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

A. 510(k) Number:
k073309

B. Purpose for Submission:
New device

C. Measurand:
Hemoglobin A1c (HbA1c)

D. Type of Test:
Quantitative turbidimetric immunoassay

E. Applicant:
Horiba ABX

F. Proprietary and Established Names:
ABX PENTRA HbA1c WB
ABX PENTRA HbA1c WB Cal
ABX PENTRA HbA1c WB Control
ABX PENTRA HbA1c WB Hemolysis Reagent

G. Regulatory Information:
1. <u>Regulation section:</u>
    21CFR §864.7470 – Glycosylated hemoglobin Assay
    21CFR §862.1150 – Calibrator, multi-analyte mixture
    21CFR §862.1660 – Quality control material (assayed and unassayed)
2. <u>Classification:</u>
    Class II
    Class II
    Class I
3. <u>Product code:</u>
    LCP - Glycosylated hemoglobin assay
    JIX -   Calibrator, multi-analyte mixture
    JJY -   Multi-Analyte Controls (Assayed and Unassayed)
4. <u>Panel:</u>
    Hematology (81) and Chemistry (75)

H. Intended Use:
1. <u>Intended use(s):</u>
    See indications for use below.

2. Indication(s) for use:
   ABX PENTRA HBA1c WB reagent with associated calibrators and controls are for quantitative in vitro diagnostic determination of Hemoglobin A1c percentage (%HbA1c) in human whole blood based on a colorimetric and turbidimetric assay. It is intended for use on ABX PENTRA 400 Clinical Chemistry Analyzer

   Percent HbA1c measurements are used in the clinical management of diabetes to assess the long-term efficacy of diabetic control.

   The ABX PENTRA HbA1c WB Cal is a calibrator for use in the calibration of quantitative Horiba ABX PENTRA HbA1c WB method on Horiba ABX clinical chemistry analyzers.

   The ABX PENTRA HbA1c WB Control is for use in quality control by monitoring accuracy and precision for the quantitative ABX PENTRA HbA1c WB method.

   The ABX PENTRA HbA1c WB Hemolysis Reagent is an additional reagent for use in combination for the quantitative ABX PENTRA HbA1c WB method.

3. Special conditions for use statement(s):
   For prescription use only
   HbS or HbC variants significantly interfere with this assay; this method should not be used to test patient samples with these hemoglobin variants.

4. Special instrument requirements:
   ABX PENTRA 400 Clinical Chemistry Analyzer

I. Device Description:

The ABX PENTRA HbA1c WB Set contains ready-to-use vials of reagents R1, R2, R3, R4, R5 and Diluent I. R1 contains particles coupled with mouse anti-human HbA1c monoclonal antibody in buffer. R2 contains agglutinator reagent containing covalent polymer-bonding hapten in buffer. R3 contains Hemoglobin denaturant containing porcine pepsin in buffer. R4 contains the total hemoglobin reagent containing sodium hydroxide and surfactant. R5 contains diluent I, a saline solution.

This assay may be used in two formats: a method for automatic hemolysis of blood samples by the ABX PENTA 400 or a method where hemolysis of blood samples is done manually before analysis by the ABX PENTA 400. The automated analyzer method uses R1, R2, R3, and R4 while the manual method uses R1, R2, R3, R4, and R5.

The calibrator kit contains ready to use vials of Calibrators 1 - 6. Each vial contains HbA1c and hemoglobin in buffer.

The control kit consists of two vials (Control 1 and Control 2). The vials contain

lyophilized hemoglobin A1c (hemolysate prepared from packed human erythrocytes) and stabilizers. One control is in the normal range and the other is in the elevated range.

The human whole blood used in the calibrators and controls is nonreactive for HBsAg, HIV-1 Ag or HIV-1 RNA, Anti- HIV-1/HIV-2, and anti-HCV or HCV RNA.

J. Substantial Equivalence Information:
1. Predicate device name(s):
   Bayer Hemoglobin A1c
   Olympus America Hemoglobin A1c Test

2. Predicate 510(k) number(s):
   k955087 (Bayer) and k031380 (Olympus)

3. Comparison with predicate:
   Reagent Similarities:

	k955087	**k031380**	**ABX Pentra HbA1c WB**
Intended Use	Determination of % HbA1c for use in clinical management of diabetes	Determination of % HbA1c for use in clinical management of diabetes	Determination of % HbA1c for use in clinical management of diabetes
Method :	Latex-enhanced turbidimetric immunoassay for detection of HbA1c and colorimetric assay for detection of total hemoglobin method. HbA1c %: determined from the HbA1c/Hb ratio.	Latex agglutination inhibition immunoassay for detection of HbA1c and colorimetric assay for detection of total hemoglobin method. HbA1c %: determined from the HbA1c/HB ratio.	Latex-enhanced turbidimetric immunoassay for detection of HbA1c and colorimetric assay for detection of total hemoglobin method. HbA1c %: determined from the HbA1c/Hb ratio.
Specimen :	Whole blood	Whole blood	Whole blood
Format	Liquid	Liquid	Liquid

Reagent Differences:

	k955087	**k031380**	**ABX Pentra HbA1c WB**
Reference method	Correction by a conversion factor to match a HPLC reference method	Correction by a conversion factor to match a DCCT reference method	Correction by a conversion factor to match a HPLC reference method (NGSP certification)

	k955087	k031380	ABX Pentra HbA1c WB
Measuring range	HbA1c%: 1.8 % – 14.7 %	HbA1c%: 2.6 % – 14.5 %	HbA1c%: 5.0 % – 15.2 %
Calibration stability		14 days	3 weeks
Open Reagent stability	Open reagent stability : until the expiry date at 2-8°C	Open reagent stability : 30 days	Stability after reconstitution of the latex antibody complex: 2 months

Calibrator Comparison:

	k031380	ABX Pentra HbA1c WB Cal
Similarities:		
Method :	Calibration for the determination of HbA1c on OLYMPUS analyzers	Calibration for the determination of: - HbA1c - Total Hemoglobin on ABX PENTRA 400 analyzers
Component matrices	Liquid chemical solutions with HbA1c hapten	Liquid chemical solutions with HbA1c hapten
Format	Liquid – 6 levels	Liquid – 6 levels
Differences:		
Calibration values and traceability	- Determined using the methods mentioned in the package insert. Traceable to IFCC reference preparations.	- Determined using HPLC method for HbA1c and the Drabkin method for total hemoglobin.

Control Comparison:

	k031380	ABX Pentra HbA1c WB Control
Intended Use	Quality control by monitoring accuracy and precision for the determination of HbA1c%	Quality control by monitoring the performances for the determination of HbA1c%
Format	2 levels – normal and high. Lyophilized	2 levels– normal and high. Lyophilized

	k031380	ABX Pentra HbA1c WB Control
Traceability	Traceable to calibrators which are traceable to IFCC reference preparation	Determined using HPLC method for HbA1c and the Drabkin method for total hemoglobin.

K. Standard/Guidance Document Referenced (if applicable):
CLSI EP05-A2: Evaluation of Precision performance of Quantitative Measurement Methods, Approved Guideline- Second Edition
CLSI EP06-A: Evaluation of the Linearity of Quantitative Measurement Procedures, A Statistical Approach; Approved Guideline
CLSI EP09-A2: Method Comparison and Bias Estimation Using Patient Samples, Approved Guideline-Second Edition
CLSI EP17-A: Protocols for the Determination of Limits of Detection and Limits of Quantitation, Approved Guideline

L. Test Principle:
HbA1c/Total Hemoglobin ratio is expressed as percentage HbA1c (units %HbA1c) after the concentrations of both HbA1c and Total Hemoglobin are determined individually. Whole blood samples are pre-treated with the Hemolysis Reagent to lyse the red cells and hydrolyze the hemoglobin chain. Total Hemoglobin is converted into alkaline haematin in the alkaline solution of a non-ionic detergent. Addition of the pre-treated blood sample to the Total Hb reagent results in a green solution, which is measured at 600 nm. HbA1c is measured from the hemolysate by a latex enhanced turbidimetric immunoassay. In the absence of HbA1c in the sample, the antibody-coated micro-particles in the HbA1c R1 and the agglutinator in R2 will agglutinate. This leads to an increase in the absorbance of the suspension. The presence of HbA1c in the sample results in a decrease in the rate of agglutination. The increase in absorbance is therefore inversely proportional to the concentration of HbA1c in the sample. The increase in absorbance is measured at 700 nm.

M. Performance Characteristics (if/when applicable):
1. Analytical performance:
   a. *Precision/Reproducibility:*
      Precision was assessed using two control samples (normal and high) and three human samples (normal, slightly elevated, and high). Within-run precision samples were prepared according to test protocol and tested 20 times in a single run on an ABX PENTRA 400 instrument. Total precision was assessed using the same samples prepared according to test protocol tested in duplicate twice a day for 20 days following the method in CLSI EP-5A (n = 80). Results for the manual method for preparing the hemolysate and the automated method are shown in the tables below:

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Precision: Pentra HbA1c WB Assay – Manual Method

Sample	Within-Run			Total Precision		
	Mean	Std Dev	CV	**Mean**	Std Dev	CV
	ng/mL	ng/mL	%	ng/mL	ng/mL	%
Control N	5.20	0.10	1.87	5.27	0.07	1.41
Control P	9.70	0.26	2.72	10.11	0.24	2.42
Normal Sample	4.95	0.07	1.51	5.27	0.11	2.18
Elevated Sample	7.77	0.12	1.60	8.52	0.19	2.21
High Sample	10.57	0.15	1.44	12.22	0.30	2.46

Precision: Pentra HbA1c WB Assay – Automated Method

Sample	Within-Run			Total Precision		
	Mean	Std Dev	CV	**Mean**	Std Dev	CV
	ng/mL	ng/mL	%	ng/mL	ng/mL	%
Control N	4.39	0.12	2.83	5.36	0.07	1.29
Control P	10.45	0.20	1.96	11.14	0.22	1.99
Normal Sample	3.65	0.10	2.84	5.21	0.13	2.49
Elevated Sample	7.93	0.24	2.98	8.10	0.30	3.71
High Sample	11.23	0.40	3.57	11.76	0.31	2.63

b. *Linearity/assay reportable range:*
   The linear range of the automatic and the manual hemolysate methods were evaluated using a high HbA1c sample diluted with a low HbA1c sample. (Samples prepared as directed for each method.) The dilutions were made as recommended in the CLSI guideline EP6-A and an analysis was carried out in accordance with the guideline by performing 1st, 2nd and 3rd order least squares regressions. The results demonstrated linearity for both datasets. In addition, the observed values were within ± 10% of the expected values for all samples tested. The results submitted demonstrated linearity across the claimed measuring range of 5.0% to 15.2% HbA1c.

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
   The sponsor has documented traceability to the NGSP's recommended accuracy base for Hbg 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 HPLC method for measuring HbA1c concentration and the Drabkin method for measuring total hemoglobin are used to assign calibrator values. Control

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values are assigned from the median of 90 measurements for each level (nine measurements per day for five days on two instruments). The stated interval is ± 20% of the median.

Assay Component Stability (storage at 2-8°C):

	Closed	Open	Reconstituted
Reagent	24 months		2 months
Calibrator	24 months	until the expiry date	N/A
Control	36 months	3 months	N/A
Hemolysis Reagent	18 months	until the expiry date	N/A

d. *Detection limit:*
   See linearity studies above.

e. *Analytical specificity:*
   Interference from endogenous substances was tested by analysis of whole blood samples spiked with up to 612 mg/dL triglycerides, 1400 mg/dL glucose, 29 mg/dL total bilirubin or 29 mg/dL direct bilirubin The results showed $< \pm 0.5$ % (absolute) interference for each substance at the levels tested. The labeling refers the user to Young *et al.* for a list of drugs and pre-analytical variables known to affect this methodology.

   The effect of different concentrations of total hemoglobin on the assay was tested. There was less than 10% difference between the test value and the expected HbA1c concentration (not %HbA1c) from 3.83 to 22.60 g/dL (14.6 to 85.7 µmol/L) of total hemoglobin.

   Interferences from Hemoglobin C, S, and F as well as interferences from carbamylated and acetylated hemoglobins were assessed for this assay. Carbamylated and acetylated hemoglobins did not interfere with the assay while HbF showed no interference up to 15% HbF. Samples containing HbS or HbC showed significant interference; this information is in the limitations section of the labeling. At the time of this decision, NGSP has a list assays used to measure HbA1C and whether the method is affected by either HbS or HbC or HbE: http://www.ngsp.org/prog/index.html .

f. *Assay cut-off:*
   Not applicable.

2. Comparison studies:
   a. *Method comparison with predicate device:*
      A method comparison study using 144 remnant whole blood samples compared the ABX Pentra 400 instrument and the predicate method (Olympus AU400).

Manual method for preparing the hemolysate:
Whole blood samples were prepared as directed. Samples ranged from 4.9%*-
12.2% HbA1c. Passing-Bablock regression analysis of the results yielded the
following: y = 0.97x + 0.36, r= 0.98

Automatic method for preparing the hemolysate:
Samples ranged from 4.9%*- 12.4% HbA1c. Passing-Bablock regression
analysis of the results yielded the following: y = 0.98x + 0.41, r= 0.98

   * = predicate device

  b. *Matrix comparison:*
     Not applicable: EDTA whole blood is the only claimed specimen.

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

N. Proposed Labeling:
The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

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