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

**A. 510(k) Number:**
k131189

**B. Purpose for Submission:**
Modification of a previously cleared glucose assay (k883181)

**C. Measurand:**
Glucose

**D. Type of Test:**
Quantitative, Spectrophotometric method

**E. Applicant:**
Beckman Coulter, Inc.

**F. Proprietary and Established Names:**
UniCel DxC SYNCHRON Systems Glucose reagent (GLUH)

**G. Regulatory Information:**

| Product Code | Classification | Regulation Section | Panel |
|---|---|---|---|
| CFR | Class II | Glucose test system (21CFR 862.1345) | 75-Chemistry |

**H. Intended Use:**

1. Intended use(s):
   See indications for use below.

2. Indication(s) for use:
   UniCel DxC SYNCHRON Systems Glucose Reagent (GLUH), when used in conjunction with UniCel DxC 600/800 SYNCHRON System(s) and SYNCHRON Systems AQUA CAL 1 and 3, is intended for the quantitative determination of glucose concentration in human serum, plasma, urine or cerebrospinal fluid (CSF).

   Glucose measurements are used in the diagnosis and treatment of carbohydrate metabolism disorders including diabetes mellitus, neonatal hypoglycemia, idiopathic hypoglycemia, and pancreatic islet cell carcinoma.

3. Special conditions for use statement(s):
   For prescription use only

4. Special instrument requirements:
   UniCel® DxC 600/800 SYNCHRON Analyzer(s)

**I. Device Description:**

The UniCel DxC SYNCHRON Systems GLUH reagent kit contains a single reagent (comes in a 104 mL bottle) and must be used with the SYNCHRON Systems AQUA CAL 1 and 3, which has been previously cleared in k965240.

The reagent consists of the following components:

- UniCel DxC SYNCHRON Systems GLUH reagent

| Reagents | Concentration |
|---|---|
| Adenosine Triphosphate | 3.8 mmol/L |
| NAD+ | 2.7 mmol/L |
| Glucose-6-phosphate dehydrogenase | 3.0 KIU/L |
| Hexokinase | 2.0 KIU/L |

**J. Substantial Equivalence Information:**

1. Predicate device name(s):
   SYNCHRON Systems LX and UniCel DxC GLU reagent

2. Predicate 510(k) number(s):
   k883181

3. Comparison with predicate:

| **Similarities and Differences** | | |
|---|---|---|
| Item | Candidate device | Predicate device |
| | UniCel DxC SYNCHRON Systems GLUH Reagent (New Device) | SYNCHRON Systems LX and UniCel DxC GLU reagent (K883181) |
| Intended Use | For the quantitative determination of glucose concentration in human serum, plasma, urine, or cerebrospinal fluid (CSF). | Same |
| Methodology | Timed endpoint method | Same |
| Fundamental Technology | Spectrophotometric detection | Same |
| Analytic Range | 5-700 mg/dL | Same |
| Reagent | REAGENT CONSTITUENTS: | Same |

| Similarities and Differences | | |
|---|---|---|
| Item | Candidate device | Predicate device |
| | Adenosine Triphosphate, 3.8 mmoi/L; NAD+, 2.7 mmoi/L; Hexokinase, 2.0 KIU/L; Glucose-6- phosphate dehydrogenase, 3.0 KIU/L; Also non-reactive chemicals necessary for optimal system performance. | |
| Sample Storage and Stability | Serum/plasma<br>1. 8 hours at 20 to 25°C<br>2. 48 hours at 2°to 8°C<br>3. > 48 hours at ≤ -15 to -20°C<br>Serum/plasma<br>One freeze/thaw cycle (when stored at -15 to -20°C) | Same |
| Linearity | Analytical range: 5-700mg/dL | Same |
| Sample type | Serum, plasma, CSF, urine | Same |
| On Board Stability | 30 days | Same |
| Calibration stability | 14 days | Same |
| Calibrator used | SYNCHRON Systems AQUA CAL | SYNCHRON MultiCal |
| Calibrator Stability (opened) | 30 days | 20 days |
| Anticoagulant | Lithium Heparin, Sodium Heparin, Potassium Oxalate/Sodium Fluoride | Ammonium Heparin, Lithium Heparin, Sodium Heparin, Potassium Oxalate/Sodium Fluoride |

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

- CLSI C28-A3, Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory
- CLSI EP14-A2,Evaluation of Matrix Effects; Approved Guideline - Second Edition
- CLSI EP-17A Protocols for Determination of Limits of Detection and Limits of Quantitation
- CLSI EP25-A, Evaluation of Stability of In Vitro Diagnostic Reagents; Approved Guideline
- CLSI EP5-A2, Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline.
- EP6-A Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline
- CLSI EP 7-A2, Interference Testing in Clinical Chemistry; Approved Guideline
- EP9-A2, Method Comparison and Bias Estimation Using Patient Samples

**L. Test Principle:**

GLUH reagent is used to measure the glucose concentration by a timed endpoint method. In the reaction, hexokinase (HK) catalyzes the transfer of a phosphate group from adenosine triphosphate (ATP) to glucose to form adenosine diphosphate (ADP) and glucose-6-phosphate. The glucose-6-phosphate is then oxidized to 6-phosphogluconate with the concomitant reduction of nicotinamide adenine dinucleotide (NAD) to reduced - nicotinamide adenine dinucleotide (NADH) by the catalytic action of glucose-6-phosphate dehydrogenase (G6PDH). The signal is measured by spectrophotometric detection.

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

1. Analytical performance:

*a. Precision/Reproducibility:*

Within-run (repeatability) and total imprecision (Intermediate precision) studies for the UniCel DxC SYNCHRON Systems Glucose (GLUH) assay were performed in accordance to CLSI Guideline EP5- A2, "Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline – Second Edition." Precision studies were performed using 3 serum based controls, 3 serum pools, 3 urine pools, and 3 CSF pools. Samples were analyzed in duplicate, twice daily, over the course of twenty working days. Precision studies were conducted on both UniCel DxC 600 and 800 analyzers. The precision results are summarized in the tables below:

**UniCel® DxC 600 SYNCHRON System**

| Analyzer | SAMPLE TYPE | | No. Data Points | Test Mean Value (mg/dL) | SD | %CV |
|---|---|---|---|---|---|---|
| Within-run (DxC600) | Serum | Control | 80 | 43 | 0.7 | 1.6 |
| | Serum | Control | 80 | 219 | 2.3 | 1.0 |
| | Serum | Control | 80 | 390 | 5.7 | 1.5 |
| | Serum | Pool 1 | 80 | 9 | 0.3 | 3.6 |
| | Serum | Pool 2 | 80 | 101 | 1.1 | 1.1 |
| | Serum | Pool 3 | 80 | 660 | 6.4 | 1.0 |
| | Urine | Pool 1 | 80 | 10 | 0.3 | 3.2 |
| | Urine | Pool 2 | 80 | 95 | 0.9 | 1.0 |
| | Urine | Pool 3 | 80 | 670 | 5.2 | 0.8 |
| | CSF | Pool 1 | 80 | 11 | 0.3 | 3.0 |
| | CSF | Pool 2 | 80 | 109 | 1.3 | 1.2 |
| | CSF | Pool 3 | 80 | 677 | 7.0 | 1.0 |

| Analyzer | SAMPLE TYPE | | No. Data Points | Test Mean Value (mg/dL) | SD | %CV |
|---|---|---|---|---|---|---|
| Total precision (DxC600) | Serum | Control | 80 | 43 | 0.8 | 1.9 |
| | Serum | Control | 80 | 219 | 2.6 | 1.2 |
| | Serum | Control | 80 | 390 | 6.5 | 1.7 |
| | Serum | Pool 1 | 80 | 9 | 0.6 | 5.9 |
| | Serum | Pool 2 | 80 | 101 | 1.6 | 1.6 |
| | Serum | Pool 3 | 80 | 660 | 8.4 | 1.3 |
| | Urine | Pool 1 | 80 | 10 | 0.6 | 5.7 |
| | Urine | Pool 2 | 80 | 95 | 1.4 | 1.5 |
| | Urine | Pool 3 | 80 | 670 | 6.1 | 0.9 |
| | CSF | Pool 1 | 80 | 11 | 0.6 | 5.3 |
| | CSF | Pool 2 | 80 | 109 | 1.6 | 1.5 |
| | CSF | Pool 3 | 80 | 677 | 8.6 | 1.3 |

**UniCel® DxC 800 SYNCHRON System**

| Analyzer | SAMPLE TYPE | | No. Data Points | Test Mean Value (mg/dL) | SD | %CV |
|---|---|---|---|---|---|---|
| Within-run (DxC800) | Serum | Control 1 | 80 | 43 | 0.5 | 1.2 |
| | Serum | Control 2 | 80 | 219 | 2.7 | 1.2 |
| | Serum | Control 3 | 80 | 389 | 6.3 | 1.6 |
| | Serum | Pool 1 | 80 | 9 | 0.3 | 3.2 |
| | Serum | Pool 2 | 80 | 101 | 1.1 | 1.1 |
| | Serum | Pool 3 | 80 | 662 | 7.5 | 1.1 |
| | Urine | Pool 1 | 80 | 10 | 0.3 | 3.0 |
| | Urine | Pool 2 | 80 | 94 | 1.2 | 1.2 |
| | Urine | Pool 3 | 80 | 668 | 7.9 | 1.2 |
| | CSF | Pool 1 | 80 | 11 | 0.3 | 2.3 |
| | CSF | Pool 2 | 80 | 108 | 1.1 | 1.0 |
| | CSF | Pool 3 | 80 | 680 | 6.7 | 1.0 |

| Analyzer | SAMPLE TYPE | | No. Data Points | Test Mean Value (mg/dL) | SD | %CV |
|---|---|---|---|---|---|---|
| Total precision (DxC800) | Serum | Control 1 | 80 | 43 | 0.7 | 1.7 |
| | Serum | Control 2 | 80 | 219 | 3.5 | 1.6 |
| | Serum | Control 3 | 80 | 389 | 7.2 | 1.9 |
| | Serum | Pool 1 | 80 | 9 | 0.3 | 3.6 |
| | Serum | Pool 2 | 80 | 101 | 1.2 | 1.2 |
| | Serum | Pool 3 | 80 | 662 | 9.4 | 1.4 |
| | Urine | Pool 1 | 80 | 10 | 0.4 | 3.7 |
| | Urine | Pool 2 | 80 | 94 | 1.3 | 1.3 |
| | Urine | Pool 3 | 80 | 668 | 8.1 | 1.2 |
| | CSF | Pool 1 | 80 | 11 | 0.4 | 3.6 |
| | CSF | Pool 2 | 80 | 108 | 1.7 | 1.6 |
| | CSF | Pool 3 | 80 | 680 | 8.1 | 1.2 |

*b. Linearity/assay reportable range:*

Linearity studies were designed in accordance with CLSI Guideline EP6-A: Evaluation of the Linearity of Quantitative Measurement Procedures. Samples were prepared by splitting two pools for each of the three sample types: serum, urine and CSF. One of the pools for each of the sample types were spiked with a glucose stock solution and then intermixed with the second pool to create 16 samples spanning the assay range. 4 replicates were tested for each of the 16 glucose samples created. Samples range tested was between 5 – 700 mg/dL. The results from regression analysis between the target values and the measured values are summarized below:

**UniCel® DxC 600 SYNCHRON System**

| | |
|---|---|
| Urine | $Y = 1.00x + 0.446$, $R^2=0.999$ |
| CSF | $Y = 1.01x + 1.516$, $R^2=0.999$ |
| Serum | $Y = 1.01x + 1.088$, $R^2=0.999$ |

**UniCel® DxC 800 SYNCHRON System**

| | |
|---|---|
| Urine | $Y = 0.991x + 2.198$, $R^2=0.999$ |
| CSF | $Y = 1.008x + 1.578$, $R^2=0.999$ |
| Serum | $Y = 1.004x + 2.197$, $R^2=0.999$ |

The results of the linearity study support the claimed measuring range of 5-700 mg/dL for glucose on the UniCel® DxC 600/800 SYNCHRON System analyzers.

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
Traceability:
The SYNCHRON Systems AQUA CAL 1 and 3 calibrators are traceable to NIST SRM 917a reference material and have been previously cleared in k965240.

d. *Detection limit:*
The Limit of Blank (LoB), Limit of Detection (LoD) and Limit of Quantitation (LoQ) of UniCel DxC SYNCHRON Systems Glucose reagent (GLUH) were determined according to CLSI EP17-A- Protocols for Determination of Limits of Detection and Limits of Quantitation. Studies were performed in the following manner:

To calculate the Limit of Blank (LoB), 4 blank samples were measured in triplicate for 5 days using 2 instrument lots on both UniCel® DxC 600 and 800 SYNCHRON System analyzers.

To estimate the LoD, 4 samples containing low levels of glucose were measured in triplicate for 5 days using 2 instrument lots on both UniCel® DxC 600 and 800 SYNCHRON System analyzers.

To estimate the LoQ, 4 samples containing low levels of glucose were measured in triplicate for 5 days using 2 instrument lots on both UniCel® DxC 600 and 800 SYNCHRON System analyzers.

Based on the study results, the following detection limit claims were made for both UniCel® DxC 600 and 800 SYNCHRON System analyzers.

| | Serum mg/dL | CSF mg/dL | Urine mg/dL |
|---|---|---|---|
| LoB | 0.19 | 0.17 | 0.19 |
| LoD | 1.74 | 1.68 | 1.78 |
| LoQ | 3.78 | 3.67 | 3.69 |

The detection limit studies support the claimed measuring range of 5-700 mg/dL.

e. *Analytical specificity:*
Interference studies were performed by evaluating 8 potential interfering substances spiked into patient serum pools at three different glucose levels, 40 to 60 mg/dL, 166 to 210 mg/dL and 400 to 480 mg/dL. Potential interferences were spiked into patient

serum pools to assess which substance would interfere with the UniCel DxC SYNCHRON Systems Glucose (GLUH) assay. Bias greater than +/- 10% between the spiked and unspiked samples defines significant interference. The following substances produced less than 10% difference when tested on the UniCel® DxC 600 and 800 SYNCHRON System analyzers at levels equal to the concentrations listed below.

| Substances | Highest Concentration Tested that showed non-significant interference |
|---|---|
| Hemoglobin | 500 mg/dL |
| Bilirubin | 24 mg/dL |
| Ascorbic Acid | 6.0 mg/dL |
| Urea | 500 mg/dL |
| Uric Acid | 40 mg/dL |
| EDTA | 16 mg/dL |
| Creatinine | 40 mg/dL |
| Lipemia | 200 mg/dL |

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

2. Comparison studies:
*a. Method comparison with predicate device:*

Serum:
A total of 120 serum samples spanning the measuring range were analyzed on the UniCel® DxC 600 and 800 SYNCHRON Systems using the candidate method and compared against the predicate method. A total of 20 samples were altered (10 samples were diluted and 10 samples were spiked). The linear regression analysis is as follows:

UniCel® DxC 600 SYNCHRON System:

Y = 0.982x – 1.02, R = 1.000, sample range tested of 5-697 mg/dL.

UniCel® DxC 800 SYNCHRON System:

Y = 0.999x – 1.60, R = 1.000, sample range tested of 5-691 mg/dL.

CSF:
A total of 100 CSF samples spanning the measuring range were analyzed on the UniCel® DxC 600 and 800 SYNCHRON Systems using the candidate method and compared against the predicate method. A total of 20 samples were altered (8 samples were diluted and 12 samples were spiked). The linear regression analysis is as follows:

UniCel® DxC 600 SYNCHRON System:

Y = 0.978x + 1.25, R = 1.000, sample range tested 8-693 mg/dL.

UniCel® DxC 800 SYNCHRON System:

Y = 1.002x – 0.61, R = 1.000, sample range tested 8-675 mg/dL.

Urine:
A total of 117 urine samples spanning the measuring range were analyzed on the UniCel® DxC 600 and 800 SYNCHRON Systems using the candidate method and compared against the predicate method. A total of 23 samples were altered (6 samples were diluted and 17 samples were spiked).The linear regression analysis is as follows:

UniCel® DxC 600 SYNCHRON System:

Y = 0.989x + 2.08, R = 1.000, sample range tested 12-689 mg/dL.

UniCel® DxC 800 SYNCHRON System:

Y = 0.973x + 2.86, R = 1.000, sample range tested 11-694 mg/dL.

*b. Matrix comparison:*
Matrix comparison studies were performed using 79 matched serum/plasma (Sodium Heparin, Lithium Heparin, and Sodium Fluoride/ Potassium Oxalate) samples and tested on the UniCel® DxC 600 SYNCHRON System and 58 matched serum/plasma samples (Sodium Heparin, Lithium Heparin, and Sodium Fluoride/ Potassium Oxalate) were analyzed on the UniCel®DxC 800 SYNCHRON System.

The following table summarizes the matrix comparaison studies:

| UniCel®DxC600 SYNCHRON System | | |
|---|---|---|
| Anticoagulant | N | Deming Regression Analysis |
| Sodium Heparin | 79 | y= 0.983x + 0.849, R= 0.999 |
| Lithium Heparin | 79 | y= 0.994x + 0.393, R= 0.999 |
| Sodium Fluoride/ Potassium Oxalate | 79 | y= 0.995x + 1.007, R= 0.999 |
| UniCel®DxC800 SYNCHRON System | | |
| Anticoagulant | N | Deming Regression Analysis |
| Sodium Heparin | 58 | y= 0.998x - 0.172, R= 0.999 |
| Lithium Heparin | 58 | y= 1.02x - 2.476, R= 1.000 |
| Sodium Fluoride/ Potassium Oxalate | 58 | y= 1.012x - 0.302, R= 0.999 |

The sponsor concluded that lithium heparin, sodium heparin and sodium fluoride/potassium oxalate plasma are acceptable to be used with the device on the

UniCel® DxC 600 and 800 SYNCHRON System.

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:

   Expected values are based on literature as follows:

| | SAMPLE TYPE | CONVENTIONAL | S.l. UNITS |
|---|---|---|---|
| Literature [1,2] | Serum or Plasma | 74- 106 mg/dL | 4.1 - 5.9 mmol/L |
| | Urine | 1 - 15 mg/dL | 0.06 - 0.83 mmol/L |
| | Urine (timed) | < 0.5 g/24 hrs | < 2.8 mmol/24 hrs |
| | CSF | 40- 70 mg/dL | 2.2 - 3.9 mmol/L |

[1] Tietz, N.W., ed., Fundamentals of Clinical Chemistry, 6th edition, W.B. Saunders, Philadelphia, PA (2007)

[2] Pagana, KD and Pagana, T J, Mosby's Manual of Diagnostic and Laboratory Tests 3rd Edition, Mosby Inc., St Louis, MO (2006)

**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.