

510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION DECISION SUMMARY

A. 510(k) Number:

k061852

B. Purpose for Submission:

New devices

C. Measurand:

Complement C3 and Complement C4

D. Type of Test:

Quantitative, Nephelometry

E. Applicant:

Dade Behring Inc

F. Proprietary and Established Names:

Dimension Vista™ C3 Flex® Reagent Cartridge

Dimension™ Vista C4 Flex® Reagent Cartridge

Dimension Vista Protein 1 Calibrator

Dimension Vista Protein 1 Control L

Dimension Vista Protein 1 Control M

Dimension Vista Protein 1 Control H

G. Regulatory Information:

1. Regulation section:

21 CFR 866.5240, Complement Components Immunological Test System

21 CFR 862.1150 Calibrator

21 CFR. 862.1660 Quality Control Material

2. Classification:

Class II

3. Product code:

CZW, complement C3 antigen, antiserum, control

DBI, Complement C4 antigen, antiserum, control

JIX, Calibrator, Multi-Analyte Mixture

JJY, Multi-Analyte Controls, all kinds (assayed and unassayed)

4. Panel:

Immunology (82)

Chemistry (75)

H. Intended Use:

1. Intended use(s):

Dimension Vista™ C3 Flex® reagent cartridge is for quantitative measurement of complement C3 serum and heparinized plasma on the Dimension Vista™ System. Measurements of C3 are used as an aid in the diagnosis of immunologic disorders associated with C3 complement protein.

Dimension Vista™ C4 Flex® reagent cartridge is for quantitative measurement of complement C4 in serum and heparinized plasma on the Dimension Vista™ System. Measurements of C4 are used as an aid in the diagnosis of immunologic disorders

associated with C4 complement protein.

Dimension Vista™ Protein 1 Calibrator is an in vitro diagnostic product for the calibration of the C3 complement (C3), C4 complement (C4), Immunoglobulin A (IgA), Immunoglobulin G (IgG) and Immunoglobulin M (IgM) on the Dimension Vista™ System.

Dimension Vista™ Protein 1 Control L, M and H are for use as an assayed intralaboratory quality controls for the assessment of precision and analytical bias in determination of C3 complement (C3), C4 complement (C4), Immunoglobulin A (IgA), Immunoglobulin G (IgG) and Immunoglobulin M (IgM) on the Dimension Vista™ System.

2. Indication(s) for use:

To aid in the diagnosis of immunologic disorders associated with complement C3 and C4 Proteins

3. Special conditions for use statement(s):

For prescription use only

4. Special instrument requirements:

For use with Dade Behring Dimension Vista™ System.

I. Device Description:

The Dade Dimension C3 and C4 devices are in the form of cartridges each with 12 wells: 1-8 contains reaction buffer, 9-12 contains antiserum to human C3 or C4. The cartridges hold all the reagents for a test method. A bar code label on the cartridge identifies the test method, lot number, expiration date, and the maximum number of tests for which the cartridge can supply reagents.

Dimension Vista Protein 1 Calibrator carton contains 6 vials of reagent with 2mL per vial. The calibrator is a liquid human serum based product containing multiple analytes namely C3, C4, IgA, IgM and IgG.

Dimension Vista Protein 1 Controls consist of three levels (low, medium and high). Each level contains 6 vials with 2 mL per vial. The controls are ready to use human serum based products containing C3, C4, IgA, IgM, IgG.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Dade Behring N Antisera to Human Complement Factors (C3c, C4)

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

k050665 (C3 and C4)

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended use	For quantitative determination of C3 and C4 protein as an aid in	Same

Similarities		
Item	Device	Predicate
	the diagnosis of C3 and C4 associated immunological disorders	
Antibody	Rabbit polyclonal	Same
Methodology	Nephelometric	Same
Traceability	CRM 470 IFCC/BCR/CAP	Same

Differences		
Item	Device	Predicate
Instrument	Dimension™ Vista System	BN™System
Sample type	Serum and lithium heparin plasma	Serum and plasma (EDTA and heparin)
Reportable range	C3-0.16-4.1 g/L C4- 0.06-1.6g/L	C3c - 0.12 – 4.1g/L C4 - 0.06 - 1.9g/L

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

CLSI EP5-A2, CLSI EP9-A2, CLSI EP7-A2.

L. Test Principle:

The method used for quantitative measurement of C3 and C4 is immunonephelometry. The samples when mixed with reagents (automatically done by the instrument) in the cartridge an immunological reaction results in forming an immune complexes with C3 or C4 contained in the sample. A light beam is passed through the complex and the intensity of light scattering is measured at 840nm. The intensity of scattered light is proportional to the concentration of the respective analyte in the sample. C3 or C4 concentrations are automatically calculated by the instrument from the multiple calibration curves.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Precision studies were performed according to CLSI EP5-A2. During each day of testing two separate samples for each test material were analyzed for 20 days. For C3, samples tested included 4 serum pools and 3 controls (low, medium and high). For C4, 3 controls (L, M, H), 2 plasma samples and 2 serum samples with different analyte concentrations. The acceptance criteria are shown below.

The maximum observed repeatability (SD)

Analyte	Concentration	Acceptable SD Maximum
C3	0.75g/L	0.16g/L
	1.2g/L	0.18g/L
C4	0.15g/L	0.02g/L
	0.23g/L	0.03g/L

The following table is a summary of the precision data:

Material	Mean g/L	Within-run SD (%CV)	Run-to-Run SD (%CV)	Day-to-Day SD (%CV)	Total Precision SD (%CV)
C3					
Protein1 Con L	0.946	0.0321 (3.4)	0.0172 (1.8)	0.0107 (1.1)	0.0380 (4.0)
Protein 1 Con M	1.499	0.035 (2.3)	0.009 (0.6)	0.000 (0.0)	0.036 (2.4)
Protein 1 Con H	1.843	0.043 (2.3)	0.000 (0.0)	0.002 (0.1)	0.043 (2.4)
Serum pool 1	1.993	0.030 (1.5)	0.039 (2.0)	0.028 (1.4)	0.057 (2.9)
Serum pool 2	1.979	0.057 (2.9)	0.018 (0.9)	0.013 (0.7)	0.061 (3.1)
Serum pool VL	0.289	0.017 (5.9)	0.000 (0.0)	0.003 (1.1)	0.017 (6.0)
Serum pool VH	3.939	0.091 (2.3)	0.078 (2.0)	0.000 (0.0)	0.120 (3.0)
C4					
Protein 1 Con L	0.1301	0.0048 (3.7)	0.0000 (0.0)	0.0017 (1.3)	0.0051 (3.9)
Protein 1 Con M	0.2052	0.0039 (1.9)	0.0017 (0.8)	0.0034 (1.7)	0.0054 (2.6)
Protein 1 Con H	0.3201	0.0051 (1.6)	0.0042 (1.3)	0.0015 (0.5)	0.0068 (2.1)
Serum low	0.1389	0.0047 (3.4)	0.0033 (2.4)	0.0000 (0.00)	0.0057 (4.1)
Serum high	1.4038	0.0449 (3.2)	0.0094 (0.7)	0.0000 (0.0)	0.0459 (3.3)
Plasma low	0.1272	0.0049 (3.8)	0.0025 (1.9)	0.0011 (0.9)	0.0056 (4.4)
Plasma high	0.4202	0.0131 (3.1)	0.0206 (4.9)	0.0000 (0.0)	0.0244 (5.8)

b. Linearity/assay reportable range:

Linearity across the assay range was determined by testing serial dilutions of a high C3 and a high C4 sample over the assay measuring range. Each dilution was tested in replicates of five. Percent recovery was calculated as mean of observed/expected concentration x 100. The mean percents recovery for C3 and C4 were 94.9% (ranged from 87.2% to 100%) and 99.5% (ranged from 92.7% to 104.1%). Linear regression analysis showed for C3, the slope was 0.989, the intercept was -0.0332 and r^2 of 0.999. For C4, the slope was 1.0108, intercept was -0.0019 and r^2 0.9996.

Measuring range (reportable range): for C3 = 0.16-4.1 g/L for initial 1:20 dilution of samples that are automatically processed by the instrument. Samples with results in excess of 4.1g/L can be repeated on a higher dilution (1:200). Samples with results less than 0.16 g/L can be repeated on a lower dilution (1:5). Samples with results less than 0.04 g/L will be reported as “less than 0.04 g/L” by the instrument.

For Compliment 4 the measuring range is 0.06-1.6 g/L. This is the measuring range for the initial 1:10 dilution of samples that are automatically processed by the instrument. Samples with excess of 1.6 g/L can be repeated on a higher dilution (1:100). Samples with results less than 0.06 g/L can be repeated on a lower dilution (1:2.5). Samples less than 0.015 g/L will be reported as “less than 0.015 g/L” by the instrument.

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

Reference standard used was ERM®-DA470 (CRM 470). C3 and C4 values of the master lots of the calibrator and controls are assigned against the reference standard.

d. Detection limit:

The detection limits was determined by assaying the diluent and Cal 1 twenty times each. The analytical sensitivity for C3 was 0.047 g/L and 0.003 g/L for C4.

e. *Analytical specificity:*

Interferences by endogenous substances namely conjugated bilirubin (60 mg/dL), unconjugated bilirubin (60 mg/dL), creatinine (30 mg/dL), hemoglobin (1000 mg/dL), IgG (5 g/dL), albumin (6 g/dL), urea (500 mg/dL), cholesterol (500 mg/dL), uric acid (20 mg/dL) and triglycerides (924 mg/dL) were spiked into aliquots of a serum sample and assayed for C3 and C4. The spiked samples were compared to the unspiked sample and % recoveries were calculated. The acceptance criterion for % recovery was $\pm 10\%$. Results showed no interference at the concentrations tested. Interference due to RF and total protein was also determined and no significant interference was observed.

In addition, drug interference was assessed. No observable interference with the drugs tested.

f. *Assay cut-off:*
Not applicable

2. Comparison studies:

a. *Method comparison with predicate device:*

Method comparison between Dimension Vista and BN ProSpec was performed on 116 samples for C3 (58 serum and plasma n=58). Passing-Bablok regression analysis yielded a slope of 0.960 (95% CI: 0.943, 0.975) and intercept of 0.041 (95% CI: 0.016, 0.069).

For C4, 66 serum samples and 60 plasma samples were tested. Passing-Bablok analysis of the results yielded a slope of 1.041 (95% CI: 1.025, 1.059) and intercept 0.006 (95% CI: 0.001, 0.016).

b. *Matrix comparison:*

Anti-coagulant effects were evaluated using 10 samples, comparing serum and plasma (lithium heparin and sodium heparin) with C3 concentrations ranging from 0.31-3.96 g/L. Linear regression analysis was performed and results are summarized below.

Analyte	Matrix	Linear Regression Analysis		
		Slope	Intercept	Correlation coefficient (r)
C3	Serum vs. lithium plasma	1.00 (95% CI: 0.99, 1.01)	-0.02	1.00
	Serum vs. sodium plasma	1.02 (95% CI: 0.99, 1.06)	-0.06	1.00
C4	Serum vs. lithium plasma	1.08 (95% CI: 1.04, 1.11)	-0.04	1.00
	Serum vs. sodium plasma	1.08 (95% CI: 1.03, 1.14)	-0.05	1.00

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 interval quoted is from literature for healthy subjects (same for both serum and plasma).
Expected values:
C3 = 0.9-1.8g/L
C4 = 0.1-0.4g/L
- 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.