

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

A. 510(k) Number:

k063610

B. Purpose for Submission:

This is a new device.

C. Measurand:

Human α_1 – antitrypsin

D. Type of Test:

Quantitative immunonephelometry

E. Applicant:

Dade Behring Inc.

F. Proprietary and Established Names:

Dimension VISTA™ α_1 – antitrypsin Flex® reagent cartridge (A1AT)

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§ 866.5130, Alpha-1-antitrypsin 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:

DEM, Alpha-1-antitrypsin, Antigen, Antiserum, Control

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™ α_1 – antitrypsin Flex® reagent cartridge (A1AT)

The A1AT method is an *in vitro* diagnostic test for the quantitative determination of alpha-1-antitrypsin in human serum, heparinized plasma or EDTA plasma on the Dimension VISTA™ system. Measurements of alpha-1-antitrypsin aid in the diagnosis of adult cirrhosis of the liver and pulmonary emphysema.

Dimension VISTA™ Protein 1 Calibrator:

PROT1 CAL is an *in vitro* diagnostic product for the calibration of the α_1 – antitrypsin (A1AT), C3 Complement (C3), C4 Complement (C4), Immunoglobulin A (IGA), Immunoglobulin G (IGG), Immunoglobulin M (IGM), and Prealbumin (PREALB) methods on the Dimension VISTA™ system.

Dimension VISTA™ Protein 1 Control L, M and H

PROT1 CON L, M and H are assayed intralaboratory quality controls for assessment of precision and analytical bias in the determination of the α_1 – antitrypsin (A1AT), C3 Complement (C3), C4 Complement (C4), Immunoglobulin A (IGA), Immunoglobulin G (IGG), Immunoglobulin M (IGM), and Prealbumin (PREALB) on the Dimension 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™ α_1 – antitrypsin Flex® reagent cartridge (A1AT) consists of N antiserum to human α_1 – antitrypsin, and reaction buffer with phosphate buffer and polyethylene glycol. All reagents are liquid and ready to use.

PROT1 CAL is a multi-analyte, liquid, human serum based product containing α_1 – antitrypsin (A1AT), C3 Complement (C3), C4 Complement (C4), Immunoglobulin A (IGA), Immunoglobulin G (IGG), Immunoglobulin M (IGM), and Prealbumin (PREALB).

PROT1 CAL is ready for use.

Dimension VISTA™ Protein 1 Control L,M and H are multi-analyte; liquid human serum-based products containing α_1 – antitrypsin (A1AT), C3 Complement (C3), C4 Complement (C4), Immunoglobulin A (IGA), Immunoglobulin G (IGG), Immunoglobulin M (IGM), and Prealbumin (PREALB). The controls are ready for use.

The other analytes in the calibrator and controls were cleared under the following premarket notifications: C3 and C4 (k061852), IgA (k061338), IgG (k051087), IgM (k061845) and Prealbumin (k062055)

The controls and calibrator are sold separately.

J. Substantial Equivalence Information:

1. Predicate device name(s):
Dade Behring N Antisera to Human α_1 –antitrypsin assay
N Protein Standard SL

N/T Protein Control SL

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

k053072

k012470

k012468

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
	Dimension VISTA™ α_1 – antitrypsin Flex® reagent	N Antisera to α_1 – antitrypsin
Indications for Use	Aid in the diagnosis of adult cirrhosis of the liver and pulmonary emphysema in conjunction with other clinical and laboratory findings.	Same
Methodology	Nephelometry	Same
Storage conditions	Refrigerate at 2-8°C until expired	Same
Standardization	Traceable to ERM® DA470	Same
Antibody	Rabbit polyclonal	Same
Sample type	human serum, heparinized plasma or EDTA plasma	Same
Components	Controls and standards are sold separately.	Same

Differences		
Item	Device	Predicate
Analyzer	Dimension VISTA™ system.	BN™ Systems
Calibrator	Dimension VISTA™PROT1 CAL	N Protein Standard SL
Calibrator constituents	A1AT, C3, C4, IgA, IgG, IgM and prealbumin	IgG, IgG1, IgG2, IgG3, IgG4, IgA, IgM, albumin, A1AT, α_2 -macroglobulin, α_1 acid glycoprotein, haptoglobin, prealbumin, hemopexin, ceruloplasmin, retinol binding protein, Ig light-kappa, Ig light-chain Lambda, soluble transferrin receptor,

Differences		
Item	Device	Predicate
		ferritin, β_2 -microglobulin and total protein
Controls	Dimension VISTA™ PROT1Control L, M and H	N/T Protein control SL L, M and H
Control constituents	A1AT, C3, C4, IgA, IgG, IgM and prealbumin	IgG, IgG1, IgG2, IgG3, IgG4, IgA, IgM, albumin, A1AT, α_2 -macroglobulin, α_1 acid glycoprotein, haptoglobin, prealbumin, hemopexin, ceruloplasmin, retinol binding protein, Ig Light-kappa, Ig Light-chain Lambda, soluble transferrin receptor, ferritin, β_2 -microglobulin and total protein
Reportable range	0.17-5.20 g/L	0.16-5.20 g/L

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 with concentrations close to the reportable range 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. The data are summarized below

Material	Mean (g/L)	Repeatability		Within-lab	
		SD	%CV	SD	%CV
PROT1 Con L	0.99	0.03	2.95	0.03	3.36
PROT1 Con M	1.42	0.04	3.09	0.05	3.27
PROT1 Con H	2.21	0.05	2.20	0.06	2.68
Serum pool	0.33	0.01	2.74	0.01	3.61
Serum pool	4.48	0.07	1.63	0.10	2.28
Plasma pool	1.23	0.02	1.72	0.05	3.80

b. *Linearity/assay reportable range:*

Linearity testing was performed on the Dimension VISTA® System by testing a calibrator with a concentration of 1.48 g/L α_1 – antitrypsin. The calibrator was serially diluted with system diluent at the following six dilutions 1:3.8, 1:8, 1:20, 1:40, 1:90 and 1:200. Each dilution was tested in replicates of three and a median is calculated. Data was analyzed using linear regression analysis (x-axis: theoretical concentration and y-axis: measured concentration). The acceptance criteria of slope between 0.9 and 1.1 and correlation coefficient ≥ 0.95 were met. Data showed a regression equation $y = 1.019x - 0.029$, r^2 of 1.00.

Additional linearity study for the Vista A1AT assay was performed by testing a serum sample with a high concentration of A1AT. The sample was serially diluted with system diluent down to the lower measuring range (4.52 to 0.22 g/L). Each dilution was tested in replicates of five. Data was analyzed using linear regression analysis (x-axis: theoretical concentration and y-axis: measured concentration). The acceptance criteria of slope between 0.9 and 1.1 and correlation coefficient ≥ 0.95 were met. Data showed a regression equation $y = 1.015x - 0.043$, r^2 of 0.99.

Linearity was observed at 0.15 to 7.978g/L. Reportable range for the device was set at 0.17 to 5.20 g/L

Prozone effect

The possibility of Prozone effect occurring when using the device was evaluated with a serum sample above the assay range (10.2 g/L). The sample was analyzed on both the BN Prospec System and the Dimension Vista instrument, indicating no hook effect up to 11.03 g/L.

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

The reference material is the ERM®-DA470 (CRM 470). Master Calibrator and Master Control concentrated human serum pool were assayed against this reference material. Commercial Calibrator and Control Lots were prepared from human serum pool at target concentrations and assayed against the master lot. Three reference curves, 4 runs, 3 vials, 4 replicates per vial tested on two instruments for

a total of 144 values were used before release of shipment.

Stability studies were performed and the following conclusions were obtained:

- On-Board Instrument Stability of opened product:
 - a. The Dimension VISTA™ α_1 – antitrypsin Flex® reagent cartridge is stable on –board the instrument for 21 days.
 - b. PROT1 CAL is stable for 9 days.
 - c. Controls are stable for 9 days.

Study duration is 24 months. Product is stored at 2-8°C throughout the testing cycle and tested on day 0 and after 12, 18, and 24 months.

- Sealed reagent cartridge on board instrument is stable up to 90 days.
- Open Punctured well:
 - a. Once the vial stopper is punctured, assigned values of PROT1 CAL and PROT1 Con L, M and H is stable for 9 days.

d. *Detection limit:*

The analytical sensitivity of the assay represents the lowest concentration of analyte that can be distinguished from zero. The value was calculated as the mean value (n=20) of System diluent plus two standard deviations. This was found to be 0.016 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 1000 mg/dL
- Bilirubin (conjugated and unconjugated) up to 60 mg/dL
- Triglycerides up to 637 mg/dL
- Immunoglobulin G up to 5000 mg/dL
- Protein: Albumin up to 6000 mg/dL
- Urea up to 500 mg/dL
- Cholesterol up to 500 mg/dL
- Creatinine up to 10 mg/dL
- Uric acid up to 20 mg/dL

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 66 serum samples and 73 plasma samples ranging from 0.23 to 4.71 g /L that were tested with the Dimension Vista™ α_1 – antitrypsin Flex® reagent cartridge (A1AT) and the predicate device Dade Behring N Antisera to Human α_1 – antitrypsin

assay. No information about age and gender was provided. The results were summarized below:

	Dimension Vista vs. BN system(Dade-Behring)
Slope	1.000(95% CI: 0.9853 to 1.0283)
Intercept	0.070 (95% CI: 0.0346 to 0.0938)
Range (g/L)	0.23to 4.71g /L
r	0.996
N	139

b. Matrix comparison:

Matrix comparison studies using matched serum, EDTA, lithium and sodium heparinized plasma samples covering the measuring range were performed on the Dimension Vista™ α_1 – antitrypsin Flex® assay. The results of the linear regression analyses are seen on the table below.

	n	Slope (95% CI)	Intercept	Correlation Coefficient
Serum vs. Lithium Heparin	10	1.0 (0.968-1.02)	0.02	0.999
Serum vs. Sodium Heparin	10	1.03 (1.008-1.05)	-0.02	0.999
Serum vs. EDTA	10	0.99 (0.976-1.00)	-0.01	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 reported expected range for Immunoglobulin A in adults (0.9 – 2.0 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).

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.