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

A. 510(k) Number:
k100010

B. Purpose for Submission:
Modification to a previously cleared device (k040767)

C. Measurand:
High Density Lipoprotein Cholesterol (HDL)

D. Type of Test:
Quantitative and semi-quantitative spectrophotometry

E. Applicant:
Beckman Coulter, Inc.

F. Proprietary and Established Names:
SYNCHRON® Systems HDL Cholesterol (HDLX) Reagent

G. Regulatory Information:
1. Regulation section:
   21 CFR § 862.1475; Lipoprotein Test System
2. Classification:
   Class I; meets limitations of exemptions under 21 CFR § 862.9 (c)(2)
3. Product code:
   LBS; LDL & VLDL Precipitation, Cholesterol Via Esterase-Oxidase, HDL
4. Panel:
   Clinical Chemistry (75)

H. Intended Use:
1. Intended use(s):
   See Indications for use below.

2. Indication(s) for use:
   HDLX reagent, when used in conjunction with SYNCHRON LX® System(s), UniCel® DxC 800 System(s) and Genzyme Liquid N-geneous® HDL Cholesterol Calibrator is intended for quantitative determination of HDL Cholesterol in the high density lipoprotein fraction of human serum or plasma.

   HDL cholesterol measurements are used in the diagnosis and treatment of lipid disorders (such as diabetes mellitus), atherosclerosis, and various liver and renal diseases, and for the assessment of the risk of developing cardiovascular disease.

3. Special conditions for use statement(s):
   For Prescription Use Only

4. Special instrument requirements:
   For use with the Unicel DxC 800 and LX20 SYNCHRON Clinical Systems.

I. Device Description:

The device consists of the SYNCHRON® Systems HDLD Reagent (BCI PN 650207). This reagent was cleared under k040767. The new device uses the cleared reagent calibrated using the Genzyme Diagnostics N-geneous Cholesterol Calibrator (PN 5272, cleared under k971162) which is not supplied with the kit.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   Olympus HDL Cholesterol Assay

2. Predicate K number(s):
   k040692

3. Comparison with predicate:

Item	Device	Predicate (k040692)
Similarities		
Intended Use	HDLX reagent, when used in conjunction with SYNCHRON LX® System(s), UniCel® DxC 800 System(s) and Genzyme Liquid N-geneous® HDL Cholesterol Calibrator is intended for quantitative determination of HDL Cholesterol in the high density lipoprotein fraction of human serum or plasma.	same
Fundamental technology	Chromogenic colored change measured by spectrophotometer	same
Sample types	Serum, heparin and EDTA plasma	same
Reagents	LIQUID stable reagents (ready to use)	same
Differences		
Range	5 – 135 mg/dL	2.5 – 200 mg/dL
Sensitivity	5 mg/dL	1 mg/dL

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

- Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline (CLSI EP6-A).
- Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline – Second Edition (CLSI EP9-A2).
- Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline (CLSI EP17-A).

L. Test Principle:

The SYNCHRON® Systems HDL Cholesterol (HDLX) Reagent is a direct HDL Cholesterol method. It is a homogeneous assay without the need for any offline pretreatment or centrifugation steps. The method depends on a unique detergent which solubilizes only the HDL lipoprotein particles and releases HDL cholesterol to react with cholesterol esterase and cholesterol oxidase in the presence of chromogens, to produce a color product. The same detergent also inhibits the reaction of the cholesterol enzymes with LDL, VLDL, and chylomicrons lipoproteins by adsorbing to their surfaces. A polyanion contained in the reagent enhances the selectivity for HDL cholesterol assay by complexing LDL, VLDL, and chylomicrons lipoproteins.

This HDLX reagent is used to measure the cholesterol concentration by a timed-endpoint method. The change in absorbance at 560 nanometers is monitored. This change in absorbance is directly proportional to the concentration of cholesterol in the sample and is used to calculate the HDL-cholesterol concentration.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

The sponsor performed a precision study designed to verify that the within-run precision has not changed as a result of changing to the new calibrator. Commercially available multi-level control materials were used. Each control level was aliquoted into 4 samples and each sample was run in 5 replicates to generate a sample number (n) of 20. The study was conducted on one UniCel DxC 800 and one LX20 SYNCHRON Clinical System. The data is summarized below:

Mean (mg/dL)	Within-run variation		Mean (mg/dL)	Within-run variation	
	S.D.	%CV		S.D.	%CV
Unicel DxC 800			LX20 SYNCHRON Clinical System		
31.82	0.53	1.66	33.13	0.35	1.05
46.56	0.39	0.85	47.56	0.37	0.77
62.33	0.51	0.82	62.61	0.55	0.87
20.20	0.37	1.83	23.11	0.38	1.64
57.63	0.65	1.13	58.94	0.78	1.33
98.75	0.84	0.85	99.79	1.39	1.39

b. Linearity/assay reportable range:

The study was performed following CLSI protocol EP6-A. Commercially available linearity standards each containing 5 levels (10 different concentration levels in total)) of HDL spanning the reportable range of the assay were used. Each level was run in 3 replicates. The study was conducted on one UniCel DxC 800 and one LX20 SYNCHRON Clinical System. The recovered HDL values were plotted against the expected values and an appropriate line was fitted by standard linear regression. The results of the data analysis are summarized below:

Instrument	Range	Linear Regression Analysis
DxC 800	5.0 – 135 mg/dL	Y = 1.004x + 1.00 r = 0.9997
LX20	5.0 – 135 mg/dL	Y = 1.004x – 3.3 r = 0.9998

The claimed reportable range of the assay is 5.0 to 135 mg/dL.

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
The calibrators to be used with this assay are manufactured by Genzyme Corporation and have been previously cleared under k971162.

Calibration Frequency: The calibration is valid for 14 days on the UniCel DxC 800 and the LX20 SYNCHRON Clinical System.

The method has not been certified or tested by the Cholesterol Reference Method Laboratory Network. The package insert includes the following statement: "This method has not been certified or tested by the Cholesterol Reference Method Laboratory Network."

d. *Detection limit:*
The sponsor performed a study designed to verify that the limit of detection (LoD) has not changed as a result of changing to the new calibrator. The study was performed in accordance with the recommendations of CLSI EP17-A. The limit of the blank (LoB) was calculated from data using a blank sample (5% human serum albumin solution) run in replicates of 20. The LoD was calculated using a low level sample (a diluted commercially available plasma-based standard) run in replicated of 20 on one UniCel DxC 800 and one LX20 SYNCHRON Clinical System. The sponsor stated that 100% of the replicates of the low level sample exceeded the calculated LoB.

The claimed LoD of the assay is 5 mg/dL.

e. *Analytical specificity:*
Established in k040767

f. *Assay cut-off:*
Not applicable

2. Comparison studies:

a. *Method comparison with predicate device:*
Studies were performed to compare the performance of the proposed device to the predicate device using 100 serum patient samples. The samples were run in singlet on the proposed device using the UniCel DxC 800 and the LX20 SYNCHRON Clinical System and in replicates of 2 on the predicate device. The results of the linear regression including the 95% confidence interval (CI) are summarized below:

Instrument	Range (mg/dL)	Slope (95% CI)	Intercept (95% CI)	R
DxC 800	6.3 to 130	1.057 (1.030 to 1.085)	-4.927 (-6.696 to -3.159)	0.991
LX20	5 to 137	1.057 (1.020 to 1.095)	-5.465 (-7.870 to -3.060)	0.984

b. Matrix comparison:

Forty eight paired samples (serum, lithium heparin plasma, sodium heparin plasma and EDTA plasma) were drawn from healthy volunteers. The samples were run in singlet on the proposed device using the UniCel DxC 800 and the LX20 SYNCHRON Clinical System. The plasma recoveries were compared to the corresponding serum recoveries for the same donor. Results of the linear regression including the 95% confidence interval (CI) are summarized below:

Lithium heparin plasma vs. serum

Instrument	Range (mg/dL)	Slope (95% CI)	Intercept (95% CI)	R
DxC 800	7 to 137	0.991 (0.977 to 1.004)	1.011 (0.018 to 2.005)	0.999
LX20	9 to 125	0.999 (0.986 to 1.013)	-0.876 (-1.864 to 0.112)	0.999

Sodium heparin plasma vs. serum

Instrument	Range (mg/dL)	Slope (95% CI)	Intercept (95% CI)	R
DxC 800	7 to 137	0.988 (0.972 to 1.004)	1.198 (0.033 to 2.363)	0.998
LX20	9 to 125	1.000 (0.986 to 1.015)	-0.867 (-1.911 to 0.176)	0.999

EDTA plasma vs. serum

Instrument	Range (mg/dL)	Slope (95% CI)	Intercept (95% CI)	R
DxC 800	7 to 137	0.977 (0.963 to 0.992)	0.264 (-0.779 to 1.307)	0.999
LX20	9 to 125	0.994 (0.977 to 1.010)	-1.724 (-2.914 to -0.535)	0.998

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 intervals listed were taken from literature*.

Cardiovascular risk	Conventional units	S.I. units
Low	≥ 60 mg/dL	≥ 1.55 mmol/L
High	< 40 mg/dL	< 1.03 mmol/L

*NIH Publication No. 01 3305, *ATP III Guidelines At-A-Glance*, Quick Desk Reference, May (2001).

*NIH Publication No. 01 3670, Third Report of National Cholesterol Education Program (NCEP) Expert Panel on Detection, *Evaluation and Treatment of High Cholesterol in Adults (Adult Treatment Panel III)*, May (2001).

The package insert includes precautionary language that each laboratory should establish its own reference intervals based upon its patient population.

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.