

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

**A. 510(k) Number:**

k061338

**B. Purpose for Submission:**

This is a new device.

**C. Measurand:**

Immunoglobulin A

**D. Type of Test:**

Quantitative, nephelometry

**E. Applicant:**

Dade Behring Inc.

**F. Proprietary and Established Names:**

Dimension VISTA™ Immunoglobulin A Flex® reagent cartridge (IgA)

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:

21CFR§ 866.5510 Immunoglobulins A, G, M, D, E Immunological Test System.

21CFR§ 862.1660, Quality Control Material (Assayed and Unassayed)

21CFR§ 862.1150, Calibrator

2. Classification:

Device and calibrator - Class II

Quality control material - Class I

1. Product code:

CFN, Method, Nephelometric, Immunoglobulins (G, A, M)

JJY, Multi-Analyte Controls (Assayed and Unassayed)

JIX, Calibrator, Multi-Analyte Mixture

4. Panel:

Immunology (82)

Chemistry (75)

**H. Intended Use:**

1. Intended use(s):

***Dimension VISTA™ Immunoglobulin A Flex® reagent cartridge (IgA):***

The IgA method is an *in vitro* diagnostic test for the quantitative measurement of immunoglobulin A in human serum and plasma on the Dimension VISTA™ system. Measurements of IgA aid in the diagnosis of abnormal protein metabolism and the body's lack of ability to resist infectious agents.

***Dimension VISTA™ Protein 1 Calibrator:***

PROT1 CAL is an *in vitro* diagnostic product for the calibration of Immunoglobulin A (IgA) and Immunoglobulin G (IgG) methods on the

VISTA™ system.

***Dimension VISTA™ Protein 1 Control L, Dimension VISTA™ Protein 1 Control M, Dimension VISTA™ Protein 1 Control H:***

For use as an assayed intralaboratory quality control for assessment of precision and analytical bias in the determination of Immunoglobulin A (IgA) and Immunoglobulin G (IgG) on the VISTA™ system.

2. Indication(s) for use:  
Same as above
3. Special conditions for use statement(s):  
For prescription use only.
4. Special instrument requirements:  
For use in the Dimension VISTA™ system (k051087)

**I. Device Description:**

The Dimension VISTA™ Immunoglobulin A Flex® reagent cartridge (IgA) consists of N antiserum to human IgA, reaction buffer with phosphate buffer and polyethylene glycol. All reagents are liquid and ready to use. PROT1 CAL is a liquid, human serum based product containing Immunoglobulin A and Immunoglobulin G (k051087). PROT1 CAL is ready for use.

Dimension VISTA™ Protein 1 Control L, Dimension VISTA™ Protein 1 Control M, and Dimension VISTA™ Protein 1 Control H are multi-analyte; liquid human serum-based product containing Immunoglobulin A and Immunoglobulin G (k051087). Values assigned to IgA and IgG are calibrated by reference to protein preparations and are lot dependent. The controls are ready for use.

The controls and calibrator are sold separately.

**J. Substantial Equivalence Information:**

1. Predicate device name(s):  
Dade Behring N Antisera (IgG, IgM, IgA) assay  
N Protein Standard SL  
N/T Protein Control SL
2. Predicate 510(k) number(s):  
k042735  
k012470  
k012468
3. Comparison with predicate:

Similarities		
Item	Device	Predicate
	Dimension Vista IgA assay	N Antisera to IgG, IgM, IgA (Dade Behring)
Indications for Use	Aid in the diagnosis of abnormal protein metabolism and the body's lack of ability to resist infectious agents.	Same

Similarities		
Item	Device	Predicate
Methodology	Nephelometry	Same
Storage conditions	Refrigerate at 2-8°C until expired	Same
Standardization	Traceable to IFCC/BCR/CAP CRM 470	Same
Antibody	Rabbit polyclonal	Same
Components	Controls and standards are sold separately.	Same

Differences		
Item	Device	Predicate
Intended Use	Quantitative measurement of IgA	Quantitative measurement of IgA, IgG, IgM
Sample type	Serum and lithium heparin plasma	Serum and plasma (EDTA, heparin) and CSF
Reportable range	0.25 – 7.5 g/L	0.25 – 0-8.0 g/L
Instrument	VISTA™ systems	BN™ systems

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

CLSI Approved Guideline for Evaluation of Precision Performance of Clinical Devices: EP5-A2

CLSI EP7-A, Interference testing in Clinical Chemistry

**L. Test Principle:**

Proteins contained in human body fluids form immune complexes in an immunochemical reaction with specific antibodies. These complexes 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 Approved Guideline for Evaluation of Precision Performance of Clinical Devices: EP5-A. Specimens at each level were analyzed in duplicate, twice a day, for 20 days. The within-run and total standard deviations (SD) and percent coefficient of variation (%CV) were calculated by the analysis of variance method. Additional testing covering the low and high end of the reportable range was performed. The data are summarized below

Material	Mean (g/L)	Repeatability		Within-lab	
		SD	%CV	SD	%CV
PROT1 Con L	1.22	0.07	5.4	0.07	5.9

Material	Mean (g/L)	Repeatability		Within-lab	
		SD	%CV	SD	%CV
PROT1 Con M	1.88	0.05	2.7	0.05	2.7
PROT1 Con H	2.47	0.05	1.9	0.06	2.4
Serum pool	2.37	0.04	1.7	0.06	2.3
Serum pool	2.99	0.08	2.7	0.08	2.8
Serum pool (VL)	0.670	.04	5.7	0.04	5.7
Serum pool (VH)	7.44	0.18	2.4	0.20	2.7

*b. Linearity/assay reportable range:*

Linearity testing was performed on the Dimension VISTA® System using a serum sample containing 9.32 g/L of IgA. The sample was serially diluted 12 times. Each dilution was tested in replicates of five and percent recovery calculated. All dilutions met the acceptance criterion of 80 to 120%.

The linear regression was calculated. The acceptance criteria of slope between 0.9 and 1.1 and correlation coefficient  $\geq 0.95$  were met. Data showed a regression equation  $y = 1.0161x - 0.038$ ,  $r^2$  of 0.9975.

Linearity was observed at 0.21 to 9.32 g/L. Reportable range for the device was set at 0.25 to 7.5 g/L.

Prozone effect

The possibility of Prozone effect occurring when using the device was evaluated with a serum sample above the assay range. The sample was analyzed on both the BN Prospec System and the Dimension Vista instrument, indicating no hook effect up to 35.8 g/L.

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

The reference material is the IFCC/BCR/CAP CRM 470. Master Calibrator concentrated human serum pool was assayed vs. CRM 470. Commercial Calibrator Lot was prepared from human serum pool at target concentrations and assayed against the master lot.

Stability studies were performed and the following conclusions were obtained:

- On-Board Instrument Stability of opened product
  - a. The Immunoglobulin A Flex reagent cartridge are stable on –board the instrument for 21 days.
  - b. PROT1 CAL is stable for 9 days.
  - c. Controls are stable for 14 days.

Study duration is labeled product shelf life plus one month. 24

months shelf life requires testing a minimum of 1 month past 24 months. Product is stored at 2-8°C throughout the testing cycle and tested on day 0 and after 6, 9, 12, 18, 24 and 25 months.

d. *Detection limit:*

Detection limit (0.25 g/L) represents the lower limit of the reportable range of IgA.

The analytical sensitivity of the assay represents the lowest concentration of IgA that can be distinguished from zero. This is defined as the mean value (n=20) plus two standard deviations of the low level 1 (1:200 dilution) using PROT1 CAL and system diluent. This was found to be 0.043 g/L.

e. *Analytical specificity:*

Interference: Interference testing was performed using guidance supplied by CLSI EP7-A, “Interference testing in Clinical Chemistry”. No significant interference was observed in:

- Hemoglobin up to 1000mg/dL
- Bilirubin (conjugated and unconjugated) up to 60 mg/dL
- Triglycerides up to 709mg/dL
- Rheumatoid Factor interference is below 10% up to 6.820 g/L.

No cross-reactivity studies have been conducted with heterophile antibodies.

Non Interfering Substance section of the package insert provides a list of drugs and other exogenous substances that do not interfere with the assay.

f. *Assay cut-off:*

Not applicable.

2. Comparison studies:

a. *Method comparison with predicate device:*

The table below shows the comparison of 50 serum samples and 50 plasma samples ranging from 0.276 to 6.864 /L that were tested with the Dimension Vista™ Immunoglobulin A Flex® reagent cartridge (IgA) and the predicate device Dade Behring N Antisera to Human IgA. No information about age and gender was provided. The results were summarized below:

	<b>Dimension Vista vs. BN system(Dade-Behring)</b>
Slope	1.022 (95% CI: 1.009 to 1.034)
Intercept	-0.036 (95% CI: -0.059 to -0.009)
Range (g/L)	0.276 to 6.864 g /L
r	0.998
N	100

b. *Matrix comparison:*

Matrix comparison studies using matched serum, lithium and sodium heparinized plasma samples covering the measuring range were

performed on the Dimension Vista™ IgA assay. The results of the linear regression analyses are seen on the table below.

Assay	Serum versus	n	Slope	Intercept	Correlation Coefficient
IgA	Lithium Heparin	13	1.04	-0.10	0.996
	Sodium Heparin	13	1.01	-0.05	0.999

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 reported expected range for Immunoglobulin A in adults (0.7 – 4.0 g/L) is from a literature:

Dati F. Schumann G, Thomas L, et al. Consensus of a Group of Professional Societies and Diagnostic Companies on Guidelines for Interim Reference Ranges for 14 Proteins in Serum base on the Standardization against the IFCC/BCR/CAP Reference Material (CRM 470). Eur J Clin Chem Biochem 34:517-520, 1996.

During childhood and adolescence, reference ranges for IgA are dependent on age and can vary over a wide range.

Each laboratory should establish its own normal ranges since values may differ depending on the population studied.

**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.