

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

A. 510(k) Number:
k042459

B. Purpose for Submission:
Change in product design

C. Analyte:
Glycosylated hemoglobin (HbA1c)

D. Type of Test:
Quantitative immunoturbidimetric assay

E. Applicant:
Beckman Coulter, Inc.

F. Proprietary and Established Names:
Synchron LX Systems Hemoglobin A1c2 Reagent

G. Regulatory Information:

1. Regulation section:
21 CFR §864.7470, Assay, glycosylated hemoglobin
2. Classification:
Class II
3. Product Code:
LCP Glycosylated hemoglobin assay
4. Panel:
Hematology (71)

H. Intended Use:

1. Intended use(s):
See below.
2. Indication(s) for use:
“The Hemoglobin A1c2 (HbA1c2) reagent kit, when used in conjunction with SYNCHRON LX System(s) and SYNCHRON Systems HbA1c2 Calibrators, is intended for the quantitative determination of hemoglobin A1c (HbA1c2) concentration as a percentage of total hemoglobin in human whole blood.

Measurement of hemoglobin A1c is accepted as a method to measure long-term glucose control in patients with diabetes mellitus (a chronic disorder associated with disturbances in carbohydrate, fat, and protein metabolism and characterized by hyperglycemia). Determination of hemoglobin A1c provides

an important diagnostic tool for monitoring the efficiency of dietary control and therapy during treatment of diabetes mellitus.”

3. Special condition for use statement(s):
This product is for prescription use only.
4. Special instrument Requirements:
Beckman Coulter Synchron LX System(s)

I. Device Description:

The device consists of two cartridges, Hb2 and A1c2, and four levels of calibrators. The Hb2 cartridge contains hemolyzing agent and a chemical for the colorimetric determination of total hemoglobin. The A1c2 cartridge contains antibodies in buffer, and the calibrators contain hemolysate (human and sheep).

J. Substantial Equivalence Information:

1. Predicate device name(s):
Synchron LX Systems HbA1c Reagent
2. Predicate K number(s):
k010748
3. Comparison with predicate:
The HbA1c2 assay is identical to the predicate in the following ways: intended use, chemical composition, analytical range, sample type, specificity, sensitivity, sample size, formulation, and calibration. The products differ in sample preparation (none required for the proposed product), test cartridge composition (the reagent cartridge now contains the hemolyzing agent that was used to process samples off-line) and there are additional limitations regarding proper mixing of whole blood and the erythrocyte sedimentation rate.

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

Area of Study	Reference Procedure	Reference Title
Method Comparison	NCCLS EP9-A	User Comparison of Quantitative Clinical Laboratory Methods Using Patient Samples
Precision	NCCLS EP5-A	User Evaluation of Precision Performance of Clinical Chemistry Devices
Linearity	NCCLS EP6-A	Evaluation of the Linearity of Quantitative Methods
Traceability	prEN ISO 17511	In vitro diagnostic medical devices -- Measurement of quantities in biological samples -- Metrological traceability of values assigned to calibrators and control materials

L. Test Principle:

The hemoglobin A1c (HbA1c) concentration is measured as a percentage of total hemoglobin (Hb). Thus, after on-board sample hemolysis, total Hb concentration is determined using a chemical colorimetric method that measures the change in

absorbance. The sample's HbA1c concentration is measured by an immunoturbidimetric reaction where anti-HbA1c antibodies bind to HbA1c to form soluble antibody-antigen complexes. Polyhaptenes from the reagent then bind with the excess antibodies, and the resulting agglutinated complex is measured turbidimetrically. The change in absorbance is inversely proportional to the concentration of HbA1c in the sample. The on-board software then calculates HbA1c as a percentage of the total hemoglobin and reports both values.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Imprecision studies were based on NCCLS Guideline EP5-A. Two levels of control material were used in a total of two assays per day, two replicates per assay, over 20 days. Imprecision results were within the acceptance criteria set by the sponsor.

Imprecision of the Beckman-Coulter HbA1c2 Reagent

Sample	Mean (%)	S.D. (%)	%CV	n=
Within-Run Imprecision				
Normal	5.5	0.07	1.21	80
Abnormal	9.8	0.09	0.95	80
Total Imprecision				
Normal	5.5	0.14	2.58	80
Abnormal	9.8	0.27	2.79	80

b. Linearity/assay reportable range:

Serial dilutions of high samples were tested in quadruplicate on the Synchron LX. Linear regression analysis showed that Hb2 recovery was linear from 5.6 g/dL to 23.5 g/dL ($y = 0.990x - 0.095$, $r = 0.9981$). Recovery of samples relative to the target value ranged from 94.5% to 99.9%. Linear regression analysis demonstrated that A1c2 recovery was linear from 0.3 g/dL to 2.45 g/dL ($y = 1.026x - 0.066$, $r = 0.998$). Recovery of samples relative to the target value ranged from 89.2% to 100.8%. Linearity was within the sponsor's acceptance specifications.

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

Beckman-Coulter makes the following stability claims for this device after performing real-time stability studies:

Stability Claims: HbA1C2 Reagent Components

Component	Unopened	Opened
Hb2 Cartridge	15 months at 2 – 8 °C	60 days at 2 – 8 °C
A1c2/Hemolyzing Reagent Cartridge	15 months at 2 – 8 °C	30 days at 2 – 8 °C

The calibrators included in the kit were cleared under the predicate device's 510(k). They are traceable to the IFCC reference method. The traceability process is based on prEN ISO 17511. Laboratories requiring certification to the National Glycohemoglobin Standardization Program (NGSP) must use an equation included in the package insert to convert the reported IFCC results to the NGSP equivalent.

d. Detection limit:

The detection limit of the assay was determined in the predicate submission. The predicate assay was also cleared for use on the Synchron LX; based on a risk analysis, the sponsor determined that the sensitivity of the assay is unaffected by the on-line sample hemolysis. In the predicate assay, the sensitivity of the total hemoglobin determination was 6 g/dL and HbA1c was 0.3 g/dL.

e. Analytical specificity:

The analytical specificity and the effect of interfering substances were determined in the predicate submission. All the components within the kit are the same; based on a risk analysis, the sponsor determined that the new on-line sample hemolysis would not affect the specificity or change the interfering substances for this assay.

f. Assay cut-off:

Not applicable to this device.

2. Comparison studies:

a. Method comparison with predicate device:

Whole blood patient samples (n=80) were tested with the predicate Synchron Systems HbA1c reagents and with the candidate Synchron LX Systems HbA1c2 reagents. Subsequent Deming regression analysis yielded the following equation: $y = 0.911x + 0.46$, $r = 0.991$.

b. Matrix comparison:

Not applicable.

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 normal range for HbA1c in non-diabetic people is 4 to 6%. The American Diabetes Association recommends a goal of <7% for effective management of diabetes and to minimize long-term diabetic complications. They suggest that

a level above 7% indicates more intensive diabetes management should be considered.

N. Conclusion:

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