

510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION DECISION SUMMARY

A. 510(k) Number:

K032035

B. Analyte:

Complement C3 and Complement C4

C. Type of Test:

Quantitative, rate turbidimetry (C3) and turbidimetry (C4)

D. Applicant:

Beckman Coulter Inc.

E. Proprietary and Established Names:

SYNCHRON LX® Systems Complement C3 (C3) Reagent

SYNCHRON LX® Systems Complement C4 (C4) Reagent

SYNCHRON LX® Systems Calibrator 1 (Cal 1)

F. Regulatory Information:

1. Regulation section:

21 CFR 866.5240, Complement components immunological test system

21 CFR 862.1150, Calibrator

2. Classification:

Class II

3. Product Code:

CZW, Complement C3, antigen, antiserum, control

DBI, Complement C4, antigen, antiserum, control

JIT, Calibrator, Secondary

4. Panel:

Immunology (82)

G. Intended Use:

C3 reagent, when used in conjunction with SYNCHRON LX® Systems and Calibrator 1, is intended for quantitative determination of Complement C3 concentration in human serum or plasma by rate turbidimetry.

C4 reagent, when used in conjunction with SYNCHRON LX® Systems and Calibrator 1, is intended for quantitative determination of Complement C4 concentration in human serum or plasma by rate turbidimetry.

The Beckman Coulter SYNCHRON LX® Systems Calibrator 1 (Cal 1), used in conjunction with SYNCHRON LX reagents, is intended for the calibration of the immunoprotein tests on SYNCHRON LX® Systems.

1. Indication(s) for use:

C3 reagent, when used in conjunction with SYNCHRON LX® Systems and Calibrator 1, is intended for quantitative determination of Complement C3 concentration in human serum or plasma by rate turbidimetry.

C4 reagent, when used in conjunction with SYNCHRON LX[®] Systems and Calibrator 1, is intended for quantitative determination of Complement C4 concentration in human serum or plasma by rate turbidimetry.

The Beckman Coulter SYNCHRON LX[®] Systems Calibrator 1 (Cal 1), used in conjunction with SYNCHRON LX reagents, is intended for the calibration of the immunoprotein tests on SYNCHRON LX[®] Systems.

2. Special condition for use statement(s):

Not applicable

3. Special instrument Requirements:

Use with automated, random access analyzers SYNCHRON LX 20 ((K965240), LX20 PRO (K011213) and LXi 725 (K023049). These systems were 510(k) cleared and belong to the same instrument family with the same intended use and measuring method. The LX20 PRO model differed from the LX20 by the addition of a near-infrared optics module. The LXi 725 model combines a LX20 PRO system, an Access[®] 2 Immunoassay analyzer and a sample handling module.

H. Device Description:

The SYNCHRON LX[®] Complement C3 or C4 Reagent kit consists of two Reagent Cartridges (100 tests each) and a lot-specific parameter card. The cartridge contains reaction buffer and polyclonal antibody to Complement C3 or C4. The assay kit has to be used with the analyzers in the SYNCHRON LX[®] family.

I. Substantial Equivalence Information:

1. Predicate device name(s):

Beckman IMMAGE[®] Complement C3 and C4 Reagents and Beckman Calibrator 1

2. Predicate K number(s):

K964842, K771603 and K791341 (the latter two are for the Calibrator)

3. Comparison with predicate:

DEVICE	PREDICATE
A. Similarities	
Intended Use. - Quantitative measurement of C3 or C4	Same
Sample Type – Serum and plasma (EDTA, sodium heparin and lithium heparin)	Same
Antibody Type and Source – Polyclonal, goat	Same
Reagent Form – Liquid, stable	Same
B. Differences	
Assay Method – Rate turbidimetry (C3) Turbidimetry (C4)	Rate nephelometry
Analytical Range – 10 - 350 mg/dL (C3) 5 - 120 mg/dL (C4)	35 - 350 mg/dL (C3) 10 - 130 mg/dL (C4)
Initial Dilution - 1:20 dilution	1:36 dilution
Extended Dilution Range –No	5.83 to 12,600 mg/dL (C3) 1.67 to 4680 mg/dL (C4)

DEVICE	PREDICATE
Instruments - LX family instruments (spectrophotometers)	IMMAGE Systems (nephelometers)
Precision (intra-assay %CV) – 0.96%-1.75% (C3)	2.5% - 2.9% (C3)
1.32% - 2.37% (C4)	2.5% - 3.4% (C4)
Precision (total %CV) – 1.23%-2.19% (C3)	3.0% - 3.6% (C3)
1.68% - 3.09% (C4)	3.4% - 5.2 % (C4)

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

None referenced.

K. Test Principle:

The SYNCHRON LX® System uses rate turbidimetry to measure C3 and turbidimetry to measure C4 in human serum or plasma. C3 or C4 in the sample combines with specific antibodies to C3 or C4 to form immunoprecipitin complexes. These complexes increase the intensity of light scatter in the reaction cuvette. The SYNCHRON LX® System monitors the change in absorbance at 340 nanometers. The change in absorbance is proportional to the concentrations of C3 or C4 in the sample. C3 or C4 concentrations are automatically calculated from the single-point adjusted, pre-determined calibration curves.

L. Performance Characteristics (if/when applicable):1. Analytical performance:a. *Precision/Reproducibility:*

Within-run and total precision studies were performed according to NCCLS Guideline EP5-A. For C3, 3 serum controls (low, medium and high) and a serum pool were assayed in duplicates, two runs per day for 20 days on a single instrument. The within-run % CV ranged from 0.96 to 1.75 and the total % CV from 1.23 to 2.19. For C4, 3 serum controls (low, medium and high) and 2 serum pools were assayed in duplicates, two runs per day for 20 days on a single instrument. The within-run % CV ranged from 1.32 to 2.37 and the total %CV ranged from 1.68 to 3.09. Results for both analytes were within acceptable limits.

b. *Linearity/assay reportable range:*

Linearity was evaluated by testing five serial dilutions of a high serum sample over the assay range. For C3, linear regression analysis yielded $y = 0.994x - 3.55$ mg/dL and $r = 0.999$ and for C4, $y = 1.0079x - 0.4617$ mg/dL and $r = 0.9988$. Results supported the linearity claim for the measuring range.

The assay measuring range for C3 is 10-350 mg/dL and for C4, 5-120 mg/dL.

c. *Traceability (controls, calibrators, or method):*

Calibrators are traceable to the IFCC reference preparation for plasma proteins, BCR-470 (EC-JRC-IRMM). Traceability process is based on prEN ISO 17511.

d. *Detection limit (functional sensitivity):*

Analytical sensitivity is defined as the lowest measurable concentration that can be distinguished from zero with 95% confidence and was determined from the mean instrument reaction absorbance (IR) of 20 replicates plus 2 SD of samples below and above the minimal dose detection (MDD) (see example below). Analytical sensitivity for C3 is 10 mg/dL and for C4 is 5 mg/dL.

Sample (C3)	Concentration (mg/dL)		Reaction Rate (Abs/min)
Below MDD	8.14	Mean IR (N=20)	0.00997
		SD	0.00088
		2SD	0.00177
		Mean IR + 2SD	0.01174
Above MDD	10.85	Mean IR (N=20)	0.01940
		SD	0.00088
		2SD	0.00177
		Mean IR + 2SD	0.01764
0.01764 > 0.01174 = PASS			

e. *Analytical specificity:*

Interference was determined either by spiking different concentrations of each interfering substance into aliquots of a positive serum pool or by mixing a positive sera with a sample containing the test substance in various proportions. Interfering substances tested include hemoglobin (500 mg/dL), bilirubin (30 mg/dL), triglyceride (3+ lipemic pool), IgM (500 mg/dL) and rheumatoid factor (300 IU/mL). Recovery results were acceptable if they were less than 9% change of the known specimen mean concentration. No significant interference was observed.

f. *Assay cut-off:*

Not applicable.

2. Comparison studies:

a. *Method comparison with predicate device:*

Method comparison studies were based on NCCLS EP9-A. Patient samples covering the assay range were tested by both predicate and new devices. Results were analyzed by Deming Regression analysis and summarized below.

Device	Concentration Range (mg/dL)	N	Slope (95% CI)	Intercept (95% CI)	Correlation Coefficient (r)
C3	10 – 350	146	1.052 (1.0317, 1.0738)	-0.459 (-3.425, 2.4227)	0.993
C4	5 – 120	179	01.088 (1.0668, 1.1099)	-1.119 (-1.8168, -0.4399)	0.991

b. *Matrix comparison:*

Anti-coagulant effects were evaluated by comparing EDTA, sodium heparin and lithium heparin plasma samples with serum samples.

For each anti-coagulant, plasma and serum samples were drawn from 56 healthy volunteers. Paired samples were analyzed using the C3 or C4 reagent on the LX System. The acceptance criterion was $r \geq 0.97$. Deming regression analysis and bias plot were used to evaluate the results which are summarized below.

Analyte	Anticoagulant	Level of Anticoagulant Tested	Deming Regression Analysis	
C3	Lithium	14 U/mL	$y = 0.966x + 0.28$	$r = 0.985$
	Sodium	14 U/mL	$y = 0.979x - 0.95$	$r = 0.979$
	EDTA	1.5 mg/mL	$y = 0.855x + 5.27$	$r = 0.988$
C4	Lithium	14 U/mL	$y = 0.899x + 1.21$	$r = 0.978$
	Sodium	14 U/mL	$y = 0.900x + 0.76$	$r = 0.992$
	EDTA	1.5 mg/mL	$y = 0.967x + 0.34$	$r = 0.985$

3. Clinical studies:

a. *Clinical sensitivity:*

Not performed.

b. *Clinical specificity:*

Not performed.

4. Clinical cut-off:

Not applicable.

5. Expected values/Reference range:

The reference interval values were previously established using the predicate device on 123 apparently healthy, non-smoking, adult male and female subjects. The values selected (95th percentile) were verified with the new devices. The C3 range is from 79-152 mg/dL and the C4 range is from 16-38 mg/dL.

M. Conclusion:

Based on the review of information provided in this 510 (k), the analytical performance of the SYNCHRON LX[®] Systems complement C3 (C3) Reagent, SYNCHRON LX[®] Systems Complement C4 (C4) Reagent and SYNCHRON LX[®] Systems Calibrator 1 (Cal 1) correlated with the performance of the IMAGE[®] Complement C3 and C4 Reagents and Beckman Calibrator and therefore, demonstrate that the new device is substantially equivalent to the marketed device.