

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY**

A. 510(k) Number:

k062035

B. Purpose for Submission:

New Device

C. Measurand:

Rheumatoid Factor

D. Type of Test:

Quantitative, nephelometry

E. Applicant:

Dade Behring Inc.

F. Proprietary and Established Names:

Dimension Vista™ Rheumatoid Factors Flex ® reagent cartridge

Dimension Vista™ Protein 2 Calibrator

Dimension Vista™ Protein 2 Control L

Dimension Vista™ Protein 2 Control H

G. Regulatory Information:

1. Regulation section:

21 CFR § 866.5775 –Rheumatoid Factor Immunological test system

21 CFR § 862.1150 –Calibrator

21 CFR § 862.1660 –Quality Control Material

2. Classification:

Class II

3. Product code:

DHR - System, Test, Rheumatoid Factor

JIX - Calibrator, multi-analyte mixture

JJY - Multi-analyte controls, all kinds (assayed and unassayed)

4. Panel:

Immunology (82)

H. Intended Use:

1. Intended use(s):

Flex® reagent cartridge: The RF method is an in vitro diagnostic reagent for the quantitative determination of rheumatoid factors (RF) in human serum and lithium heparin plasma on the Dimension Vista™ System. Measurements are used as an aid in the diagnosis of rheumatoid arthritis.

Protein 2 Calibrator: PROT2 CAL is an in vitro diagnostic product for the calibration of the C-reactive protein (CRP), high sensitivity CRP (hsCRP) and Rheumatoid Factors (RF) methods on the Dimension Vista™ System.

Protein 2 Controls L and H: PROT2 CON L and H are assayed intra-laboratory quality controls for the assessment of precision and analytical bias in the determination of C-reactive protein (CRP) and Rheumatoid Factor (RF) on the Dimension Vista™ System.

2. Indication(s) for use:

Same as Intended Use.

3. Special conditions for use statement(s):
Prescription use only
4. Special instrument requirements:
Dimension Vista™ System

I. Device Description:

Dimension Vista™ Rheumatoid Factors Flex® reagent cartridge (RF): RF reagent consists of polystyrene particles coated with an immunocomplex consisting of human-IgG/anti-human IgG from sheep and RF supplement reagent consisting of a phosphate buffer and polyethylene glycol.

Dimension Vista™ Protein 2 Calibrator:

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

Dimension Vista™ Protein 2 Control L and H:

PROT2 CON L and H are liquid, multi-analyte, human serum based products containing C-reactive protein and Rheumatoid Factors in two concentration ranges: low and high.

J. Substantial Equivalence Information:

1. Predicate device name(s) and 510(k) numbers:
 ROCHE Tina-Quant RF II assay k032535
 N Rheumatology Standard SL k964527
 N/T Rheumatology Control SL k962373
2. Comparison with predicate:

Dimension Vista™ Rheumatoid Factors Flex® reagent cartridge

Similarities		
Item	Device	Predicate
Intended Use	For the quantitative determination of rheumatoid factors (RF) in human serum and lithium heparin plasma	For the quantitative in vitro determination of rheumatoid factors in human serum and plasma
Indications for Use	Measurements are used as an aid in the diagnosis of rheumatoid arthritis.	Same
Measurement type	Quantitative	Same
Stability: Unopened	90 days 2-8°C	Same

Differences		
Item	Device	Predicate
Method	Immunonephelometry	Immunoturbidimetry
Capture Antibody	Immune complexes of human immunoglobulin and sheep anti-human IgG antibody	Human IgG
Instrument system	Dimension Vista™ System	ROCHE/Hitachi 917 analyzer

Differences		
Item	Device	Predicate
Plasma	lithium heparin plasma	lithium heparin plasma and EDTA plasma
Measuring Range	10-600 IU/mL	7-650 IU/mL
Expected values	<15 IU/mL	<14 IU/mL
Stability: Open	21 days 2-8°C	90 days 2-8°C

Dimension Vista™ Protein 2 Calibrator

Similarities		
Item	Device	Predicate
Intended Use	For the calibration of the specified methods	For establishment of reference curves for specific immunonephelometric determinations
Composition	Pooled Human sera	Same
Reagent Preparation	Liquid, Ready-for-Use	Same
Traceability	1 st British Standard 64/002	Same

Differences		
Item	Device	Predicate
Analytes	C-reactive protein (CRP), high sensitivity CRP (hsCRP) and Rheumatoid Factors (RF)	Rheumatoid factors (RF), anti-Streptolysin O (ASL) and C-reactive protein (CRP)
Instrument system	Dimension Vista™ System	BN Systems
Stability: Open	12 days 2-8°C	14 days 2-8°C
Materials Provided	6 vials, 2 mL per vial	3 vials, 1 mL per vial

Dimension Vista™ Protein 2 Control L and H

Similarities		
Item	Device	Predicate
Intended Use	Assayed intra-laboratory quality controls for the assessment of precision and analytical bias in the determination of specific assays	Assayed controls for accuracy and precision in the quantitative determination of specific analytes
Composition	Pooled human sera	Same
Reagent Preparation	Liquid, Ready to use	Same
Concentration Range	Low and High	Same

Differences		
Item	Device	Predicate
Analytes	C-reactive protein (CRP) and Rheumatoid Factor (RF)	Rheumatoid factors (RF), anti-streptolysin O (ASL) and C-reactive protein (CRP)
Instrument system	Dimension Vista™ System	BN Systems and the TurbiTime System
Stability Open	12 days 2-8°C	14 days 2-8°C
Materials Provided	6 vials, 2 mL per vial	3 vials, 1 mL per vial

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

CLSI Evaluation of Precision Performance of Clinical Devices Approved Guideline: EP5-A2; CLSI Method Comparison and Bias Estimation Using Patient Samples Approved Guideline EP9-A2; CLSI Interference Testing in Clinical Chemistry Approved Guideline EP7-A2.

L. Test Principle:

Polystyrene particles coated with an immunocomplex consisting of human-IgG/anti-human IgG from sheep are aggregated when mixed with samples containing RF. 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 performed in accordance with CLSI EP5-A2. Four samples derived from serum pools representing RF concentrations that span the measuring range, and the PROT2 CON L and H were analyzed in duplicate, for 20 days, two times per day. The repeatability and within-lab standard deviations (SD) and percent coefficient of variation (%CV) were calculated. Repeatability imprecision was <6%, and within-lab imprecision was ≤6.2%.

Material	Mean IU/mL	Repeatability		Within-Lab	
		SD	%CV	SD	%CV
PROT2 CON L	73.7	1.5	2.0	1.6	2.2
PROT2 CON H	183.9	3.5	1.9	3.9	2.1
Serum pool* VL	14.5	0.9	5.9	0.9	6.2
Serum pool VL	30.5	0.8	2.6	1.8	5.9
Serum pool L	90.0	2.1	2.3	2.3	2.6
Serum pool H	544.3	21.7	4.0	23.9	4.4

*Tested for 5 days

b. *Linearity/assay reportable range:*

Linearity across the assay range of 10-600 IU/mL was confirmed by testing a

calibrator with high concentration of RF. The calibrator was serially diluted in 7, two-fold increments (measuring range from 8.36 to 836.86 IU/mL). Each dilution was tested in replicates of three. Data were analyzed using linear regression analysis with the following results:

Slope	Y-Intercept IU/mL	Correlation Coefficient	n
1.040	-2.348	1.0	21

A recovery study using 1st British Standard 64/002 (5 replicates) showed that % recovery ranged from 96.4 to 98.6% with a mean recovery of 97.9%

- c. *Traceability, Stability, Expected values (controls, calibrators, or methods):* Calibration material values were referenced to the 1st British Standard 64/002.
- d. *Detection Limit*
Limit of Detection: 10 IU/mL represents the lower limit of the reportable range of the RF assay.
Analytical sensitivity was determined by assaying analyte-free System Diluent 20 times and determining the mean value plus two SDs: 0.814 IU/mL.
- e. *Analytical specificity:*
 - i. Interference Studies: Interference testing was performed according to CLSI EP7-A2, to determine the effect of various exogenous substances on the Dimension Vista™ RF assay. The following exogenous interferents were tested by spiking into test samples containing two concentrations of RF (one at the clinical decision point 12-15 IU/mL and one higher), and compared to a control sample without interferent: bilirubin (conjugated and unconjugated, 60 mg/dL), hemoglobin (1000 mg/dL), creatinine (30 mg/dL), albumin (6 g/dL), urea (500 mg/dL), cholesterol (500 mg/dL), uric acid (20 mg/dL). Minimal interference (<8%) was observed. Interference by triglycerides (native and clarified) was tested on 5 test samples containing RF concentrations between 12 and 25 IU/mL, and minimal interference (<7%) was observed. Additionally, 41 potentially interfering drugs were also assayed and shown to exhibit minimal interference (<10%).
 - ii. Cross-reactivity with autoimmune antibodies common to other systemic autoimmune diseases was not tested.
 - iii. Antigen Excess: the effect of antigen excess was evaluated using a serum sample above the assay range. No effect was seen up to 2877 IU/mL. Samples above this level are reported as exceeding assay range (>600 IU/mL).
- f. *Assay cut-off:*
The assay cut-off of 15 IU/mL was determined by measuring 300 normal blood donors from Europe and taking the mean between the 95th and 97.5th percentile value.
2. Comparison studies:
 - a. *Method comparison with predicate device:*
The Dimension Vista™ RF assay was compared to the ROCHE Tina-Quant

RF II assay on the Hitachi 917 Analyzer by assaying 120 serum samples with concentrations ranging from 10-520 IU/mL on both systems. Passing Bablock regression analysis of these results yielded the following statistics:

Comparative Method	Slope (95% CI)	Y-Intercept (IU/mL) (95% CI)	Correlation Coefficient	n
ROCHE Tina-Quant RF II/Hitachi 917	0.953 (0.898 to 1.024)	-9.71 (-16.192 to -6.021)	0.95	120

b. Matrix comparison:

Fourteen matched serum and lithium heparin plasma samples, containing concentrations of RF spanning the measuring range (10-515 IU/mL), were assayed and compared. Regression analysis showed no significant bias between the two matrices and yielded the following information:

% recovery in Li-Hep plasma vs. serum	Slope (95% CI)	Y-Intercept (IU/mL)	Correlation Coefficient	n
Mean = -2.5% (Range = -9.7% to 2.3%)	0.98 (0.94-1.01)	-0.04	1.00	14

3. Clinical studies:

a. Clinical Sensitivity:

Not provided

b. Clinical specificity:

Not provided

c. Other clinical supportive data (when a. and b. are not applicable):

Not applicable.

4. Clinical cut-off:

See Assay cut-off

5. Expected values/Reference range:

Testing of serum from 300 European blood donors resulted in a 95th percentile of <10 IU/ml and a 97.5th percentile of 19.5 IU/ml. The expected value of the normal healthy adults is <15 IU/ml.

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.