



**ASVCP Guidelines:
Quality Assurance for Portable Blood Glucose Meter (Glucometer) Use in
Veterinary Medicine**

Version 1.0 (September 2015)

Karen L. Gerber¹, Kathleen P. Freeman²

¹ College of Public Health, Medical and Veterinary Sciences, James Cook University, Townsville, Queensland, Australia. ² IDEXX Laboratories, Ltd, Wetherby, West Yorkshire, UK

Developed by the American Society for Veterinary Clinical Pathology (ASVCP) Quality Assurance and Laboratory Standards (QALS) Committee

Suggested citation:

“If citing this document, the following format is suggested: American Society for Veterinary Clinical Pathology (ASVCP). Quality Assurance for Portable Blood Glucose Meter (Glucometer) Use in Veterinary Medicine. Version 1. 2015. Available at: <http://www.asvcp.org/pubs/index.cfm> Accessed [Date].”

Table of Contents

Table of Contents	2
1.0 Abbreviations	3
2.0 Introduction.....	4
3.0 Scope	4
4.0 PBGM methods & technology overview.....	5
5.0 Considerations for glucose meter testing.....	6
5.1 Minimizing pre-analytical error	6
5.1.1 Operator proficiency	6
5.1.2 Timing of sample collection.....	6
5.1.3 Specimen collection and handling.....	6
5.1.4 Sample matrix.....	8
5.2 Minimizing analytical error.....	8
5.2.1 Standardization of glucose reporting (plasma equivalent value)	9
5.2.2 Sources of PBGM inaccuracy	11
5.3 Minimizing post-analytical error.....	14
5.3.1 Units of measurement.....	14
5.3.2 Records.....	15
6.0 Specific quality management recommendations for PBGM	15
6.1 Allowable (desirable) total error (TEa)	15
6.2 Control material and control rule selection specific for PBGM	16
6.3 External quality assessment (EQA)	16
6.3.1 Participation in an external quality assurance program.....	17
6.3.2 Comparability Testing with a Reference Laboratory	17
6.4 Multiple glucose meters at one site	18
6.4.1 PBGM Harmonization	19
6.5 Non-Statistical Quality Assurance Procedures	20
6.6 Recommendations for Pet Owners	21
7.0 Instrument Procurement.....	21
8.0 Summary	21
9.0 Acknowledgements	21

1.0 Abbreviations

ASVCP	American Society of Veterinary Clinical Pathology
CLSI	Clinical Laboratory Standards Institution (formerly the National Committee for Clinical Laboratory Standards, or NCCLS)
CV	Coefficient of variation (expressed in units of %)
EQA	External Quality Assurance
GDH	Glucose dehydrogenase enzyme
GDH-PQQ	Glucose dehydrogenase pyrroloquinoline enzyme
GO	Glucose oxidase enzyme
HCT	Hematocrit
MCV	Mean cell (corpuscular) volume
PBGM	Portable blood glucose meter (glucometer)
Ped	Probability of error detection
Pfr	Probability of false rejection
POCT	Point of care test (or testing)
QA	Quality Assurance
QALS	Quality Assurance and Laboratory Standards
QC	Quality Control
RBC	Red blood cells
SD	Standard deviation
TEa	Allowable (desirable) total error

2.0 Introduction

Portable blood glucose meters (PBGM, a.k.a. glucometers) are a convenient, cost effective, and quick means to assess patient blood glucose concentration. They can provide rapid results in patients with clinical signs suggestive of hypoglycemia and assist critical short term therapeutic strategies. They can be used as a screening tool to identify potential diabetes mellitus which can then be confirmed by laboratory glucose analysis. They are also convenient when multiple glucose measurements are needed within a short time interval (e.g., to construct glucose curves), can be helpful when monitoring critically ill patients to pre-empt hypoglycemic incidents, and can be used as part of a pre-operative blood screen.

PBGM offer a faster turnaround time and require a smaller sample volume compared to reference laboratory chemistry analyzers. The number of commercially available PBGM is constantly increasing, making it challenging to determine whether certain meters may have benefits over others for veterinary testing. The challenge in selection of an appropriate glucose meter from a quality perspective is compounded by the variety of analytical methods used to quantify glucose concentrations and disparate statistical analysis in many published studies.

The FDA has produced draft guidelines to industry setting stricter pre-manufacturer requirements for PBGMs intended for use by professionals in hospital (medical) settings compared to those intended for use by lay persons in a home setting with the aim to improve the accuracy of PBGMs used for tight glycemic control by medical professionals.¹

This document presents general information about PBGM. Specific brands of glucometers are mentioned in this document when tests with information pertinent to accuracy of results and QA and QC have been studied. This does not represent an endorsement or criticism of the brands mentioned, but provides information that may be useful to clinical pathologists whose advice is sought by veterinarians, veterinary technicians or nurses, or other relevant operators considering using PBGMs.

3.0 Scope

The purpose of this guideline is to provide clinical pathologists and laboratorians with background knowledge & specific recommendations for QA/QC to improve the quality of results obtained when using PBGMs. Strengths and weaknesses of different analytical methods used by PBGM are presented to help clinical pathologists understand the effects of methodology on results and to assist them with analysis of the scientific and marketing literature. Causes of pre-analytical, analytical and post-analytical error are presented to help clinical pathologists advise clinicians and veterinary technicians or nurses, or other relevant operators on how to minimize the effect of these factors on the accuracy of their PBGM results. One of the current biggest analytical contributors to the production of erroneous glucose results is the inbuilt calculation formulae in many PBGM models which convert a whole blood glucose result and report a calculated plasma equivalent result. Prior knowledge of the impact of this functional aspect of their design is required to help clinical pathologists who interpret glucose results submitted by veterinarians for comparative purposes as part of QA/QC of their PBGMs or answering queries regarding the difference in results between PBGMs and laboratory chemistry analyzers. Clinical pathologists can also educate veterinarians on the implications of a calculated plasma equivalent result so that they can intervene and correct results where possible or select another brand of PBGM. Clinical pathologists should take note of the known variation in performance of PBGMs at

extremes of glucose concentration (hypo- & hyperglycemia) due to the wide variety of methodology employed in these instruments so they can disseminate the information to veterinarians, veterinary technicians or nurses or other relevant operators to prevent these limitations leading to incorrect clinical decisions and treatment. Instructions are given for how to use external quality assessment programs or comparability studies with a local reference laboratory for ongoing QA. Step-by-step procedures to characterize the performance of individual PBGM and to harmonize multiple PBGM in larger practices/institutions are also presented so clinical pathologists can assist veterinarians in implementing these measures as components of their quality planning and management. These recommendations are not intended to be all-inclusive; rather, they represent a minimum standard for PBGM management in veterinary clinical settings.

4.0 PBGM methods & technology overview

PBGM are biosensors that detect glucose via enzymatic activity (interaction between glucose and an enzyme, with resulting consumption or production of a physical or chemical product that is subsequently measured). Enzymes used in PBGM vary and include hexokinase, glucose oxidase, or glucose dehydrogenase. Broadly, PBGM are divided into optical (light detecting) and electrochemical (electric current detecting) systems. **Table 1** lists the various PBGM analytical methods, where a variety of enzymes may be combined with either optical or electrochemical detection methods.

Each batch of glucose meter test strips has a code describing the performance of the batch and the calibrating relationship between the photometric or electrochemical signal and the concentration of the glucose.²

It is beyond the scope of this document to discuss all the systems but a few particularly important points are mentioned below because of their effect on the outcome of glucose results, which are discussed in later sections. Most modern glucose strips utilize thick film technology, where the film is composed of several layers, each with a specific function. For example in photometric systems a spreader layer is necessary, whereas electrochemical strips use capillary fill systems. In some photometric systems the RBCs are trapped in the first semipermeable membrane/ separation layer, preventing them from entering the matrix, and analysis is performed on the resultant plasma.² This may be important since the results from this type of system are more comparable with serum or plasma glucose results from biochemistry analyzers, than those that measure glucose in whole blood. In electromechanical systems, coulometry provides more accurate results from a smaller sample size and is less affected by temperature and patient hematocrit because it evaluates the total charge generated instead of steady state current used in amperometry.³ This is important in environments that may have extremes of temperature or in veterinary patients that may have hematocrits that differ from that of adult humans (hematocrit range typically 40-50%) for which most PBGM are designed.

Newer multilayer slide systems contain extra pads to concurrently measure two different analytes, such as glucose and hemoglobin. This is advantageous because the hemoglobin measurement can be used to calculate the hematocrit and make adjustments for patients that have a hematocrit outside of the normal human range for which most PBGMs are designed. Exceptions include animals with iron deficiency and camelids where the calculation of HCT is not equal to three times the Hgb concentration. In the latter circumstances these PBGMs that measure both glucose and hemoglobin might lead to

inaccuracies. The relationship between glucose and hematocrit is discussed in more detail in section 5.2.1 and 5.2.2.

5.0 Considerations for glucose meter testing

Considerations for glucose meter testing include knowledge of sources of pre-analytical, analytical and post-analytical errors and strategies to minimize these during routine testing.

5.1 Minimizing pre-analytical error

Sources of pre-analytical error that should be considered include operator proficiency, timing of sample collection, specimen collection and handling, and sample matrix.

5.1.1 Operator proficiency

Operator proficiency should be addressed by adequate staff training, both initially & ongoing, ensuring that a standardized operating procedure (protocol) is written and subsequently maintained. Further detail regarding operator proficiency is available in ASVCP Guidelines: Quality Assurance for Point -of-Care Testing in Veterinary Medicine, Chemistry, Section 2.4.⁴

5.1.2 Timing of sample collection

Hypertriglyceridemia in a post-prandial sample can cause pseudohypoglycemia (falsely low glucose concentration) with some methods.⁵ Refer to section 5.2.2.3 for explanation.

Repeat sampling for comparative purposes should be performed at the same time of day relative to fasting or feeding. Diagnosis of diabetes mellitus requires evaluation of fasting blood glucose (minimum fast 8 hours).⁶

5.1.3 Specimen collection and handling

5.1.3.1 Preparation of patient skin surface

If isopropyl alcohol is used to clean the skin surface prior to blood sampling, it should be allowed to dry prior to collection of the specimen in order to avoid contamination that may cause interference with results.⁷

5.1.3.2 Sample volume

Operators should ensure that PBGM test strips are adequately filled, with insufficient sample being of more concern. (Overfilling has not been associated with inaccuracy of glucose results.⁸ Some of the older PBGM fail to detect under-filling of test strips. This can lead to erroneous results, as the measuring process will start regardless of sample volume.^{8,9,10} Insufficient sample volume is unlikely to occur in the new generation of PBGM, because the size of a drop from a routine blood sample collection (22 to 24 g needle) is sufficient to fill the PBGM analyzer.⁸

5.1.3.3 Sample collection tube additives (anticoagulants &/or preservatives)

International quality standards (ISO & CCLS)^{11, 12} and this guideline recommend that manufacturers' instructions for proper sample tube use should be followed. A few veterinary (dogs & cats) studies concluded that glucose results from blood collected into plain (no anticoagulant), EDTA or lithium- heparin were similar^{8, 10, 13} In contrast, fluoride anticoagulated blood of cats¹⁰ and dogs⁸, using one meter brand, the "SureStep" (GO methodology) consistently underestimated the glucose concentration. Fluoride is not a routinely used anticoagulant in veterinary practice in the United States but it is commonly used in Europe, Africa, and Australia. In the latter countries, it is the anticoagulant of choice to inhibit glycolysis in samples submitted for glucose testing by chemistry analyzers if there is an anticipated delay between sample acquisition and handling such that the plasma will not be tested within 60 minutes of collection.¹⁴ In countries where fluoride oxalate is routinely used to submit glucose samples to laboratories, clinicians should be aware of its limitations for glucose testing by PBGMs to avoid this potential source of error.^{8, 10}

An avian study identified no significant difference in glucose results between blood taken into microtainer tubes with no anticoagulant or heparin but glucose concentration was significantly lower if blood was collected into microtainer tubes with EDTA.¹⁵

5.1.3.4 Site of Collection – capillary, venous, and arterial samples

PBGM are predominantly designed for use with fresh whole blood obtained from capillaries. Some models are designed for use with capillary, venous and arterial blood. Glucose results between capillary, venous and arterial samples vary, and this variation is partly meter and method specific. Prandial status, pO₂ and tissue perfusion are additional variables which may influence comparative results.

In a fasting state, capillary blood glucose is 5 mg/dL (0.27 mmol/L) higher than venous blood, as glucose is absorbed by the tissues as an energy source at the capillary level.^{16, 17} In the postprandial state (1 hour in humans) capillary blood glucose may be 20-25% or greater than venous levels.^{5, 18, 19, 20, 21} Additionally, the hemoglobin concentration in capillary blood is slightly higher than venous blood,²² and this might contribute to additional variation if samples from different sites are compared. Finally, the partial pressure of oxygen (pO₂) is higher in capillary blood compared to venous blood. The impact of the partial pressure of oxygen (pO₂) on glucose results is method dependent. In meters measuring glucose by an electrochemical method (which utilize GO in a two-step reaction), capillary blood glucose results can be lower than venous blood in humans²³ and cats.^{24, 25} However, in meters employing photometric detection, the pO₂ does not influence the result and capillary blood results are slightly higher than those obtained in venous blood.²⁵

Veterinary literature comparing capillary and venous samples is scarce. Some studies identified differences, but concluded they were not

clinically significant.^{24, 25} A limitation of these studies was the exclusion of samples with HCTs outside reference intervals.²⁵

The wider blood glucose range tolerated in veterinary patients could account for the acceptance of the level of difference between sample sites found unacceptable in human medicine. Bearing this in mind, it is prudent to minimize the number of variables when performing serial glucose tests by consistently using the same sampling technique, site, and method of testing.

5.1.4 Sample matrix

Each species has a unique sample matrix, which includes blood viscosity, rheology etc. (**Figure 1**)^{26,27, 28, 29, 30, 31,32} which may lead to inaccurate glucose results measured on glucose meters designed for samples from mature human patients. The error will depend on the matrix property and the specific methodology of the glucose meter. When these matrix-based factors are present, results should be interpreted with caution and preferably followed with confirmation at a reference laboratory.

An important matrix-related variable is the distribution of glucose between RBCs and plasma. In humans, glucose is distributed equally within RBCs and plasma. In contrast, dogs have been reported to have 12.5% of glucose in RBCs and 87.5% in plasma and cats have 7% of glucose in RBCs.³⁰ Rabbits have 15% of glucose bound in RBCs.³³ Avian RBCs do not have protein-mediated uptake of glucose like mammals, thus the ratio of plasma to RBC glucose may be much higher with a greater concentration difference.³⁴ A PBGM marketed for veterinary species, which claimed to account for the difference in species RBC glucose binding capacity using proprietary algorithms performed favorably in some testing aspects.^{35,36} However, this claim was not supported by published studies or data on specific species validation or species-specific algorithms.³⁶

PBGMs also underreport blood glucose in avian species^{15, 34,37} even those with a psittacine-specific (proprietary) glucometer correction algorithm (although the bias is much less than concurrently tested human PBGMs). This could be due to the sample matrix difference, i.e. presence of nuclei in avian RBCs which potentially reduce the current flow needed for accurate electrochemical glucose measurement^{34,37} although this remains to be proven.³⁷ Other potential explanations included the higher normal avian HCT and glucose concentration compared to humans, although both were within the PBGMs published ranges.³⁴ Finally the correction factor in PBGMs to accommodate for the difference between whole blood and plasma is designed for humans and not avian species, which could account for the negative bias compared to chemistry analyzers.³⁴

5.2 Minimizing analytical error

Possible sources of analytical error that should be considered include standardization of glucose result reporting and knowledge of possible sources of and contributions to analytical inaccuracy.

5.2.1 Standardization of glucose reporting (plasma equivalent value)

PBGMs vary in their method of glucose detection as well as the actual sample quantity they report. Meters either detect glucose concentration in molarity or glucose activity in molality. The reported glucose quantity may be whole blood, serum, plasma or calculated plasma activity.

Private diagnostic or university laboratories utilizing large biochemistry analyzers measure and report serum or plasma glucose as a concentration; the majority of PBGM measure glucose in whole blood. PBGM may report whole blood glucose, plasma glucose or “plasma equivalent” (calculated) glucose. What an individual PBGM measures and reports can be obtained from the user’s manual or other literature provided by the PBGM manufacturer.

Whole blood and serum/plasma glucose results are not interchangeable; direct comparison poses a risk of misinterpretation. Plasma glucose concentration is roughly 10 to 15% higher than whole blood glucose, requiring different reference intervals and clinical decision limits³⁸ as illustrated in a study involving cattle and sheep.³⁹ These values differ because glucose content is measured in the aqueous (water) component of a sample. The amount of glucose per unit water mass (glucose concentration) is the same throughout a blood sample. However, the amount of water in RBCs (77%) is less than that in plasma (93%). This explains why the water content of whole blood varies with its HCT. Therefore, the amount of glucose in whole blood (plasma +RBCs) is less than an equivalent volume of plasma or serum (no RBCs).

Some PBGM first remove the RBC component through a filter and then the resultant plasma is tested for glucose content. These actual plasma glucose values may agree well with serum or plasma glucose determinations measured with chemistry analyzers as the water content per volume of sample tested is similar.

Reporting glucose concentrations as plasma equivalent values has been recommended by the International Federation of Clinical Chemistry (IFCC) in an attempt to standardize and facilitate comparison of glucose results between diagnostic laboratories (measuring serum or plasma) and PBGM (measuring glucose in whole blood).⁴⁰

The problem arises when the PBGM reads the glucose concentration in whole blood and either reports the concentration in whole blood or a plasma equivalent value (calculated value), due to differences in sample water content as explained above.

There are two conversion equations which attempt to adjust for the different water content in the various types of samples:

Equation A

$$[Glucose_{plasma}] = [Glucose_{whole\ blood}] \times 1.11$$

In this equation, plasma and whole blood glucose must be expressed in the same units, either as mg/dL or mmol/L. The factor of 1.11 in equation

A is based on a single PCV or HCT of 40 to 50%.^{41,42} The equation is therefore only accurate if the patient's PCV is in this range.

Equation B^{43,44}

$$[Glucose_{plasma}] = \frac{[Glucose_{whole\ blood}]}{1.0 - (0.0024 \times Hct\%)}$$

In this equation, plasma and whole blood glucose must be expressed as mg/dL and the equation includes an assessment of the patient's PCV/HCT. **Figure 2**⁴⁵ demonstrates the outcome of application of equation A and B to determine plasma equivalent glucose result. When the hematocrit is outside of the normal human reference, of 40 to 50%, (on which the factor of 1.11 is based), Equation A produces erroneous calculated plasma glucose concentrations but Equation B, which incorporates the patient's actual hematocrit, is more accurate. Figure 2 also demonstrates that a measured whole blood glucose value is closest in concentration to a measured or calculated plasma glucose value in anemic samples because there are fewer RBCs and there is less of a difference in the water content between the two sample types. As expected, when the patient HCT is within the 40-50%, PBGM results are similar for both equations.

Due to the variety of PBGM methodologies with respect to what they measure (whole blood or serum/plasma) and report (whole blood, serum/plasma or calculated plasma equivalent) various scenarios exist:

1. In meters that measure glucose in whole blood and report values in whole blood, the operator can convert the whole blood glucose result to a plasma equivalent result by selecting Equation B in all circumstances or Equation A if the patient's HCT is within the range of 40 to 50%. In these circumstances the operator would have to determine the patient's hematocrit by means of another test, a calculated value from an automated analyser (HCT) or a spun PCV using a microhematocrit centrifuge (assuming other QA/QC have been achieved). Either method is acceptable as long as it was standardized within the same patient if performing serial testing.
2. The few meters that can concurrently measure glucose and the patient HCT report an accurate plasma equivalent glucose value^{43,44} except in iron deficient animals and camelids, as mentioned in section 4.0. Equation B is used by these meters, and the patient's actual hematocrit determines the factor with which whole blood is multiplied to convert it to a plasma equivalent value. In these meters the results are accurate throughout the entire range of possible HCT concentrations in health and disease.
3. The majority of current meters that provide results in plasma equivalent glucose concentration do not measure HCT and use equation A. In all patients with a HCT/PCV outside the range of 40 to 50%, either due to

disease such as anemia or polycythemia or difference in the “normal” reference interval this can lead to erroneous results.

The situation is further complicated in that whole blood glucose concentrations in tested samples are not only influenced by the HCT/PCV, but the effect of the HCT/PCV in turn is influenced by the actual glucose concentration. This means that the effect a given HCT has on water content of a sample and thus the glucose content of whole blood sample is different in hypoglycemic, normoglycemic and hyperglycemic patients. These complex dependencies are system (meter type & its method) dependent,^{31, 46, 47} the explanation of which is beyond the scope of this document.

Therefore, with meters that measure glucose concentration in whole blood and report a calculated plasma equivalent glucose concentration, as recommended by the IFCC, users should take note of the equation used to determine this result. If the PBGM cannot determine the HCT concurrently, the operator should evaluate the patient’s HCT/PCV independently. If the HCT/PCV is outside of 40-50% then meters using equation A may be inaccurate.

If operators wish to compare results from a PBGM that measures and reports the glucose concentration in whole blood to a chemistry analyser result they should also convert the result to a plasma equivalent concentration using equation B and the patient’s actual hematocrit.

5.2.2 Sources of PBGM inaccuracy

Sources of inaccuracy include variation due to instrument use, the environment, and variables related to physiology of the patient and concurrent disease. The following sections highlight factors affecting glucometer results and strategies to minimize or eliminate possible error or variation.

5.2.2.1 Instrument use

- Test strip batch

Check the expiry date of strips prior to each use. Out-dated reagent strips and incorrect strip storage, such as open vials or exposure to direct light will affect glucose meter performance.⁴⁸

Strip lot-to-lot variation should be minimized by entering or scanning the key code if one is required (some are automatic on insertion of the strip) and running QC material each time a new lot of strips is opened. Lot-to-lot variation may be a major factor in result accuracy, affecting precision and bias.^{9, 49, 50, 51, 52, 53}

- Operational procedure

The correct species code should be entered in a veterinary-specific PBGM. Failure to do this can lead to error. For example, where insertion of a dog code for cat samples produced glucose levels 1-4mmol/L higher than the true value.³⁵

Sufficient time should be given for temperature equilibration of the instrument and test strips, otherwise the temperature estimated by the meter will be incorrect. Temperature estimation is

used in a correction calculation (temperature compensation algorithm) to accommodate for the temperature dependence of the measurement methodology.⁵⁴ This type of system failure can happen when strips are stored in the fridge and the ambient environment temperature is higher.⁴⁹

In meters that measure glucose and hemoglobin simultaneously, the strips contain extra layers and it is important to cover the whole strip. In addition, the procedure may have to be timed if results are calculated at a particular time interval.²

- Control material

If high and low concentration controls are used, care should be taken not to reverse liquid control levels, by checking the labels carefully every time they are run. Control materials should be stored and handled according to manufacturer's recommendations.

5.2.2.2 Environment

Meters must not be operated under environmental conditions outside those set by the manufacturer.^{48, 54} Extremes in humidity (>85%), temperature (>40°C) and altitude (see blood oxygen pressure below) may contribute to production of erroneous results.

5.2.2.3 Physiological & Disease

The concentrations at which substances interfere with performance are *instrument specific* (meter & method) and can be found in product labelling/inserts or manuals. If levels might be exceeded or if results do not fit with other clinical data for the patient, it is recommended that glucose results should be confirmed by reference laboratory methods. Some of these variables are highlighted below.

- Glucose concentration

PBGMs perform differently at extremes of blood glucose concentration (hypoglycemia and hyperglycemia) in humans^{55, 56, 57} and animals.^{8, 10, 13, 25, 28, 35, 58, 59, 60, 61} It may be easier to clinically compensate for a meter that consistently under or overestimates glucose in a specific range than a meter where the direction of error relative to a reference method is unpredictable. Inconsistent under or over estimation of glucose results was identified in a PBGM marketed for veterinary application in a study in dogs³⁶ and another study in alpacas.⁶⁰

- Hematocrit

Increased HCT can decrease the glucose measurement; conversely, a decreased HCT can increase glucose measurements (in human medicine).^{26, 46, 47, 49, 62, 63, 64, 65} This inverse relationship is more pronounced in the hyperglycemic range in humans.⁶⁶

HCT affects the accuracy of many glucose meters for several reasons. Its effect on meters with inbuilt conversion factors has been discussed in section 5.2.1. Another reason may be an increased

diffusion rate of plasma to the reagent pad with reduced numbers of erythrocytes.^{26, 46, 47, 62, 63} Studies^{49, 51, 63, 67} have indicated that this error can occur even if the manufacturer states that HCT has no effect in the instrument's HCT measurement range. In meters where RBCs are lysed prior to measuring the glucose concentration, HCT appears to have less of an effect.⁶⁵

Newer technology, using a whole blood glucose biosensor has a lower sensitivity to the effects of HCT based on an impregnated porous carbon electrode that excludes erythrocytes. This technology thus allows testing of capillary, venous, arterial or neonate blood in humans over a wide range (20-70%) of HCT.⁶⁸ More recently dynamic electrochemistry which involves complex PBGM mathematical algorithms based on differences in kinetics of electrochemical reactions of glucose and potential interfering substances, have become available that can correct for some interfering substances and variation in HCT.⁶⁹

Similar to reports in humans, HCT can affect the accuracy of glucose readings in animals.^{8, 10, 59, 60, 70, 71} In a few veterinary studies which did not find an association between glucose and HCT^{13, 28} one indicated that their study had limitations (low sample number with abnormal PCV) and required further investigation.²⁸ Ultimately, clinicians should interpret glucose concentrations in anemic or hemoconcentrated cats,¹⁰ dogs,⁸ horses,⁷¹ rabbits⁵⁹ and alpacas⁶⁰ with caution.

- Lipemia/hyperlipidemia

Lipemia may interfere with some methodologies. If the meter measures glucose molality, variations in water content of the sample will influence measurements, as proteins and lipids displace water. In other PBGM methods elevated cholesterol or triglycerides may interfere with the way light is reflected producing erroneous results⁷². Endocrinopathies or parental nutrition may result in artifactually lower glucose results. False high glucose readings can occur with GDH-PQQ methodology when triglyceride > 5000mg/dL (56.5 mmol/L)⁷³ or >265 mg/dL (3 mmol/L).⁷⁴

- Bilirubin

Studies testing the effect of bilirubin on plasma glucose measurement by PBGM are limited and some results are discordant with the same methodology, (**Table 2**).

Where interference was detected glucose results could be up to 21% inaccurate and this could change clinical decisions.⁷⁵

- Blood oxygen pressure

The effect of pO₂ on glucose measurement by PBGMs depends on the method of measurement^{54, 62, 76, 77, 78, 79}. A low pO₂ due to high altitude, hypoxia, or young age can cause falsely elevated glucose, in meters with GO methodology in humans.^{54, 62, 76, 77}

A high pO₂ e.g. oxygen therapy, mechanical ventilation can cause a false decrease in glucose with GO methodology.^{62, 77, 78, 79} This occurs

in meters utilizing GO methodology because oxygen acts as a competing electron acceptor. The GDH method does not appear to be affected by high/low blood oxygen pressure.⁷⁷

- Blood pH

Blood pH may affect activity of the enzymes used to measure blood glucose. Acidosis may falsely decrease glucose readings and alkalosis may falsely increase glucose readings in glucose meters using GO methods.^{26, 80} This could be due to insufficient buffering capacity of the test strip in these circumstances to maintain pH in a range needed for optimal enzyme activity.⁸⁰

As with other variables, there are inconsistent results across studies. Some studies show little effect on glucose results of blood pH in the range 6.80 to 7.55 in meters with GO methodology.⁶² In contrast, others have found significant changes in glucose at pH <6.95 and >7.85.²⁶ Severe ketoacidosis or other acid-base disorders combined with an abnormality in HCT⁸⁰ or marked hyperglycemia⁸¹ may result in misleading glucose results (particularly with instruments using GO methods). Glucose results should be interpreted with caution in patients with potential ketoacidotic diabetes.⁸⁰

5.2.2.4. Administered drugs or treatments

PBGM manufacturer's instructions should be consulted for information concerning substances which may be used in medications that could interfere with individual meters.

Drugs or other therapeutic compounds may falsely increase or decrease the measured glucose concentration,^{73, 82, 83, 84} including commonly used antimicrobials (e.g. tetracycline⁸⁵), anti-inflammatory drugs (e.g. aspirin and acetaminophen), potassium bromide and hemoglobin substitutes. Interference depends on the type of enzyme (GO or GDH) and the method of detection (photometric vs. electrochemical) in PBGMs. Potential explanations for these effects include consumption of intermediate products in photometric systems or direct oxidation in electrochemical systems with some commonly used drugs or supplements like acetaminophen or ascorbic acid. Substances like mannitol may interfere directly with measurement. For lists of other potential interferents refer to the FDA website⁷² or textbooks (e.g. Tietz).⁸⁵

5.1 Minimizing post-analytical error

Post-analytical error may occur with inadvertent change in units of measurement and/or in keeping of records related to PBGM testing.

5.3.1 Units of measurement

Operators should check which unit the meter displays because inadvertent change in the units of measurement could lead to misinterpretation of results and inappropriate medical decisions. One type of

unit display should be used, either mmol/L or mg/dL. (Conversion factor: Glucose mmol/L x 18.018 = mg/dL; Glucose mg/dL x 0.0555 = mmol/L).

5.3.2 Records

Accurate records must be kept for all aspects of glucose testing, as with other POCT.⁴ One extra item specific to PBGM is to record battery change dates.

6.0 Specific quality management recommendations for PBGM

6.1 Allowable (desirable) total error (TEa)

Performance testing should be done on PBGM to ensure that repeated results from the same patient fall within the allowable total error (TEa) of 10% for values below the reference interval or 20% for values within and above the reference interval.⁸⁶

Such assessment should be performed in each of the three diagnostically relevant glucose ranges; hypoglycemia, normoglycemia and hyperglycemia.^{57, 87} This is necessary because of the overwhelming evidence in the literature that PBGM performance varies across the glycemic range in human^{56, 57} and veterinary^{8, 10, 13, 25, 58, 59, 88} studies.

This assessment is even more important in veterinary medicine where there is currently no consensus regarding the range (hypo-, normo- or hyperglycemia) within which more error occurs or whether the PBGM under- or over-estimate the glucose concentration in that range.^{8,10,13, 89, 90} A recent study which evaluated performance in all three glycemic ranges (**Table 3**) in rabbits using a human and veterinary PBGM found that the TEa guideline recommended by the ACVCP was exceeded in all categories with the veterinary meter except for the euglycemic range on the feline setting. The specific human meter used in that study performed better, with TEa within the ASVCP guideline except for the hypoglycemic category.⁵⁹ The same veterinary meter had a lower bias than a human PBGM in a study with ferrets, but only euglycemic and rare hypoglycemic samples were assessed.⁹¹ Additionally, the veterinary PBGM overestimated glucose and hypoglycemic patients might not be identified.⁹¹ These findings emphasise the importance of performance evaluation in all three glycemic ranges in the target species.⁵⁹

Glucometers currently being marketed with FDA approval are designed to have 95% of the results fall within +/- 20% for glucose results ≥ 75 mg/dL (4.16 mmol/L) and within +/- 15% for glucose results < 75 mg /dL (4.16 mmol/L).¹¹ Possible revisions of standards and recommendations by various organizations indicate that requirements may change to require 99% of results to fall within +/-15%, regardless of the level of the glucose result. This means that newer glucometers may have different performance specifications compared to older meters and that organizations using glucometers should be aware to inquire about this aspect when evaluating glucometers.⁹²

More strict quality specifications (lower TEa) may decrease the likelihood of insulin dose errors based on monitoring of blood glucose levels using PBGMs. In a study using mathematical models for human glucose results with PBGM with 5% and

10% TEa, dosage errors occurred in 8-23% and 16-45% of cases, respectively, depending on the insulin dosage rules used and the range of blood glucose. Large errors of insulin dose (two-step or greater) occurred >5% of the time when the CV and/or bias exceeded 10-15%. To provide the intended insulin dosage 95% of the time required that both the bias and the CV of the glucose meter be <1% or <2%, depending on mean glucose concentrations and the rules for insulin dosing. Most PBGM are not able to meet these quality requirements. The authors of this study concluded that the effects of such dosage errors on blood glucose and on patient outcomes requires further study.⁹³ To the author's knowledge, no studies of this type have been conducted for veterinary species.

6.2 Control material and control rule selection specific for PBGM

Customization of quality control (QC) protocols for individual PBGM is recommended.⁴ PBGM manufacturers may provide 1 to 3 control material "levels" (glucose concentrations). This is in contrast to the recommendation for other biochemistry analytes, where an alternate source of control materials other than the instrument manufacturer is recommended.⁹⁴ This exception is due to the commutability of various control materials applicable to PBGM and the variation in methodology employed in PBGMs. If not supplied by the manufacturer, then control material levels can be purchased from suppliers of in-clinic chemistry instruments or any other independent reputable suppliers.

Establishing the minimum number of control materials and control rules tailored specifically to a particular PBGM can be achieved through the process of QC validation, which requires an instrument performance study (assessment of precision and bias for the particular PBGM). Detail on these procedures along with information regarding the recommended 1_{3s} control rule which is preferred for in-clinic use because of its simplicity can be found in the ASVCP Guidelines for Allowable Total Error⁸⁶ and ASVCP Guidelines: Quality Assurance for Point-of-Care Testing in Veterinary Medicine.⁴

The POCT guideline contains a table adapted from a recent publication (Rishniw, et al.)⁹⁵ that may be used to decide whether PBGM performance is suitable for statistical QC using the 1_{3s} rule.⁴

The recommendation for optimal QC is to analyze quality control materials once daily or whenever patient samples are run (if not run daily). In addition to the general recommendations for when QC should be performed listed in the POCT Section 2, QC in glucose meters should also be performed:

- a. After changing the meter battery.
- b. When a new vial/packet/lot of test strips is opened.
- c. If the meter has potentially been damaged.

6.3 External quality assessment (EQA)

This may be achieved by participation in an EQA program or comparability testing by periodic comparison to a referral laboratory. Refer to ASVCP quality assurance guidelines: external quality assessment and comparability testing for reference and in-clinic laboratories.⁹⁴

6.3.1 Participation in an external quality assurance program

External QA programs apply with single or multiple PBGMs.

- The sample provided by the external QA program can be used for testing on an in house chemistry analyzer and/or just the glucose meter to be tested.
- It is crucial to indicate in the sample submission that the instrument is a glucose meter and which method the meter uses. If the submitter fails to do this the comparative results will be meaningless.
- Results are considered acceptable if they fall within $\pm TEa$ from the peer group mean. Although other recommendations by ASVCP guidelines indicate that ± 2 or $3 SD$ or $\pm TEa$ may be used as criteria for EQA performance, for glucometers $\pm TEa$ is preferred due to the relatively strict recommended quality requirement of 10% for values below the reference interval or 20% for values within and above the reference interval.⁸⁶

Current External QA programs specific for PBGM include:

- The Norwegian centre** for external quality assurance in primary care (Norsk senter for kvalitetssikring av laboratorieanalyser utenfor sykehus - **NOKLUS).^{50,52,96}
- Eurotrol***, who offer whole blood glucose quality control samples and a website where an unlimited number of PBGMs can be included.⁹⁷
Eurotrol operate from the Netherlands in Europe and Massachusetts in the US.

External QA programs specific for PBGMs in the US are currently limited in human medicine because they are present on the CLIA (regulate laboratory testing) list of “waived” tests.

6.3.2 Comparability Testing with a Reference Laboratory

QA may be obtained by comparing glucose meter results to results obtained by a chemistry analyzer in a reference laboratory or a bench top biochemistry analyzer used in the in-clinic laboratory (as long as the latter is also part of a robust QA program to ensure it is a valid reference method). Ideally, the enzyme used by the reference method and that in the PBGM are the same. 

Comparison is achieved by split sample analysis⁹⁹ following CLSI guidelines.¹⁰⁰

1. Split the sample, run one whole blood sample in house on the PBGM and process the other sample to submit it to a referral diagnostic laboratory or in-clinic laboratory to run on a chemistry analyzer.
2. Prompt separation of the serum or plasma from the latter sample is important because the glucose concentration can decrease by 5-7% per hour or 0.33-1.33 mmol/L/hour (6-24 mg/dL/hour) while the plasma/serum is in contact with the erythrocytes that metabolize glucose by glycolysis.^{101,102, 103} Plasma should be separated within 5 minutes of collection¹² and serum at 25 degrees Celsius should be separated from the clot within 2 hours in dogs and within 4 hours in horses and alpacas.¹⁰⁴ Glucose concentration in avian samples is stable up to 4 hours

after collection in heparin because their RBCs do not rely on glycolysis for energy.^{34,105}

3. Compare the PBGM results with the chemistry analyser glucose result. If the PBGM reads & reports whole blood glucose then convert it to calculated plasma glucose using Equation B (see section 1.4.2.1) to enable comparison to the chemistry analyzer result. If the meter methodology separates and measures plasma and reports plasma glucose or if the meter reads whole blood glucose and sample HCT simultaneously and then reports calculated plasma glucose by internal use of equation B then direct comparison with the serum chemistry analyzer is possible. However, if the meter measures whole blood glucose and converts it internally using Equation A (see section 5.2.1) the operator must be aware of the limitations and potential error associated with this type of PBGM when the patients haematocrit falls outside the 40 – 50 % range.
4. If the PBGM glucose result falls within the laboratory chemistry analyzer glucose result \pm TEa recommended by ASVCP then glucose meter performance is satisfactory (**Table 4**).
5. If the PBGM glucose result falls outside the laboratory chemistry analyzer glucose result \pm TEa(**Table 4**), recommended by ASVCP, then the operator should re-evaluate glucose meter performance by checking all potential sources of error including pre-analytical (e.g. sample preparation), analytical (check methodology of PBGM and chemistry analyzer are comparable) and post – analytical error. It is particularly important to check the patient HCT and method of result reporting, e.g. whole blood, plasma or calculated plasma equivalent (see item 5.2.1)¹⁰⁶ If no such errors can be identified and the chemistry analyser is performing as expected, then the PBGM should not be used until results of repeat evaluation are within acceptable performance. This may require consultation with the technical service representative of the PBGM manufacturer.

6.4 Multiple glucose meters at one site

Each meter should be clearly marked for easy identification. All results from any patient should be recorded in such a way that they are traceable to a specific PBGM and operator.

All PBGM results should be reported in the same format, preferably plasma or plasma equivalent. If conversions from whole blood are required, the same method for conversion should be used (see section 5.2.1).

Ideally if more than one reading is made for a patient, the same PBGM should be used. However, if this is not possible the operator should be able to compare results between meters with reasonable confidence. This is possible if all the PBGMs are involved in regular (minimum quarterly) EQA program or comparability testing with a referral laboratory or in house analyzer (as long as the latter is also part of a robust QA program to ensure it is a valid reference method). If this method is followed all the PBGM's must have results equivalent to the EQA mean or chemistry instrument mean \pm TEa for that glucose concentration range recommended by

ASVCP. A more robust program involves in-clinic harmonization, which can be achieved following the guidelines provided below.

6.4.1 PBGM Harmonization

The in-clinic harmonization procedure ideally should be performed for existing instruments and then each time a new batch of meter strips is used to calibrate the meters (for applicable models) or a new instrument is purchased. Table 5 provides a practical example using the steps outlined below to achieve harmonization of multiple PBGMs to a primary meter.

1. Execute an instrument performance evaluation for each PBGM. Refer to the ASVCP TEa guideline document for instructions.⁸⁶ This involves establishing the CV, mean and the bias of each PBGM compared to manufacturers' mean using all 3 levels of control material.
2. Choose the primary PBGM preferably as the one with least bias to manufacturers' mean or less favorably the first purchased PBGM.
3. Determine if the bias of the comparative meters relative to the primary PBGM are acceptable for inclusion in a PBGM harmonization program. This is achieved by establishing the maximum allowable bias of the comparative meter relative to the primary PBGM.
 - a. The bias for the primary glucometer is considered to be zero since it is the standard by which the comparative glucometers are judged.
 - b. Establish the CV for each of the comparative PBGMs and the primary PBGM.
 - c. Calculate the combined inherent impression using the following equation $\sqrt{CV^2_{\text{primary glucometer}} + CV^2_{\text{comparative glucometer}}}$.
 - d. Derive the max comparative instrument bias. $TEa = \text{bias} + 2 \text{ CV}$, therefore $\text{Bias} = TEa - 2 (\text{combined inherent imprecision})$
 - e. Calculated bias compared to the primary glucometer = $[\text{Result primary glucometer} - \text{Result comparative glucometer} / \text{Result primary glucometer}] \times 100$
 - f. If the calculated bias compared to the primary glucometer is < the maximum bias for the comparative glucometer, then the performance is ACCEPTABLE relative to the primary PBGM.
 - g. If the calculated bias compared to the primary glucometer is NOT < the maximum bias for the comparative glucometer, then the performance is UNACCEPTABLE relative to the primary PBGM.
4. If the bias of the comparative PBGM is acceptable relative to the primary meter then continued performance evaluations of the PBGMs in the harmonization should be carried out as follows:

- a. The primary PBGM should be evaluated quarterly by means of participation in an EQA program or comparison to a referral laboratory or in house chemistry analyzer.
In these instances, performance of the primary PBGM is considered acceptable if the mean of the PBGM is within the mean of the EQA group mean or chemistry analyser result \pm TEa set by the ASVCP for that concentration of glucose. This test should be performed with samples containing glucose within all three glucose concentration ranges (hypo/normo & hyperglycemia).
- b. The comparative glucometers can then be compared to the primary glucometer as the standard for ongoing performance evaluations. The primary glucometer mean result for each control material or patient sample used for comparative test will be used as the 'best estimate' of the true result for all glucometers within the organization.
- c. All comparative glucometers should have a result that falls within mean primary glucometer \pm TEa for the material or patient sample that is tested.
- d. If the glucose result of the comparative meter does not fall within the mean of the primary meter \pm TEa set for that glucose concentration range then performance is considered unacceptable. Potential causes for unacceptable performance could include operator error, recording error, different strip lots etc. Further investigation should include re-evaluation of PBGM performance to establish CV, SD and bias. If any of the later results change to the extent that the TEa set by the ASVCP cannot be achieved for all 3 glucose concentration levels then the manufacturer should be contacted for assistance or the PBGM should be replaced.

5. Annual performance evaluation of the primary PBGM should ensure that the precision remains the same (or very close to the same) as the instrument ages. Should there be any question regarding a shift in the bias or change in precision with the primary instrument, it should no longer be used as a basis for the ongoing assessment of the other glucometers within the organization. A new primary glucometer should be chosen and all comparative glucometers re-evaluated based on the new primary glucometer.

6. This approach to harmonization aims to maintain the total analytical error within the ASVCP guidelines to improve patient care from a testing perspective.

6.5 Non-Statistical Quality Assurance Procedures

All criteria listed in item 2.6.5 of Section 2 – Quality Assurance Guidelines for Veterinary Point-of-Care Chemistry Testing are relevant, but medical review criteria deserve particular attention with PBGM.⁴

Staff should be trained to report and document glucose concentrations that require the immediate attention of a veterinarian in a timely manner. Repeat criteria

should be in place to determine whether further action (repeat testing or verification by sending out to a reference laboratory or confirmed by an in-clinic biochemistry analyzer) is needed.

6.6 Recommendations for Pet Owners

Owners using PBGM for home monitoring of diabetic pets should receive training in the collection of samples, running tests, handling and storage of test strips, as well as use of one or more control materials. They should be instructed how to clean and store the glucometer between evaluations. The PBGM performance should be evaluated prior to its use for home monitoring and periodic participation in EQA and comparative testing with a reference laboratory or in-clinic laboratory biochemistry analyzer is recommended to help ensure ongoing production of reliable and accurate results.

7.0 Instrument Procurement

If multiple PBGM are needed at one hospital or testing site, then ideally the organization should purchase multiple units of the same instrument. If this is not possible, purchasing PBGM using the same analytical methodology and that have been calibrated by the manufacturer to the same analytical method is recommended. **Appendix 1** provides criteria for considering with instrument procurement and tabulates some system function advantages in a quick review format.

8.0 Summary

PBGM are valuable POCT instruments. A basic knowledge of the variety of methods employed in these devices and their associated limitations may assist clinical pathologists advising clinicians on how to gauge the degree of confidence they can place in their PBGM results. Minimizing variables listed under considerations for glucose meter testing in this document including pre-analytic, analytic and post analytical errors will reduce the occurrence of inaccurate results. Clinical pathologists should encourage and assist veterinarians to establish and maintain a quality management program for all PBGMs in an organization by applying the ASVCP recommendations. They include customizing QC for each instrument by QC validation, utilizing control materials, harmonization of instruments when multiple instruments are present at one location or within a system of clinics, and participating in comparability testing with their local laboratory or external quality assessment to ensure the accuracy of results produced by PBGMs and provide a high quality of patient care.

9.0 Acknowledgements

The authors would like to thank Dr. Bente Flatland¹, Dr. Tracy Stokol² and Dr. Melinda Camus³ for their thorough review of this manuscript and contributions to its content.

¹Department of Biomedical and Diagnostic Sciences, College of Veterinary Medicine, University of Tennessee, Knoxville, TN, USA; ²Department of Population Medicine and

Diagnostic Sciences, College of Veterinary Medicine Cornell University, Ithaca, NY, USA.

³Department of Pathology, University of Georgia College of Veterinary Medicine, Athens, GA, USA

Footnotes

#SureStep portable blood glucose monitor (marketed under the name Gluco Touch in Europe), LifeScan Inc, Milpitas, Calif.

* HemoCue B-glucose system (HemoCueAB, Angelhom, Sweden) & (HemoCueAmerica, Brea, CA, USA) Accessed 30 April, 2014.

**NOKLUS, Bergen, Norway. <http://www.noklus.no/English.aspx> . Email: noklus@noklus.no

***Eurotrol, Inc. Burlington, Massachusetts, USA & Eurotrol B.V., Ede, Netherlands.

<https://www.eurotrol.com/index.php/products/diabetes-care/glucotrol-wb> Accessed 5 December 2013

Disclaimer

This list is for informational purposes only and does not constitute a legal contract or endorsement between ASVCP and any person or entity unless otherwise specified. The ASVCP does not endorse any particular vendor or manufacturer.”

10.0 References

1. Blood Glucose Monitoring Test Systems for Prescription Point-of-Care Use. Draft Guidance for Industry and Food and Drug Administration Staff. Draft Guidance. Available at <http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm380325.pdf>. Accessed April 28, 2014.
2. Price CP, St. John A. Point -of-Care Testing. In: Burtis CA, Ashwood ER, Bruns DE, eds. Tietz *Fundamentals of clinical chemistry*. 6th ed. Missouri: Saunders; 2008: 190 – 193.
3. Feldman B, Mc Garraugh G, Heller A, et al. FreeStyle: a small-volume electrochemical glucose sensor for home blood glucose testing. *Diabetes Tehnol Ther*. 2000; 2: 221-229.
4. American Society for Veterinary Clinical Pathology (ASVCP) Guidelines: Quality Assurance for Point -of-Care Testing in Veterinary Medicine, Chemistry, Section 2.4. Available at <http://www.asvcp.org/pubs/qas/index.cfm>. Accessed January 20, 2014.
5. Tonyushkina K, Nichols JH. Glucose Meters: A Review of Technical Challenges to Obtaining Accurate Results. *Journal of Diabetes Science and Technology*. 2009; 3 (4): 971-980.
6. Stockham SL, Scott MA. *Fundamentals of Veterinary Clinical Pathology*. 2nd ed. Ames, IA: Blackwell; 2008:714.
7. Grazaitis DM, Sexson WR. Erroneously high Dextrostix caused by isopropyl alcohol.

Pediatrics. 1980; 66(2): 221-223.

8. Wess G, Reusch C. Evaluation of five portable blood glucose meters for use in dogs.

JAVMA. 2000; 216 (2): 203 – 209.

9. Kristensen GBB, Nerhus K, Thue G, Sandberg S. Standardized Evaluation of Instruments for Self-Monitoring of Blood Glucose by Patients and a Technologist. *Clinical Chemistry*.

2004; 50 (6): 1068- 1071.

10. Wess G, Reusch C. Assessment of five portable blood glucose meters for use in cats.

AJVR. 2000; 61 (12): 1587- 1592.

11. International Organization for Standardization. In Vitro Diagnostic Test Systems— Requirements for Blood-Glucose Monitoring Systems for Self-Testing in Managing Diabetes Mellitus. ISO 15197:2003(E). Geneva: International Standards Organization, 2003.

12. Clinical and Laboratory standards Institute (CCLIS): Point-of-Care Blood Glucose Testing in Acute and Chronic Care Facilities; Approved Guideline, 2nd ed. CCLIS (formerly NCCLS) document C30-A2. Wayne, PA: NCCLS, 2002.

13. Dobromylskyj MJ, Sparkes AH. Assessing portable blood glucose meters for clinical use in cats in the United Kingdom. *Veterinary Record*. 2010; 167: 438-442.

14. Sacks DB. Carbohydrates. In: Wu AHB, Tietz NW, eds. Tietz clinical guide to laboratory tests. 4th ed. St. Louis: Saunders/Elsevier; 2006:869.

15. Lieske CL, Ziccardi MH, Mazet JAK, Newman SH, Gardner IA. Evaluation of 4 Handheld Blood Glucose Monitors for Use in Seabird Rehabilitation. *Journal of Avian Medicine and Surgery*. 2002; 16(4): 277-285.

16. Larsson-Conn U: Differences between capillary and venous blood glucose during oral glucose tolerance tests. *Scand J Clin Lab Invest*. 1976; 36: 85–88.

17. Poirier JY, Le Prieur N, Campion L, Guilhem I, Allannic H, Maugendre D: Clinical and statistical evaluation of self-monitoring blood glucose meters. *Diabetes Care*. 1998; 21: 1919–1924.

18. Arabadjief D, Nichols JH: Assessing glucose meter accuracy. *Curr Med Res Opin*. 2006; 22: 2167–174.

19. Service FJ. Hypoglycaemic disorders. *N Engl J Med*. 1995; 332:1144-52.

20. Ellison JM, Stegmann JM, Colner SL, et al. Rapid changes in postprandial blood glucose produce concentration differences at finger, forearm, and thigh sampling sites. *Diabetes Care*. 2002; 25: 961–4.

21. Farrer M, Albers CJ, Neil HAW, Adams PC, Laker MF, Alberti KGMM. Assessing the impact of blood sample type on the estimated prevalence of impaired glucose tolerance and diabetes mellitus in epidemiological surveys. *Diabet Med.* 1995; 12(4): 325–9.
22. Schalk E, Heim MU, Koenigsmann M, Jentsch-Ullrich K. Use of capillary blood count parameters in adults. *Vox Sanguinis.* 2007; 93: 348-53.
23. Baum J. Patient-use performance summary of the Glucometer Elite blood system. In: Clinical Summary Report, Information Material. Bayer Corporation, USA. 1997.
24. Thompson M., Taylor SM, Adams VJ, Waldner CL, Feldman EC. Comparison of glucose concentrations in blood samples obtained with a marginal ear vein nick technique versus from a peripheral vein in healthy cats and cats with diabetes mellitus. *JAVMA*; 221 (3): 389-392.
25. Wess G, Reusch C. Capillary blood sampling from the ear of dogs and cats and use of portable meters to measure glucose concentrations. *Journal of small Animal Practice.* 2000; 41: 60-66.
26. Kilpatrick ES, Rumley AG, Myint H, Dominiczak MH, Small M. The effect of variation in haematocrit, mean cell volume and red blood cell count on reagent strip tests for glucose. *Ann Clin Biochem.* 1993; 30: 485-7.
27. Kaplan, M, Blondheim, O, Alon, I, et al. Screening for hypoglycemia with plasma in neonatal blood of high hematocrit value. *Crit Care Med.* 1989; 17(3):279-282.
28. Hollis AR, Dallap Schaer BL, Boston RC, Wilkins PA. Comparison of the Accu-Chek Aviva Point-of-care Glucometer with Blood Gas and Laboratory Methods of Analysis of Glucose Measurements in Equine Emergency Patients. *J Vet Internal Med.* 2008; 22: 1189-1195.
29. Russel C, Palmer JE, Boston RC, Wilkins PA. Agreement between point-of-care glucometry, blood gas and laboratory-based measurement of glucose in an equine neonatal intensive care unit. *Journal of Veterinary Emergency and Critical Care.* 2007; 17(3):236-242.
30. Coldman MF, Good W. The distribution of sodium, potassium and glucose in the blood of some mammals. *Comp. Biochem. Physiol.* 1967; 21: 201-206.
31. Lyon ME, Lyon AW. Patient acuity exacerbates discrepancy between whole blood and plasma methods through error in molality to molarity conversion: "Mind the gap!" *Clinical Biochemistry.* 2011; 44 (5-6): 412-417
32. Haeckel R, Hanecke P. Problems of Comparing Blood Glucose Molality and Molarity Determined with an Omni, an EML 105 and an Ebio Analyser. *Clin Chem Lab Med.* 2003; 41 (7): 950-957.

33. Andreen-Svedberg A. On the distribution of sugar between plasma and corpuscles in animal and human blood. *Skand Arch Physiology* 1933; 66: 113-190.
34. Acierno MJ, Schnellbacher R, Tully TN. Measuring the Level of Agreement Between a Veterinary and a Human Point-of-Care Glucometer and a Laboratory Blood Analyzer in Hispaniolan Amazon Parrots (*Amazona ventralis*). *Journal of Avian Medicine and Surgery*. 2012; 26 (4): 221-224.
35. Zini E, Moretti S, Tschuor F, Reusch CE. Evaluation of a new portable glucose meter designed for use in cats. *Schweiz. Arch. Tierheilk.* 2009; 151(9):448-451.
36. Cohen TA, Nelson RW, Kass PH, Christopher MM, Feldman EC. Evaluation of six portable blood glucose meters for measuring blood glucose concentration in dogs. *JAVMA*. 2009; 235(3): 276-280.
37. Acierno MJ, Mitchell MA, Schuster PJ et al. Evaluation of the agreement among three handheld blood glucose meters and a laboratory blood analyser for measurement of blood glucose concentration in Hispaniolan Amazon parrots (*Amazona ventralis*). *AJVR*. 2009; 70 (2): 172- 175.
38. Sacks DB. Carbohydrates. In: Burtis CA, Ashwood ER, Bruns DE, eds. *Tietz Fundamentals of clinical chemistry*. 6th ed. Missouri: Saunders; 2008:390-91.
39. Katsoulos PD, Minas A, Karatzia M, Pourliotis K, Christodouloupoulos G. Evaluation of a portable glucose meter for use in cattle and sheep. *Vet Clin Pathol*. 2011; 40 (2): 245-247.
40. Burnett RW, D’Orazio PD, Fogh-Andersen N, et al. IFCC recommendation on reporting results for blood glucose. *Clinica Chimica Acta*. 2001; 307: 205-209.
41. D’Orazio P, Burnett RW, Fogh-Andersen N, Jacobs E, et al. Approved IFCC recommendation on reporting results for blood glucose: International Federation of Clinical Chemistry and Laboratory Medicine Scientific Division, Working Group on Selective Electrodes and Point-of-Care Testing (IFCC-SD-WG-SEPOCT). *Clin Chem Lab Med*. 2006; 44(12):1486–90.
42. Post H, van Keulen GJ, Muller WJ, Miedema K. TNO Quality Guideline PG/TG/2001.045: Portable in-vitro blood monitoring systems for (Self)-Monitoring–Blood Glucose Monitors–Particular Requirements and Test Methods. Netherlands Organisation for Applied Scientific Research (TNO), Leiden, the Netherlands, November 2001 (No. 011.51275/01.02).
43. Astles JR, Sedor FA, Toffaletti JG. Evaluation of the YSI 2300 Glucose analyser: Algorithm-corrected results are accurate and specific. *Clinical Biochemistry*. 1996; 29 (1): 27-31.

44. Rao LV, Jakubiak F, Sidwell JS, Winkelman JW, Snyder ML: Accuracy evaluation of a new glucometer with automated hematocrit measurement and correction. *Clin Chim Acta*. 2005; 356: 178–183.
45. Stockham SL, Scott MA. *Fundamentals of Veterinary Clinical Pathology*. 2nd ed. Ames, IA: Blackwell; 2008:712.
46. Karon BS, Griesmann L, Scott R. Evaluation of the impact of hematocrit and other interference on the accuracy of hospital based glucose meters. *Diabetes Technol Ther*. 2008; 10: 111-20.
47. Tang Z, Lee JH, Louie RF, Kost GJ. Effects of different hematocrit levels on glucose measurements with handheld meters for point-of-care testing. *Arch Pathol Lab Med*. 2000; 124: 1135-40.
48. Bamberg R, Schulman K, MacKenzie M, Moore J, Olchesky S: Effect of adverse storage conditions on performance of glucometer test strips. *Clin Lab Sci*. 2005; 18:203–209.
49. Kristensen GBB, Monsen G, Skeie S, and Sandberg S. Standardized Evaluation of Nine Instruments for Self-Monitoring of Blood Glucose. *Diabetes Technology & Therapeutics*. 2008; 10 (2).
50. Kristensen GBB, Christensen NG, Thue G, Sandberg S: Between- lot variation in external quality assessment of glucose: clinical importance and effect on participant performance evaluation. *Clin Chem* 2005; 51:1632–1636.
51. Skeie S, Thue G, Nerhus K, Sandberg S. Instruments for self-monitoring of blood glucose: comparisons of testing quality achieved by patients and a technician. *Clin Chem*. 2002; 48: 994–1003.
52. Kristensen GBB, Nerhus K, Thue G, Sandberg S. Results and Feasibility of an External Quality Assessment Scheme for Self-Monitoring of Blood Glucose. *Clinical Chemistry*. 2006; 52 (7): 1311–1317.
53. Flore KMJ, Fiers T, Delanghe JR. Critical evaluation of connectivity-based point of care testing systems of glucose in a hospital environment. *Clin Chem Lab Med* .2008; 46(12): 1763-1768.
54. Heinemann L. Quality of Glucose Measurement with Blood Glucose Meters at the Point-of-Care: Relevance of Interfering Factors. *Diabetes Technology & Therapeutics*. 2010; 12 (11): 847 – 857.
55. Khan AI, Vasquez Y, Gray J, Wians Jr FH, Kroll MH. The Variability of Results Between Point-of-Care Testing Glucose Meters and the Central Laboratory Analyzer. *Arch Pathol Lab Med*. 2006; 130: 1527-1532.

56. Brunner GA, Ellmerer M, Sendlhofer G, Wutte A, et al. Validation of home blood glucose meters with respect to clinical and analytical approaches. *Diabetes Care*. 1998; 21(4): 585-591.
57. Chen ET, Nichols JH, Duh S, Hortin G. Performance Evaluation of Blood Glucose Monitoring Devices Diabetes. *Technology & Therapeutics*. 2003; 5 (5):749- 768.
58. Johnson BM, Fry MM, Flatland B, Kirk CA. Comparison of a human portable blood glucose meter, veterinary portable blood glucose meter, and automated chemistry analyser for measurement of blood glucose concentrations. *JAVMA*. 2009; 235 (11): 1309-1313.
59. Selleri P, Di Girolamo N, Novari G. Performance of two portable meters and a benchtop analyser for blood glucose concentration measurement in rabbits. *JAVMA*. 2014; 245 (1): 87-98.
60. Tennent-Brown BS, Koenig A, Williamson LH, Boston RC. Comparison of three point-of-care blood glucose meters for use in adult and juvenile alpacas. *J Am Vet Med Assoc*. 2011; 239: 380-386.
61. Wittrock JAM, Duffield TF, LeBlanc SJ. Short communication: Validation of a point-of-care glucometer for use in dairy cows. *J. Dairy Sci*. 2012; 96: 4514-4518.
62. Louie RF, Tang Z, Sutton, DV, Lee JH, Kost GJ: Point-of-care glucose testing: effects of critical care variables, influence of reference instruments, and a modular glucose meter design. *Arch Pathol Lab Med*. 2000; 124: 257-266.
63. Balion C, Grey V, Ismaila A, Blatz S, Seidlitz W: Screening for hypoglycemia at the bedside in the neonatal intensive care unit (NICU) with the Abbott PCx glucose meter. *BMC Pediatr*. 2006; 6: 28.
64. Devreese K, Leroux-Roels G. Laboratory assessment of five glucose meters designed for self-monitoring of blood glucose concentration. *Eur J Clin Chem Clin Biochem*. 1993; 31: 829–837.
65. Wiener K. An assessment of the effect of haematocrit on the HemoCue blood glucose analyser. *Ann Clin Biochem*. 1993; 30: 90-93.
66. Wiener K. The effect of haematocrit on reagent strip tests for glucose. *Diabet Med*. 1991; 8: 172-5.
67. *Scandinavian Evaluation of Laboratory Equipment for Primary Health Care (SKUP). Evaluation # SKUP/2007/59 Ascensia BREEZE2. Pdf. <http://www.skup.nu>. Accessed April 2012.*

68. Forrow NJ, Bayliff SW: A commercial whole blood glucose biosensor with a low sensitivity to hematocrit based on an impregnated porous carbon electrode. *Biosens Bioelectron.* 2005; 21: 581-587.
69. Musholt PB, Schipper C, Thome N, et al. Dynamic Electrochemistry Corrects for Hematocrit Interference on Blood Glucose Determinations with Patient Self- Measurement Devices. *Journal of Diabetes Science and Technology.* 2011; 5 (5):1167-1175.
70. Paul AEH, Shiel RE, Juvet F, Mooney CT, Mansfield CS. Effect of hematocrit on accuracy of two point-of-care glucometers for use in dogs. *AJVR.* 2011; 72 (9): 1204-1208.
71. Hackett ES, McCue PM. Evaluation of a Veterinary Glucometer for Use in Horses. *J Vet Intern Med* 2010; 24: 617-621.
72. US Department of Health and Human Services. Public Health Service. Food and Drug Administration (FDA). Center for Devices and Radiological Health. Review Criteria Assessment of Portable Blood Monitoring In Vitro Diagnostic Devices Using Oxidase, Dehydrogenase or Hexokinase Methodology. Available at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm094134.htm> Accessed 10 Dec, 2012.
73. Eastham JH, Mason D, Barnes DL, Kollins J. Prevalence of interfering substances with point-of-care glucose testing in a community hospital. *Am J Health Syst Pharm.* 2009; 15; 66 (2):167-70.
74. Ashworth L, Gibb I, Alberti KGMM. HemoCue: Evaluation of a Portable Photometric System for Determining Glucose in Whole Blood. *Clin. Chem.* 1992; 38(8): 1479-1482.
75. Girouard J., Forest J., Massé J. et al. Multicenter Evaluation of the Glucometer Elite XL Meter, an Instrument Specifically Designed for Use With Neonates. *Diabetes Care.* 2000; 23: 1149–1153.
76. Ginsberg B. Factors affecting blood glucose monitoring: sources of error in measurement. *J Diabetes Sci Technol.* 2009; 3:9 03-913.
77. Kost GJ, Vu H, Lee JH et al. Multicenter study of oxygen-insensitive handheld glucose point-of-care testing in critical care/hospital/ambulatory patients in the United States and Canada. *Critical Care Medicine.* 1998; 26 (3): 581-590.
78. Kiyoyasu K, Hideo M, Yutaka U, Masahide O: Influence of blood sample oxygen tension on blood glucose concentration measured using an enzyme electrode method. *Crit Care Med.* 1997; 25: 231–235.

79. Dungan K, Chapman J, Braithwaite S, Buse J. Glucose Measurement: Confounding Issues in Setting Targets for Inpatient Management. *Diabetes Care*. 2007; 30 (2): 403-409.
80. Tang Z, Du X, Louie RF, Kost GJ. Effects of pH on Glucose Measurements with Handheld Glucose Meters and a Portable Glucose Analyzer for Point-of Care Testing. *Arch Pathol Lab Med*. 2000; 124: 577-582.
81. Blank FSJ, Miller M, Nichols J et al. Blood glucose measurements in patients with suspected diabetic ketoacidosis: A comparison of Abbott Medisense PCx point-of-care meter values to reference laboratory values. *Journal of Emergency Nursing*. 2009; 35: 93-96.
82. Tang Z, Du X, Louie RF, Kost GJ. Effects of drugs on glucose measurements with handheld glucose meters and a portable glucose analyser. *Am J Clin Pathol* .2000; 113: 75-86.
83. Kost GJ, Nguyen TH, Tang Z. Whole-blood Glucose and Lactate Trilayer Biosensors, Drug Interference, Metabolism, and Practice Guidelines. *Arch Pathol Lab Med*. 2000; 124: 1128-1134.
84. Schleis TG. Interference of maltose, icodextrin, galactose, or xylose with some blood glucose monitoring systems. *Pharmacotherapy*. 2007; 27 (9): 1313-1321.
85. Sacks DB. Carbohydrates. In: Wu AHB, Tietz NW, eds. *Tietz clinical guide to laboratory tests*. 4th ed. St. Louis: Saunders/Elsevier; 2006:870.
86. American Society for Veterinary Clinical Pathology (ASVCP). Guidelines for Allowable Total Error (Biochemistry). Available at <http://www.asvcp.org/pubs/qas/index.cfm>. Accessed January 20, 2014.
87. Klonoff DC. The need for separate performance goals for glucose sensors in the hypoglycaemic, normoglycaemic and hyperglycaemic ranges. *Diabetes Care*. 2004; 27: 834-836.
88. Beemer O, Byers S, Bohn A. Evaluation of Four Point-of-Care Glucose Meters in Alpacas. *J Vet Intern Med*. 2013; 27: 990-995.
89. Joseph RJ, Allyson K, Graves TK, et al. Evaluation of two reagent strips and three reflectance meters for rapid determination of blood glucose concentrations. *J Vet Intern Med* 1987; 1:170–174.
90. Cohn LA, McCaw DL, Tate DJ, Johnson JC. Assessment of five portable blood glucose meters, a point-of-care analyser, and color test strips for measuring blood glucose concentrations in dogs. *JAVMA*. 2000; 216 (2):198-202.
91. Petritz OA, Antinoff N, Chen S, Kass PH, Paul-Murphy JR. Evaluation of portable blood glucose meters for measurement of blood glucose concentration in ferrets (*Mustela putorius furo*). *JAVMA*. 2013; 242 (3): 350-354.

92. Malone, B. Blood Glucose Meters: Is FDA ready to tighten up accuracy standards? *Clinical Laboratory News*, 36(5), May 2010.
<http://www.aacc.org/publications/cln/2010/december/Pages/default.aspx>
Accessed 13 May 2014.
93. Boyd JC, Bruns DE. Quality specifications for glucose meters: assessment by simulation modelling of errors in insulin dose. *Clin Chem*. 2001; 47(2):209-214.
94. American Society for Veterinary Clinical Pathology (ASVCP). Guideline for External Quality Assessment (EQA) and Proficiency Testing in Veterinary Medicine (draft document). In development.
95. Rishniw M, Pion PD, Maher T. The quality of veterinary in-clinic and reference laboratory testing. *Veterinary Clinical Pathology* 2012; 41(1):92-109.
96. Sandberg S, Christensen NG, Jevnaker M, Thue G, Klovning A. External quality assurance in Norwegian primary health care. Available at <http://www.uib.no/isf/people/sverre.htm>. Accessed 31 Mar, 2012.
97. Eurotrol. Available at <https://www.eurotrol.com/index.php/products/diabetes-care/glucocontrol-wb> Accessed December 5, 2013.
98. Mahoney JJ, Ellison JM: Assessing glucose monitor performance—a standardized approach. *Diabetes Technol Ther*. 2007; 9: 545–552.
99. International Organization of Standardization. In vitro diagnostic medical devices – measurement of quantities in biological samples – metrological traceability of values assigned to calibrators and control materials. International Standard ISO 17511:2003. Geneva, Switzerland: ISO, 2003.
100. National Committee for Clinical Laboratory Standards. Method comparison and bias estimation using patient samples. NCCLS Document EP9-A2. Wayne, PA: NCCLS, 2003.
101. Chan AY, Swaminathan R, Cockram CS. Effectiveness of sodium fluoride as a preservative of glucose in blood. *Clin Chem*. 1989(2); 35: 315–7.
102. Weissman M, Klein B. Evaluation of glucose determinations in untreated serum samples. *Clin Chem*. 1958; 4(5):420–2.
103. Sidebottom RA, Williams PR, Kanarek KS. Glucose determinations in plasma and serum: Potential error related to increased hematocrit. *Clin Chem*. 1982; 28: 190–192.

104. Collicutt NB, Garner B, Camus MS, Hart K. Effect of delayed serum separation and storage temperature on rate of serum glucose concentration decline in four species. [abstract] *Vet Clin Pathol.* 2013; 43: 119.

105. Mathew A, Grdisa M, Johnstone RM. Nucleosides and lutamine are primary energy substrates for embryonic and adult chicken red cells. *Biochem Cell Biol.* 1993; 71: 288-295.

106. Wood WG, Hanke R, Meissner D, Reinauer H. Experience with an external quality assessment program for point- of- care-testing (POCT) devices for the determination of blood glucose. *Clin Lab.* 2003; 49: 151-159.

11.0 Appendix 1

Criteria	Preference
Technology & Methodology	Enzyme & transducer type Multiple meters in an organization should be the same product or if not possible, use the same methodology
Specimen type	Venous whole blood, venous plasma/serum, capillary blood
Measurement range	Wide range. Establish performance over the entire glycemic range (hypo/normo/hyperglycemic).
Hematocrit/packed cell volume range	The range of HCT/PCV within which glucose measurement is accurate may be broader in meters designed for use by professionals than those intended for home use.
Reported result	Plasma –equivalent calculated result or plasma calibrated preferred.
Reported unit	Fixed to one unit mmol/l or mg/dl is preferred
Number and range of quality control materials (QCM)	3 QCM are preferred for performance evaluation. Number of QCM and control rules ideally should be based on QC Validation using performance data from the performance valuation study.

Properties to Look For When Choosing a Glucometer**System Function Advantages**

- Systems that automatically calibrate and do not require user involvement
- Automatic start and timing of measurement
- If insufficient sample is applied the meter should fail to start reading, flash a warning light or audible warning message
- Prevent use of incorrectly inserted or previously used or damaged strips
- List of limitations and interferences (levels) and measures taken to avoid them
- Training - Instruction manuals and education charts and materials

Valuable manufacturer's services

- Technical support
- Training
- Enrolment into EQA schemes for glucose measurement
(human schemes are acceptable)

Ability to reserve a single batch of test strips for long term use

12.0 Tables**Table 1. Analytical and detection methods used by portable blood glucose meters**

Analytical Method Enzyme (reacts with glucose)	Detection Method Transducer (measures glucose)	
	Type	Specific Method
Hexokinase Glucose Oxidase (GO) Glucose Dehydrogenase (DHD)	Optical	Spectrophotometry
		Photometry
	Electromechanical	Potentiometry
		Amperometry
		Coulometry

Table 2 Bilirubin concentrations at which interference resulting in inaccuracy was detected on portable blood glucose meters with different methodologies

Method	Glucose oxidase	Glucose dehydrogenase
No interference	Up to 1.4 mg/dL ⁷⁸	26.5 mg/dL ⁷⁴
Interference	17.5 mg/dL ⁷⁵	20 mg/dL ⁷³

Table 3 Example of performance evaluation using total allowable error (TE) recommendations of the American Society of Veterinary Clinical Pathology for human and veterinary portable blood glucose meters (PBGM) in rabbits.⁵⁹ Total error recommendations for the study were $<\pm 10\%$ for results below the established reference interval and $<\pm 20\%$ for results within or above established reference interval. In this study, the veterinary PBGM yielded unsatisfactory performance for rabbits using the canine and feline setting for most of the tested glycemic states whereas the human PBGM performed better than the veterinary instrument

ASVCP TEa guideline	Human PBGM	Veterinary PBGM Canine setting	Veterinary PBGM Feline setting
Hypoglycemia $<10\%$	TE=15.0% exceeded	TE=31.6% exceeded	TE=18.9% exceeded
Euglycemia $<20\%$	TE=10.7% acceptable	TE=24.8% exceeded	TE=7.3% acceptable
Hyperglycemia $< 20\%$	TE=10.9% acceptable	TE=36.4% exceeded	TE=23.2% exceeded

Table 4 Comparability testing: Examples of acceptable & unacceptable results for PBGM as compared to a reference laboratory chemistry analyzer (gold standard)

Reference laboratory chemistry analyzer result	Total allowable error	TEa range of values for chemistry analyzer result	Portable blood glucose meter (PBGM) result	Acceptability of PBGM result compared to reference laboratory result
5.27 mmol/L (95 mg/dL)	20%	5.27 $\pm 20\%$ 4.2 - 6.3 mmol/L (76-114 mg/dL)	5.55 mmol/L (100 mg/dL)	Acceptable
4.99 mmol/L (90 mg/dL)	20%	4.99 $\pm 20\%$ 4-5.98 mmol/L (72-108 mg/dL)	3.88 mmol/L (70 mg/dL)	Unacceptable
2.89 mmol/L (52 mg/dL)	10%	2.89 $\pm 10\%$ 2.6-3.18 mmol/L (46.8-57.2 mg/dL)	2.77 mmol/L (50 mg/dL)	Acceptable

Table 5. Example of harmonization evaluation of multiple portable blood glucose meters used in a single organization. The primary meter was used as the reference to which the two comparative glucometers (1 and 2) were compared.

Manufacturer values	Hypoglycemic Target mean = 2.2 mmol/L (40 mg/dL)	Normoglycemic Target mean = 5.9 mmol/L (106 mg/dL)	Hyperglycemic Target mean = 19.1 mmol/L (345 mg/dL)
PBGM	Data from initial performance evaluation SD (CV)		
Primary	0.06 mmol/L (2.9%)	0.2 mmol/L (3.4%)	0.7 mmol/L (3.7%)
Glucometer 1	0.07 mmol/L (3.2%)	0.4 mmol/L (6.8%)	1.0 mmol/L (5.2%)
Glucometer 2	0.07 mmol/L (3.2%)	0.35 mmol/L (5.9%)	1.2 mmol/L (6.3%)
	Combined inherent imprecision for each glucometer and the primary glucometer = $\sqrt{(CV^2_{\text{primary glucometer}} + CV^2_{\text{comparative glucometer}})}$.		
Glucometer 1	$\sqrt{(2.9^2 + 3.2^2)} =$ $\sqrt{18.65} = 4.3\%$	$\sqrt{(3.4^2 + 6.8^2)} =$ $\sqrt{57.80} = 7.6\%$	$\sqrt{(3.7^2 + 5.2^2)} = \sqrt{40.73}$ $= 6.4\%$
Glucometer 2	$\sqrt{2.9^2 + 3.2^2} =$ $\sqrt{18.65} = 4.3\%$	$\sqrt{3.4^2 + 5.9^2} =$ $\sqrt{46.37} = 6.8\%$	$\sqrt{3.7^2 + 6.3^2} = \sqrt{53.38}$ $= 7.3\%$
	Maximum bias for each comparative glucometer Max Bias = TEa – 2*(combined inherent imprecision)		
Glucometer 1	Max Bias = $10 - 2(4.3) =$ $10 - 8.6 = 1.4\%$	Max Bias = $20 - 2(7.6) =$ $20 - 15.2 = 4.8\%$	Max Bias = $20 - 2(6.4) =$ $20 - 12.8 = 7.2\%$
Glucometer 2	Max Bias = $10 - 2(4.3) =$ $10 - 8.6 = 1.4\%$	Max Bias = $20 - 2(6.8) =$ $20 - 13.6 = 6.4\%$	Max Bias = $20 - 2(7.3) =$ $20 - 14.6 = 5.4\%$
EQA samples	Hypoglycemia range	Normoglycemia range	Hyperglycemia range
Primary Meter	2.50 mmol/L	6.1 mmol/L	21 mmol/L
Glucometer 1	2.53 mmol/L	6.4 mmol/L	20 mmol/L

Calculated Bias of Glucometer 1 relative to Primary meter	$= (2.5 - 2.53 / 2.5) \times 100$ $= 0.03 / 2.5 \times 100$ $= 1.20\%$	$= (6.1 - 6.4 / 6.1) \times 100$ $= 0.3 / 6.1 \times 100$ $= 4.9\%$	$= (21 - 20 / 21) \times 100$ $= 1 / 21 \times 100$ $= 4.8\%$
Performance of Glucometer 1 relative to Primary meter	<p>The calculated bias of 1.20% is < max bias of 1.4% for the hypoglycemic range</p> <p>= Acceptable Performance</p>	<p>The calculated bias of 4.9% is >max bias of 4.8 % for the normoglycemic range</p> <p>= Unacceptable performance</p>	<p>The calculated bias of 4.8% is < max bias of 7.2 % for the hyperglycemic range</p> <p>= Acceptable Performance</p>

13.0 Figures

Figure 1 Sample Matrix properties which may affect PBGM accuracy

<p>Patient age – neonate lower [glucose] compared to adults^{26, 27}</p> <p>HCT^{26, 27}</p> <p>RBC count^{26, 27}</p> <p>MCV^{26, 27}</p> <p>Color – e.g. pigment like bilirubin, hemoglobin (hemolysis)^{26, 27}</p> <p>Rouleaux – equine samples²⁸</p> <p>Microclots^{26, 29}</p> <p>Inflammation – increased fibrinogen^{26, 29}</p> <p>Proportion of glucose bound in RBC versus plasma (species difference)^{30, 33, 34}</p> <p>Plasma water content – variation due to disease³¹ or species³⁴ (If PBGM is designed around the human plasma water fraction mean of 0.95.³²)</p>

Figure 2⁴⁵ Comparison of application of Equations A and B in Figure 2 to calculate and report plasma glucose equivalent results in portable blood glucose meters (PBGM) that measure whole blood glucose

Example: Whole blood glucose = **3.33** mmol/L

Whole blood glucose on a PBGM = 3.33 mmol/L (60 mg/dl)			
Calculated plasma glucose reported by PBGM	Equation A	Equation B	HCT
	3.69 mmol/L (62mg/dl)	3.45 mmol/L (62mg/dl)	15%
	3.69 mmol/L (62mg/dl)	3.68 mmol/L (66mg/dl)	40%
	3.69 mmol/L (62mg/dl)	3.89 mmol/L (70mg/dl)	60%

Equation A

$$[Glucose_{plasma}] = [Glucose_{whole\ blood}] \times 1.11$$

HCT	15%	40%	60%
	$[Glucose_{plasma}] = [3.33] \times 1.11$	$[Glucose_{plasma}] = [3.33] \times 1.11$	$[Glucose_{plasma}] = [3.33] \times 1.11$
	= 3.69 mmol/L	= 3.69 mmol/L	= 3.69 mmol/L

Equation B

$$[Glucose_{plasma}] = \frac{[Glucose_{whole\ blood}]}{1.0 - (0.0024 \times Hct\%)}$$

When the plasma equivalent glucose concentration is calculated from a whole blood glucose result, then the higher the HCT of the patient sample the smaller the denominator will be thus giving a greater relative calculated plasma equivalent glucose result compared a sample with a lower HCT.

HCT	15%	40%	60%
	$\frac{[Glucose_{plasma}]}{[3.33\text{mmol/L}]}$	$\frac{[Glucose_{plasma}]}{[3.33\text{mmol/L}]}$	$\frac{[Glucose_{plasma}]}{[3.33\text{mmol/L}]}$
	$= \frac{[3.33\text{mmol/L}]}{1.0 - (0.0024 \times 15\%)}$	$= \frac{[3.33\text{mmol/L}]}{1.0 - (0.0024 \times 40\%)}$	$= \frac{[3.33\text{mmol/L}]}{1.0 - (0.0024 \times 60\%)}$
	$= \frac{[3.33\text{mmol/L}]}{1.0 - (0.036)}$	$= \frac{[3.33\text{mmol/L}]}{1.0 - (0.096)}$	$= \frac{[3.33\text{mmol/L}]}{1.0 - (0.144)}$
	$= \frac{[3.33\text{mmol/L}]}{0.964}$	$= \frac{[3.33\text{mmol/L}]}{0.904}$	$= \frac{[3.33\text{mmol/L}]}{0.856}$
	$= 3.45\text{ mmol/L}$	$= 3.68\text{ mmol/L}$	$= 3.89\text{ mmol/L}$

14.0 PBGM Guideline Compliance Checklist

Compliance with ASVCP guidelines is voluntary. Purpose of this checklist is to facilitate guideline implementation and practical application.

(The numbers in the first column correspond to the item numbers in the PBGM Guideline.)

Guideline Recommendation	Compliant?	Auditor Comment(s)
4.0 PBGM operators are knowledgeable regarding the operation, principle of measurement, and potential errors associated with the methodology used on the instrument.	<input type="checkbox"/> Yes <input type="checkbox"/> No	
5.1.1 PBGM operators have received adequate initial and ongoing training, which is documented.	<input type="checkbox"/> Yes <input type="checkbox"/> No	
5.1.2, 5.1.3 PBGM operators understand patient preparation requirements for the desired application of the test.	<input type="checkbox"/> Yes <input type="checkbox"/> No	
5.1.3 PBGM operators are aware of the sample collection vacutainer and volume requirements needed for the instrument.	<input type="checkbox"/> Yes <input type="checkbox"/> No	
5.1.3 PBGM operators understand the importance of standardization of the sample type and collection site to minimize variation due to these pre-analytical variables.	<input type="checkbox"/> Yes <input type="checkbox"/> No	
5.1.4 Operators of PBGM are aware of the potential of erroneous results due to different animal sample rheological properties if meters have not been validated for veterinary use.	<input type="checkbox"/> Yes <input type="checkbox"/> No	

5.2.1 Operators of PBGM know and understand the importance of the sample type the PBGM reports i.e. whole blood, plasma or calculated plasma equivalent.	<input type="checkbox"/> Yes <input type="checkbox"/> No	
5.2.1 Operators of PBGMs know when and how to apply glucose meter conversion equations.	<input type="checkbox"/> Yes <input type="checkbox"/> No	
5.2.2.1 Test strips are stored according to manufacturer's recommendations and are in date.	<input type="checkbox"/> Yes <input type="checkbox"/> No	
5.2.2.1 Key code or other instructions regarding batches of test strips are followed.	<input type="checkbox"/> Yes <input type="checkbox"/> No	
5.2.2.1 Correct species codes are used, if applicable.	<input type="checkbox"/> Yes <input type="checkbox"/> No	
5.2.2.1 Manufacturer's recommendations for temperature equilibration of test strips are followed.	<input type="checkbox"/> Yes <input type="checkbox"/> No	
5.2.2.1 Manufacturer's instructions for timing of reactions (if applicable) are followed.	<input type="checkbox"/> Yes <input type="checkbox"/> No	
5.2.2.2 Manufacturer's instructions regarding environmental temperature, humidity and altitude are followed.	<input type="checkbox"/> Yes <input type="checkbox"/> No	
5.2.2.3 Operators of PBGMs are aware that the performance (accuracy) of PBGMs may vary at different glucose concentrations.	<input type="checkbox"/> Yes <input type="checkbox"/> No	
5.2.2.3 Operators of PBGMs know whether HCT is concurrently measured, whether the instrument is HCT independent, or if this needs to be done as a separate procedure. Operators understand the effect of ranges of HCT on glucometer results and actions that should be taken.	<input type="checkbox"/> Yes <input type="checkbox"/> No	

5.2.2.3, 5.2.2.4 Procedures are in place to indicate possible test interference from substances such as lipids, bilirubin, changes in pO ₂ or pH, drugs, if known and applicable at time of testing.	<input type="checkbox"/> Yes <input type="checkbox"/> No	
5.3.1 PBGM operators should be aware of units in which the glucose result is reported to avoid possible inadvertent change and misinterpretation of results in a different unit.	<input type="checkbox"/> Yes <input type="checkbox"/> No	
5.3.2 Records regarding instrument performance, maintenance, battery change dates and QC are present and maintained.	<input type="checkbox"/> Yes <input type="checkbox"/> No	
6.1 ASVCP-recommended guidelines for Total Allowable Error (TEa) are used to evaluation instrument performance at hypo/normo & hyperglycemic ranges prior to clinical use.	<input type="checkbox"/> Yes <input type="checkbox"/> No	
6.2 Choice of quality control materials and rules has been tailored for the specific instrument.	<input type="checkbox"/> Yes <input type="checkbox"/> No	
6.2 Periodic QC is performed and frequency justified.	<input type="checkbox"/> Yes <input type="checkbox"/> No	
6.2 QC is performed and documented following battery change, new lot/vial/batch of test strips, instrument damage (e.g. dropped), or if there is any concern regarding result accuracy.	<input type="checkbox"/> Yes <input type="checkbox"/> No	
6.3 The laboratory participates in an External Quality Assurance program for all PBGMs or does comparative testing with a reference laboratory.	<input type="checkbox"/> Yes <input type="checkbox"/> No	

6.3. EQA or comparative testing performance is documented along with appropriate actions if a problem is identified.	<input type="checkbox"/> Yes <input type="checkbox"/> No	
6.4 If multiple PBGMs are used, these should be of the same type (manufacturer) or use the same methodology.	<input type="checkbox"/> Yes <input type="checkbox"/> No	
6.4 If multiple PBGMs are used at one site, the PBGM identification is recorded with the patient result and serial evaluations conducted with the same PBGM (if possible).	<input type="checkbox"/> Yes <input type="checkbox"/> No	
6.4. If multiple PBGMs are used at one site, they should all be included in EQA or comparative testing or harmonized to ensure comparable results.	<input type="checkbox"/> Yes <input type="checkbox"/> No	
6.5 Appropriate non-statistical QC/QA procedures are used and documented, such as repeat testing, critical medical decision limit notification, and/or verification testing.	<input type="checkbox"/> Yes <input type="checkbox"/> No	
6.6 Pet owners operating PBGMs for their diabetic pets should be trained to operate PBGMs for daily use and application of quality control measures.	<input type="checkbox"/> Yes <input type="checkbox"/> No	
6.6 Performance of PBGMs used by pet owners should be evaluated prior to home use and periodically in an EQA or comparative test program.	<input type="checkbox"/> Yes <input type="checkbox"/> No	