

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

A. 510(k) Number:

k063272

B. Purpose for Submission:

New devices

C. Measurand:

Human β_2 -microglobulin

D. Type of Test:

Quantitative, immunonephelometry

E. Applicant:

Dade Behring, Inc.

F. Proprietary and Established Names:

Dimension Vista® β_2 -Microglobulin Flex® reagent cartridge (B2MIC)

Dimension Vista® Protein 1 Calibrator (CAL)

Dimension Vista® Protein 1 Control Medium (M)

Dimension Vista® Protein 1 Control High (H)

G. Regulatory Information:

1. Regulation section:

21 CFR § 866.5630 Beta-2-Microglobulin 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:

JZG, System, Test, Beta-2-Microglobulin Immunological

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® System β_2 -Microglobulin Flex® reagent cartridge:

The B2MIC method is an *in vitro* diagnostic test for the quantitative determination of β_2 -Microglobulin in human serum or heparinized or EDTA plasma on the Dimension Vista® System. Measurements of β_2 -Microglobulin aid in the diagnosis of renal dysfunction.

Dimension Vista® System Protein 1 Calibrator:

PROT 1 CAL is an *in vitro* diagnostic product for the calibration of the β_2 -Microglobulin (B2MIC), C3 complement (C3), C4 complement (C4), Immunoglobulin A (IGA), Immunoglobulin G (IGG), Immunoglobulin M (IGM), Prealbumin/Transthyretin (PREALB) methods on the Dimension Vista® System.

Dimension Vista® System Protein 1 Control M (medium):

PROT1 CON M is an assayed intralaboratory quality control for assessment of precision and analytical bias in the determination of β_2 -Microglobulin (B2MIC), C3 complement (C3), C4 complement (C4), Immunoglobulin A (IGA), Immunoglobulin G (IGG), Immunoglobulin M (IGM), Prealbumin/Transthyretin (PREALB) on the Dimension Vista® System.

Dimension Vista® System Protein 1 Control H (high):

PROT1 CON H is an assayed intralaboratory quality control for assessment of precision and analytical bias in the determination of β_2 -Microglobulin (B2MIC), C3 complement (C3), C4 complement (C4), Immunoglobulin A (IGA), Immunoglobulin G (IGG), Immunoglobulin M (IGM), Prealbumin/Transthyretin (PREALB) on the Dimension Vista® System.

Calibrators and controls are not included in the device and are sold separately.

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® System (k051087)

I. Device Description:

Dimension Vista® System B2MIC Flex® reagent cartridge carton contains 2 cartridges (12 wells per cartridge which generates approximately 100 tests/cartridge) with mouse monoclonal antiserum to human β_2 -Microglobulin, phosphate buffer, and polyethylene glycol sorbitan monolaurate. Reagent is in ready-to-use liquid form.

Dimension Vista® System Protein 1 Calibrator carton contains 6 vials (2 mL per vial), with a multi-analyte human serum based product containing β_2 -Microglobulin, C3, C4, IgA, IgG, IgM and Prealbumin. Reagent is in ready-to-use liquid form.

Dimension Vista® System Protein 1 Control M, and Control H cartons contain 6 vials per carton (2 mL per vial), with a multi-analyte human serum based products containing β_2 -Microglobulin, C3, C4, IgA, IgG and IgM and Prealbumin. Reagents are ready-to-use liquid form.

J. Substantial Equivalence Information:

1. Predicate device name(s):
Dade Behring N Latex β_2 -Microglobulin assay
Dade Behring N Protein Standard SL
Dade Behring N/T Protein Controls SL
2. Predicate 510(k) number:
k002731 (Antisera)
k012470 (Protein Standard)
k012468 (Controls)
3. Comparison with predicate:

Similarities		
Item	Dimension Vista® System β_2 -Microglobulin Flex® reagent cartridge	Dade Behring N Latex β_2 -Microglobulin assay
Intended Use/Indication for Use	An <i>in vitro</i> diagnostic test for the quantitative determination of β_2 -Microglobulin to aid in the diagnosis of renal dysfunction	Same
Technology	Immunonephelometry	Same
β_2 -Microglobulin antisera mammal source	Mouse Monoclonal	Same

Differences		
Item	Dimension Vista® System β_2 -Microglobulin Flex® reagent cartridge	Dade Behring N Latex β_2 -Microglobulin assay
Sample type	Serum and plasma (EDTA; lithium and sodium heparin)	Serum, plasma (EDTA; sodium, lithium and ammonium heparin), urine and CSF
Reportable range for serum and plasma	0.72 – 23.0 mg/L	0.70 – 23.0 mg/L
Reportable range for urine	Urine is not a matrix	0.2 – 6.0 mg/L
International Reference standard material	Traceable to Highly purified proteins 1 st International Standard (NIBSC)	Traceable to Highly Purified Proteins
Storage conditions	Unopened product: Refrigerate at 2-8°C until expired. Opened product: stable for 21 days on board analyzer	Unopened product: Refrigerate at 2-8°C until expired. Opened product: stable for 4 weeks at 2-8°C
Analyzer	Dimension Vista® System	Dade Behring BN™ Systems

Similarities		
Item	Dimension Vista® System Protein 1 Calibrator	Dade Behring N Protein Standard SL
Intended Use/Indication for Use	For the calibration of specific serum protein assays	Establishment of the reference curves for the determination of specific serum protein assays

Similarities		
Item	Dimension Vista® System Protein 1 Calibrator	Dade Behring N Protein Standard SL
Material source	Human serum	Same
Reagent preparation	Ready-to-use, liquid	Same

Differences		
Item	Dimension Vista® System Protein 1 Calibrator	Dade Behring N Protein Standard SL
Analytes	7 analytes: β_2 -Microglobulin, C3, C4, IgA, IgG, IgM and Prealbumin	27 analytes: 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, Ig/L-chain Kappa, Ig/L-chain Lambda, soluble transferrin receptor, ferritin, β_2 -microglobulin, total protein
International Reference standard material	Traceable to Highly purified proteins 1 st International Standard (NIBSC)	Traceable to Highly Purified Proteins
Storage conditions	Unopened product: Refrigerate at 2-8°C until expired. Opened product: stable for 9 days on board analyzer	Unopened product: Refrigerate at 2-8°C until expired. Opened product: stable for 14 days at 2-8°C
Analyzer	Dimension Vista® System	Dade Behring BN™ Systems

Similarities		
Item	Dimension Vista® System Protein 1 Control	Dade Behring N/T Protein Controls SL
Intended Use/Indication for Use	Assayed intralaboratory quality controls for assessment of precision and analytical bias in the determination of specific protein assays	For use as assayed accuracy controls and precision controls in the determination of specific serum protein assays
Material source	Human serum	Same

Similarities		
Item	Dimension Vista® System Protein 1 Control	Dade Behring N/T Protein Controls SL
Reagent preparation	Ready-to-use, liquid	Same

Differences		
Item	Dimension Vista® System Protein 1 Control	Dade Behring N/T Protein Controls SL
Analytes	7 analytes: β_2 -Microglobulin, C3, C4, IgA, IgG, IgM and Prealbumin	27 analytes: 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, Ig/L-chain Kappa, Ig/L-chain Lambda, soluble transferrin receptor, ferritin, β_2 -microglobulin, total protein
Storage conditions	Unopened product: Refrigerate at 2-8°C until expired. Opened product: stable for 9 days on board analyzer	Unopened product: Refrigerate at 2-8°C until expired. Opened product: stable for 14 days at 2-8°C
Analyzer	Dimension Vista® System	Dade Behring BN™ Systems
Levels	Medium and High	Low, Medium, and High

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

CLSI/NCCLS, EP 5-A2: Evaluation of Precision Performance of Clin Chem Devices

CLSI/NCCLS, EP 7-A2: Interference Testing in Clinical Chemistry

CLSI/NCCLS, EP 9-A2: Method Comparison and Bias Estimation

L. Test Principle:

Polystyrene particles coated with specific antibodies to human β_2 -Microglobulin are aggregated when mixed with samples containing human β_2 -Microglobulin. 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:*

Reproducibility testing was done in accordance with CLSI/NCCLS document

EP5-A2, ‘Approved Guideline for Evaluation of Precision Performance of Clinical Devices’. The intra-assay reproducibility was determined by testing six samples in duplicate twice a day for 20 days. The samples included the M and H controls (β_2 -Microglobulin concentration of 1.88 and 4.86 mg/L respectively), two serum pools (concentrations of 2.13 and 20.35 mg/L) and two plasma pools (concentrations of 1.76 and 5.69 mg/L). The controls had %CV ranging from 2.07% to 2.57%, the serum pools 2.13% to 3.01% and the plasma pools 1.97% to 2.22%.

The inter-assay reproducibility was determined by testing the same six samples in duplicate twice a day for 20 days. The %CV for the controls ranged from 3.10% to 3.56 %, the sera pools 3.23% to 4.08% and the plasma pools 2.94% to 3.28%. The data are summarized below:

Material	Mean mg/L	Intra-assay		Inter-assay	
		SD	%CV	SD	%CV
PROT 1 CON M	1.88	0.048	2.57	0.067	3.56
PROT 1 CON H	4.86	0.101	2.07	0.151	3.10
Serum pool	2.13	0.045	2.13	0.069	3.23
Serum pool	20.35	0.612	3.01	0.831	4.08
Plasma pool	1.76	0.039	2.22	0.052	2.94
Plasma pool	5.69	0.112	1.97	0.186	3.28

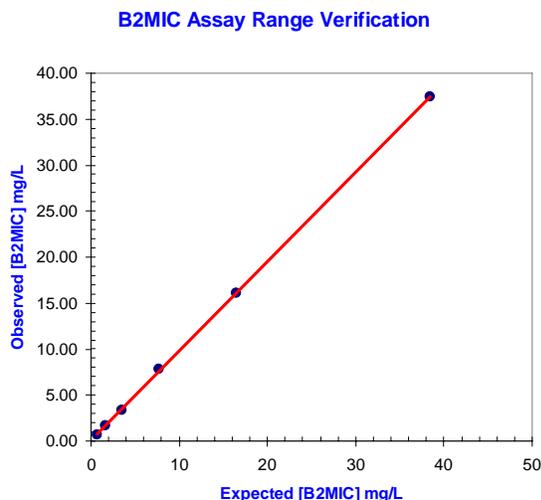
b. Linearity/assay reportable range:

Linearity across the assay range was confirmed by testing a calibrator with high concentration (37.42 mg/L) of β_2 -Microglobulin. This calibrator was serially diluted 6 times with System Diluent down to the lower measuring range (0.66 mg/L). Each dilution was tested in replicates of three.

The linear regression analysis was performed. The acceptance criteria for the slope (0.9 and 1.1) and correlation of coefficient ≥ 0.95 were met. (Slope = 0.973, Intercept = 0.087, Correlation coefficient = 1.00. See figure below).

Linearity was observed between 0.66 to 37.42 mg/L.

Reportable range for the device was set at 0.72 – 23.0 mg/L



High Dose Hook Effect:

The possibility of hook occurring when using the Dimension Vista® B2MIC assay was evaluated with serum sample above the assay range. The sample was analyzed on both the BN ProSpec® System and the Dimension Vista® System and results indicated no hook effect was observed up to 122 mg/L.

- c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
The calibrator is traceable to the reference material Highly Purified Protein 1st International Standard (3/17/04 NIBSC).

Device Stability

The expiration date claims for the reagents are as follows:

Unopened reagent cartridges and closed vials:

Dimension Vista® B2MIC Flex® reagent cartridge – 24 months

Dimension Vista® Protein 1 Calibrator – 24 months

Dimension Vista® Protein 1 Control M and H – 24 months

On-board Instrument products:

Dimension Vista® B2MIC Flex® reagent sealed cartridge – 90 days

Dimension Vista® B2MIC Flex® open well reagent cartridge – 21 days

Dimension Vista® Protein 1 Calibrator open vial – 9 days

Dimension Vista® Protein 1 Control M and H open vial – 9 days

- d. *Detection limit:*
Detection limit (0.72 mg/L) represents the lower limit of the reportable range of β_2 -Microglobulin.

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 System Diluent plus two standard deviations. It was determined to be 0.176 mg/L.

- e. *Analytical specificity:*
Interference testing was performed according to CLSI document EP7A2, ‘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 1000 mg/dL, Triglycerides up to 1313 mg/dL, Creatinine up to 30 mg/dL, Albumin up to 6000 mg/L, Immunoglobulin G (IgG) up to 5000 mg/L, Urea up to 500 mg/dL, Cholesterol up to 500 mg/dL, Uric Acid 16 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 71 serum and 72 plasma samples ranging from 0.81 to 22.69 mg/L β_2 -Microglobulin that were tested with the Dimension Vista™ β_2 -Microglobulin assay and the predicate device BN ProSpec® System. Regression analysis of these samples is summarized in the table below:

	N	Slope (95%CI)	Intercept (95%CI)	r
Dimension Vista® vs. BN ProSpec®	143	0.942 (0.931, 0.954)	-0.029 (-0.062, 0.011)	0.998

b. *Matrix comparison:*

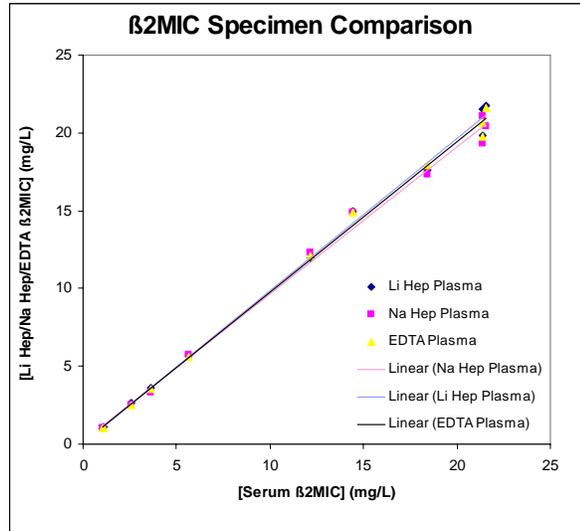
Sera and plasma (EDTA; lithium and sodium heparin) samples, covering the β_2 -Microglobulin assay measuring range (1.01 – 21.78 mg/L) were compared to determine if any significant bias existed between matrices. The correlation coefficients were acceptable and no bias was observed. Regression analyses of the comparison results are summarized below:

	n	Slope	Intercept	r
Lithium heparin plasma vs. serum	11	0.98	0.11	0.998*
Sodium heparin plasma vs. serum	11	0.95	0.20	0.997**
EDTA plasma vs. serum	11	0.97	0.11	0.998***

* The range of β_2 -Microglobulin values in the correlation study was 1.05-21.78 mg/L

** The range of β_2 -Microglobulin values in the correlation study was 1.07-21.08 mg/L

*** The range of β_2 -Microglobulin values in the correlation study was 1.01-21.64 mg/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 β₂-Microglobulin in adults (0.7 – 1.8 mg/L) is from literature Lammers M, et al Determination of *beta2-microglobulin* by a *particle-enhanced immunonephelometric assay*. Clin Chem 2002; 48: A-119.

Each laboratory should establish its own expected values for β₂-Microglobulin 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.