**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION**
**DECISION SUMMARY**
**ASSAY ONLY TEMPLATE**

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

k173909

**B. Purpose for Submission:**

Addition of a diagnostic claim to an existing device

**C. Measurand:**

Glycosylated Hemoglobin (HbA1c).

**D. Type of Test:**

Quantitative turbidimetric inhibition assay

**E. Applicant:**

Siemens Healthcare Diagnostics Inc.

**F. Proprietary and Established Names:**

Dimension Hemoglobin A1c Assay

**G. Regulatory Information:**

1. Regulation section:

   21 CFR 862.1373

2. Classification:

   Hemoglobin A1c Test System.

3. Product code:

   PDJ

4. Panel:

   Clinical Chemistry, 75

## H. Intended Use:

1. Intended use(s):

   See indications for use below.

2. Indication(s) for use:

   The Dimension Hemoglobin A1c assay is an in vitro diagnostic assay for the quantitative determination of %HbA1c (DCCT/NGSP) and mmol/mol HbA1c (IFCC) in human anticoagulated venous whole blood for use on the Dimension clinical chemistry system. Measurement of Hemoglobin A1c is used as an aid in diagnosis of diabetes and monitoring of long-term blood glucose control in patients with diabetes mellitus and as an aid in the identification of patients at risk for developing diabetes mellitus.

3. Special conditions for use statement(s)

   The Dimension Hemoglobin A1c assay has significant interference with fetal hemoglobin (HbF). Samples containing HbF may produce a negative bias (lower than actual results) with the Dimension Hemoglobin A1c assay. Hemoglobin A1c results are invalid for patients with abnormal amounts of HbF, including those with known Hereditary Persistence of Fetal Hemoglobin. For additional information on the interference of the HbF variant, refer to Interfering Substances.

   For prescription use only

   The Dimension Hemoglobin A1C Assay is designed only for accurate and precise measurement of mmol/mol HbA1c (IFCC) and % HbA1c (DCCT/NGSP). The individual results for total Hb and HbA1c concentration are not reported.

   The Dimension A1C assay should not be used to diagnose diabetes during pregnancy. Hemoglobin A1c reflects the average blood glucose levels over the preceding 3 months (the average life span of a red blood cell) and therefore may be falsely low during pregnancy or any other condition associated with recent onset of hyperglycemia and/or decreased red blood cell survival.

   The Dimension A1C assay should not be used to diagnose or monitor diabetes in patients with the following conditions: hemoglobinopathies except as demonstrated to produce acceptable performance (such as, sickle cell trait), abnormal red blood cell turnover (such as, anemias from hemolysis and iron deficiency), malignancies, and severe chronic hepatic and renal disease.

   In cases of rapidly evolving Type 1 diabetes, the increase of HbA1c values might be delayed compared to the acute increase in glucose concentrations. In these conditions, diabetes mellitus must be diagnosed based on plasma glucose concentrations and/or the typical clinical symptoms.

   This test should not replace glucose testing for patients with Type 1 diabetes, pediatric patients or pregnant women.

   Any cause of shortened red blood cell survival (for example, hemolytic anemia or other

hemolytic diseases, pregnancy, or recent significant blood loss) will reduce the exposure of red blood cells to glucose with a consequent decrease in A1c values, Results of HbA1c are not reliable in patients with chronic blood loss and consequent variable erythrocyte lifespan

4. Special instrument requirements

   Performance data below was collected on the Dimension RxL Clinical Chemistry System.

## I. Device Description:

The Dimension Hemoglobin A1c assay consists of three reagents packaged in Dimension Flex cartridges, that contain the antibody, buffers and reagents, are used with the Dimension RxL instrument. The HbA1c measurement is based on a turbidimetric inhibition immunoassay principle, and the measurement of total hemoglobin is based on a modification of the alkaline hematin reaction. Using the values obtained for each of these two analytes, the relative proportion of the total hemoglobin that is glycated is calculated and reported.

## J. Substantial Equivalence Information:

1. Predicate device name(s):

   Roche Diagnostics Cobas c513 Tina-Quant HbA1cDx Gen.3 Assay

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

   k160571

3. Comparison with predicate:

| Similarities | | |
|---|---|---|
| **Item** | **Device (Dimension Hemoglobin A1c Assay)** | **Predicate (Roche Diagnostics Cobas c513 Tina-Quant HbA1cDx Gen.3 Assay)** |
| Intended Use | Intended for the the quantitative determination of mmol/mol HbA1c (IFCC) and % HbA1c (DCCT/NGSP) as an aid in the diagnosis of diabetes mellitus, as an aid to identify patients who may be at risk for developing diabetes | Same |

| | | |
|---|---|---|
| | mellitus, and for the monitoring of longterm blood glucose control in individuals with diabetes mellitus. | |
| Instrument platform | Absorbance spectroscopy | Same. |
| Assay principle | Quantitative turbidimetric inhibition immunoassay | Same |
| Traceability | The assigned HbA1c and total hemoglobin values are certified with the National Glycohemoglobin Standardization Program (NGSP). | Same |
| Reporting Units | % HbA1c NGSP/DCCT and mmol/mol IFCC | Same |

| **Differences** | | |
|---|---|---|
| **Item** | **Device** | **Predicate** |
| Measuring range | %HbA1c (NGSP units)<br>3.8 to 14.0%<br><br>HbA1c (IFCC units)<br>18 to 130 mmol/mol | %HbA1c<br>4.2 to 15.5%<br><br>HbA1c<br>23 to 146 mmol/mol |
| Sample Type | Anticoagulated venous whole blood. Acceptable anticoagulants include:<br>$K_2$-EDTA<br>$K_3$-EDTA<br>Na Fluoride/$Na_2$-EDTA<br>Lithium Heparin<br>Na Fluoride/K-Oxalate | Anticoagulated whole blood or hemolysate Acceptable anticoagulants for both the hemolysate and whole blood applications include:<br>Li-Heparin<br>K2-EDTA<br>K3-EDTA<br>NaF/K-Oxalate |

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

CLSI EP05-A3 Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline – Third Edition

CLSI EP06-A Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline

CLSI EP07-A2 Interference Testing in Clinical Chemistry; Approved Guideline – Second Edition

CLSI EP17-A2 Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline – Second Edition

CLSI EP25-A Evaluation of Stability of In Vitro Diagnostic Reagents; Approved Guideline

## L. Test Principle:

HbA1c determination is based on the turbidimetric inhibition immunoassay (TINIA) for hemolyzed whole blood. Glycohemoglobin in the sample reacts with anti-HbA1c to form soluble antigen-antibody complexes. Polyhaptens react with excess anti-HbA1c to form an insoluble antibody-polyhapten complex which can be measured turbidimetrically. This method uses tetradecyltrimethylammonium bromide (TTAB) as the detergent in the hemolyzing reagent. Sample pretreatment to remove labile HbA1c is not necessary. The instrument calculates the %HbA1c from the HbA1c/Hb ratio according to a user selected protocol and the percentage of HbA1c is displayed as the % HbA1c (DCCT/NGSP).

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

1. Analytical performance:

*a. Precision/Reproducibility:*

Samples consisted of two (2) commercial quality controls (BioRad QC) and four (4) venous whole blood patient pools in K2-EDTA with target values of 5.0%, 6.5%, 8.0%, and 12.0% HbA1c.

Testing was performed at one site over twenty (20) testing days by two (2) operators using three (3) instruments and three (3) reagent lots on each instrument. One (1) calibration was performed over the duration of the study. Each testing day, two (2) runs were performed (with a minimum of 2 hours in between) each with two replicates for a total of 720 results for each sample. Results are summarized in the tables below:

**Precision (All Instruments, all reagent lots, %HbA1c)**

| Mean %HbA1c | Repeatability | | Between Run | | Between Day | | Between Lot | | Between Instrument | | Total | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | SD | CV | SD | CV | SD | CV | SD | CV | SD | CV | SD | CV |
| Human1, 5.3% | 0.05 | 0.9 | 0.04 | 0.7 | 0.01 | 0.1 | 0.07 | 1.4 | 0.09 | 1.6 | 0.13 | 2.4 |
| Human2, 6.4% | 0.05 | 0.7 | 0.03 | 0.5 | 0.03 | 0.4 | 0.09 | 1.4 | 0.00 | 0.0 | 0.11 | 1.7 |
| Human3, 7.8% | 0.06 | 0.8 | 0.04 | 0.5 | 0.03 | 0.3 | 0.10 | 1.3 | 0.00 | 0.0 | 0.13 | 1.6 |

| Mean %HbA1c | Repeatability | | Between Run | | Between Day | | Between Lot | | Between Instrument | | Total | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | SD | CV | SD | CV | SD | CV | SD | CV | SD | CV | SD | CV |
| Human4, 11.9% | 0.09 | 0.8 | 0.05 | 0.0 | 0.05 | 0.0 | 0.06 | 0.0 | 0.18 | 0.3 | 0.22 | 1.8 |
| QC 1, 5.2% | 0.05 | 1.0 | 0.04 | 0.8 | 0.02 | 0.4 | 0.03 | 0.5 | 0.11 | 2.1 | 0.13 | 2.6 |
| QC 2, 9.5% | 0.08 | 0.8 | 0.06 | 0.7 | 0.03 | 0.3 | 0.12 | 1.2 | 0.03 | 0.3 | 0.16 | 1.7 |

**Precision (Instrument 1, all reagent lots, %HbA1c)**

| Mean %HbA1c | Repeatability | | Between Run | | Between Day | | Between Lot | | Total | |
|---|---|---|---|---|---|---|---|---|---|---|
| | SD | CV | SD | CV | SD | CV | SD | CV | SD | CV |
| Human1, 5.4% | 0.05 | 0.9 | 0.04 | 0.7 | 0.02 | 0.3 | 0.11 | 2.1 | 0.13 | 2.4 |
| Human2, 6.5% | 0.05 | 0.8 | 0.04 | 0.6 | 0.02 | 0.3 | 0.07 | 1.1 | 0.10 | 1.5 |
| Human3, 8.0% | 0.06 | 0.8 | 0.05 | 0.7 | 0.01 | 0.2 | 0.01 | 0.2 | 0.08 | 1.0 |
| Human4, 11.9% | 0.10 | 0.8 | 0.04 | 0.4 | 0.04 | 0.3 | 0.24 | 2.0 | 0.27 | 2.3 |
| QC 1, 5.3% | 0.06 | 1.1 | 0.06 | 1.2 | 0.01 | 0.1 | 0.12 | 2.3 | 0.15 | 2.8 |
| QC 2, 9.6% | 0.07 | 0.8 | 0.05 | 0.5 | 0.03 | 0.4 | 0.00 | 0.0 | 0.09 | 1.0 |

**Precision (Instrument 2, all reagent lots, %HbA1c)**

| Mean %HbA1c | Repeatability | | Between Run | | Between Day | | Between Lot | | Total | |
|---|---|---|---|---|---|---|---|---|---|---|
| | SD | CV | SD | CV | SD | CV | SD | CV | SD | CV |
| Human1, 5.4% | 0.05 | 0.9 | 0.04 | 0.7 | 0.00 | 0.0 | 0.07 | 1.3 | 0.09 | 1.7 |
| Human2, 6.4% | 0.04 | 0.7 | 0.03 | 0.5 | 0.04 | 0.6 | 0.03 | 0.4 | 0.07 | 1.1 |
| Human3, 7.8% | 0.06 | 0.7 | 0.04 | 0.6 | 0.04 | 0.5 | 0.05 | 0.6 | 0.09 | 1.2 |
| Human4, 11.9% | 0.09 | 0.7 | 0.07 | 0.6 | 0.07 | 0.6 | 0.16 | 1.3 | 0.21 | 1.8 |
| QC 1, 5.2% | 0.04 | 0.8 | 0.02 | 0.4 | 0.03 | 0.6 | 0.08 | 1.6 | 0.10 | 1.9 |
| QC 2, 9.5% | 0.08 | 0.8 | 0.07 | 0.7 | 0.04 | 0.4 | 0.03 | 0.3 | 0.12 | 1.2 |

**Precision (Instrument 3, all reagent lots, %HbA1c)**

| Mean %HbA1c | Repeatability | | Between Run | | Between Day | | Between Lot | | Total | |
|---|---|---|---|---|---|---|---|---|---|---|
| | SD | CV | SD | CV | SD | CV | SD | CV | SD | CV |
| Human1, 5.3% | 0.05 | 1.0 | 0.04 | 0.7 | 0.00 | 0.0 | 0.11 | 2.1 | 0.13 | 2.4 |
| Human2, 6.4% | 0.05 | 0.8 | 0.02 | 0.4 | 0.02 | 0.3 | 0.05 | 0.8 | 0.08 | 1.3 |
| Human3, 7.8% | 0.07 | 0.9 | 0.01 | 0.2 | 0.03 | 0.3 | 0.04 | 0.5 | 0.08 | 1.0 |
| Human4, 1.9% | 0.08 | 0.7 | 0.03 | 0.3 | 0.04 | 0.3 | 0.15 | 1.3 | 0.18 | 1.5 |
| QC 1, 5.1% | 0.05 | 1.0 | 0.04 | 0.7 | 0.02 | 0.4 | 0.12 | 2.4 | 0.14 | 2.7 |
| QC 2, 9.4% | 0.09 | 0.9 | 0.07 | 0.7 | 0.02 | 0.2 | 0.03 | 0.3 | 0.12 | 1.2 |

b. *Linearity/assay reportable range:*

Linearity testing was conducted in accordance with CLSI EP06-A, Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline. Nine (9) samples were used with %HbA1c levels that spanned the assay range. The sponsor performed first order linear regression.

The following table summarizes the linear regression results.

| Units | Slope | y-intercept | Correlation coeffecient |
|---|---|---|---|
| NGSP (%HbA1c) | 0.9719 | 0.3264 | 0.9986 |
| IFCC (mmol/mol) | 0.9774 | 2.1431 | 0.9976 |

The linearity results support the claimed reportable measuring range of 3.8-14.0 % HbA1c (18 to 130 mmol/mol).

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

*Traceability:*

The Hemoglobin A1C assay on the Dimension RxL system is certified with the National Glycohemoglobin Standardization Program (NGSP). See NGSP website for current certification at http://www.ngsp.org.

The International Federation of Clinical Chemistry (IFCC) units of mmol/mol are calculated using the Master Equation NGSP (%) = 0.09148 x IFCC (mmol/mol) + 2.152. HbA1c results are provided to the customers using two different units: NGSP equivalent units (%) and IFCC equivalent units (mmol/mol).

d. *Detection limit:*

Limit of Blank (LoB) and Limit of Detection (LoD) testing was conducted in accordance with CLSI EP17-A2, Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures. LoB and LoD were determined for HbA1c (%), total hemoglobin (tHb) (g/dL) and HbA1c (g/dL).

LoB testing was performed over three testing days by one operator using one instrument and two kit lots. One calibration was performed for each kit lot (total of two). On each testing day, five replicate measurements were taken for each of five blank samples for a total of 75 replicates for each kit lot.

LoD testing was performed over three testing days by one operator using one instrument and two kit lots. One calibration was performed for each kit lot (total of two). On each testing day, four replicate measurements were taken for each of five (5) low level patient samples for a total of 75 total replicates for each kit lot.

Calculations were performed following the classical approach described in EP17-A2. LoB was calculated using the Nonparametric Option and LoD was calculated using Parametric Analysis.

The detection limits are summarized in the table below:

| | **Limit of Blank** | **Limit of Detection** |
|---|---|---|
| tHb | 0.0 g/dL | 0.5 g/dL |
| HbA1c | 0.21 g/dL | 0.23 g/dL |
| % HbA1c | 3.6 % | 3.7 % |

*e. Analytical specificity:*

i. Endogenous interferents

Interference studies were performed to assess endogenous substances that could interfere with the Dimension Hemoglobin A1c Assay. The interfering substances were evaluated in venous whole blood K2 EDTA samples. Four replicates for each interferent were tested on the Dimension Hemoglobin A1c Assay at each of 2 target HbA1c levels: 6.5 ± 1% and 8.0 ± 1%. The sponsor's definition of definition of non-significant interference is ≤5.0% mean relative deviation between the tested and the control samples.

**Concentrations at which no significant interference (≤5.0%) was observed.**

| **Endogenous interfering factor** | **Concentration** |
|---|---|
| Bilirubin (Conjugated) | 66 mg/dL |
| Bilirubin (Unconjugated) | 66 mg/dL |
| Glucose | 2000 mg/dL |
| Rheumatoid Factor | 750 IU/mL |
| Protein: Total | 22 g/dL |
| Triglycerides | 600 mg/dL |

ii. Exogenous Interference

Interference studies were performed to assess common or known exogenous substances that could interfere with the Dimension Hemoglobin A1c Assay. The interfering substances were evaluated in venous whole blood K2-EDTA samples. Four replicates for each interferent were tested on the Dimension Hemoglobin A1c Assay at each of 2 target HbA1c levels: 6.5 ± 1% and 8.0 ± 1%. The sponsor's definition of non-significant interference is ≤5.0% mean relative deviation between the tested and the control samples. Results demonstrated that no significant interference was observed with the following substances up to the listed concentrations:

| Substance | Highest Concentration Tested with no Significant Interference |
|---|---|
| Acetaminophen | 20 mg/dL |
| Ampicillin | 100 mg/dL |
| Acetylsalicylic acid | 100 mg/dL |
| Ascorbic acid | 30 mg/dL |
| Calcium dobesilate | 20 mg/dL |
| Cefoxin sodium | 250 mg/dL |
| Cholesterol | 503 mg/dL |
| Cyclosporin | 1.66 mg/dL |
| Doxycycline hyclate | 5 mg/dL |
| Heparin | 5 U/mL |
| Ibuprofen | 50 mg/dL |
| Insulin | 593 µU/mL |
| Intralipid | 1000 mg/dL |
| Levodopa | 2 mg/dL |
| Metformin | 4 mg/dL |
| Methyldopa | 2 mg/dL |
| Metronidazole | 20 mg/dL |
| N-acetylcysteine | 166.3 mg/dL |
| Phenylbutazone | 40 mg/dL |
| Rifampicin | 6 mg/dL |
| Rosiglitazone | 0.8mg/dL |
| Salicylic acid | 60 mg/dL |
| Theophylline | 10 mg/dL |

iii. Cross Reactivity with Hemoglobin Derivatives

Testing to evaluate potential interference of hemoglobin derivatives on the Dimension Hemoglobin A1c Assay was performed according to CLSI EP07-A2, Interference Testing in Clinical Chemistry; Approved Guideline – Second Edition.

The effect of each hemoglobin derivative was evaluated using a paired difference analysis that compared HbA1c values between control samples (Anticoagulated K2-EDTA venous whole blood) and test samples (Anticoagulated K2-EDTA venous whole blood spiked with the derivative being tested). Four replicates were tested for each sample at three HbA1c levels: 5.0 ± 1.0%, 6.5 ± 1.0%, and 8.0 ± 1.0%. The results demonstrate no significant cross reactivity with Acetylated Hb up to 50 mg/dL of acetylsalicylic acid, Carbamylated Hb up to 10 mmol/L of Cyanate, or Labile Hb up to 1500 mg/dL of Glucose.

To verify that HbA1a, HbA1b, or HbA0 derivatives did not interfere with assay

performance, the sponsor evaluated the assay's HbA1c recovery of venous whole blood K2-EDTA patient samples with known HbA1c, HbA1a, HbA1b, and HbA0 concentrations. The highest concentrations tested with no interference were 2.2, 1.0, and 84.1% for HbA1a, HbA1b, and HbA0, respectively. The data support the sponsor's claim that HbA0, HbA1a, and HbA1b do not interfere with assay results.

iv. Hemoglobin Variants

Interference testing to determine the effect of hemoglobin variants on the Dimension Hemoglobin A1c Assay was performed in accordance with CLSI EP07-A2, Interference Testing in Clinical Chemistry; Approved Guideline – Second Edition.

Anticoagulated (K2-EDTA) human venous whole blood samples with known concentrations of hemoglobin variant were obtained from several commercial sources. The effect of each hemoglobin variant on assay performance was evaluated by analyzing these samples and comparing the %HbA1c values obtained by using the candidate assay on the Dimension RxL system to comparator %HbA1c values obtained on the Trinity Biotech Ultra 2 (HbC, HbD, HbE, HbS, HbA2), Tosoh HLC-723G8 (HbA2, HbF), and Bio-Rad Variant II Turbo (HbC). Four replicates were tested for each sample. Results are shown below:

**Hb Variant Distribution**

| Hb Variant | Number of Samples | % Concentration of Variant in Sample | %HbA1c Concentration Range |
|---|---|---|---|
| HbC | 37 | 26.1 – 40.0% | 4.4 – 15.7 % |
| HbD | 20 | 24.8 – 38.4% | 5.0 – 13.0% |
| HbE | 22 | 19.7 – 30.4% | 4.7 – 11.0% |
| HbS | 22 | 27.2 – 36.3% | 5.3 – 14.0% |
| HbA2 | 23 | 4.3 – 6.2% | 5.1 – 8.4% |
| HbF | 20 | 4.3 – 29.3% | 4.3 – 10.1% |

**Hb Variant Results**

| Hb Variant | % Bias (Range of % Bias) for ~6% HbA1c | % Bias (Range of % Bias) for ~8% HbA1c |
|---|---|---|
| HbC | -1.0% [-5.0% to 4.9%] | -0.9% [-4.6% to 4.4%] |
| HbD | -2.2% [-4.9% to 4.4%] | -2.5% [-4.4% to -1.3%] |
| HbE | -2.1% [-4.9% to 3.1%] | -2.5% [-4.3% to -1.0%] |
| HbS | -1.3% [-4.7% to 4.9%] | -2.0% [-4.9% to 3.5%] |
| HbA2 | 0.1% [-4.8% to 3.6%] | -2.0% [-3.0% to -1.1%] |
| HbF | HbF interferes with this assay | |

Significant interference was defined by the sponsor as ≥ ±5% change in HbA1c value in the presence of the hemoglobin variant relative to control. The results show there was no significant interference for HbS (≤36.3%), HbC (≤40.0%), HbD (≤38.4%),

HbE (≤30.4%), and HbA2 (≤6.2%) at the concentrations tested in this study.

The labeling contains the following limitation:

*This device has significant negative interference with fetal hemoglobin (HbF). HbA1c results are invalid for patients with abnormal amounts of HbF including those with known Hereditary Persistence of Fetal Hemoglobin.*

*f. Assau cut-off:*

Not applicable

2. Comparison studies:

*a. Method comparison with predicate device:*

Method comparison testing was performed in accordance with CLSI EP09-A3, Measurement Procedure Comparison and Bias Estimation Using Patient Samples; Approved Guideline – Third Edition. 147 human venous K2-EDTA whole blood samples with values spanning the assay range (4.5 to 12.6%) were tested. The candidate device results were compared to those obtained from testing at a NGSP secondary reference laboratory on the Tosoh G8 method. The distribution of samples spanning the measuring interval were as follows:

**Distribution of Samples**

| Range of Results (%HbA1c) | Percentage of Samples | Number of Samples |
|---|---|---|
| <5 | 4.8% | 7 |
| 5 – 6 | 12.2 | 18 |
| 6 – 6.5 | 20.4 | 30 |
| 6.5 – 7 | 21.8 | 32 |
| 7 – 8 | 14.3 | 21 |
| 8 – 9 | 8.2 | 12 |
| >9 | 18.4 | 27 |
| Total | 100% | 147 |

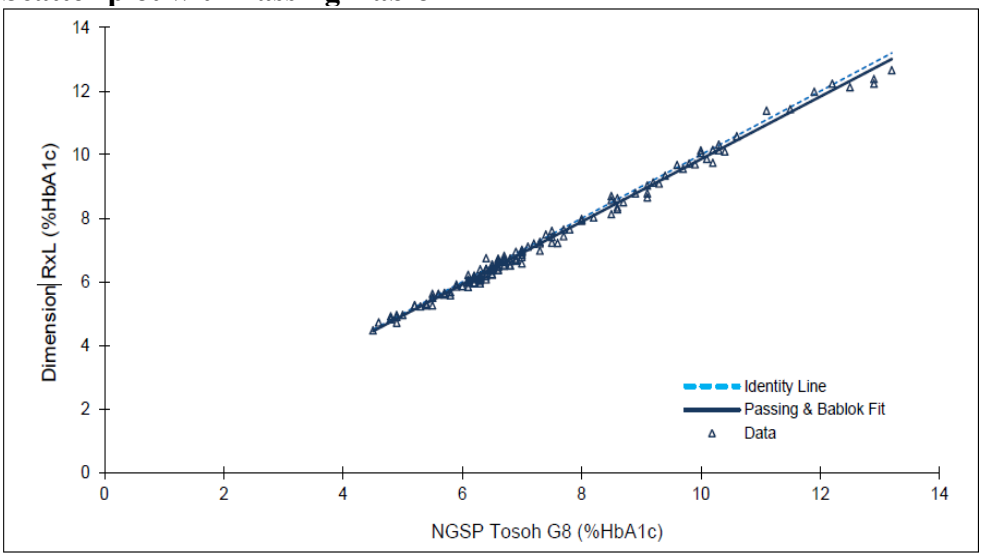
Deming and Passing-Bablok regression analysis was performed for the candidate system results versus the NGSP assigned comparator value. A summary is provided below:

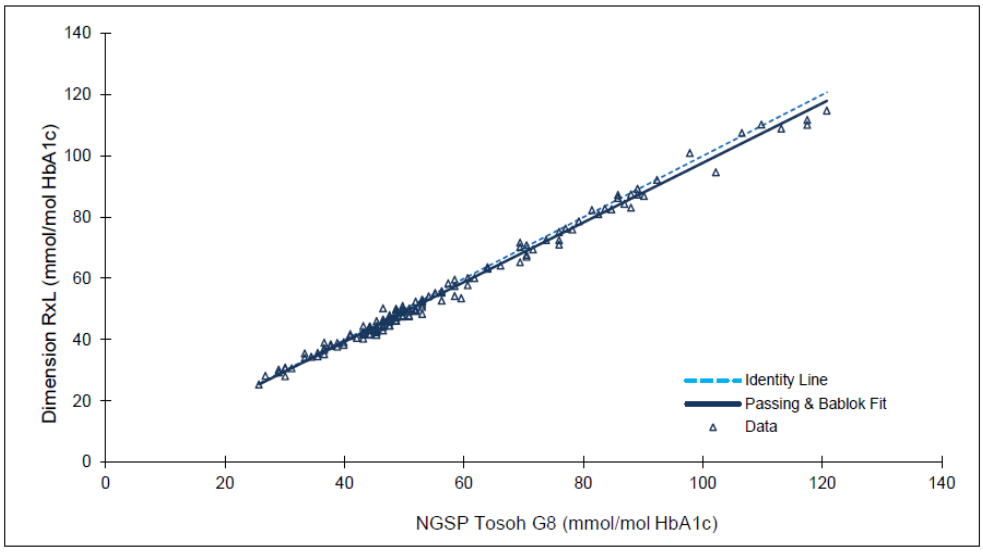
N=147, sample range 4.8 – 13.2% HbA1c and 25.7 – 120.8 mmol/mol.

**Method Comparison Regression**

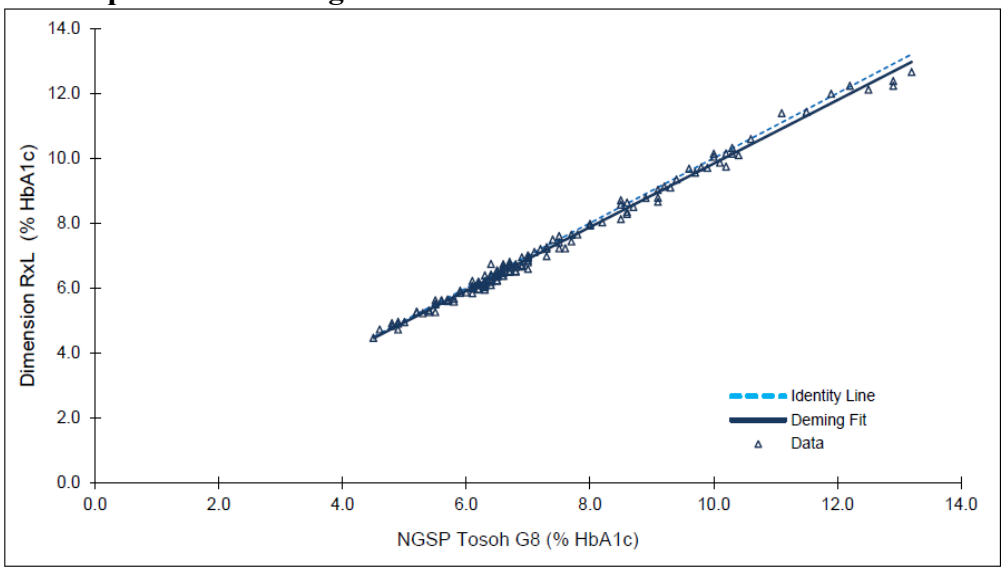
| Units | Regression | Slope | 95 % CI | y-intercept | 95 % CI | Pearson correlation coefficient (r) |
|---|---|---|---|---|---|---|
| NGSP | Passing-Bablok | 0.983 | [0.966; 1.001] | 0.030 | [-0.095; 0.144] | 0.996 |
| | Deming | 0.978 | [0.957; 1.000] | 0.052 | [-0.094; 0.198] | |
| IFCC | Passing-Bablok | 0.973 | [0.955; 0.992] | 0.437 | [-0.474; 1.450] | 0.996 |
| | Deming | 0.970 | [0.948; 0.992] | 0.532 | [-0.603; 1.666] | |

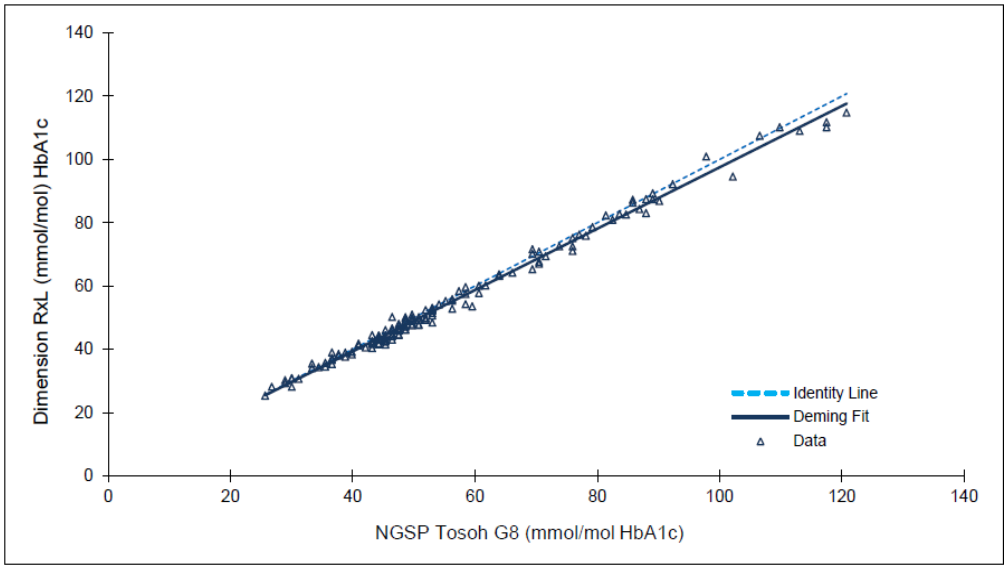
**Scatter plot with Passing-Bablok**



**Scatter plot with Deming**




i. Bias Estimation Table

**Bias Estimation Table, Passing-Bablok**

| %HbA1c | Bias | % Bias |
|---|---|---|
| 5.00 | -0.05 | -1.10 |
| 6.50 | -0.08 | -1.24 |
| 8.00 | -0.11 | -1.33 |
| 12.00 | -0.17 | -1.45 |

**Bias Estimation Table, Deming**

| %HbA1c | Bias | % Bias |
|---|---|---|
| 5.00 | -0.06 | -1.16 |
| 6.50 | -0.09 | -1.40 |
| 8.00 | -0.12 | -1.55 |
| 12.00 | -0.21 | -1.77 |

ii. Total Error Calculation and Estimation Table

The bias estimation values determined in the method comparison study and precision estimates determined in the precision study were used to determine the total error at each of the levels listed in the tables below. Total error was calculated by the following equation:

%TE = |%Bias| + (1.96 x %CV) x (1 + %Bias/100)

**Total Error Summary, Passing-Bablok**

| %HbA1c | % Bias | % CV | % TE |
|---|---|---|---|
| 5.0 | -1.10 | 2.4 | 5.8 |
| 6.5 | -1.24 | 1.7 | 4.5 |
| 8.0 | -1.33 | 1.6 | 4.4 |
| 12.0 | -1.45 | 1.8 | 4.9 |

**Total Error Summary, Deming**

| %HbA1c | % Bias | % CV | % TE |
|---|---|---|---|
| 5.0 | -1.16 | 2.4 | 5.8 |
| 6.5 | -1.40 | 1.7 | 4.7 |
| 8.0 | -1.55 | 1.6 | 4.6 |
| 12.0 | -1.77 | 1.8 | 5.2 |

*b. Matrix comparison:*

Matrix comparison testing was conducted to demonstrate equivalence between five different anticoagulants using 79 matched sets of whole human blood collected in all five anticoagulant tubes containing K2 EDTA, K3 EDTA, Na Fluoride/Na2 EDTA, Lithium Heparin, and Na Fluride/K-Oxalate. Regression analysis was used to analyze the measured values with K2-EDTA values as the comparator. Pearson correlation coefficient between K2-EDTA compared to the five other anticoagulants was 0.999 for each pair.

**Deming Regression Analysis**

| Anticoagulant | Comparator | N | Slope | y-intercept |
|---|---|---|---|---|
| K3 EDTA | K2 EDTA | 79 | 0.997 | 0.011 |
| Na Fluoride/Na2 EDTA | K2 EDTA | 79 | 1.003 | -0.033 |

| Anticoagulant | Comparator | N | Slope | y-intercept |
|---|---|---|---|---|
| Lithium Heparin | K2 EDTA | 79 | 1.008 | -0.042 |
| Na Fluoride/K-Oxalate | K2 EDTA | 79 | 1.007 | -0.018 |

**Passing-Bablok Regression Analysis**

| Anticoagulant | Comparator | N | Slope | y-intercept |
|---|---|---|---|---|
| K3 EDTA | K2 EDTA | 79 | 0.994 | 0.030 |
| Na Fluoride/Na2 EDTA | K2 EDTA | 79 | 0.997 | 0.006 |
| Lithium Heparin | K2 EDTA | 79 | 1.006 | -0.038 |
| Na Fluoride/K-Oxalate | K2 EDTA | 79 | 1.010 | -0.037 |

These results support the use of the Dimension Hemoglobin A1c Assay with samples collected in K2-EDTA, K3-EDTA, Na Fluoride/Na2-EDTA, Na Fluoride/K-Oxalate or Lithium Heparin tubes.

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):*

      Not applicable

4. Clinical cut-off:

   Not applicable

5. Expected values/Reference range:

   The reference interval was taken from the American Diabetes Association, Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care* 2017; 40 (Supplement 1): S11-S24.7

| Suggested Diagnosis | HbA1c (%) | HbA1c (mmol/mol) |
|---|---|---|
| Diabetic | ≥ 6.5 | ≥ 48 |
| Prediabetic | 5.7-6.4 | 39-47 |
| Normal | <5.7 | <39 |

**N. Proposed Labeling:**

The labeling is sufficient and it satisfies the requirements of 21 CFR Parts 801 and 809, as applicable, and the special controls for this device type under 21 CFR 862.1373.

**O. Conclusion:**

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