

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

A. 510(k) Number:

k061845

B. Purpose for Submission:

New Devices

C. Measurand:

Immunoglobulin IgM

D. Type of Test:

Quantitative, Nephelometry

E. Applicant:

Dade Behring, Inc.

F. Proprietary and Established Names:

Dimension Vista™ Immunoglobulin M Flex® reagent cartridge (IgM)

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:

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

21 CFR § 862.1150, Calibrator

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

2. Classification:

Class II, Devices and Calibrator

Class I, Quality Control Material

3. Product code:

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

JIX, Calibrator, Multi-Analyte Mixture

JJY, Multi-Analyte Controls, All kinds (Assayed and Unassayed)

4. Panel:

Immunology (82)

Chemistry (75)

H. Intended Use:

1. Intended use(s):

Dimension Vista™ IgM Flex® reagent cartridge:

The IgM method is an *in vitro* diagnostic test for the quantitative determination of immunoglobulin M in human serum and heparinized plasma on the Dimension Vista™ System. Measurements of IgM aid in the diagnosis of abnormal protein metabolism and the body's lack of ability to resist infectious agents.

Dimension Vista™ IgM Protein 1 Calibrator:

Protein 1 Calibrator is an *in vitro* diagnostic product for the calibration of the Immunoglobulin A (IgA), Immunoglobulin G (IgG), Immunoglobulin M (IgM) methods on the Dimension Vista™ System.

Dimension Vista™ IgM Protein 1 Control L:

PROT1 CON L is an assayed intralaboratory quality controls for assessment of precision and analytical bias in the determination of Immunoglobulin A (IgA), Immunoglobulin G (IgG), Immunoglobulin M (IgM) on the Dimension Vista™ System.

Dimension Vista™ Protein 1 Control M:

PROT1 CON M is an assayed intralaboratory quality controls for assessment of precision and analytical bias in the determination of Immunoglobulin A (IgA), Immunoglobulin G (IgG), Immunoglobulin M (IgM) on the Dimension Vista™ System.

Dimension Vista™ Protein 1 Control H:

PROT1 CON H is an assayed intralaboratory quality controls for assessment of precision and analytical bias in the determination of Immunoglobulin A (IgA), Immunoglobulin G (IgG), Immunoglobulin M (IgM) on the Dimension Vista™ System.

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

I. Device Description:

Dimension Vista™ IgM Flex® reagent cartridge carton contains 2 cartridges (12 wells per cartridge) with rabbit polyclonal antiserum to human IgM, phosphate buffer, and polyethylene glycol. Reagent is in ready-to-use liquid form.

Dimension Vista™ IgM Protein 1 Calibrator carton contains 6 vials with 2 mL per vial, with multi-analyte human serum based product containing Immunoglobulin IgA, IgG, and IgM. Reagent is in ready-to-use liquid form.

Dimension Vista™ IgM Protein 1 Control L, Control M, and Control H cartons contain 6 vials per carton with 2 mL per vial, with multi-analyte human serum based products containing Immunoglobulin IgA, IgG and IgM. Reagents are ready-to-use liquid form.

J. Substantial Equivalence Information:

1. Predicate device name(s):
Dade Behring N Antisera to Human Immunoglobulins (IgG, IgA, IgM)
Dade Behring N Protein Standard SL
Dade Behring N Protein Controls SL
2. Predicate 510(k) number:
k042735 (Antisera)
k012470 (Protein Standard)
k012468 (Controls)

3. Comparison with predicate:

Similarities		
Item	New Device	Predicate Device
Technology	Nephelometric	Same
IgM antisera mammal source	Rabbit polyclonal	Same
Calibrator material source	Human serum	Same
Control material source	Human serum	Same
International Reference standard material	Traceable to IFCC/BCR/CAP 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 IgM Antisera	Dimension Vista™ IgM Flex® reagent cartridge: The IgM method is an <i>in vitro</i> diagnostic test for the quantitative determination of Immunoglobulin M in human serum and heparinized plasma on the Dimension Vista™ System. Measurements of IgM 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 human urine and 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 Immunoglobulin A (IgA), Immunoglobulin G (IgG), Immunoglobulin M (IgM) methods on the Dimension Vista™ System.	Establishment of the reference curves for the determination of IgG, IgG1, IgG2, IgG3, IgG4, IgA, IgM, IgE, C3c, C4, Transferrin, Albumin, α ₁ -antitrypsin, α ₂ -macroglobulin, haptoglobin, α ₁ -acid glycoprotein, Prealbumin (transthyretin), hemopexin, ceruloplasmin, RbP, IgL-

Differences		
Item	New Device	Predicate
		chain Kappa, IgL-chain Lambda, soluble transferrin receptor, ferritin, β_2 -microglobulin total protein on the Dade Behring Systems, as well as of IgM, C3c, ceruloplasmin, IgL-chains (types kappa, and lambda), by RID using Partigen plates.
Control	PROT 1 CON L, CON M, and CON H are assayed intralaboratory quality controls for assessment of precision and analytical bias in the determination of Immunoglobulin A (IgA), Immunoglobulin G (IgG), Immunoglobulin M (IgM) on the Dimension Vista™ System.	The N/T Protein Controls SL/L, M, H are for use as assayed accuracy controls and precision controls in the determination of the following human serum proteins by immunonephelometry with the BN Systems, by immunoturbidimetry with the TurbiTime System and by RID with Partigen plates: IgG, IgG1, IgG2, IgG3, IgG4, IgA, IgM, IgE, C3c, C4, Transferrin, Albumin, α_1 -antitrypsin, α_2 -macroglobulin, haptoglobin, α_1 -acid glycoprotein, Prealbumin, hemopexin, ceruloplasmin, RbP, IgL-chain Kappa, IgL-chain Lambda, soluble transferrin receptor, ferritin, β_2 -microglobulin total protein.
Sample type	Serum and plasma (lithium and sodium heparin)	Serum, plasma (EDTA; sodium, lithium and ammonium heparin), urine and CSF
Analyzer	Dimension Vista™ System	Dade Behring BN™ Systems
Reportable range	0.20 – 6.40 g/L	0.21 – 6.40 g/L

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

CLSI/NCCLS, EP 7-A: Interference Testing in Clinical Chemistry

CLSI/NCCLS, EP 5-A: Evaluation of Precision Performance of Clinical Chemistry

Devices

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:*

Reproducibility testing was done in accordance with CLSI document EP5-A, 'Approved Guideline for Evaluation of Precision Performance of Clinical Devices'. The intra-assay reproducibility was determined by testing seven samples in duplicate twice a day for 20 days. The samples included the L, M and H controls (IgM concentration of 0.567, 0.682, and 0.894 g/L respectively), two serum pools (IgM concentrations of 0.294 and 4.717 g/L) and two plasma pools (IgM concentrations of 0.631 and 1.980 g/L). The controls had %CV ranging from 1.8% to 2.9%, the serum pools 3.0% to 4.8% and the plasma pools 2.9% to 3.0%.

The inter-assay reproducibility was determined by testing the same seven samples in duplicate twice a day for 20 days. The %CV for the controls ranged from 2.0% to 3.6 %, the sera pools 3.6% to 4.8% and the plasma pools 3.3% to 3.8%. The data are summarized below:

Material	Mean g/L	Intra-assay SD (%CV)	Inter-assay SD (%CV)
PROT 1 CON L	0.567	0.017 (2.9)	0.021 (3.6)
PROT 1 CON M	0.682	0.016 (2.3)	0.020 (3.0)
PROT 1 CON H	0.894	0.016 (1.8)	0.018 (2.0)
Serum pool	0.294	0.014 (4.8)	0.014 (4.8)
Serum pool	4.717	0.140 (3.0)	0.172 (3.6)
Plasma pool	0.631	0.019 (3.0)	0.024 (3.8)
Plasma pool	1.980	0.058 (2.9)	0.065 (3.3)

b. *Linearity/assay reportable range:*

Linearity across the assay range was confirmed by testing a serum sample with high concentration (6.7 g/L) of IgM. This sample was serially diluted 12 times with System Diluent down to the lower measuring range (0.35 g/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% with a mean recovery of 98.1%.

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 $y = 0.9852x - 0.0203$, r^2 of 0.9986. Linearity

was observed between 0.33 to 6.70 g/L.
Reportable range for the device was set at 0.21 – 6.4 g/L

Antigen Excess Effect:

The possibility of antigen excess occurring when using the device was evaluated with serum sample 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 49.558 g/L.

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

The calibrator is traceable to the reference material IFCC/BCR/CAP CRM 470.

Stability

The expiration date claims for the reagents are as follows:

Unopened reagent cartridges and closed vials:

Dimension Vista™ IgM Flex® reagent cartridge (IGM) – 24 month

Dimension Vista™ Protein 1 Calibrator – 24 months

Dimension Vista™ Protein 1 Control L, M and H – 24 months

On-board Instrument products:

Dimension Vista™ IgM Flex® reagent sealed cartridge (IGM) – 90 days

Dimension Vista™ IgM Flex® open well reagent cartridge (IGM) – 21 days

Dimension Vista™ Protein 1 Calibrator open vial – 9 days

Dimension Vista™ Protein 1 Control L, M and H open vial – 14 days

d. Detection limit:

Detection limit (0.21 g/L) represents the lower limit of the reportable range of IgM.

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 twenty replicates of 1:20 dilution of PROT 1 Cal and system diluent plus two standard deviations. It was determined to be 0.02 g/L.

e. Analytical specificity:

Interference testing was performed according to CLSI document EP7A, ‘Interference testing in Clinical Chemistry’ guidance. 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, Triglycerides up to 924 mg/dL, Creatinine up to 30 mg/dL, Albumin up to 6 g/L, Immunoglobulin G (IgG) up to 5 g/L, Urea up to 500 mg/dL, Cholesterol up to 500 mg/dL, Uric Acid 20 mg/dL, Rheumatoid factor up to 500 IU/mL, Total Protein up to 12 g/L.

Non-interfering substances section of the device 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 69 serum and 74 plasma samples

ranging from 0.23 to 6.28 g/L IgM that were tested with the Dimension Vista™ IgM assay and the predicate device BN ProSpec® System. Regression analysis of these samples is summarized below:

	N	Slope	Intercept	r
Dimension Vista™ vs. BN System (Dade Behring)	143	1.020	-0.089	0.995

b. Matrix comparison:

Sera and plasma (lithium and sodium heparin) samples, covering the IgM assay measuring range (0.41 – 6.20 g/L) were compared to determine if any significant bias existed between matrices. The correlation coefficients were acceptable and no bias was observed. Regression analyses of the comparison results are summarized below:

	n	Slope	Intercept	r
Lithium heparin plasma vs serum	10	0.98	0.11	1.00*
Sodium heparin plasma vs serum	10	0.97	0.14	0.99**

* The range of IgM values in the correlation study was 0.41-6.20 g/L

** The range of IgM values in the correlation study was 0.42-6.19 g/L

3. Clinical studies:

a. Clinical Sensitivity and specificity:

Not Applicable

b. Other clinical supportive data:

Not Applicable.

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

The reported expected range for the Immunoglobulin M (IgM) in adults (0.4 – 2.3 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 IgM are dependent on age and can vary over a wide range.

Each laboratory should establish its own expected values for IgM 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.