

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

A. 510(k) Number:

k063322

B. Purpose for Submission:

New Device

C. Analyte:

Transferrin

D. Type of Test:

Quantitative, immunonephelometry

E. Applicant:

Dade Behring, Inc.

F. Proprietary and Established Names:

Dimension Vista™ Transferrin Flex® reagent cartridge

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 §866.5880- Transferrin immunological test system

21CFR §862.1150- Calibrator

21CFR §862.1660- Quality control material

2. Classification:

Class II

3. Product Code:

DDG - Transferrin, antigen, antiserum, control

JIX - Calibrator, multi-analyte mixture

JJY - Multi-analyte controls, all kinds (assayed and unassayed)

4. Panel:

Immunology (82)

H. Intended Use:

1. Intended use(s):

Transferrin Flex® reagent cartridge: The TRF method is an in vitro diagnostic test for the quantitative determination of transferrin in human serum, heparinized plasma or EDTA plasma on the Dimension Vista™ System. Measurements of transferrin aid in the diagnosis of malnutrition, acute inflammation, infection, and iron deficiency anemia.

Protein 1 Calibrator: PROT1 CAL is an in vitro diagnostic product for the calibration of the C3 complement (C3), C4 complement (C4), Immunoglobulin A (IGA), Immunoglobulin G (IGG), Immunoglobulin M (IGM), Prealbumin (PREALB) and Transferrin (TRF) methods on the Dimension Vista™ System.

Protein 1 Controls L, M and H: PROT 1 CON L, M, and H are assayed intra-laboratory quality controls for assessment of precision and analytical bias in the determination of C3 complement (C3), C4 complement (C4), Immunoglobulin A

(IGA), Immunoglobulin G (IGG), Immunoglobulin M (IGM), Prealbumin (PREALB) and Transferrin (TRF) methods on the Dimension Vista™ System.

2. Indication(s) for use:
Same as intended use.
3. Special condition for use statement(s):
Prescription use only.
4. Special instrument Requirements:
Dimension Vista™ System

I. Device Description:

Dimension Vista™ Flex® reagent cartridge (TRF): TRF reagent consists of a Reaction buffer and an antiserum to polyclonal rabbit antiserum to human transferrin.

Dimension Vista™ Protein 1 Calibrator:

PROT1 CAL is a multi-analyte, liquid, human serum based product containing C3, C4, IgA, IgG, IgM, prealbumin and transferrin.

Dimension Vista™ Protein 1 Control L and H:

PROT1 CON L, M and H are multi-analyte, liquid, human serum based products containing C3, C4, IgA, IgG, IgM, prealbumin and transferrin.

J. Substantial Equivalence Information:

1. Predicate device name(s) and 510(k) numbers:
Dade Behring N Antisera to Human Transferrin assay (k053075)
N Protein Standard SL (k012470)
N/T Protein Control SL (k012468)
2. Comparison with predicate:

Dimension Vista™ Transferrin Flex® reagent cartridge

Similarities		
Item	Device	Predicate
Intended Use	For the quantitative determination of transferrin in human serum, heparinized plasma, or EDTA plasma on the Dimension Vista™ System.	For the quantitative in vitro determination of transferrin and haptoglobulin in human serum, heparinized and EDTA plasma, as well as of transferrin in human urine by means of immunonephelometry on the BN Systems.
Indications for Use	Measurements are used as an aid in the diagnosis of malnutrition, acute inflammation, infection, and iron deficiency anemia.	Same
Method	Immunonephelometry	Same

Similarities		
Item	Device	Predicate
Measurement type	Quantitative	Same
Capture Antibody	Rabbit polyclonal	Same
Measuring Range	0.35 to 5.6 g/L	Same
Reference Interval (Expected values)	2.0 – 3.6 g/L	Same
Storage: Unopened	2-8°C	Same

Differences		
Item	Device	Predicate
Instrument system	Dimension Vista® System	BN ProSpec® System
Matrices	Serum, lithium heparin plasma, EDTA plasma	Serum, lithium heparin plasma, EDTA plasma and urine.
Stability: Open	21 days 2-8°C	4 weeks 2-8°C
Stability: On board	Unopened 90 days	5 days 8 hr/day for 5 ml vials; 3 days for 2ml vials

Dimension Vista™ Protein 1 Calibrator

Similarities		
Item	Device	Predicate
Intended Use	PROT1 CAL is an in vitro diagnostic product for the calibration of the C3 Complement (C3), C4 Complement (C4), Immunoglobulin A (IGA), Immunoglobulin G (IGG), Immunoglobulin M (IGM), Prealbumin (PREALB), and Transferrin (TRF) methods on the Dimension Vista™ System	For establishment of reference curves for specific immunonephelometric determinations
Composition	Pooled human sera	Same
Reagent Preparation	Liquid, Ready-to-use	Same
Traceability	ERM®-DA470 (CRM 470) L, M, and H	Same

Differences		
Item	Device	Predicate
Analytes	7 analytes	26 analytes
Instrument system	Dimension Vista® System	BN Systems
Stability: Open	9 days 2-8°C	14 days 2-8°C

Dimension Vista™ Protein 1 Control L, M and H

Similarities		
Item	Device	Predicate
Intended Use	Assayed intra-laboratory quality controls for the assessment of precision and analytical bias in the determination of specific assays	Assayed controls for accuracy and precision in the quantitative determination of specific analytes
Composition	Pooled human sera	Same
Reagent Preparation	Liquid, Ready-to-use	Same
Differences		
Item	Device	Predicate
Analytes	7 analytes	26 analytes
Instrument system	Dimension Vista™ System	BN Systems and the TurbiTime System
Concentration Range	Low, medium and High	Low and High
Stability Open	9 days 2-8°C	14 days 2-8°C

- K. Standard/Guidance Document Referenced (if applicable):**
 CLSI Evaluation of Precision Performance of Clinical Devices; Approved Guideline: EP5-A2, CLSI Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline EP9-A2, CLSI Interference Testing in Clinical Chemistry; Approved Guideline EP7-A2.
- 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 EP5-A2. Two samples derived from serum pools and two samples derived from plasma pools representing TRF concentrations that span the measuring range, and the PROT1 CON L, M and H were analyzed in duplicate, for 20 days, two runs per day. The repeatability and within-lab standard deviations (SD) and percent coefficient

of variation (%CV) were calculated by the analysis of variance method. Repeatability imprecision was <3.3%, and Within-Lab irreproducibility was <3.5%.

Material	Mean g/L	Repeatability		Within-Lab	
		SD	%CV	SD	%CV
PROT2 CON L	1.99	0.047	2.36	0.057	2.85
PROT1 CON M	2.66	0.058	2.18	0.083	3.13
PROT2 CON H	3.97	0.093	2.35	0.112	2.82
Serum pool	1.53	0.023	1.53	0.031	1.99
Serum pool	4.3	0.087	2.01	0.112	2.60
Plasma pool	0.79	0.026	3.27	0.027	3.46
Plasma pool	2.55	0.036	1.41	0.060	2.37

b. *Linearity/assay reportable range:*

Linearity across the range was confirmed by testing a calibrator with a high concentration of transferrin. The calibrator was serially diluted in 5, approximately two fold increments (measuring range from 0.28 to 6.95 g/L). Each dilution was tested in replicates of three. Data were analyzed using linear regression analysis: regression analysis of theoretical concentration versus measured concentration produced the following results:

Slope	Y-Intercept g/L	Correlation Coefficient	n
1.038	-0.045	0.999	15

Recovery testing with European reference material ERM ®-DA470* was performed with 5 replicates of a TRF sample 2.45 g/L. Results ranged from 97.1 -100.2% with a mean recovery of 98.8%.

c. *Traceability (controls, calibrators, or method):*

Calibration material values were referenced to the European reference material ERM ®-DA470*.

d. *Detection limit:*

Analytical sensitivity was determined by assaying analyte-free System Diluent 20 times and determining the mean value plus two SDs: 0.062 g/L.

e. *Analytical specificity:*

- i. Interference Studies Interference testing was performed according to CLSI EP7-A2, to determine the effect of various endogenous and exogenous substances on the Dimension Vista™ TRF assay. For the following interferents, the percent bias was determined by testing a control samples without the interferent and comparing it to the value obtained from a test sample to which the potential interferent was added: bilirubin (conjugated and unconjugated, 60 mg/dL), hemoglobin (1000 mg/dL), creatinine (30 mg/dL), albumin (6 g/dL), urea (500 mg/dL), cholesterol (500 mg/dL), uric acid (20 mg/dL). Minimal interference (<8%) was observed. Interference by

triglycerides (native and clarified) was tested on 5 test samples containing a known amount of triglycerides and comparing results from the same sample after centrifugation. Interference was less than 6%. Samples containing rheumatoid factor (>500 IU/ml) or total protein >120 g/L were mixed 1:1 with TRF concentrations and % recovery was compared to samples without RF using 5 replicates. No interference was observed up to 350 IU/ml and 88 g/L TP. Additionally, 41 potentially interfering drugs were also assayed and shown to exhibit minimal interference (<10%).

- ii. Cross-reactivity with autoimmune antibodies common to other systemic autoimmune diseases was not tested.
- iii. Antigen Excess: The effect of antigen excess was evaluated using a serum sample with a high concentration of transferrin (above the assay range). No effect was seen up to 9.46 g/L. Samples whose values exceed 5.6 g/L using the initial 1:20 dilution are reported as “exceeds assay range” to alert the user to repeat the assay using a higher dilution.

f. *Assay cut-off*:
See Expected values

2. Comparison studies:

a. *Method comparison with predicate device*:

The Dimension Vista™ TR assay was compared to the Dade Behring N Antisera to Human Transferrin assay on the BN ProSpec ® System by evaluating serum and plasma samples with concentrations ranging from 0.79 to 5.43 g/L. Regression analysis of these results yielded the following statistics:

Comparative Method	Slope (95% CI)	Y-Intercept (g/L) (95% CI)	Correlation Coefficient	n
N Antisera to Human Transferrin on the BN ProSpec ®	1.087 (1.071 to 1.102)	0.060 (-0.088 to -0.032)	0.992	180

b. *Matrix comparison*:

Ten matched samples of serum, EDTA, lithium heparin and sodium heparin plasma containing concentrations of transferrin spanning the measuring range (0.37 to 4.92 g/L), were assayed and compared. Regression analysis showed no significant bias between the four matrices and yielded the following information:

% Recovery statistics for anticoagulant-plasma vs. serum		Slope (95% CI)	Y-Intercept (g/L)	Correlation Coefficient	n
Lithium heparin plasma	Mean = -0.5% (Range = -4.5%-4.4%)	0.98 (0.956-1.01)	0.03	0.998	10
Sodium heparin plasma	Mean = 0.8% (Range = -2.7%-5.0%)	1.02 (0.987-1.05)	-0.02	0.998	10

% Recovery statistics for anticoagulant-plasma vs. serum		Slope (95% CI)	Y-Intercept (g/L)	Correlation Coefficient	n
EDTA plasma	Mean = -2.9% (Range = -7.9%-1.5%)	0.95 (0.920-0.98)	0.03	0.998	10

3. Clinical studies:

a. *Clinical sensitivity:*

Not provided

b. *Clinical specificity:*

Not provided

c. *Other clinical supportive data (when a and b are not applicable):*

Not applicable.

4. Clinical cut-off:

See assay range

5. Expected values/Reference range:

A reference range for normal transferrin levels is provided and supported by additional testing using the Dimension Vista™ TRF assay supplied by sponsor. Results support the reference interval 2.0-3.6g/L. This reference interval applies to serum samples from healthy adults.

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.