

Blood Glucose Measurement Traceability to a Primary Reference Measurement Procedure (IDMS); a Key Step for Evaluating POC Glucose methodologies

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Background and aim: There is considerable discussion about the accuracy of hospital and self-monitoring glucose meters. Studies undertaken with the same POC glucose meters have shown different results and this is often related to the different comparative methods used. With new FDA, ISO and CLSI guidelines emerging it is important that evaluations are standardised to a true and traceable definitive reference method. We advocate the use of an isotope dilution GC Mass Spectrometry (ID-GCMS) aligned hexokinase method on a central laboratory analyzer (Roche Modular) for undertaking evaluations combined with pre-treatment of samples with perchloric acid to haemolyse and deproteinise samples, and describe our validation method for achieving this.

Methods: The definitive ID-GCMS reference method was calibrated using a bracketing technique using varying concentrations of glucose in water (primary standards). NIST secondary protein based standards were then evaluated to demonstrate the performance of the ID-GCMS definitive method and its agreement with the NIST assigned target values as compared to the primary standards. The alignment of our perchloric acid hexokinase method (PCA-HK) to the ID-GCMS method was undertaken with NIST standards and Eurotrol whole blood and plasma samples. The correlation of the ID-GCMS aligned PCA-HK to the routine HK method was further assessed with patient samples.

Results: Excellent linearity was obtained between PCA-HK and IDMS GCMS method using NIST standards ($y = 1.0164x - 0.04$ ($R^2 = 0.9974$)). Mean bias was -0.11 mmol/L with sd of -0.27 mmol/L and an overall mean %bias of -0.98% . Excellent correlation was obtained between PCA-HK and routine plasma hexokinase method for clinical patient samples ($n = 100$) R statistic = 0.99995 95% CL = 1.0 to 10 2-tailed $p = <.0001$.

Conclusion; The missing element from emerging glucose performance standards is defining an acceptable primary reference method. In our facility the PCA-HK method is closely aligned to IDMS GCMS method for plasma glucose measurements and also the routine plasma hexokinase method is closely aligned to the PCA-HK method. This type of method traceability approach is essential in evaluations of POC glucose methods.