

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

A. 510(k) Number:

k063655

B. Purpose for Submission:

New Device

C. Measurand:

Ceruloplasmin

D. Type of Test:

Quantitative, nephelometric.

E. Applicant:

Dade Behring, Inc.

F. Proprietary and Established Names:

Dimension Vista[™] Ceruloplasmin Flex[®] reagent cartridge (CER)

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 866.5210; Ceruloplasmin Immunological Test System

21 CFR 862.1150; Calibrator

21 CFR 862.1660; Quality Control Material (assayed and unassayed)

2. Classification:

Class II; Ceruloplasmin test system and Calibrator

Class I; Control

3. Product code:

CHN; Immunochemical, Ceruloplasmin

JIX; Calibrator, Multi-Analyte Mixture

JJY; Multi Analyte Controls

4. Panel:

Immunology 82; Clinical Chemistry (75)

H. Intended Use:

1. Intended use(s):

Dimension Vista[™] CER Flex[®] reagent cartridge:

The CER method is an *in vitro* diagnostic test for the quantitative determination of ceruloplasmin in human serum, heparinized plasma or EDTA plasma on the Dimension Vista[®] System. Measurements of ceruloplasmin aid in the diagnosis of copper metabolism disorders.

Dimension Vista[™] Protein 1 Calibrator:

PROT1 CAL is an *in vitro* diagnostic product for the calibration of the C3 Complement (C3), C4 Complement (C4), Ceruloplasmin (CER), Immunoglobulin A (IGA), Immunoglobulin G (IGG), Immunoglobulin M (IGM) and Prealbumin (PREALB) methods on the Dimension Vista[®] System.

Dimension Vista™ Protein 1 Control L, M and H:

PROT1 CON L, M and H are assayed intralaboratory quality controls for assessment of precision and analytical bias in the determination of C3 complement (C3), C4 complement (C4), ceruloplasmin (CER), immunoglobulin A (IGA), immunoglobulin G (IGG), immunoglobulin M (IGM) and prealbumin (PREALB) 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:
For use on the Dade Behring Dimension Vista® System

I. Device Description:

Dimension Vista™ CER Flex® reagent cartridge

Dimension Vista™ CER Flex® reagent cartridge consists of 12 wells containing reaction buffer: phosphate buffer and polyethylene and rabbit antiserum to human ceruloplasmin.

Dimension Vista™ Protein 1 Calibrator

Protein 1 Calibrator is a multi-analyte, liquid, human serum based product containing C3 complement, C4 complement, ceruloplasmin (CER), immunoglobulin A (IGA), immunoglobulin G (IGG), immunoglobulin M (IGM) and prealbumin (PREALB).

Dimension Vista™ Protein 1 Control L, M and H

Protein 1 Control L, M and H are multi-analyte, liquid, human serum based products containing C3 complement, C4 complement, ceruloplasmin (CER), immunoglobulin A (IGA), immunoglobulin G (IGG), immunoglobulin M (IGM) and prealbumin (PREALB).

Calibrators and Controls are sold separately.

J. Substantial Equivalence Information:

1. Predicate device name(s):
Dade Behring N Antisera to Human Ceruloplasmin
Dade Behring N Protein Standard SL
Dade Behring N/T Protein Control SL
2. Predicate 510(k) number(s):
k053074; k012470; k012468
3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	For the quantitative determination of ceruloplasmin	Same
Antibody	Rabbit polyclonal	Same
Reportable Range	0.07 to 2.2 g/L	Same
Controls	L, M and H	Same

Similarities		
Item	Device	Predicate
Traceability	Calibrators traceable to ERM® DA470 reference standard	Same
Differences		
Item	Device	Predicate
Sample matrix	Serum, heparinized plasma or EDTA plasma	Serum or heparinized plasma
Instrumentation	Dimension Vista® System	BN™ Systems
Calibrator	Dimension Vista™ Protein 1 Calibrator	N Protein Standard SL
Calibrator Constituents	C3, C4, ceruloplasmin, IgA, IgG, IgM, and prealbumin	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, retinol binding protein, Ig Light-chain kappa, Ig Light-chain lambda, soluble transferrin receptor, ferritin, β_2 -microglobulin and total protein
Control	Dimension Vista™ Protein 1 Control L, M and H	N/T Protein Control SL L, M and H
Control Constituents	C3, C4, ceruloplasmin, IgA, IgG, IgM, and prealbumin	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, retinol binding protein, Ig Light-chain kappa, Ig Light-chain lambda, soluble transferrin receptor, ferritin, β_2 -microglobulin and total protein.

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

None

L. Test Principle:

Proteins contained in human body fluids form 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 relevant 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 Study

Specimens at various levels (Protein 1 Control L, M, H; Serum High, Serum Pool High and Plasma High) were analyzed in duplicate, twice a day, for 20 days. The repeatability and within-lab standard deviations (SD) and percent coefficient of variation (%CV) were calculated and a summary of the precision data is presented in the Table below.

Material	Mean Value (g/L)	Within-run SD (%CV)	Within-Lab SD (%CV)
PROT1 CON L	0.22	0.01 (3.81)	0.01 (4.53)
PROT1 CON M	0.26	0.01 (3.02)	0.01 (3.42)
PROT1 CON H	0.41	0.02 (3.94)	0.02 (4.01)
Serum High	1.63	0.04 (2.54)	0.05 (3.08)
Serum Pool High	2.13	0.03 (1.54)	0.04 (1.78)
Plasma Pool	0.51	0.01 (2.65)	0.03 (5.22)

b. *Linearity/assay reportable range:*

Linearity across the assay range was confirmed by testing a calibrator with a high concentration of ceruloplasmin. This calibrator was serially diluted with System Diluent (3.40 to 0.07 g/L). Each dilution was tested in replicates of three. Data were analyzed using linear regression analysis. The acceptance criteria of slope between 0.9 and 1.1 and correlation coefficient ≥ 0.95 were met. A summary of the linearity data is presented in the table below.

Linearity Data Summary

Dimension Vista™	n	Slope	Intercept	Correlation Coefficient
CER	6	1.018	-0.015	1.000

High Dose Hook Effect

The possibility of hook effect occurring when using the Dimension Vista™ CER assay was evaluated with a serum sample above the assay range. The sample was analyzed on both the BN ProSpec® System and the Dimension Vista® System, indicating no hook effect up to 4.441 g/L. A summary of the hook effect data are presented below.

BN ProSpec® System Ceruloplasmin Concentration (g/L)	Dimension Vista® Test Dilution	Dimension Vista™ CER Concentration (g/L)
4.13	1:10	>2.2 (exceeds assay range)
	1:100	4.441

- c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
The analyte in the calibrator and controls is traceable to ERM® DA470 reference standard.
- d. *Detection limit:*
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 the System Diluent plus 2SD and was determined to be 0.14 g/L.
- e. *Analytical specificity:*
Potentially interfering endogenous substances
Interference testing was performed to determine the effect of various endogenous and exogenous substances on the Dimension Vista™ CER assay. For all interferents except Triglycerides, RF, and Total Protein, 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. A bias exceeding $\pm 10\%$ was considered a significant interference.
For each spiked sample, the % recovery was determined [% Recovery = (Test result/Baseline) x 100]. The acceptance criterion of $\pm 10\%$ relative deviation from the base pool was met for all interferents tested. A summary of the results is presented below.

Exogenous Substance	Concentration in sample	95% Sample + 5% Stock solution		
		Test sample Mean g/L	Control g/L	Recovery (%)
Bilirubin (conjugated)	60 mg/dL	0.46	0.44	103%
Bilirubin (unconjugated)	60 mg/dL	0.45	0.44	100%
Creatinine	30 mg/dL	0.44	0.44	100%
Hemoglobin	1000 mg/dL	0.44	0.44	98%
Immunoglobulin G (IgG)	5000 mg/dL	0.34	0.32	106%
Protein: Albumin	6000 mg/dL	0.39	0.39	101%
Urea	500 mg/dL	0.45	0.44	102%
Cholesterol	500 mg/dL	0.43	0.42	102%
Uric Acid	20 mg/dL	0.44	0.44	100%

Triglyceride interference was evaluated by testing five samples containing a known amount of triglycerides and compared to results from the same sample after centrifugation. Results showed no significant change in CER recovery after centrifugation. This study however, only showed effect of centrifugation but did not address the triglyceride interference since the actual CER concentration in these samples without triglycerides were not known. The package insert was revised to state that lipemic samples should be avoided in the specimen handling section.

To evaluate interference from total protein (TP) and rheumatoid factor (RF), samples which had RF concentrations > 500 IU/mL and TP concentrations > 120 g/L and samples with no detectable RF concentration or low TP concentrations were used to prepare samples for the study. A (1+1) mixture of

samples with high concentrations of RF and TP were prepared and the ceruloplasmin concentrations determined in replicates of five on the Dimension® Vista System. For each sample preparation, the % recovery was calculated [% Recovery = (measured result/calculated result) x 100]. The acceptance criterion of $\pm 10\%$ relative deviation from the calculated result was met. No significant interference was found with the Dimension Vista® CER method from the presence of RF up to 685 IU/mL or from elevated Total Protein at 127 g/L at CER concentrations ranging from 0.19 to 0.754 g/L. Results for TP and RF interference are presented in the following tables:

	<i>TP (g/L)</i>	<i>CER (g/L)</i>
Sample A	213	0.173
Sample B	217	0.419
Sample C	209	0.707
Sample D	131	0.191
Sample E	128	0.447
Sample F	132	0.755
Sample G	40.9	0.206
Sample H	33.1	0.327
Sample I	35.3	0.666

Sample ID	Dilution 1+1	TP (g/L)	CER calculated (g/L)	CER measured (g/L)	Recovery (%)
1	Sample A + G	127	0.190	0.196	103
2	Sample B + H	125	0.373	0.374	100
3	Sample C + I	122	0.687	0.693	101
4	Sample D + G	86.0	0.198	0.203	102
5	Sample E + H	80.6	0.387	0.392	101
6	Sample F + I	83.7	0.711	0.791	111

	<i>RF (IU/mL)</i>	<i>CER (g/L)</i>
Sample A	922	0.248
Sample B	1370	0.443
Sample C	1340	0.762
Sample D	504	0.207
Sample E	774	0.470
Sample F	423	0.628
Sample G	< 9.6	0.185
Sample H	< 9.6	0.430
Sample I	< 9.6	0.746

Sample ID	Dilution 1+1	RF (IU/mL)	CER calculated (g/L)	CER measured (g/L)	Recover (%)
1	Sample A + G	461	0.216	0.219	101
2	Sample B + H	685	0.415	0.415	100

Sample ID	Dilution 1+1	RF (IU/mL)	CER calculated (g/L)	CER measured (g/L)	Recover (%)
3	Sample C + I	670	0.754	0.733	97
4	Sample D + G	252	0.196	0.194	99
5	Sample E + H	387	0.450	0.461	102
6	Sample F + I	212	0.507	0.506	100

f. Assay cut-off:

No change.

2. Comparison studies:

a. Method comparison with predicate device:

The Dimension Vista™ CER assay was compared to the Dade Behring N Antisera to Human Ceruloplasmin assay on the BN ProSpec® System by evaluating 60 serum samples, 32 Li plasma and 38 NH-plasma samples with concentrations ranging from 0.09 g/L to 2.20 g/L. Regression analysis of these results yielded the following results:

Method Comparison Study

Comparative Method	n	Slope	Intercept (g/L)	Correlation Coefficient
N Antisera to Human Ceruloplasmin on BN ProSpec® (95% CI)	130	1.009 (0.986-1.036)	0.008 (0.00-0.02)	0.994

b. Matrix comparison:

Serum versus Plasma Comparison:

A comparison was performed with matched specimens of serum, and EDTA, lithium heparin, and sodium heparin plasma (10 for each serum/plasma pairs) assayed on the Dimension Vista® System. The samples covered the reportable range. Linear regression analysis showed agreement between the serum and the plasma samples tested.

Linear Regression vs. Serum			
	Li Hep	Na Hep	EDTA
Slope:	0.99	1.02	0.97
Y-int (g/L):	0.00	-0.02	0.01
r:	0.999	0.998	1.000
Syx:	0.03	0.05	0.02
Slope 95% CI	0.971-1.01	0.986-1.06	0.955-0.99
% Recovery Statistics			
Mean:	-0.8%	-1.0%	-0.4%
Min:	-4.9%	-5.1%	-5.8%
Max:	5.3%	4.2%	5.7%

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:
Expected Values: 0.2 – 0.6 g/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.