

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

**A. 510(k) Number:**

k081299

**B. Purpose for Submission:**

Add urine as a sample type for the previously cleared assay

**C. Measurand:**

Transferrin

**D. Type of Test:**

Quantitative, nephelometry

**E. Applicant:**

Seimens Healthcare Diagnostics, Inc.

**F. Proprietary and Established Names:**

Dimension Vista® System TRF Flex reagent cartridge

Dimension Vista® System Protein 1 Calibrator

Dimension Vista® System Protein 3 Control

**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 measurement of transferrin in human serum, heparinized plasma, EDTA plasma or urine 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 Dimension Vista® System for  $\alpha_1$ -Acid Glycoprotein (A1AG),  $\alpha_1$ - Antitrypsin (A1AT),  $\beta_2$ - 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, IGG-C\*), 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, TRF-U).

Protein 3 Control: PROT3 CON is an assayed intra-laboratory quality control for assessment of precision and analytical bias on the Dimension Vista® System in the quantitative determination of  $\alpha_1$ -Microglobulin, (A1MIC), Immunoglobulin G (IGG-C\*), Microalbumin (MALB), specialty albumin (sALB\*), and Transferrin (TRF-U\*\*).

\* For cerebrospinal fluid

\*\* For urine

2. Indication(s) for use:  
Same as intended use
3. Special conditions for use statement(s):  
Prescription use only
4. Special instrument requirements:  
Dimension Vista™ System (k051087)

**I. Device Description:**

Transferrin Flex® reagent cartridge: Reagents are contained in 12 segregated wells in a plastic cartridge. Wells 1 through 8 contain buffers and polyethylene glycol. Wells 9 through 12 contain liquid rabbit polyclonal antiserum to human transferrin.

PROT1 CAL: is a multi-analyte, liquid human serum based product consisting of 6 vials (2.0 mL per vial).

PROT3 CON: is a multi-analyte, lyophilized, polygeline and rabbit albumin based product consisting of 4 vials (1.0 mL per vial).

**J. Substantial Equivalence Information:**

1. Predicate device K numbers and name(s):  
k053075      N Antisera to Human Transferrin  
k012470      N Protein Standard SL  
k032237      N/T Protein Control LC

3. Comparison with predicate:

**Transferrin Flex reagent cartridge**

<b>Similarities</b>		
Item	Device	Predicate
Intended Use	For the quantitative measurement of transferrin in human serum, heparinized plasma, EDTA plasma or urine on the Dimension Vista™ System. Measurements of transferrin aid in the diagnosis of malnutrition, acute inflammation, infection, and iron deficiency anemia.	Same
Method	Immunonephelometry	Same
Specimen types	Serum, Plasma, Urine	Same
Capture antibody	Rabbit anti-human	Same

<b>Similarities</b>		
Item	Device	Predicate
	transferrin; polyclonal	
Storage	2-8°C	Same

<b>Differences</b>		
Item	Device	Predicate
Instrumentation	Dimension Vista <sup>®</sup> System	BN <sup>™</sup> Systems
Stability; Open	21 days for wells 1-12	28 days

### **PROT1 Calibrator**

<b>Similarities</b>		
Item	Device	Predicate
Traceability for TRF-U	Protein reference preparation ERM <sup>®</sup> -DA470 (CRM 470)1,	Same
Composition	Ready-to-use	Same
Level	One	Same
Storage	2-8°C	Same

<b>Differences</b>		
Item	Device	Predicate
Analytes	Multi-analyte: α1-Acid Glycoprotein (A1AG) Immunoglobulin G (IGG, IGG-C*) α1-Antitrypsin (A1AT) Immunoglobulin G Subclass 1 (IGG1) β2-Microglobulin (B2MIC) Immunoglobulin G Subclass 2 (IGG2) C3 Complement (C3) Immunoglobulin G Subclass 3 (IGG3) C4 Complement (C4) Immunoglobulin G Subclass 4 (IGG4) Ceruloplasmin (CER) Immunoglobulin M (IGM) Haptoglobin (HAPT) Prealbumin (PREALB) Hemopexin (HPX) Retinol binding Protein (RBP) Homocysteine (HCYS) soluble Transferrin Receptor (STFR) Immunoglobulin A (IGA) Transferrin (TRF, TRF-U**)	IgG IgG 1 IgG 2 IgG 3 IgG 4 IgA IgM IgE C3c C4 Transferrin Albumin α1-antitrypsin (α1-proteinase inhibitor) α2-macroglobulin Haptoglobin α1-acid glycoprotein Prealbumin (transthyretin) Hemopexin Ceruloplasmin RbP Ig/L-chain, Kappa Ig/L-chain, Lambda soluble Transferrin Receptor (sTfR) Ferritin b2 -Microglobulin

<b>Differences</b>		
<b>Item</b>	<b>Device</b>	<b>Predicate</b>
	Immunoglobulin E (IGE) * For cerebrospinal fluid (CSF) ** For urine	Total protein
Instrument System	Dimension Vista	BN Systems
Stability; Open	9 days	14 days
Quantity	6 vials, 2.0 mL per vial	3 vials, 1 mL per vial

**PROT 3 Control**

<b>Similarities</b>		
<b>Item</b>	<b>Device</b>	<b>Predicate</b>
Traceability for TRF-U	Protein reference preparation ERM®-DA470 (CRM 470)1,	Same
Composition	Lyophilized	Same
Stability; Open	14 days	Same
Storage	2-8°C	Same

<b>Differences</b>		
<b>Item</b>	<b>Device</b>	<b>Predicate</b>
Analytes	$\alpha$ 1-Microglobulin (AIMIC) specialty Albumin (sALB*) Immunoglobulin G (IGG-C*) Transferrin (TRF-U**) Microalbumin (MALB) * For cerebrospinal fluid (CSF) ** For urine	IgG in CSF, IgA in CSF, transferrin in urine, albumin in urine and CSF, $\alpha$ 1-microglobulin in urine and total protein in urine and CSF
Instruments	Dimension Vista System	BN and TurbiTime Systems
Quantity	4 vials, 1.0 mL per vial	3 vials, 1 mL per vial

**K. Standard/Guidance Document referenced (if applicable):**

Guidance for Industry and FDA Staff- Assayed and Unassayed Quality Control Material.

**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):**

The performance characteristics for Transferrin in serum and plasma are available in the Decision Summary for k063322.

1. Analytical performance:
  - a. *Precision/Reproducibility:*

CLSI EP5-A2 was followed. During each day of testing, two separate runs, with two test samples, for each test material, were analyzed for 20 days. The urine matrix precision data are attached below. The test samples consisted of two additional urine pools at different concentrations, and the Dimension Vista® System Protein 3 Control. One operator, one reagent and one instrument were used.

**TRF for urine:**

Material	Mean		Standard Deviation mg/dL [mg/L] (% CV)					
	mg/dL	[mg/L]	Repeatability			Within-Lab		
PROT3 CON	1.53	[15.30]	0.04	[0.42]	(2.7)	0.06	[0.61]	(4.0)
Urine pool	0.59	[5.89]	0.02	[0.20]	(3.4)	0.02	[0.23]	(3.8)
Urine pool	2.7	[26.99]	0.05	[0.48]	(1.8)	0.09	[0.89]	(3.3)

- b. *Linearity/assay reportable range:*

Linearity testing was performed according to CLSI EP06-A using one urine sample (concentration 31.6 mg/L) serially diluted with System Diluent and run in replicates of 5 per dilution level. The TRF-U measuring range is 2.00 - 31.0 mg/L. Linearity for the extended measuring range was evaluated as well. Linearity data using weighted least squares regression analysis is shown below:

Sample range (mg/L)	Slope (95%CI)	Y-intercept (mg/L) (95%CI)	Correlation Coefficient	n
(1.57 to 31.44)	1.009 ± 0.008	0.129 ± 0.135	0.9999	12
(20.1 to 334.9)	0.955 ± 0.025	1.755 ± 1.478	0.9993	12

A test report message (flag or comment) is provided for the results that fall outside the measuring ranges.

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

The calibrator and control are traceable to protein reference preparation ERM®-DA470 (CRM 470).

- d. *Detection limit:*

Limit of Quantitation (LoQ) was established using a testing protocol outlined in CLSI EP17-A Section 5.1 and a total analytical error of 30% based on imprecision experience for this transferrin assay and consistent with similar plasma proteins. Three independent samples at the target concentration were assayed in 5 runs, three replicates per run. Testing performed in one day with a single reagent lot, calibrator lot, instrument and operator. The LoQ was determined to be 2 mg/L (=0.2 mg/dL).

e. *Analytical specificity:*

Interference Studies:

Test samples were prepared by spiking the potential interferent into Urine. Urine transferrin concentrations ranged from 7.22 - 23.83 mg/L. Interference testing was performed based on CLSI EP7-A2 to determine the effect of various endogenous and exogenous substances on the Dimension Vista® System TRF assay. For all interferents the percent bias was determined by testing a control sample without the interferent and comparing it to the value obtained from a test sample to which the potential interferent had been added. For urine samples, ten replicates were tested for each substance. Recovery for the interferents tested ranged from 95% to 109% and met the acceptance criteria of bias <10%.

Substance Tested	Substance concentration	TRF in urine	% Bias
Hemoglobin	115 mg/dL	5.00 mg/L	-5%
		25.00 mg/L	+5%
Bilirubin (conjugated)	3 mg/dL	5.00 mg/L	+7%
		25.00 mg/L	+8%
Bilirubin (unconjugated)	2 mg/dL	5.00 mg/L	-5%
		25.00 mg/L	0%

The following substances do not interfere with the TRF method when present *in urine* at the concentrations indicated. Inaccuracies (biases) due to these substances are less than 10 % at transferrin concentrations of 0.72 mg/dL to 2.38 mg/dL [7.22 mg/L to 23.83 mg/L].

Substance	Test Concentration	SI Units
Acetone	1000 mg/dL	217 mmol/L
Ascorbic acid	600 mg/dL	27.2 mmol/L
Boric acid	1000 mg/dL	161.7 mmol/L
Bovine serum albumin	500 mg/dL	5 g/L
Creatinine	500 mg/dL	44.2 mmol/L
Ethanol	1000 mg/dL	217 mmol/L
Glucose	2000 mg/dL	111 mmol/L
Human serum albumin	400 mg/dL	4 g/L
Immunoglobulin G (IgG)	100 mg/dL	1 g/L
Oxalic acid	10 mg/dL	0.8 mmol/L
Riboflavin	7.5 mg/dL	200 µmol/L
Sodium azide	1000 mg/dL	153.8 mmol/L
Sodium fluoride	900 mg/dL	214.5 mmol/L
Urea	6000 mg/dL	1 mol/L

**pH:** Effect of pH on TRF-U was evaluated. Ten replicates of a urine sample were evaluated across a pH range 3 to 9. Sample bias was less than 10%.

*Hook Effect:*

The possibility of hook effect occurring when using the Dimension Vista® System TRF-U assay was evaluated for urine. Testing indicated no hook effect up to 663 mg/L for urine.

*f. Assay cut-off:*

Not applicable

2. Comparison studies:

*a. Method comparison with predicate device:*

Matched urine samples containing transferrin (sample concentration range from 2.0 mg/L to 24.4 mg/L) were tested with the Seimens TFR-U assay and predicate device following CLSI EP9-A2. A total of 63 urine samples were analyzed in singlicate (33 native ranging 2.0 to 24.4 mg/L, and 30 spiked ranging 10 to 20.7 mg/L). Passing-Bablok regression yielded the following statistics:

Comparative Method	Slope (95%CI)	Y-Intercept (mg/L) (95%CI)	Correlation Coefficient	n
N Antisera to Human Transferrin on the BN ProSpec®	0.983 (.950-1.013)	-0.00059 (-0.336 – 0.230)	0.991	63

*b. Matrix comparison:*

Not applicable

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 concentration of transferrin in urine of healthy individuals is below the detection limit of detection for this method (less than 0.20 mg/dL [2.00 mg/L]) and is based on the following literature reference Rifai N, Gubar K, Silverman LM. Immunoturbidimetry: an attractive technique for the determination of urinary albumin and transferrin. Clin Biochem 1987; 20:179-81. This was confirmed by performing a reference interval transference study evaluating TRF-U levels in 20 apparently 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.