

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION  
DECISION SUMMARY  
ASSAY AND INSTRUMENT COMBINATION TEMPLATE**

**A. 510(k) Number:**

k062658

**B. Purpose for Submission:**

New device

**C. Measurand:**

Glycosylated hemoglobin (Hgb A1C)

**D. Type of Test:**

Quantitative, boronate affinity method

**E. Applicant:**

Primus Corporation

**F. Proprietary and Established Names:**

Primus A1care Assay

Primus TRI $\blacklozenge$ stat<sup>TM</sup> Instrument

**G. Regulatory Information:**

1. Regulation section:

21CFR 864.7470 and 21 CFR 862.2160

2. Classification:

Class II

3. Product code:

LCP and JJE

4. Panel:

Hematology (81) and Chemistry (75)

**H. Intended Use:**

1. Intended use(s):

See indications for use below

2. Indication(s) for use:

The Primus A1care Assay A1c test, for use with the TRI♦stat™ Instrument, is a rapid *in vitro* diagnostic test for measurement of the percent of glycated hemoglobin (%HbA1c) level in human blood from finger stick or venous samples for clinical laboratory and point-of-care use. Measurement of percent HbA1c is used to monitor long-term glucose control in individuals with diabetes mellitus.

3. Special conditions for use statement(s):

The device is for in vitro diagnostic prescription use.

In the package insert the manufacturer has stated the following limitations:

1. Not for use with anemia, splenectomy, uremia, or after blood transfusion.
2. Incompletely filled EDTA tubes may contain an excess concentration of EDTA and may give slightly altered results. It is recommended that only properly (completely) filled EDTA blood collection tubes be used for A1c testing in TRI♦stat™.
3. **Do not** use with patients who have Hemoglobin F.

4. Special instrument requirements:

Primus TRI♦stat™ Instrument

**I. Device Description:**

Primus TRI♦stat™ Instrument is a small (10"W x11"Lx4"H), in vitro diagnostic instrument used with the Primus A1C assay test to quantitate HbA1C using patented two-phase optical method. The TRI♦stat™ is capable of analyzing a total of 3 samples simultaneously.

Each TRI♦stat™ instrument package contains:

One (1) TRI♦stat™ Instrument

One (1) Power Supply

One (1) Instrument Operator Manual

One (1) Warranty Card

One (1) A1care start-up kit containing: 1. One reagent tube holding rack  
2. One Quick Reference Guide

Primus A1care assay kit contains:

1. 24 reagent tubes: Each reagent tube contains 700 µl of 10% immobilized m-aminophenylboronic acid on 6% cross linked agarose in a glycine buffer containing MDC12, NaCl, triton X100, NaOH, Ethyl alcohol and distilled water.
2. 24 blood collection capillary tubes: Each tube contains EDTA for collecting 4µl of whole blood from finger stick or venous samples.
3. One Key Card (contains reagent lot number and calibration information)

**J. Substantial Equivalence Information:**

1. Predicate device name(s):

Primus HPLC, model CLC 330 analyzer

2. Predicate 510(k) number(s):

k891235

3. Comparison with predicate:

<b>Similarities and differences between the predicate and candidate devices</b>		
<b>Item</b>	<b>Predicate Device</b>	<b>Candidate Device</b>
Device name	Primus HPLC, model CLC 330 analyzer (k891235)	Primus A1care Assay On TRI $\blacklozenge$ stat™ Instrument
Method	Conventional HPLC column chromatography with a boronate affinity matrix suitable for HPLC	Use same boronate affinity principle with a boronate modified agarose matrix suitable transparency for optical reading
Instrument	Primus HPLC analyzer	Primus TRI $\blacklozenge$ stat™ Instrument
Buffer used	Ammonium acetate buffer at pH 9.0	Glycine buffer at pH 9.1
Sample type	Venous EDTA or finger-stick	Same
Calibration	With each run	Factory calibrated
Traceability	Traceable to Diabetes Control and Complications Trial (DCCT) method	Same

**K. Standard/Guidance Document Referenced (if applicable):**

1. CLSI Guideline, EP5-A2 *Evaluation of Precision Performance of Clinical Chemistry Devices; Approved Guideline Second edition*
2. CLSI Guideline, EP6-A *Evaluation of the Linearity of Quantitative Analytical Methods; Approved Guideline*
3. CLSI Guideline, EP7-A2 *Interference Testing in Clinical Chemistry; Approved Guideline- Second edition*
4. CLSI Guideline, EP9-A2 *Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline Second edition*
5. EN ISO 17511: 2003, *Metrological Traceability of Values Assigned to Calibrator and Control Materials.*

**L. Test Principle:**

The Primus A1care assay used the boronate affinity in a patented two-phase optical assay. The sample is mixed in an optical cuvette with a suspension of the solid phase particles in a fluorescent buffer. The buffer also contains a lysing agent to break up the red blood cells. After the glycated hemoglobin (HbA1C) adheres to the solid phase, gel particles with A1C attach separately by sedimentation. The HbA1C –gel sedimentation process is monitored by an optical system examining fluorescence intensities generated between the suspension and the settled solid phase, the proportion of which is factory calibrated to give results comparable to known standards. Optical measurement of hemoglobin is by fluorescence quenching. The wavelength of light absorbance by hemoglobin overlaps the wavelength of excitation of the fluorescent dye. In the presence of hemoglobin there is less light available to excite fluorescence (the quenching effect), and this effect is linear with hemoglobin concentration. The patented two phase assay optically examines the position where the solid phase particles settle. The measurement is made before settling for total hemoglobin, and after complete settling for Hemoglobin A1c only. Optical measurements are automatically completed, calculations automatically performed, and the patient's HbA1c test value is displayed.

**M. Performance Characteristics (if/when applicable):**

1. Analytical performance:

a. *Precision/Reproducibility:*

The sponsor has obtained certification from the National Glycohemoglobin Standardization Program (NGSP) for the Primus A1Care assay by performing a direct comparison with a Secondary Reference Laboratory (SRL) using 40 fresh human specimens. The sponsor has met the NGSP's acceptance criteria of precision  $\leq 4\%$

and bias  $\leq 1\%$ .

Precision studies were performed internally by the manufacturer and externally at three Point-of-care sites according to the CLSI EP5-A2 guideline.

#### Internal study performed at Primus

An internal precision study was performed in house using two whole blood controls materials. Each control was run in triplicate with two runs per day for 20 days with the following results:

	Level 1	Level 2
N	60	60
Mean Hgb A1C	5.68	9.87
Within run %CV	3.3	3.0
Between day %CV	1.4	1.4
Between run %CV	2.4	1.4
Total precision %CV	3.6	3.3

#### External study

An external precision study was performed in 3 different Point-of-Care sites with 6 untrained operators, 2 different operators for each POC site. Two whole blood controls were used in all 3 sites. In addition, site 3 ran two additional venous EDTA samples with 2 different levels of Hgb A1C. Between-run precision was performed once a run for a total of 20 runs. Within-run precision was performed 20 times in one run. Precision results are summarized below:

Site	N	Samples	Mean	Within Run CV%		Between Run CV%		Within Site CV%	Total CV%
				Operator 1	Operator 2	Operator 1	Operator 2		
1	20	Control 1	6.71	2.85	1.98	3.10	4.70	3.36	
	20	2	10.48	4.24	4.79	1.71	6.70	4.58	
2	20	1	6.32	4.26	4.47	3.52	1.55	3.72	
	20	2	10.48	4.72	2.63	3.60	2.43	3.80	
3	20	1	6.23	5.02	3.39	3.81	2.64	4.74	
	20	2	9.32	2.12	4.83	5.17	2.37	6.65	
All Sites	60	1	6.43	5.01		6.36			5.72
	60	2	10.09	7.27		8.49			7.93
3	20	EDTA 1	5.34	3.61	4.54	7.42	9.37	7.72	
	20	EDTA 2	8.61	3.02	7.83	3.74	5.06	6.71	

*b. Linearity/assay reportable range:*

A recovery study was performed according to the CLSI EP6-A guideline using two EDTA whole blood samples. The first sample has an A1c value of 17% by HPLC method and was diluted with various amount of a low liquid control (5.4% A1c) to yield a series stretching from 17% down to 6%. The second sample has an A1c value of 5.2% by HPLC method and was diluted with various amount of a non-A1c (A0) blood sample to yield a series down to 2.6%. All samples were tested on the TRI $\diamond$ stat<sup>TM</sup> instrument in triplicates. The mean percent recovery ranges from 93.4% to 110.6%. A straight line is observed in the regression plot from 2.6% to 17%. The correlation coefficient equation is  $Y = 1.061X - 0.05$ ,  $r = 0.998$ .

Based on the linearity study and the method comparison study, the sponsor claimed that the linearity/reportable range are 2.6-17% A1c with hemoglobin in the normal range of 11-16 mg/dL.

*c. Traceability, Stability, Expected values (controls, calibrators, or methods):*

Primus A1Care assay is traceable to the Diabetes Control and Complications Trial (DCCT) Method for Measurement of HbA1c. HbA1c values are reported according to the National Glycohemoglobin Standardization Program (NGSP) recommendations at the DCCT level.

The sponsor has documented traceability to the NGSP's recommended accuracy base for Hgb A1c by performing a direct comparison with a Secondary Reference Laboratory (SRL) using 40 fresh human specimens. NGSP certifications expire after one year. Current certifications are posted on the NGSP website at:

<http://www.ngsp.org/prog/index.html>

A whole blood sample (EDTA) stability study was performed to show that EDTA sample is stable up to 14 days when stored in the refrigerator.

*d. Detection limit:*

See linearity study above.

*e. Analytical specificity:*

i.) Studies were performed to assess common or known substances that could interfere with the A1Care assay. The interfering substances were evaluated in whole blood EDTA samples that had different Hgb A1C concentrations (from a normal patient and a diabetic patient). The sponsor's acceptable criterion is that the analyte recovery should not vary from the base recovery by  $\pm 10\%$ . No significant interference was defined as the % recovery of  $\leq 10\%$ .

The sponsor claimed that there was no significant interference by the following interferents:

- Bilirubin up to 15.0 mg/dL
- Protein up to 6 g/dL
- Triglycerides up to 500 mg/dL
- Acetate up to 30µg/mL

ii.) To study the interference from labile A1c on the A1Care assay, two EDTA whole blood patients' samples representing normal and diabetic A1c levels were split into aliquots. These aliquots were supplemented by the addition of an aqueous glucose stock solution; up to 1400 mg/dL of glucose solution was tested. The samples were incubated for three hours at 37°C to facilitate formation of labile A1c. The samples were then run on the TRI♦stat™ instrument. The acceptance criterion is  $\leq 10\%$  recovery between the tested and the control conditions.

The sponsor concluded that labile A1c concentrations up to 5.2% in non-diabetic patients and up to 10.9% in diabetic patients do not interfere with the assay.

The sponsor claimed that Hemoglobin variants such as Hgb S, C, Chicago, and E do not affect their device because it has been shown that affinity method do not have interference on these Hgb variants according to the literature.\* Reference: "National Glycohemoglobin Standardization Program. In Factors that interfere with GHB (HbA1c) Test Results." <http://www.ngsp.org/prog/factors.htm>

*f. Assay cut-off:*

Not applicable.

## 2. Comparison studies:

### *a. Method comparison with predicate device:*

Method comparison studies were performed internally by the manufacturer and externally at three Point-of-care sites. Precision studies were performed according to the CLSI EP9-A2 guideline.

#### Internal study performed at Primus

A method comparison study was performed in-house using 117 venous EDTA samples on the TRI♦stat™ instrument against the HPLC reference method (predicate method). Sample range tested was 4.8%- 15% with Hgb value of 11-16 mg/dL. The linear regression correlation was calculated as follows:

$$Y = 1.0155X + 0.038, r = 0.974. (X = \text{HPLC method}, Y = \text{TRI♦stat™ method})$$

In addition, 35 capillary samples were collected and run on the TRI♦stat™ instrument and results were compared to the venous samples on the HPLC reference method.

Sample range tested was 4.8%- 12.5% with Hgb value of 11-16 mg/dL. The linear regression correlation was calculated as follows:

$$Y = 1.0686X - 0.6093, r^2 = 0.9527. (X = \text{HPLC method}, Y = \text{TRI}\blacklozenge\text{stat}^{\text{TM}} \text{ method})$$

#### External study

Nine untrained point-of care operators from three different sites performed a method comparison against the HPLC method. A total of 85 patients were used in collecting the finger-stick samples. Each patient tested provided two finger-stick samples (one sample for the POC operator to run on the candidate device and one sample for the HPLC method, which is the predicate device). In addition, the venous whole blood samples from the same individuals were tested on the TRI $\blacklozenge$ stat<sup>TM</sup> instrument vs. the HPLC method. The linear regressions results were summarized as follow:

For finger-sticks samples:

TRI $\blacklozenge$ stat<sup>TM</sup> instrument (candidate device) vs. HPLC method (predicate device):

$$Y = 0.958X + 0.946, r = 0.928, N = 85, \text{ sample range was } 4.9\text{-}15.1\%$$

For venous whole blood samples:

TRI $\blacklozenge$ stat<sup>TM</sup> instrument (candidate device) vs. HPLC method (predicate device):

$$Y = 0.975X + 0.817, r = 0.947, N = 85, \text{ sample range was } 5.1\text{-}15.5\%$$

Finger-stick samples vs. venous whole blood samples on the TRI $\blacklozenge$ stat<sup>TM</sup> instrument:

$$Y = 0.958X + 0.366, r = 0.961, N = 85, \text{ sample range was } 4.9\text{-}15.5\%$$

#### *b. Matrix comparison:*

See method comparison studies above. The sponsor claimed that whole blood samples from finger-stick or EDTA venous samples are the recommended samples.

### 3. Clinical studies:

#### *a. Clinical Sensitivity:*

Not applicable

#### *b. Clinical specificity:*

Not applicable



c. *Other clinical supportive data (when a. and b. are not applicable):*

See 2.a. above

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

The expected %HbA1c value for patients with diabetes will depend on physician discretion. The American Diabetes Association's (ADA) most recent Clinical Practice Recommendation of diabetes specifies a treatment goal of 7% or less and suggests additional action when the HbA1c level is above 8%.

The table below provides ADA guidelines<sup>5</sup> and NGSP standardized A1c test determinations to DCCT values<sup>6</sup>. A test result in the "Action Suggested" category should be promptly reviewed with a physician and as directed.

% A1c	Mean Plasma Glucose		Mean Blood Glucose	Interpretation
	mmol/L	mg/dL	mg/dL	
4	3.5	65	61	Non-Diabetic Range
5	5.5	100	92	
6	7.5	135	124	
7	9.5	170	156	ADA Target for Diabetes Control
8	11.5	205	188	Action Suggested (ADA Guidelines)
9	13.5	240	219	
10	15.5	275	251	
11	17.5	310	283	
12	19.5	345	314	

**N. Instrument Name:**

Primus TRI $\blacklozenge$ stat<sup>TM</sup> instrument

**O. System Descriptions:**

1. Modes of Operation:

This is a small analyzer with the capability of running three samples at the same time. The reagent tube contains all the reagents necessary for the determination of the analyte to be measured. The sample material is collected using the blood collection device, which

is a capillary manufactured to draw the exact sample volume (4 µl) from either a finger-stick or a venous sample. The blood collection device is placed directly back into the reagent tube before the reagent tube is insert into the Primus TRI♦stat™ instrument. The analyzing process is fully automated after inserting the reagent tube into the analyzer; the process starts by inserting the reagent tube in a barcode scanning station. Up to three reagent tubes can be run at a time.

All assay and lot specific information necessary for the analyzer to process a test is read from the barcode fixed to the reagent tube. All reagent tubes are single use and shall be disposed after use.

2. Software:

FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

Yes \_\_\_\_ X \_\_\_\_ or No \_\_\_\_\_

The sponsor referenced FDA's Guidance Document for software:

<http://www.fda.gov/cdrh/comp/guidance/1553.html>

Level of Concern: Moderate

3. Specimen Identification:

Samples are identified by manually labeling the reagent tube and by logging the patient ID into the analyzer prior to inserting the reagent tube into the analyzer, or during the analyzing process. The patient ID cannot be read by the analyzer.

4. Specimen Sampling and Handling:

The sample is collected using the blood collection device, which is a capillary manufactured to draw the exact sample volume from a finger-stick or a sample tube. The blood collection device is placed back into the reagent tube before it is inserted into the analyzer. All further processing of the sample is performed inside the reagent tube.

5. Calibration:

The TRI♦stat™ instrument is factory calibrated and is not field or user adjustable. However, each lot of reagent tubes comes supplied with a Key Card (barcode) for automatic transfer of lot specific information into the instrument for use.

6. Quality Control:

The TRI♦stat™ instrument has an internal quality control system that performs operational self-checks at power on and during the processing of each sample. Corresponding error messages are displayed. Primus recommends that controls be periodically tested and resulting values verified and follow federal, stat, and local requirements for quality control testing. External quality control materials must be purchased separately from Primus. The manufacturer recommends that two levels of external controls (a low and a high) be ran daily to verify the performance of the device. It also recommends that controls are run:

- Before the first use of a new instrument.
- For the first use of each new lot of reagents.
- For any doubt about the validity of a test result.
- Before use following long periods of instrument or reagent storage.

**P. Proposed Labeling:**

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

**Q. Conclusion:**

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.