Review Criteria Assessment of Portable Blood Glucose Monitoring In Vitro Diagnostic Devices Using Glucose Oxidase, Dehydrogenase or Hexokinase Methodology

DRAFT DOCUMENT

This guidance document is being distributed for comment purposes only.

Clinical Chemistry and Toxicology Devices Branch
Division of Clinical Laboratory Devices
Office of Device Evaluation

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Comments and suggestions regarding this draft document should be submitted within 60 days of the above release date to: Joseph Hackett, Ph.D., Associate Director, Division of Clinical Laboratory Devices, HFZ-440, 2098 Gaither Road, Rockville, MD 20850. Comments and suggestions received after this may not be acted upon by the Agency until the document is next revised or updated. For questions regarding the draft document, contact Dr. Kaiser Aziz or Dr. Joseph Hackett via phone (301) 594-3084 or fax (301) 594-5940.

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration
Center for Devices and Radiological Health

REVIEW CRITERIA FOR ASSESSMENT OF PORTABLE BLOOD GLUCOSE MONITORING IN VITRO DIAGNOSTIC DEVICES USING GLUCOSE OXIDASE, DEHYDROGENASE, OR HEXOKINASE METHODOLOGY

VERSION 02/14/96

This is a flexible document presenting current guidance on the preparation of premarket notifications (510(k)s) for glucose in vitro diagnostics devices employing enzymatic methodologies. It is based on 1) current technology, 2) clinical experience, 3) previous submissions by manufacturers to the Food and Drug Administration (FDA), and 4) Safe Medical Devices Act of 1990 and regulations in the Code of Federal Regulations (CFR). So that we may revise the draft as necessary, please send your comments to

http://www.fda.gov/cdrh/ode/gluc.html
DEFINITION: Portable blood glucose devices are intended for use in hospitals, at point of care, in physicians' offices, and over-the-counter as in vitro diagnostic tests for quantitative and semi-quantitative measurement of glucose by glucose oxidase, dehydrogenase, or hexokinase based methodologies. These do not include the larger clinical chemistry analyzers or the dedicated glucose analyzers used to perform routine and stat glucose testing on plasma, serum, urine, and CSF.

PRODUCT CODE: CGA, CFR, LFR

REGULATION: 21 CFR 862.1345

(a) Identification.

A glucose test system is a device intended to measure glucose quantitatively in blood and other body fluids. Glucose measurements are used in the diagnosis and treatment of carbohydrate metabolism disorders including diabetes mellitus, neonatal hypoglycemia, and idiopathic hypoglycemia, and of pancreatic islet cell tumors.

(b) Classification. II

REVIEW REQUIRED: 510(k)

PURPOSE

The purpose of this document is to provide guidance on information to present to the FDA before a device may be cleared for marketing. This notification enables FDA to make better informed decisions based on a more consistent data base. We hope that such documents will lead to more reliable, reproducible and simple to use commercial devices.

I. Background

Glucose monitoring has become a major adjunct to the care of individuals with diabetes mellitus in the past decade. It is now possible for the individual with diabetes and the health-care professional to measure and record blood glucose levels frequently with portable devices. In the hospital, blood glucose monitors are often used instead of routine laboratory glucose testing methods to quickly obtain blood glucose concentrations from patients in the ER, ICU, CCU, OR, or other bedside locations. Used at home, these devices allow individuals with diabetes to monitor and treat fluctuations in blood glucose levels daily.¹

Despite some problems with blood glucose monitors, a Consensus Panel of physicians, diabetes educators, and laboratorians has recommended blood glucose monitoring (BGMg) testing for insulin-treated diabetes. The Panel, sponsored by the American Diabetes Association, FDA, NIH, and CDC, http://www.fda.gov/cdrh/ode/gluc.html 8/3/2006
stated that most of the problems with current monitoring systems involve the user and not the system itself.2 Thus, emphasis should be placed on educating users and following up on their performance. The Panel recommended that manufacturers help by developing systems with memory to allow comparison of patient's recorded meter glucose results with their laboratory glucose results and by building in quality control checks that must be performed before samples can be run.3

The primary intended use for glucose monitoring is to assist in the evaluation and management of individuals with diabetes. On November 17-19, 1986, the Consensus Panel of the American Diabetes Association recommended BGMg for the following uses:

- Pregnancy complicated by diabetes
- Individuals with a propensity for severe ketosis or hypoglycemia
- Individuals prone to hypoglycemia who may not experience the usual warning symptoms
- Individuals on intensive treatment programs, especially those using portable insulin-infusion devices and multiple daily insulin injections
- Individuals with abnormal renal glucose thresholds

The Panel indicated that although controversial, BGMg may be useful for individuals with diabetes not treated with insulin. However, the Panel cautioned that BGMg must not be used to diagnose diabetes mellitus, and the role of BGMg systems in screening remains uncertain. The Panel remained silent on the use of these systems with neonates. However, some BGMg systems have been validated for use with neonatal specimens. (See FDA's Review Criteria for Portable Glucose Monitoring Devices Intended for Bedside use in the Neonate Nursery).4

A broad spectrum of issues were identified for glucose monitoring. These include 1) intended and actual use, 2) adequacy of calibration and quality control, 3) accuracy and precision of these devices, 4) types of users, 5) training, 6) the adequacy of user instruction, and 7) procedural and technical limitations,2 8) specimen types (arterial, capillary, venous, whole blood, plasma), and 9) Hct effects. Additionally, more recent reports indicate environmental factors i.e., temperature, humidity, and altitude may also affect results.

The consensus document expressed the following performance goals: a) "The goal of all future Self Monitoring Blood Glucose (SMBG) systems should be to achieve a variability (system plus user) of 10% at glucose concentrations of 30-400 mg/dL 100% of the time. However, the panel is aware that the accuracy required for clinical management has not been rigorously defined." , b) "With current systems, SMBG measurements should be within 15% of the results of the reference measurements." , c) "Approximately 50-70% of individuals who receive some sort of formal training are capable of obtaining a result within 20% of the reference method; however, performance may deteriorate over time."2

II. Device Description

Most blood glucose monitoring devices consist of glucose test strips and a reflectometer to determine glucose concentrations in whole blood. Some systems depend on a glucose oxidase-colorimetric reaction that occurs when a drop of blood is placed on a reagent-impregnated pad. The test pad contains the
enzymes glucose oxidase and peroxidase, and color indicators. When whole blood is placed on the test pad, glucose is oxidized to gluconic acid and hydrogen peroxide with glucose oxidase acting as a catalyst. The hydrogen peroxide that results from this reaction oxidizes an oxygen acceptor in the presence of peroxidase to form a color change, the intensity of which is directly proportional to the amount of glucose in the blood sample.\(^1\)

A reflectance photometer or an amperometric system can be used to measure the reaction that takes place on the reagent strip. To accomplish this, the reagent strip is inserted into the test chamber. When light shines on the reagent pad, light is reflected. This reflected light is measured electronically and a blood glucose concentration value is displayed.

Absorbance photometry is another method which uses two wavelengths to measure glucose concentration rather than the single wavelength used by most reflectance photometry systems.

Other systems use electrochemical methodologies. These monitors quantify glucose amperometrically by measuring the current that is produced when glucose oxidase catalyzes the oxidation of glucose to gluconic acid or when glucose dehydrogenase catalyzes the oxidation of glucose to gluconolactone. The electrons generated during this reaction are transferred from the blood to the electrodes. The magnitude of the resultant current is proportional to the concentration of glucose in the specimen and is converted to a readout displayed on the monitor.

Some blood glucose monitoring systems are based on a reflectometric hexokinase method. When blood is applied to the reagent strip, glucose is phosphorylated to glucose-6-phosphate. This is later oxidized with concurrent reduction of NAD. The NADH formed is directly proportional to the amount of glucose present in the sample. Then the NADH, in the presence of another enzyme, reduces the dye and a colored product is generated. The strip which is inserted in the photometer after application of the sample, measures the reaction reflectance, uses an algorithm to calculate glucose, and displays the result.

Some monitors have features such as electronic voice capability and programs for organizing/managing data and glucose history. In addition, many models have memory chips that allow one to store and recall test results. These features may include the following:

1. A real time clock to display daytime references for blood glucose values.
2. A recall button used to display results one reading at a time.
3. Event marker buttons to identify special situations or delete a result from computation.
4. Sufficient memory to record and display 100 or more entries such as blood glucose values, date, and time.
5. On demand, an average blood glucose value for the last 14 or more days will be displayed.

All meters are battery-powered and use solid-state electronics.\(^5\) The effective concentration range depends on the system but generally covers the clinically relevant range. Size, shape, and calibration technique vary by manufacturer. Some require no timing or wiping and are factory-calibrated. Most monitoring systems use check strips to periodically evaluate optical and electrical components of the monitor. Most monitor manufacturers have glucose control solutions with a specific range of glucose values that must be run periodically to check operation of the test strips and the monitor together, as well as operator technique.\(^1\) However, they do not monitor the quality of the collection procedure or proper

http://www.fda.gov/cdrh/ode/gluc.html
application of blood to the test strip.

Absorption spectroscopy blood glucose monitoring techniques that do not require the user to draw blood are in development. One monitor, which is available for research use only, is a noninvasive monitor that measures the absorption of near-infrared light in vivo to determine blood glucose concentrations. In addition to not requiring fingersticks, chemical reactions, or timing and wiping, the procedure allows for instantaneous and continuous measurement. Implantable continuous monitoring systems are also being developed.

III. Human Factors Studies

Since 1984, the Food and Drug Administration (FDA) has received many reports of problems with blood glucose meters. A large number of these problems have been attributed to users': (a) failure to maintain the meter properly, (b) incorrect techniques or operating procedures, or (c) failure to follow the instructions for meter use.

Ergonomic factors to be considered include meter size, display size, the placement of buttons, and meter carrying case. These factors sometimes play an important part in user performance. For example, the height of numerals displayed may be an important consideration. Human factors design considerations indicate that 5 mm should be considered the minimum acceptable character size for effective meter use by diabetics with no uncorrected visual deficits.6

Human factor considerations also indicated that the preference for the number of buttons ranged from one, which controlled all functions, to more than three buttons, each controlling different functions. The surface area of the push-button must be large enough for the finger to press it easily and apply the necessary force without slipping. Grandjean (1982) recommended a push-button diameter of 12-15 mm. The surface can also provide tactile cues to aid users in positioning their finger properly. This can be done by providing a rough or textured push-button surface or by making it slightly concave to fit the convex shape of the underside of the finger.6

Optimum meter design can be important in reducing user error. Users should be encouraged to provide feedback about the design of meters through user surveys. The survey can employ a numerical rating scale (1 to 5).

The following features may be considered for instruments:

Appearance
Size
Color
Button size
Button color
Display readout size
Flagging of procedural errors and analytical errors
Readout visibility
Reaction visibility
Reaction start procedure
Warning beeps
Ease of use
Convenience
Ease of cleaning/maintenance

Batteries and replacement
Memory features and use
Carrying or storage case
Check strip and controls
Method quick reference card(s)

The following features may be considered for reagent strips:

Size and shape
Appearance
Pad appearance
Quantity of blood needed
Ease of application
Wipe method
Wipe materials
Warning beep usefulness
Pad reaction color
Reaction color uniformity
Timing
Visually-read color chart for confirming/checking meter performance
Storage, handling and stability

An FDA-funded human factors study, was performed to evaluate the sequence of operations required to perform a correct reading. Blood sampling, a function that is independent of meter type but that is highly dependent upon technology of strip chemistry, was identified as having the greatest potential for error. This is the point at which the user must draw the blood and place it on the strip.6

The second most error prone function is the testing itself. Here, the primary sources of error identified were timing, wiping or blotting, and inserting the strip into the meter. Most of the mistakes that can occur in this function can affect the meter reading and will probably not be detected by the user. These procedures are generally specific to the type of meter being tested.

IV. Performance Considerations for Regulatory Clearance

Appropriate studies to evaluate the device include precision, linearity, hematocrit effects, interferences, and comparisons to laboratory glucose method(s). Manufacturers are encouraged to study the effect of environmental factors such as temperature, humidity and altitude as well.

A. Precision

Blood Glucose Meters typically are designed for optimum performance with a specific matrix, usually capillary or venous blood. Therefore, precision studies should be conducted using matrix appropriate material. It must be kept in mind that a number of BGMs give precise, but incorrect, glucose results with venous blood. This is particularly true of biosensors which depend on the oxygen levels of capillary blood, and give high results (+20%-30% in some cases) with venous blood due to the fact that oxygen "poisons" the biosensors, causing venous blood (with 50-60% lower pO₂) to show higher reaction rates as a result of lower oxygen content.

FDA recommends following the NCCLS precision guidelines EP5-T2 or equivalent when evaluating and stating label precision claims.7 Additionally, it is suggested that the following glucose

http://www.fda.gov/cdrh/ode/gluc.html
concentrations be prepared from spiked samples with maleimide added to prevent glycolysis. Similar concentrations should be considered when aqueous control solutions are used.

1. 30-50 mg/dl
2. 51-110 mg/dl
3. 111-150 mg/dl
4. 151-250 mg/dl
5. 251-400 mg/dl

Precision studies should be performed on-site at 3 independent physicians' office laboratories (POLs) if intended for POL use; at 3 different hospitals or 3 different settings within a hospital, e.g. ER, ICU, etc., if intended for use at point-of-care (POC); or at the manufacturing site. Additionally, the same lot of blood glucose strips should be used over the study period. This along with the protocol used for determining precision should be included in the premarket notification submission, i.e. 510(k).

B. Linearity

Follow the NCCLS linearity guidelines EP6-P or equivalent when defining and evaluating label claims. 8

C. Hematocrit Studies

Over and under estimation of glucose due to hematocrit effect is a common source of error. Studies should be performed at physiologically meaningful levels and submitted with the protocol and results.

D. Bias

The % bias of the proposed assay relative to the comparative method can be calculated as follows:

\[
\% \text{ bias} = \frac{\text{Proposed Method Result} - \text{Comparative Result}}{\text{Comparative Result}} \times 100
\]

Report the Total Error for the glucose monitor.

The overall bias can be calculated from the least squares linear regression line of the proposed assay and the comparative method. Additionally, the Clark Error Grid may be used to estimate the clinical significance of bias results between the two methods.

The protocol used for estimating bias should be included in the 510(k).

E. Interference Studies

Follow the NCCLS guidelines outlined in EP7-P or equivalent for testing various analytes or drugs for interference. 9 Include exogenous and endogenous substances. Common interferants to be considered for testing are the following: acetaminophen, ascorbic acid, bilirubin, cholesterol, creatinine, dopamine, ephedrine, ibuprofen, L-dopa, methyl dopa, salicylate, tetracycline, tolazamide, tolbutamide, triglycerides, and uric acid. Preservatives should be included here as well.

An aliquot of whole blood can be taken and supplemented with glucose concentrations in various ranges. The same target glucose value should be used for a series of 4 to 5 aliquots and utilized for
studying each interferant. Each aliquot should be supplemented with a specific concentration of the compound under investigation. The specific concentration of each compound in an experimental series should be chosen to bracket the physiological or therapeutic concentrations expected in blood. Replicate measurements should be made of each aliquot.

F. Correlation Studies

Capillary blood is suggested for correlation determinations with the whole blood glucose hexokinase deproteinization method as the comparative method. Alternatively, a well characterized clinical laboratory method or a legally marketed glucose meter employing hexokinase or glucose oxidase may be used. For neonatal testing, refer to the Guidance Document on glucose monitoring specific to neonates.

Capillary blood specimens covering the analytical range of approximately 40-400 mg/dL should be analyzed with the proposed device. The same specimens should be analyzed by the comparative method. Follow the NCCLS guidelines EP9-T or equivalent. Linear regression should be used to express the relationship between the results obtained by the proposed and comparative methods. Include calculations for the slope, intercept, correlation coefficient, and confidence intervals. Because the reliability of the estimates of slope and intercept can be affected by nonlinearity in the data set, outliers, a narrow range of data, and variability of the comparison method, samples preferably should cover the complete range of concentrations that might be encountered, and standard deviations of slope and intercept should be given.

1. Consumer Studies

Field testing of the device under actual conditions of use is important. Patients should be selected as they present themselves at an outpatient clinic and/or physician's office. Patients should be of varying age, sex, background and education. The total number of patients should include a minimum number of 100 different patient samples.

Each patient selected for the comparison study should perform their own fingerstick and test on the subject device following device instructions. A trained technician should perform a fingerstick on the patient immediately after and perform the test on the same device. Separate results should be recorded by patient and technician and masked. Another blood sample should be collected within 5 minutes for testing by a well-characterized laboratory method. Capillary blood is the specimen of choice. When a venous sample must be used, it is important to take into account variables introduced when comparing capillary, venous, whole blood and plasma samples. Serum or plasma values are an average of 1.18 times whole blood values. (True for Hct of ~ 63%, but for "average" Hct of 43%, the factor is ~ 1.11.)

2. Point-Of-Care (POC)/Physician's Office Laboratory (POL)

Personnel typical of the intended setting should perform fingersticks and testing using the proposed device. Within 5 minutes, another specimen should be obtained from the patient for testing with the comparative device. For POC use, it is recommended that data be collected from a minimum of three POC sites either within the hospital or three different hospitals. For POL use, it is recommended that data be collected from a minimum of three independent POL sites for both accuracy and precision. At least 40 specimens should be collected and analyzed per POC/POL site.
G. Software Verification and Validation

In view of the increase in software features, it is important that the premarket notifications for such devices contain adequate documentation of software verification, validation, and testing. This documentation should describe activities performed to assess and improve the quality of the software throughout development by determining conformance to function and design specifications and by testing to assure that safeguards against potential hazards function properly. A certified statement summarizing the documentation should be submitted.

V. Labeling

The package insert for blood glucose devices should be simple, concise, and easy to understand. Graphics, i.e. line drawings, illustrations, symbols, icons, photographs, tables, and graphs are very useful tools. Also, it’s helpful to include color coded reagent containers. The size of the type should be 12 or 14 points, especially for elderly or visually impaired users, in addition to specifying that adequate lighting is needed for testing. Additionally, the same term should be used to identify the device and its parts throughout the labeling. Synonyms or alternate phrases should be avoided.

Labeling should follow 21 CFR § 809.10 and address the following specific considerations:

1. The intended use statement (section 809.10 (a)(2)) should clearly indicate on the outside package container the type of procedure that is offered and the intended use. The intended use statement in the package insert should reiterate this information. Refer to 809.10 (b).

2. A separate information section, interpretation of test results, should be presented and include information specified by section 809.10 (b)(10), limitation of the procedure.

3. General warnings and precautions should be highlighted, e.g. bolded, and appear in appropriate insert section.

4. A brief, non-technical discussion of the correlation studies should be included in the package insert.

5. Precision data obtained at the manufacturing site or POC/POL settings should be included in the package insert. The precision data should be representative of performance obtained by users. Pooling of site data may bias results and may not be allowable.

In view of the issues presented in Section VII, Limitations, it is suggested that the limitation section of the package insert/instruction manual contain the following cautionary statements as appropriate:

1. Extended exposure to air and light may alter results. It is recommended that the strips be stored in the original capped vial at temperatures below 30 °C (86 °F). Avoid exposure to excessive humidity; do not freeze.

2. Hematocrits below 35% or above 55% can affect results in either direction. 11

3. Grossly lipemic (fatty) samples may interfere with some methodologies. To be aware of such interferences, patients under the supervision of their physician should have baseline glucose values established by a clinical laboratory method prior to starting home glucose monitoring. These baseline values should be checked periodically thereafter.

4. Meter read capillary blood glucose values may be significantly lower than "true glucose levels" in
the hyperglycemic- hyperosmolar state, with or without ketosis. Include a clear statement in the
product insert that critically ill patients should not be tested by BGM, or tested with extreme
cautions.

5. Caution is advised in the interpretation of glucose values below 50 mg/dL or above 250 mg/dL.
Consult a physician as soon as possible if values in this range are obtained.

6. Health care professionals should evaluate their technique and their patients' technique at periodic
intervals. To accomplish this, it is recommended that BGMg results be compared with a
concurrently obtained laboratory measurement on the same blood sample. A well characterized
clinical laboratory method employing hexokinase or glucose oxidase should be used as the
comparative method.

7. Fluoride should not be used as a preservative for venous specimens when using blood glucose
monitors.

8. Hands and fingers contaminated with sugar from foods or beverages may cause falsely elevated
results. Include directions to wash hands in warm soapy water, rinse and dry before testing.

9. Severe dehydration and excessive water loss may cause inaccurately low results.

10. Differences in whole blood and serum/plasma values may cause variability in results.

11. Storage of strips near bleach as well as bleach containing products will affect results of glucose
oxidase strips.

12. The use of cellular phones and other radio transmitting devices should be prohibited in areas
where testing occurs.

13. Inaccurate results may be obtained at high altitudes as a result of the lower oxygen concentration
\(pO_2\).

14. Include a precautionary statement that color blind individuals should not use visual color
procedures.

Labeling for the instrument instruction manual should contain, at a minimum, the items outlined in
809.10 (b)(6), as well as troubleshooting information, question and answer section, company emergency
telephone numbers for assistance (1-800#), and hours of operation for assistance.

The National Committee for Clinical Laboratory Standards has published a document on Labeling of
Home Use In Vitro Testing Products (GP-14P). It contains very useful information including the SMOG
Readability Formula to assess the readability level of package inserts. CDRH has written a Home Use
Guidance Document, a Computer Controlled Medical Devices Guidance Document, and a Book on
Developing Home Use Instruction Manuals. Valuable information can be derived from these
documents as well. For more information, contact the FDA's Division of Small Manufacturers
Assistance at 1-800-638-2041.

VI. Quality Control
The Consensus Panel of the American Diabetes Association noted that in general, quality control practices are inadequate.\(^3\) The essential components of a quality control program include 1) calibration checks to ensure that meter performance is adequate, 2) the measurement of control solutions of known glucose concentration to evaluate the performance of reagent strips and meters, 3) comparison of results with a well characterized laboratory comparative method, and 4) periodic review of user technique with correction of deficiencies by a qualified health-care professional.

Differences in the reagent-strip chemistries used by various manufacturers raise issues that should be considered in the design of an external quality-control program based on a single aqueous glucose control.\(^15\) In a comparison of blood glucose meters, Brooks et al.\(^16,17\) highlighted anomalous results obtained with both aqueous and serum-based control materials. Some investigators believe solution viscosity is a major factor affecting reactivities of different reagent strips.\(^15\) It may be necessary to use viscosity-adjusted control material to minimize these effects in the design of a quality control program.

Quality control solutions do not measure errors generated during collection and application of blood to the reagent strip. Therefore, the precision and accuracy of all facets of the BGMg technique should be evaluated at regular intervals by comparing the patient's BGMg results with a concurrently obtained measurement on the same blood sample by a well characterized comparative method. The same blood sample should be used with both the meter and the laboratory method to avoid uncertainty introduced by differences among capillary, venous, whole blood, and plasma samples.\(^2\) Calibration and quality control procedures should be discussed in an appropriate section of the instrument manual.

### VII. Limitations

In actual patient-care situations, glucose monitors may not always be adequate for making clinical decisions.\(^2,18\) Various factors may affect precision and accuracy. Listed below are some of the factors.

1. **User variability.**

   BGMg is technique sensitive. It has been noted that up to 50\% of the values may vary more than 20\% from the reference values in general use (an error of > 20\% is accepted by some physicians as the amount of change that can result in an inappropriate adjustment of insulin dose).

2. **Hematocrit.**

   Anemia falsely elevates and polycythemia and dehydration falsely depress blood glucose values. The magnitude of this effect may vary 4-30\% for every 10\% change in hematocrit, depending on the systems.\(^3\) High hematocrits are common in neonates. If the system has not been validated for use on neonates, include this as a limitation.

3. **Hypoglycemia and hyperglycemia.**

   Caution should be exercised in interpreting values in the hypoglycemic (less than 50 mg/dL) or severe hyperglycemic ranges (greater than 250 mg/dL).

4. **Elevated cholesterol and triglyceride levels.**

   Elevated cholesterol and triglyceride levels may interfere with the way light is reflected producing erroneous meter results.

5. **High altitude effect.**

   It has been shown that decreased oxygen tension at high altitudes may interfere with the amount of oxygen present for reaction, resulting in inaccurate results.

6. **Electromagnetic Interference (EMI).**

   Recent studies have shown that EMI can cause electronic medical device performance degradation and could lead to inappropriate therapy.\(^{19}\)

**Summary**

Frequent monitoring of blood glucose has been recommended for use in the management of patients with diabetes. Major issues needing consideration are to ensure quality control and to be certain that data from BGMg systems are accurate and precise. Premarket notification review objectives are to document consumer performance and human factor considerations, and to ensure that labeling contains appropriate quality control and limitations for use. Readability tests, and user questionnaires in conjunction with consumer studies, may allow one to draw conclusions about adequacy and simplicity of instructions for use.

**VIII. Bibliography**


11. Wiene R.K., The Effect of Hematocrit on Reagent Strip Tests for Glucose, Diabetes Medical,


**ABBREVIATIONS**

BGM - Blood Glucose Monitor  
BGMg - Blood Glucose Monitoring  
CDC - Center for Disease Control  
CDRH - Center for Devices and Radiological Health  
FDA - Food and Drug Administration  
IVD - In Vitro Diagnostic  
NCCLS - National Committee for Clinical Laboratory Standards  
NIH - National Institutes of Health  
NIST - National Institute for Standards and Technology  
POC - Point-of-Care  
POL - Physician's Office Laboratory  
SMBG - Self Monitoring Blood Glucose

**Checklist**

Instructions: Use this checklist for premarket notifications for Portable Blood Glucose Meters as a guide in preparing your submission.

- CDRH Premarket Submission Cover Sheet

• Truthful and Accurate statement verbatim as required by 21 CFR 807.87(j). Additions and deletions are not permitted.

• 510(k) summary or statement as required by 21 CFR 807.92 or 21 CFR 807.93 respectively.

• Indications for use on a separate page.

• Labeling for in vitro diagnostic products as required by 21 CFR 809.10(b) specific to portable blood glucose monitors.

  o Intended Use

    Device Identification
    User Identification
    Matrix
    Home Use
    Point of Care Use (POC)
    Physicians' Office Laboratory Use (POL)
    Quantitative
    Semi-Quantitative/Qualitative (visual interpretation, color block or color chart)

  o Storage/Maintenance

    Blood Glucose System (strips, meter, control(s)) Strip Meter (battery installation, cleaning recommendations)

  o Specimen Collection/Preparation

    Capillary Whole Blood (finger stick)
    Venous Whole Blood
    Arterial Whole Blood

  o Testing Procedures

    Step by Step Procedure preferably with illustrations

  o Limitations / Warnings and Precautions applicable to this meter

  o Performance Characteristics

    Site specific correlation studies using adequate samples covering the assay range with a well characterized laboratory method.
    Matrix appropriate precision studies at medical decision levels.
    Bias calculation.
    Linearity Studies

  o Interferences

  o Quality Control/Calibration

http://www.fda.gov/cdrh/ode/gluc.html
Easy to follow Procedure in Package Insert and/or Users' Manual

- **Expected Values**

  - **Labeling recommended for portable blood glucose meters not required by 21 CFR 809.10(b)**

    Type Size - 12 or 14 Point
    Specify Adequate Lighting
    Terminology - Use clear and concise terms throughout

- **Training (Optional)**
  
  Video Tape
  Audio Tape
  Other

- **Toll-free number for consumer support**

- **Consumer Studies Field Testing (OTC)**
  
  Provide Study Protocol and results on minimum of 100 users
  Users must represent broad range of demographic characteristics
  Consumer testing Survey

- **Point-of-Care (POC)/Physician's Office Laboratory**
  
  40 Patients/Site Site testing personnel description Study Protocol Results: accuracy and precision by site

- **Hematocrit Study**
  
  Study Protocol
  Results

- **Altitude Study**
  
  Study Protocol
  Results

- **Human Factors Study**
  
  Ease of Use Protocol
  Results

- **Software Validation/Verification**

  Updated March 21, 1997

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http://www.fda.gov/cdrh/ode/gluc.html