

## Accuracy and Reproducibility of a Rapid, Fingerstick Method for Measuring A1C Certified by the NGSP

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### Abstract

Hemoglobin A<sub>1c</sub> (A1C) is an essential test for monitoring long-term glycemic control in individuals with diabetes mellitus. Standardization ensures clinically meaningful A1C results that are traceable to the Diabetes Control and Complications Trial (DCCT). The National Glycohemoglobin Standardization Program (NGSP) certifies A1C methods that meet stringent criteria for accuracy and precision. The Cholestech GDX™ System is a CLIA-waived, boronate affinity method enabling A1C results in less than five minutes using 10 µL of whole blood from a fingerstick or venous sample. Precision of the GDX A1C method was determined with whole blood pools using the NCCLS protocol required by the NGSP. Comparing GDX A1C results with those determined in an NGSP network laboratory assessed accuracy. Total precision coefficients of variation (CVs) met NGSP requirements in all years, including the new, tighter 4% CV in 2002. GDX A1C values were highly correlated with NGSP network laboratory values ( $r = 0.99$ ) in four separate studies. The differences between methods were within  $\pm 1\%$  A1C for all samples. GDX A1C is a rapid, NGSP-certified method for measuring A1C that meets the same stringent requirements for accuracy and precision as methods used in clinical diagnostic laboratories.

### Introduction

The Diabetes Control and Complications Trial (DCCT) showed that the risk for development and progression of the chronic complications of type 1 diabetes is closely related to the degree of glycemic control, as measured by hemoglobin A<sub>1c</sub> (A1C).<sup>1</sup> Similar observations for type 2 diabetes were made in the UK Prospective Diabetes Study (UKPDS).<sup>2</sup> Monitoring A1C at regular intervals is now the standard for medical care of diabetic patients.<sup>3</sup>

Standardization is essential to enable clinically meaningful interpretation of A1C results relative to these two landmark trials. In the US and much of the rest of the world, standardization of A1C methods is achieved via the National Glycohemoglobin Standardization Program (NGSP). The NGSP, a network of reference laboratories in the US and Europe, works with manufacturers to certify A1C test methods as traceable to the DCCT (the method used in the UKPDS was tightly aligned with the method used in the DCCT).

A1C can be measured in less than 5 minutes using 10 µL of whole blood obtained by fingerstick applied to the CLIA-waived Cholestech GDX System. This testing methodology enables baseline and follow-up assessments during a patient visit with a physician or other allied health professional.

The NGSP has set stringent criteria for precision and accuracy for all A1C methods. In the present study, the precision of the GDX A1C method was assessed and accuracy of GDX A1C was determined by comparison with an NGSP network reference laboratory.

### Methods

All specimens were analyzed using A1C test cartridges and the Cholestech GDX Analyzer. Comparing

GDX results on 40 fresh, diabetic patient specimens with the NGSP network laboratory assessed A1C accuracy. A 20-day study of twice daily measurement of two samples (normal and abnormal A1C levels) assessed precision according to NCCLS (National Committee for Clinical Laboratory Standards) protocol EP5-A, Evaluation of Precision Performance of Clinical Chemistry Devices; Approved Guidelines (1998). These studies were completed for NGSP certification in 2000, 2001, 2002, and 2003.

The 95% confidence interval of the differences between A1C test results must be within  $\pm 1\%$  A1C to meet the NGSP criterion for accuracy. As of 2002 precision (CV) must not be statistically greater than 4%; it was 5% in 2001 and 2000.

### Results

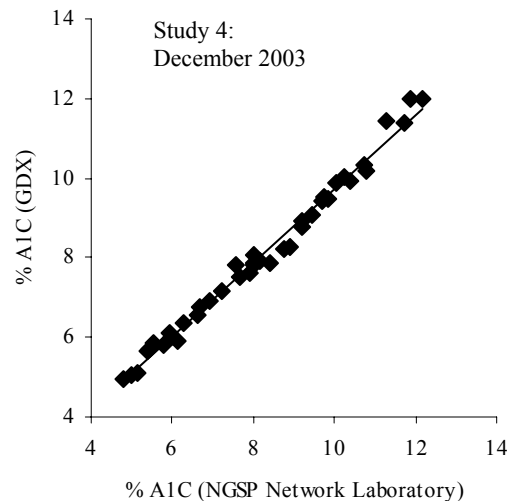
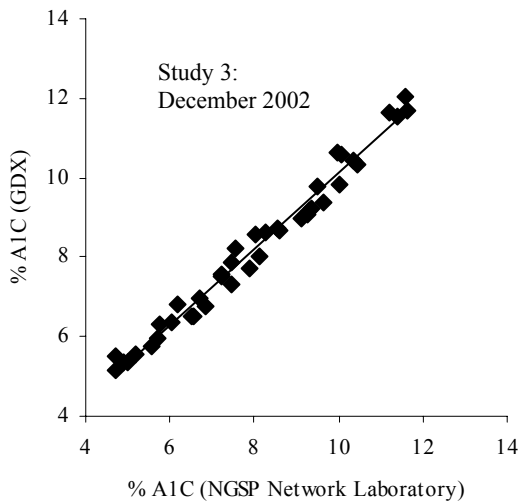
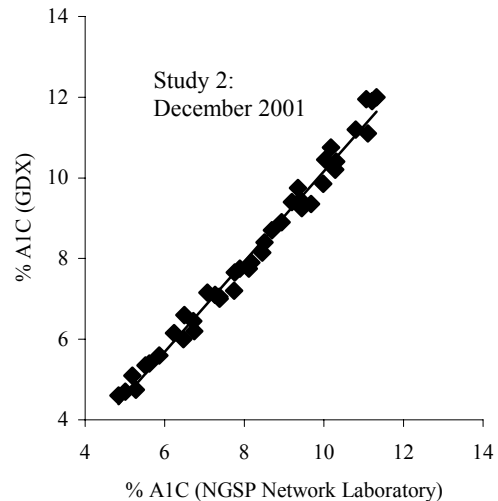
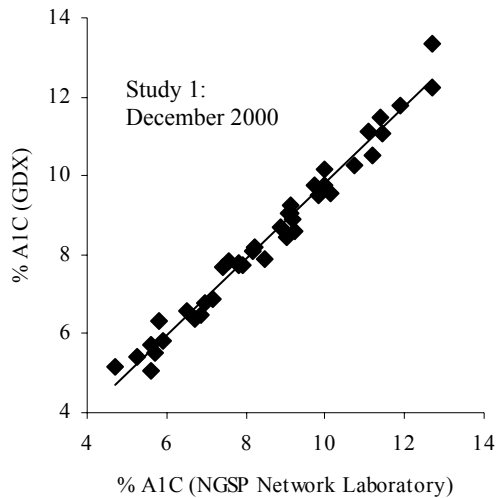
Total precision of the GDX A1C test cartridges was less than the applicable NGSP CV criteria for each year (Table). GDX A1C values were highly correlated with A1C values measured by the NGSP network laboratory ( $r = 0.99$ ; Figures). In all studies, 100% of the differences between A1C test results were within  $\pm 1\%$  A1C, exceeding the 95% requirement of the NGSP.

### Conclusions

Accuracy and reproducibility of the Cholestech GDX A1C test met NGSP requirements for certification in four successive years. This included the greater precision to meet the 2002 4% CV criterion. GDX A1C results are therefore traceable to the DCCT. This simple, CLIA-waived, fingerstick method provides A1C result in less than 5 minutes that meet the same stringent requirements for accuracy and precision as methods used in clinical diagnostic laboratories.

**Table. Precision of Cholestech GDx A1C**

	Study 1: December 2000		Study 2: December 2001		Study 3: December 2002		Study 4: December 2003	
	Normal	Abnormal	Normal	Abnormal	Normal	Abnormal	Normal	Abnormal
Mean (% A1C)	5.2	9.9	5.3	10.5	5.4	10.4	5.4	9.6
Total CV (%)	4.7	3.4	4.7	2.9	3.9	2.9	3.3	2.4

**Figures. Comparisons Between the Cholestech GDx A1C Method and the NGSP Network Reference Laboratory****References**

1. The Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med* 1993; 329:977-86.
2. UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). *Lancet* 1998; 352:837-53.
3. American Diabetes Association. Clinical Practice Recommendations 2002: standards of medical care for patients with diabetes mellitus. *Diabetes Care* 2002; 25 Suppl 1:S33-49.