

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

A. 510(k) Number:

k061825

B. Purpose for Submission:

New Submission

C. Measurand:

C-Reactive Protein

D. Type of Test:

Quantitative Immuno-nephelometric assay

E. Applicant:

Dade Behring, Inc.

F. Proprietary and Established Names:

Dimension Vista CRP Flex Reagent Cartridge, Protein 2 Calibrator, Control Low
And Control High

G. Regulatory Information:

1. Regulation section:

21CFR§-866.5270-C-reactive protein immunological test system

21CFR§-862.1150-Calibrator

21CFR§-862.1660-Quality control material (assayed and unassayed)

2. Classification:

Class II, II, and I reserved, respectively

3. Product code:

DCN- System, Test, C-Reactive Protein

JIX - Calibrator, Multi-Analyte Mixture

JJY - Multi-Analyte Controls, All Kinds (Assayed And Unassayed)

4. Panel:

Chemistry (75)

H. Intended Use:

1. Intended use(s):

See indications for use below

2. Indication(s) for use:

Dimension Vista™ CRP Flex® reagent cartridge:

The CRP method is an in vitro diagnostic test for the quantitative measurement of C-reactive protein (CRP) in human serum and heparinized plasma by means of particle enhanced immunonephelometry on the Dimension Vista™ System. In acute phase response, increased levels of a number of plasma proteins, including C-reactive protein, are observed. Measurement of CRP is useful for the detection and evaluation of infection, tissue injury, and inflammatory disorders.

Dimension Vista™ Protein 2 Calibrator:

Protein 2 Calibrator is an in vitro diagnostic product for the calibration of the C-reactive protein (CRP) method on the Dimension Vista™ System.

Dimension Vista™ Protein 2 Control L and Dimension Vista™ Protein 2 Control H:

Protein 2 Control L and H are for use as assayed intra laboratory quality controls for the assessment of precision and analytical bias in determination of C-reactive protein (CRP) on the Dimension Vista™ System.

3. Special conditions for use statement(s):

Prescription use

4. Special instrument requirements:

Dade Dimension Vista™ System

I. Device Description:

Reagents are in the following cassette format

Wells	Form	Ingredient	Concentration	Source
1-8	Liquid	CRP Supplement Reagent: Phosphate buffer Polidocanol	1.9 g/L	
9-12	Liquid	CRP Reagent: Polystyrene particles Monoclonal antibodies	1 g/L 13 mg/L	Mouse

PROT2 CAL is a liquid, human serum based product containing C-reactive protein.

CONROL L &H are liquid, human serum based product containing C-reactive protein

J. Substantial Equivalence Information:

1. Predicate device name(s):
Dade Behring CardioPhase® hsCRP assay, N Rheumatology Standard SL and N/T Rheumatology Control SL
2. Predicate 510(k) number(s):
k033908, k964527, k962373
3. Comparison with predicate:

Feature	Dade Behring CardioPhase® hsCRP Assay	Dimension Vista™ CardioPhase® hsCRP Assay
1. Intended Use:	CardioPhase® hsCRP is an <i>in vitro</i> diagnostic reagent for the quantitative determination of C-reactive protein (CRP) in human serum, and heparin and EDTA plasma by means of particle enhanced immunonephelometry using BN™ Systems. In acute phase response, increased levels of a number of plasma proteins, including C-reactive protein, is observed. Measurement of CRP is useful for the detection and evaluation of infection, tissue injury, inflammatory disorders and associated diseases. High sensitivity CRP (hsCRP) measurements may be used as an independent risk marker for the identification of individuals at risk for future cardiovascular disease. Measurements of hsCRP, when used in conjunction with traditional clinical laboratory evaluation of acute coronary syndromes, may be useful as an independent marker of prognosis for recurrent events, in patients with stable coronary disease or acute coronary syndromes.	The CRP method is an <i>in vitro</i> diagnostic test for the quantitative measurement of C-reactive protein (CRP) in human serum and heparinized plasma by means of particle enhanced immunonephelometry on the Dimension Vista™ System. In acute phase response, increased levels of a number of plasma proteins, including C-reactive protein, are observed. Measurement of CRP is useful for the detection and evaluation of infection, tissue injury, and inflammatory disorders.
2. Principle:	Same	Same
3. Standardization:	Same	Same
4. Antibody:	Same	Same
5. Reportable Range:	0.16 – 200 mg/L	3.1 – 190 mg/L
6. Calibrator:	N Rheumatology Standard SL	Dimension Vista™ Protein 2 Calibrator
Form:	Liquid, human serum	Liquid, human serum
Constituents:	RF, ASL and CRP	CRP

Feature	Dade Behring CardioPhase [®] hsCRP Assay	Dimension Vista [™] CardioPhase [®] hsCRP Assay
Traceable to:	known as CRM 470	CRM 470
Levels:	1	1
7. Control:	N/T Rheumatology Control SL 1/2	Dimension Vista [™] high sensitivity CRP Control L and H
Form:	Liquid, human serum	Liquid, human serum
Constituents:	RF, ASL and CRP	CRP
Traceable to:	International Reference Preparation – RF and ASL CRM 470 - CRP	CRM 470
Levels	Low and High	Low and High
8. Analyzer:	BN [™] Systems	Dimension Vista [™] System

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

CLSI - Evaluation of Precision Performance of Clinical Chemistry Devices - EP05-A2

CLSI - Interference Testing in Clinical Chemistry - EP07-A2

L. Test Principle:

Polystyrene particles coated with monoclonal antibodies specific to human CRP are aggregated when mixed with samples containing CRP. These aggregates scatter a beam of light passed through the sample. The intensity of the scattered light is proportional to the concentration of the respective protein in the sample. The result is evaluated by comparison with a standard of known concentration.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Precision testing was done in accordance with CLSI/NCCLS Approved Guideline for Evaluation of Precision Performance of Clinical Devices: EP5-A2. Specimens at each level were analyzed in duplicate, twice a day, for 20 days. The repeatability and within-lab standard deviations (SD) and percent coefficient of variation (%CV) were calculated by the analysis of variance method. The data are summarized below.

CRP Precision Data Summary

Material	Mean mg/L	Repeatability SD (%CV)	Within-Lab SD (%CV)
PROT2 CON L	11.91	0.57 (4.8)	0.72 (6.0)
PROT2 CON H	49.47	1.83 (3.7)	2.14 (4.3)
Serum pool	5.69	0.30 (5.3)	0.38 (6.7)
Serum pool	44.79	2.17 (4.9)	2.32 (5.2)
Serum pool	176.7	6.5 (3.7)	6.8 (3.8)

b. *Linearity/assay reportable range:*

The reportable range of 3.1 – 190 mg/L is based on linearity and method comparison.

Linearity across the assay range was confirmed by testing serum samples with high concentrations of CRP. These samples were serially diluted with System Diluent down to the lower measuring range (171.6 to 4.8 mg/L). Each dilution was tested in replicates of five. Percent recovery was calculated using the formula: Mean of test/ expected concentration X 100. All dilutions met the acceptance criterion of recovery of 80 to 120%.

The linear regression [x-axis: theoretical concentration versus y-axis: measured concentration] was also calculated. The acceptance criteria of slope between 0.9 and 1.1 and correlation coefficient ≥ 0.95 were met. A summary of the linearity data is presented below.

Slope	Intercept	Correlation Coefficient
1.041	1.745	0.995

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

Standard values are assigned to a master calibrator lot using CRM 470. Values are then assigned to the commercial calibrator (human pooled at target concentration) versus master calibrator using three reference curves, 4 runs, 3 vials, 4 replicates per vial tested on two nephelometric instruments for a total of 144 measurements.

Control values are assigned to a master control lot using CRM 470. Values are then assigned to the commercial control (human pooled at target concentration) versus master control using three reference curves, 4 runs, 3 vials, 4 replicates per vial tested on two nephelometric instruments for a total of 144 measurements.

Standard stability is tested real time for stored at +2 to +8°C and opened/punctured on board instrument.

d. *Detection limit:*

Limit of Detection: 3.1 mg/L

The limit of detection represents the lower limit of the reportable range of CRP based on the sensitivity, functional sensitivity, and historical variability of the calibrator, which represents the lower cutoff point of the reportable range of CRP.

e. *Analytical specificity:*

HIL Interference

The CRP method was evaluated for interference according to CLSI/NCCLS EP7-A2. Bias is the difference in the results between the control sample (without the interferent) and the test sample (contains the interferent)

expressed in percent. Bias exceeding 10% is considered interference.

Substance Tested	Substance Concentration	S. I. Units	CRP Concentration mg/L	Bias %
Hemoglobin (hemolysate)	1000 mg/dL	0.62 mmol/L	13.68	-1
Bilirubin (unconjugated)	60 mg/dL	1026 µmol/L	13.70	-6
Bilirubin (conjugated)	60 mg/dL	1026 µmol/L	13.70	-1
Lipemia (Triglycerides)	1455 mg/dL	16.44 mmol/L	52.96	-1

Non Interfering Substances

The following substances do not interfere with the CRP method when present in serum and plasma at the concentrations indicated. Inaccuracies (biases) due to these substances are less than 10% at CRP concentration of 3.09 mg/L to 125.47 mg/L.

Substance	Test Concentration	S. I. Units
Acetaminophen	0.025 mg/dL	1.66 µmol/L
Amikacin	15 mg/dL	256 µmol/L
Ammonium heparin	3 U/mL	3000 U/L
Ampicillin	5.3 mg/dL	152 µmol/L
Ascorbic acid	5 mg/dL	227 µmol/L
Caffeine	6 mg/dL	308 µmol/L
Carbamazepine	3 mg/dL	127 µmol/L
Chloramphenicol	5 mg/dL	155 µmol/L
Chlordiazepoxide	1 mg/dL	33.3 µmol/L
Chlorpromazine	0.2 mg/dL	6.27 µmol/L
Cholesterol	500 mg/dL	12.9 mmol/L
Cimetidine	2 mg/dL	79.2 µmol/L
Creatinine	30 mg/dL	2652 µmol/L
Dextran 40	6000 mg/dL	1500 µmol/L
Diazepam	0.5 mg/dL	17.6 µmol/L
Digoxin	5 ng/dL	6.15 nmol/L
Erythromycin	6 mg/dL	81.6 µmol/L
Ethanol	400 mg/dL	86.8 mmol/L
Ethosuximide	25 mg/dL	1770 µmol/L
Furosemide	6 mg/dL	181 µmol/L
Gentamicin	12 mg/dL	251 µmol/L
Ibuprofen	50 mg/dL	2425 µmol/L
Immunoglobulin G (IgG)	5 g/dL	50 g/L
Lidocaine	1.2 mg/dL	51.2 µmol/L
Lithium chloride	2.3 mg/dL	3.2 mmol/L
Lithium heparin	3 U/mL	3000 U/L

Substance	Test Concentration	S. I. Units
Nicotine	0.1 mg/dL	6.2 µmol/L
Penicillin G	25 U/mL	25000 U/L
Pentobarbital	8 mg/dL	354 µmol/L
Phenobarbital	10 mg/dL	431 µmol/L
Phenytoin	5 mg/dL	198 µmol/L
Primidone	4 mg/dL	183 µmol/L
Propoxyphene	0.2 mg/dL	4.91 µmol/L
Protein Albumin	6 g/dL	60 g/L
Protein Total	10 g/dL	100 g/L
Rheumatoid Factor	500 IU/mL	500 IU/mL
Salicylic acid	60 mg/dL	4.34 mmol/L
Sodium heparin	3 U/mL	3000 U/L
Theophylline	4 mg/dL	222 µmol/L
Urea	500 mg/dL	83.3 mmol/L
Uric Acid	20 mg/dL	1190 µmol/L
Valproic acid	50 mg/dL	3467 µmol/L

The CRP method shows no hook effect up to 1347.9 mg/L.

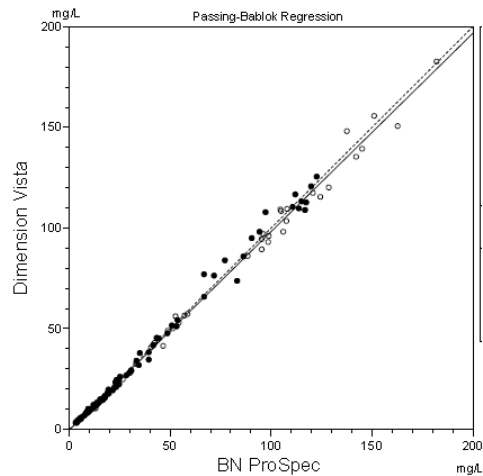
- f. Assay cut-off:*
See limit of detection above.

2. Comparison studies:

a. Method comparison with predicate device:

The Dimension Vista™ CRP assay was compared to the Dade Behring CardioPhase® hsCRP assay on the BN ProSpec® System by evaluating serum and plasma samples with concentrations ranging from 3.36 to 182.76 mg/L. Regression analysis of these results yielded the following equation:

Method Comparison Study				
	n	Slope	Intercept	Correlation Coefficient
Dimension Vista™ CRP	140	0.985	-0.353	0.997



b. Matrix comparison:

Sample	Serum	Li Hep	Na Hep
1	5.74	5.74	5.65
2	35.21	34.38	34.19
3	9.51	9.51	9.44
4	8.86	8.13	8.32
5	12.93	11.97	12.18
6	5.20	5.51	5.10
7	87.96	87.79	89.10
8	113.90	116.23	110.93
9	130.36	128.40	128.74
10	157.35	155.94	159.25
11	177.41	172.07	178.74

Linear Regression vs Serum

Slope:	0.99	1.00
Y-int:	0.14	-0.58
r:	1.000	1.000
Syx:	1.71	1.42
Slope 95% CI		
Low:	0.97	0.99
Slope 95% CI		
High:	1.00	1.02

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 for healthy individuals as noted in the literature are typically ≤ 3 mg/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.