols clearly define the limitations of the glucose meter test.
5. Review published alerts and adverse or sentinel events pertaining to glucose meter testing.