

1 December 2009

Proposed self monitoring of blood glucose evaluation protocol and requirements for funding in New Zealand

PHARMAC is seeking feedback on a proposed evaluation protocol and requirements for the evaluation of meters for self monitoring of blood glucose (SMBG) in New Zealand before PHARMAC makes decisions on funding of new brands of meters and test strips.

Up until recently, PHARMAC's requirements have been based on the 1996 American Diabetes Association standard for diabetes meters. The Diabetes Subcommittee of the Pharmacology and Therapeutics Advisory Committee (PTAC) has recommended that PHARMAC adopt a new protocol based on international standards and consensus recommendations.

In summary, the requirements, for all new funding decisions, would include:

- a formal evaluation of at least 50 patients who have diabetes to compare the analytical performance of blood glucose meters on capillary whole blood samples versus reference laboratory analysis of venous plasma glucose; and
- separate field testing (including ease of use for all age groups) and associated computer software assessment by the Diabetes Subcommittee of PTAC. We anticipate that all field testing would be completed during negotiations between PHARMAC and suppliers.

Feedback sought

PHARMAC welcomes feedback on this proposal. Specifically we seek the following feedback on:

- the proposed protocol, timing of testing and any exemptions to it which may be appropriate;
- what information from the evaluation results that health professionals would like provided to them after the testing is completed;
- what information from the evaluation results that suppliers would like provided to them after the testing is completed; and
- expressions of interest from Diabetes Centres that may be able to undertake such evaluations (including costs and timing involved in completing evaluations).

To provide feedback, please submit it in writing by **5 pm Tuesday, 22 December 2009** to:

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Details of the proposal

Using trained staff with appropriate quality oversight, the aim of the proposed evaluation requirements is to compare the analytical performance of the blood glucose meter on capillary whole blood samples versus reference laboratory analysis of venous plasma glucose.

The performance of SMBG meters would be assessed by comparing capillary blood sample results from two meters of each make, with a simultaneously collected venous sample. The venous samples should be spun down immediately and be analysed promptly by a reference laboratory. Samples would be collected from 50 outpatients with diabetes, with either type 1 or type 2 diabetes (aiming to have a wide spread of glucose results) and a current haematocrit >0.30 . The capillary glucose result used in the final analysis would be the mean of the two results collected from each make of meter.

Imprecision of the meters would be assessed by repeating glucose estimation 20 times on high and low test solutions as supplied by the supplier and also using patient's venous whole blood samples stabilised in a fluoride tube.

We anticipate that the cost of the evaluation would be met by the supplier and that the supplier would provide the evaluator with sufficient consumables (including two different batches of test strips). The supplier would be given the opportunity to provide the evaluator with a face-to-face instruction on the use of the meter and test strips but any additional communications with the supplier would be via PHARMAC only.

Meter performance would be assessed in the ambulatory (outpatient) setting only; i.e. there is no expectation that performance would be assessed in specialist settings such as neonatal ICU.

It is anticipated that the diabetes centre undertaking the evaluation would obtain regional ethics committee approval, however we would be interested in any proposals that could streamline this process.

Accuracy should be assessed relative to the reference method by Bland–Altman plots, Passing and Bablok regression analysis, and both Clarke and consensus (Parkes) error grid analyses. The results would then be provided to the supplier and PHARMAC and used to inform funding decisions. We propose that the results would be owned by PHARMAC.

We propose that the final evaluation requirements would be attached to PHARMAC's funding application guidelines as an Appendix.

Background

New Zealand consumers with diabetes and their health professionals expect capillary glucose meter results to reflect a corresponding laboratory venous glucose value. Thus, although the true glucose concentration of a capillary sample tends to be higher than that of a corresponding venous sample, consumers expect their capillary glucose meter and strip system to be calibrated to read as a venous sample.

At its August 2009 meeting, the Diabetes Subcommittee noted an article by Mahoney et al (Diabetes Technol and Ther 2009; 9:545-552) that established a 14-point checklist for SMBG evaluation (with associated references applicable to international standards and consensus recommendations). The Subcommittee considered this was an acceptable

protocol with the exception that the subjects need to total 50 (not 40) and that all patients have diabetes.

The Christchurch Diabetes Centre recently undertook testing on newly funded meters using the methodology as outlined in this consultation. The Diabetes Subcommittee considered that the methodology of this evaluation was appropriate and similar to the checklist developed by Mahoney et al.

The Mahoney et al 14-point checklist is as follows:

Topic	Recommendations	References
1 Study design	Prospective study design	STARD; ISO 15197; CLSI C30-A2 and EP9-A2; SKUP; FDA; TNO; China GB/T 19634
2 Study population	Review monitor labelling and determine appropriate exclusion and inclusion criteria. Report these criteria as well as demographics, location, and sampling plan.	STARD; CLSI C30-A2; FDA
3 Glucose monitor system calibration and units	Glucose monitor calibration is plasma-equivalent; conversion factor of 1.11; mmol/L units preferred.	IFCC; TNO
4 Number of donors	Minimum of 40 human blood donors and their associated blood samples; a range of glucose is desired.	CLSI C30-A2; CLSI EP9-A2; ISO 15197; SKUP; FDA
5 Operators of glucose monitor system	Describe number and skill of operators. Train all operators to manufacturer's instructions.	STARD; CLSI C30-A2; EP9-A2; SKUP, MHRA; FDA
6 Blood sample type	Use a sample that is appropriate for monitor. Use appropriate sample additives (if any). Blood hematocrit tested and within range of monitor	STARD; CLSI C30-A2; EP(-A2; MHRA; FDA; China GB/T 19634
7 Glucose monitor system testing	Store, handle, and use glucose monitor system components according to manufacturer's instructions. Test in duplicate according to manufacturer's instructions.	ISO 15197; STARD; CLSI C30-A2A; FDA; SKUP
8 Reference method testing	Capable of testing serum or plasma glucose. Quality control checks for stability. Check with NIST SRM materials or other traceable materials.	STARD; CLSI C20-A2; SKUP; ISO 15197
9 Methodology	See text. Split-sample design is preferred. Obtain samples for the reference method before and after duplicate monitor tests. Test reference method with each sample within 5 min of monitor test, or else blood is centrifuged within 5 min and plasma/serum tested within 60 min of monitor tests.	STARD; CLSI C30-A2; SKUP; TNO, China GB/T 19634; ISO 15197
10 Sample stability evaluation	Check that the difference between the two reference tests is within 4 % or 0.22 mmol/L (4mg/dL) or else excluded.	CLSI C30-A2; ISO 15197; SKUP
11 Statistical analysis	Compare individual monitor results to average of the two reference tests. Calculate differences in percent for glucose ≥ 4.2 mmol/L (75 mg/dL) of mean reference value.	ISO 15197; CLSI C30-A2; FDA; SKUP
12 Results	Use difference plots. Use tables (see text) to show average difference by glucose concentration.	ISO15197; CLSI C30-A2; SKUP; FDA
13 Acceptance criteria	The monitor is acceptable if at least 95% of results are accurate. Accuracy defined as within ± 0.83 mmol/L (15 mg/dL) for glucose < 4.2 mmol/L (75 mg/dL) or $\pm 20\%$ for glucose ≥ 4.2 mmol/L (75 mg/dL) of mean reference value.	ISO 15197; CLSI C30-A2; SKUP; FDA; China GB/T 19634
14 Discussion	Describe protocol deviations, timing, adverse events, outliers, and ease of use. Discuss clinical applicability of findings.	ISO 15197; CLSI C30-A2; EP9-A2; SKUP; START