

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

A. 510(k) Number:

k073561

B. Purpose for Submission:

Cerebrospinal fluid (CSF) sample matrix is added to existing devices. In addition, modifications are made to the serum/plasma assay measuring ranges; stability of on-board and open-well reagent cartridges.

C. Measurand:

Immunoglobulin IgG

D. Type of Test:

Quantitative, Nephelometry

E. Applicant:

Dade Behring, Inc.

F. Proprietary and Established Names:

Dimension Vista® System Immunoglobulin G Flex® Reagent Cartridge

Dimension Vista® Protein 1 Calibrator

Dimension Vista® Protein 3 Control

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
CFN: Method Nephelometric, Immunoglobulins (G, A, M)	Class II, Devices	21 CFR § 866.5510, Immunoglobulins A, G, M, D, and E Immunological test system.	Immunology (82)
JIX: Calibrator, Multi-analyte Mixture	Class II, Calibrator	21 CFR § 862.1150, Calibrator	Chemistry (75)
JJY: Multi-analyte Controls, All kinds (Assayed and Unassayed)	Class I, Quality Control Material	21 CFR § 862.1660, QC material (Assayed and Unassayed)	Chemistry (75)

H. Intended Use:

1. Intended use(s):

Dimension Vista® System Immunoglobulin G Flex® reagent cartridge:

The IGG method is an *in vitro* diagnostic test for the quantitative measurement of immunoglobulin G in human serum, heparinized plasma and cerebrospinal fluid (CSF) on the Dimension Vista® System. Measurements of IgG aid in the diagnosis of abnormal protein metabolism and the body's lack of ability to resist infectious agents.

Dimension Vista® System Protein 1 Calibrator (PROT1 CAL):

PROT1 CAL is an *in vitro* diagnostic product for the calibration of the Dimension Vista® System for: α_1 -Acid Glycoprotein (A1AG), α_1 -Antitrypsin (A1AT), β_2 -Microglobulin (B2MIC), C3 Complement (C3), C4 Complement (C4), Ceruloplasmin (CER), Haptoglobin (HAPT), Hemopexin (HPX), Homocysteine (HCYS), Immunoglobulin A (IgA), Immunoglobulin E (IgE), Immunoglobulin G (IgG) [serum/ plasma] and (IgG-C) [cerebrospinal fluid], Immunoglobulin G Subclass 1 (IgG1), Immunoglobulin G Subclass 2 (IgG2), Immunoglobulin G Subclass 3 (IgG3), Immunoglobulin G Subclass 4 (IgG4), Immunoglobulin M (IGM), Prealbumin (PREALB), Retinol Binding Protein (RBP), soluble Transferrin Receptor (STFR), and Transferrin (TRF).

Dimension Vista® System Protein 3 Control (PROT3 CON):

PROT3 CON is an assayed, low level intralaboratory quality control for assessment of precision and analytical bias on the Dimension Vista® System in the determination of α_1 -Microglobulin(A1MIC), specialty Albumin (sALB)*, Immunoglobulin G (IgG -C)* and Microalbumin (MALB).

* For Cerebrospinal fluid (CSF)

2. Indication(s) for use:
Same as Intended Use.
3. Special conditions for use statement(s):
For Prescription only.
4. Special instrument requirements:
Dimension Vista® Analyzer (k051087)

I. Device Description:

Dimension Vista® System Immunoglobulin G Flex® reagent cartridge carton contains 2 cartridges (12 wells/cartridge). Wells 1 through 8 contain buffers and polyethylene glycol. Wells 9 through 12 contain liquid rabbit polyclonal antisera to human IgG. Reagent is in ready-to-use liquid form.

Dimension Vista® System Protein 1 Calibrator carton contains 6 vials with 2 mL per vial, with multi-analyte, serum based product containing A1AG, A1AT, B2MIC, C3, C4, CER, HAPT, HPX, IgA, IgE, IgG, IgM, PREALB, RBP, STRF, TRF, IgG1, IgG2, IgG3, IgG4 and HPX. Reagent is in ready-to-use liquid form.

Dimension Vista® System Protein 3 Control carton contains 4 vials with 1 mL per vial, with multi-analyte polygelatin and rabbit albumin based product containing urinary α_1 -A1AG and serum albumin and IgG of human origin. Reagent is in lyophilized form.

J. Substantial Equivalence Information:

1. Predicate device name(s):
Dade Behring N Antisera to Human Immunoglobulins (IgG, IgA, and IgM)
Dade Behring Dimension Vista® System Protein 1 Calibrator
Dade Behring Dimension Vista® System Protein 3 Control
2. Predicate 510(k) number(s):
k042735 (Antisera)
k071980 (Protein Standard)
k072435 (Control)

3. Comparison with predicate:

Similarities		
Item	New Device	Predicate Device
Technology	Nephelometric	Same
IgG antisera mammal source	Rabbit polyclonal	Same
Calibrator material source	Human serum	Same
Control material source	Human serum and rabbit albumin	Same
International Reference standard material	Traceable to ERM® DA 470 (CRM 470)	Same
Storage conditions	Refrigerate at 2-8°C until expired.	Same
Components	Controls and standards are sold separately	Same

Differences		
Item	New Device	Predicate
Intended Use/Indication for Use: Reagent IgG Antisera	Dimension Vista™ IgG Flex® reagent cartridge: The IgG method is an <i>in vitro</i> diagnostic test for the quantitative determination of Immunoglobulin G in human serum, heparinized plasma and cerebrospinal fluid (CSF) on the Dimension Vista™ System. Measurements of IgG aid in the diagnosis of abnormal protein metabolism and the body's lack of ability to resist infectious agents.	<i>In vitro</i> diagnostic reagents for the quantitative determination of immunoglobulins (IgA, IgG, IgM) in human serum, heparinized and EDTA plasma as well as IgG in cerebrospinal fluid (CSF) by means of immunonephelometry on the Dade Behring BN Systems.
Calibrator	The PROT 1 CAL is an <i>in vitro</i> diagnostic product for the calibration of the Dimension Vista® System for: A1AG, A1AT, B2MIC, C3, C4, CER, HAPT, HPX, HCYS, IgA, IgE, IgG [serum/ plasma] and	For the calibration of the Dimension Vista® System for: A1AG, A1AT, B2MIC, C3, C4, CER, HAPT, HPX, HCYS, IgA, IgE, IgG, IgG1, IgG2, IgG3, IgG4, IgM, PREALB, RBP, STFR, and TRF.

Differences		
Item	New Device	Predicate
	(IgG-C) [cerebrospinal fluid], IgG1, IgG2, IgG3, IgG4, IgM, PREALB, RBP, STFR and TRF	
Control	PROT3 CON is an assayed, low level intralaboratory quality control for assessment of precision and analytical bias on the Dimension Vista [®] System in the determination of A1MIC, sALB*, IgG -C* and MALB. *For CSF	For assessment of precision and analytical bias on the Dimension Vista [®] System in the determination A1MIC, sALB*, and MALB. *For CSF
Sample type	Serum, plasma (lithium heparin), and CSF	Serum, plasma (EDTA; lithium heparin), and CSF
Analyzer	Dimension Vista [™] System	Dade Behring BN [™] Systems
Measuring ranges	Serum/ plasma: 1.4 – 40.0 g/L Undiluted CSF: 4.4 – 123 mg/L	Serum/ plasma: 1.4 – 46.0 g/L Undiluted CSF: 3.6 – 115.0 mg/L

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

Standard Document:

CLSI/NCCLS, EP 9-A2: Method Comparison

CLSI/NCCLS, EP 5-A2: Precision Performance of Quantitative Measurement

CLSI/NCCLS, EP 7-A: Interference Testing

Guidance Document:

OIVD/ DIHD Guidance Document Number 785: 510(k) Submission for IgA,G,M,D,E Immunological System IVD (9/1/1992)

OIVD Guidance Document Number 2231: For Industry and FDA Staff: Assayed and Unassayed Control Material (6/7/2007)

L. Test Principle:

Proteins contained in human body fluids react with specific antibodies in the reagent, to form immune complexes in an immunochemical reaction. These complexes in the reaction mixture cause the scatter of a beam of light passed through the samples. The intensity of the scattered light is proportional to the concentration of IgG 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:*

Reproducibility testing was done in accordance with CLSI document EP5-A. The intra-assay reproducibility was determined by testing four samples in duplicate twice a day for 20 days. The samples included one serum pool (12.99 g/L), two human source CSF pools (19.28 mg/L and 110.58 mg/L), and one Protein 3 Control (20.25 mg/L). The serum pool had %CV of 2.7%; CSF pools 3.1% and 3.9%; Prot 3 control 1.2%,

The inter-assay reproducibility was determined by testing the same four samples in duplicate twice a day for 20 days. The serum pool had %CV of 3.4%; the CSF pools 3.9% and 3.2%; Prot 3 Control 3.9%. The data are summarized below:

Material	Mean	Intra-assay		Inter-assay	
		SD	%CV	SD	%CV
Serum pool	1299 mg/dL	1.870	2.7	1.870	3.4
CSF pool 1	19.28 mg/L	3.152	3.1	3.152	3.9
CSF pool 2	110.58 mg/L	14.744	2.3	14.744	3.2
PROT 3 CON	20.25 mg/L	3.304	1.2	3.304	3.9

b. Linearity/assay reportable range:

Linearity across the assay range was confirmed by testing a human CSF with high concentration (129 mg/L) of IgG. This sample was serially diluted 12 times with System Diluent down to the lower measuring range (4.39 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 criteria of 80 to 120%.

The linear regression analysis was performed. The acceptance criteria of slope between 0.9 and 1.1 and correlation of coefficient ≥ 0.95 were met. Data showed a regression equation $y = 1.0041 + 0.3351x$, r^2 of 0.9995.

Reportable range for IgG-C device was set at 4.4 - 123 mg/L

Antigen Excess Effect:

The possibility of antigen excess occurring when using the device was evaluated with serum and CSF samples above the assay range. The sample was analyzed on both the BN ProSpec® System and the Dimension Vista™ instrument, indicating no antigen excess effect up to 1960 mg/L for CSF IgG and 78.3 g/L for serum IgG.

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

The calibrator is traceable to the reference material ERM® DA 470 (CRM 470).

Stability

The expiration date claims for the reagents are as follows:

Unopened reagent cartridges and closed vials:

Dimension Vista™ IgG Flex® reagent cartridge (IGG) – 24 months

Dimension Vista™ Protein 1 Calibrator – 24 months

Dimension Vista™ Protein 3 Control – 24 months

On-board Instrument products:

Dimension Vista™ IgG Flex® reagent sealed wells – 90 days

Dimension Vista™ IgG Flex® open well reagent cartridge – 21 days

Dimension Vista™ Protein 1 Calibrator open vial – 9 days

Dimension Vista™ Protein 3 Control open vial – 14 days

d. Detection limit:

Detection limit (4.4 mg/L) represents the lower limit of the reportable range of CSF IgG. The analytical sensitivity is defined as the minimal detectable level of analyte, which can be distinguished from zero. The value was calculated as the mean value of fifteen replicates of three CSF samples and system diluent. It was determined to be 3.87 mg/L.

e. Analytical specificity:

Interference testing was performed according to CLSI document EP7A2. No significant interference was observed in the presence of the following interferents: Bilirubin (conjugated and unconjugated) up to 60 mg/dL, Hemoglobin up to 750 mg/dL.

Non-interfering substances section of the device package insert provides a list of 39 drugs and other exogenous substances that do not interfere with the assay at the concentrations indicated for serum/ plasma and CSF sample matrices.

The package insert states the following: ‘Lipemic samples should be avoided’ and ‘Inaccuracies (biases) due to the listed 39 substances are less than 10% at IgG concentrations of 842 - 2651 mg/dL in serum and plasma; and 2.67 – 5.48 mg/dL in CSF.

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

The table below shows the comparison of 75 CSF samples ranging from 4.6 – 118.2 mg/L IgG that were tested with the Dimension Vista™ IgG assay and the predicate device BN ProSpec® System. Results were analyzed by Passing-Bablok regression analysis and are summarized below:

	N	Slope (95% CI)	Intercept (95%CI)	R
Dimension Vista™ vs. BN System	75	1.018 (0.987, 1.042)	0.048 (-0.603, 2.317)	0.990

b. Matrix comparison:

Not applicable.

3. Clinical studies:

a. Clinical Sensitivity and specificity:

Not applicable.

b. Other clinical supportive data (when a. is not applicable):

Not applicable.

4. Clinical cut-off:

Not applicable.

5. Expected values/Reference range:

The reported expected range for the Immunoglobulin G (IgG) in adults (7.0 – 16.0 g/L) is from 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 based on the standardization against the IFCC/BCR/CAP Reference Material (CRM 470). Eur J Clin Chem Clin Biochem 34: 517-20, 1996).

During childhood and adolescence, reference ranges for IgG are age dependent. (Refer to Ritchie RF et al in J Clin Lab Anal 1998;12:363-70).

The CSF IgG reference range (≤ 34.0 mg/L or 3.40 mg/dL) is from literature (Reiber H et al in Lab Med 1988;12:101-109).

[Note in P.I.: CSF IgG reference intervals in the strict sense exist only for CSF/serum ratios]

Each laboratory should establish its own expected values for IgG as performed on the Dimension Vista® System

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.