510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:
k051456

B. Purpose for Submission:
This is a new device.

C. Measurand:
Ceruloplasmin

D. Type of Test:
Quantitative immunoturbidimetric

E. Applicant:
Sentinel CH. S.r.l.

F. Proprietary and Established Names:
Sentinel Ceruloplasmin

G. Regulatory Information:

1. Regulation section:
   21 CFR§ 866.5210 Ceruloplasmin Immunological Test System
2. Classification:
   Class II
3. Product code:
   JFR, Indirect Copper Assay, Ceruloplasmin
4. Panel:
   (82) Immunology

H. Intended Use:

1. Intended use(s):
   Quantitative immunoturbidimetric determination of ceruloplasmin [Cerul] in serum and plasma using AEROSET® System and ARCHITECT® *c*8000 System.
2. Indication(s) for use:
   The Sentinel Ceruloplasmin assay is used for the quantitation of ceruloplasmin (copper transporting serum protein) levels in human serum or plasma. Measurements of ceruloplasmin aid in the diagnosis of copper metabolism disorder.
3. Special conditions for use statement(s):
   The device is for prescription use only.
4. Special instrument requirements:
   AEROSET® (k980367) cleared on 4/01/9898 and ARCHITECT® c8000 Systems (k980367/A002) cleared on 1/17/01).

I. Device Description:

The device consists of the following: Reagent 1 – 20 mmol/L (pH 7.5) phosphate buffer with ≥5% PEG, 150 mmol/L sodium chloride, and <0.1% sodium azide; Reagent 2 – goat anti-ceruloplasmin polyclonal anti-serum with <0.1% sodium azide These reagents are ready to use.
Calibrators and controls are sold separately.
The calibrator used with the Sentinel Ceruloplasmin is the Sentinel Plasmaproteins

Cal 3x cleared under k051457. Any Immuno controls can be used for this application.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   Roche Ceruloplasmin on the Roche/Hitachi 911
2. Predicate 510(k) number(s):
   k921661
3. Comparison with predicate:

Similarities		
Item	Device	Predicate
	Sentinel Ceruloplasmin	**Roche Ceruloplasmin on the Roche/Hitachi 911**
Intended Use	Quantitation of ceruloplasmin	Same
Sample type	Serum or plasma	Same
Assay Principle	Immunoturbidimetry	Same
Standardization	CRM 470 (RPPHS-Reference Preparation for Proteins in Human Serum)	Same
Components	Controls and calibrators are sold separately	Same

Differences		
Item	Device	Predicate
Assay range	2 to 110 mg/dL	10 to 140 mg/dL
Instrument	AEROSET and ARCHITECT c8000	Roche/Hitachi 911
Source of antibody	Goat	Rabbit

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

None referenced.

L. Test Principle:

The determination of ceruloplasmin is based on the specific immunoturbidimetric reaction which occurs between the anti-ceruloplasmin polyclonal antiserum and its corresponding antigen under optimal pH conditions and in the presence of polyethylene glycol (PEG). The turbidity of the immune complex is proportional to the concentration of the analyte in the sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:
   a. *Precision/Reproducibility:*
      Precision on the AEROSET system (within-run, between-run and total), was determined by analyzing three control levels in duplicate twice a day, over a period of 10 days (n=40) using one reagent/calibrator lot and one operator. Precision on the ARCHITECT c8000 system (within-run, between-run and

total), was determined by analyzing three control levels in 4 replicates twice a day, over a period of 5 days (n=40) using one reagent/calibrator lot and one operator.
The following results are obtained:

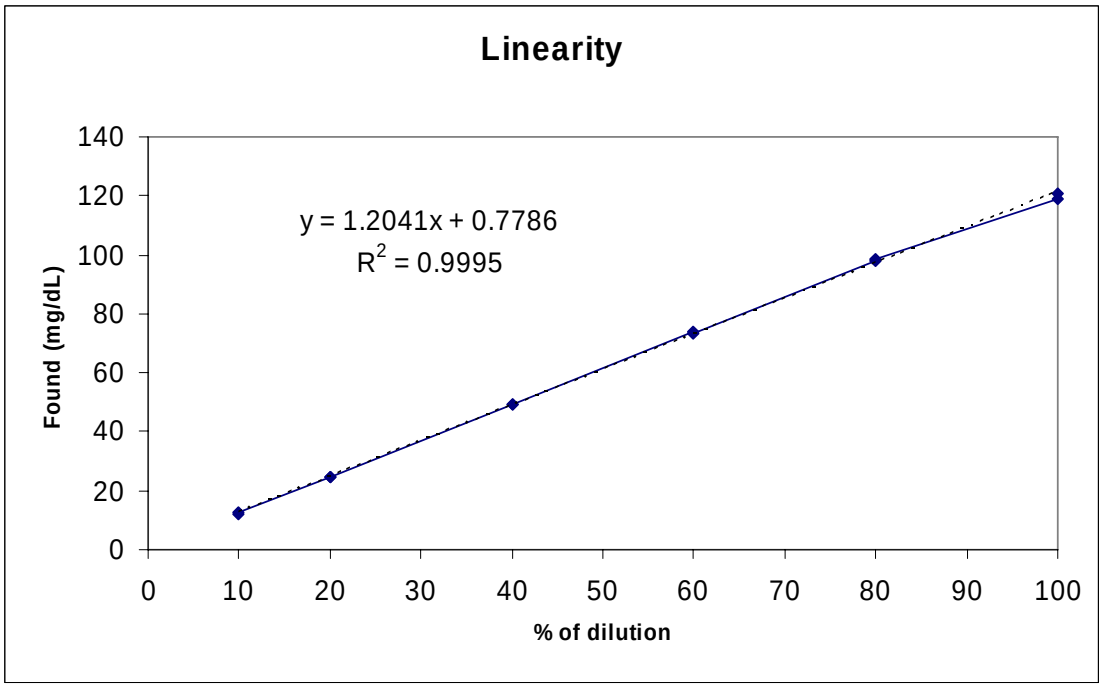
AEROSET

Level	N	Mean (mg/dL)	Within-run Mean %CV	Between-run Mean %CV	Total %CV
1	40	20.47	1.66	2.78	3.69
2	40	29.44	1.25	4.74	5.33
3	40	70.27	2.23	2.94	4.33

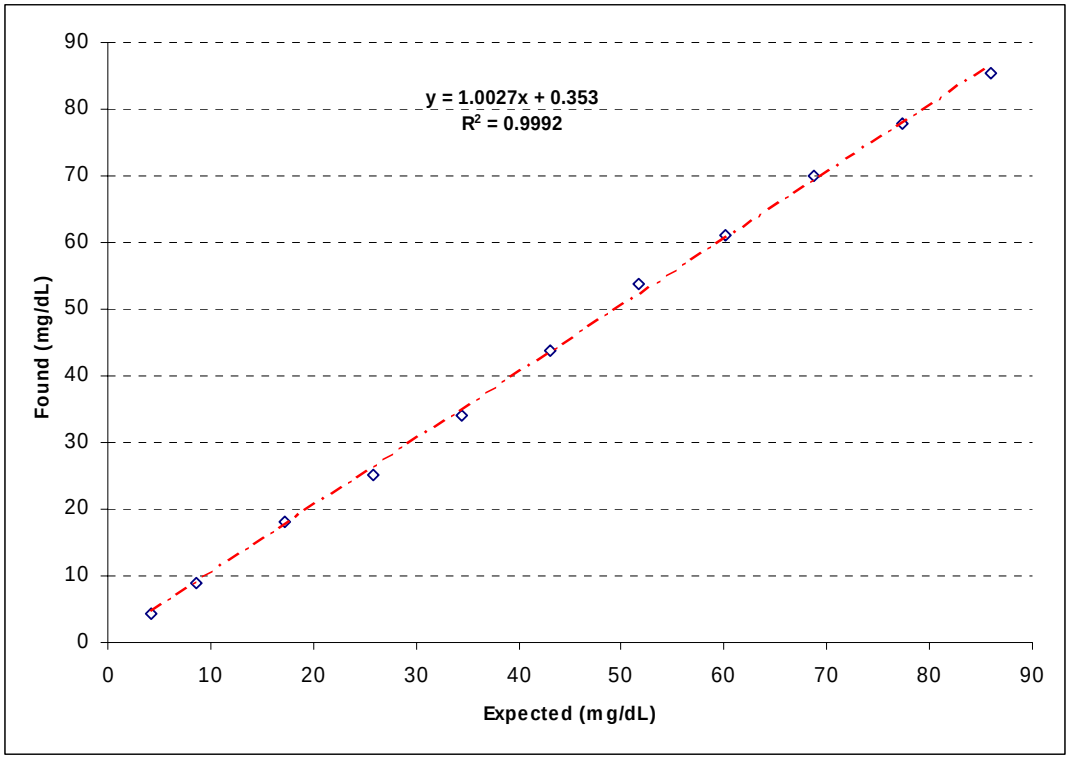
ARCHITECT

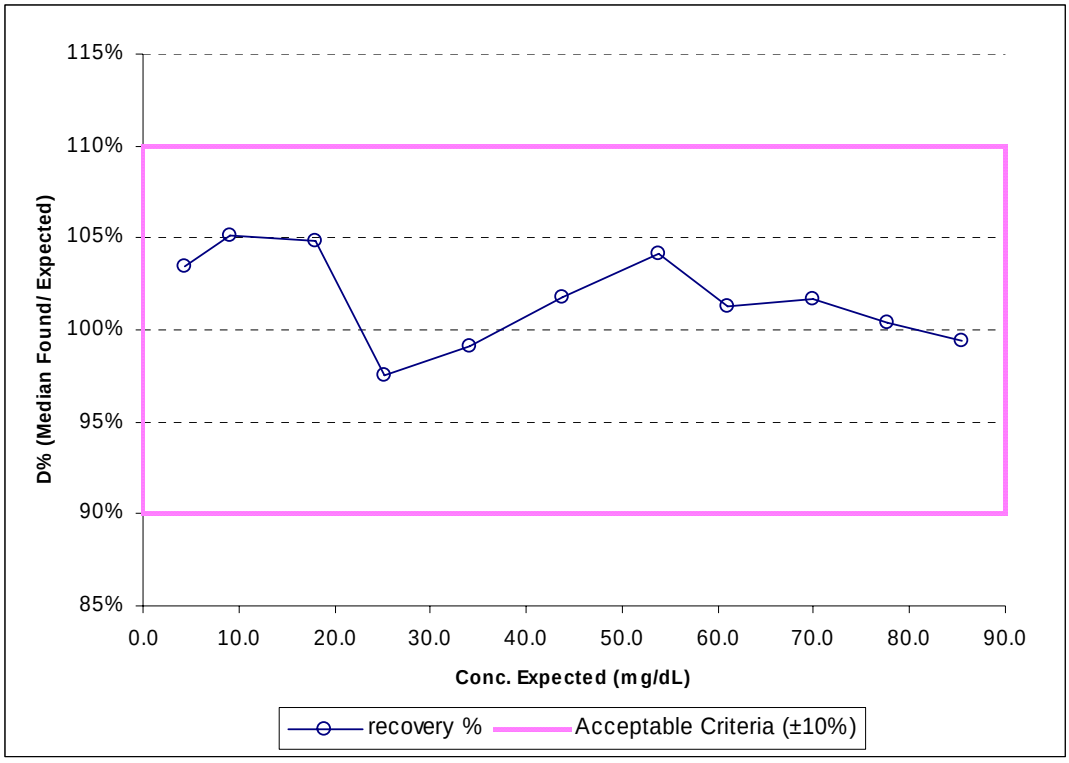
Level	N	Mean (mg/dL)	Within-run Mean %CV	Between-run Mean %CV	Total %CV
1	40	13.30	1.86	3.81	4.06
2	40	49.70	1.69	2.77	3.70
3	40	65.70	1.13	0.85	1.28

b. *Linearity/assay reportable range:*
Linearity testing was performed on an AEROSET® System using a serum sample containing 120 mg/dL of Ceruloplasmin diluted in physiologic saline at 6 different dilutions (10%, 20%, 40%, 60%, 80%, and 100%). Each dilution was analyzed in quadruplicate. Data generated indicate acceptable linearity up to 120 mg/dL, with a regression equation $y = 1.2041x + 0.7786$, $r^2 = 0.9995$. The claim for this assay is 2 to 110 mg/dL.



An additional linearity study was done on the ARCHITECT c8000 per the reviewer's request but due to the lack of a highly concentrated sample, a serum sample with a concentration of 86 mg/dL was used. The spline calibration method was used which would linearize the response in absorbance of the reactive against the actual concentration. The serum sample was diluted in physiologic saline at10 different dilutions (5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, and 100%). Each dilution was analyzed in triplicate. Median of the result was compared with the expected calculated value. % recovery of the median result found against the expected value must be within 10% (90-110%). The following results were obtained.





c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
The traceability of the method is verified using CRM 470 (Certified Reference Material) from BCR (EC Community Bureau of Reference) corresponding to RPPHS (Reference Preparation for Protein in Human Serum) lot numbers 91/06 19. Once this lyophilized material is reconstituted, it is aliquoted and stored frozen at -20 ^{o}C (master lot). The Sentinel Plasmaproteins Cal 3x value assignment is assessed by testing a new lot of calibrator with a master lot. In the assignment testing, five replicates per 3 runs are assessed for ceruloplasmin assay. The assigned value is calculated as the average of all replicates for the assay. Quality control materials are used to verify the assay performance at every step of the test.

d. *Detection limit:*
Sensitivity was determined on the AEROSET and ARCHITECT c8000 from 6 serial dilutions (2.5%, 5%, 10%, 15%, 25%, and 50%) of a sample containing 26.44 mg/dL ceruloplasmin with normal saline. Each dilution was tested over 20 replicates for the AEROSET and 10 replicates for the ARCHITECT c8000. For immunoturbidimetric methods, the sensitivity represents the lowest measurable concentration of analyte that can be distinguished from the zero standard. Results showed sensitivity to be less than 1.0 mg/dL for both instruments. The claim for this assay is 2.0 mg/dL.

e. *Analytical specificity:*
Interfering substances
Interference testing was performed by spiking a sample containing ceruloplasmin. For each interfering substance, the sample was split in two aliquots, one spiked with a concentrated interfering substance and the other

with normal saline. Each dilution was assayed in triplicate. %Recovery of spiked samples vs. non-spiked was calculated. An acceptance criterion is 100 ± 10%. No significant interference was observed in:

- Bilirubin up to 30 mg/dL
- Hemoglobin up to 500 mg/dL
- Triglycerides up to 1000 mg/dL
- Rheumatoid Factor up to 70 IU/mL

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

A total of 75 patient samples, (one replicate per run) covering the reportable range of the analyte were tested using Sentinel Ceruloplasmin on the AEROSET® analyzer and the predicate device Roche Ceruloplasmin on the Hitachi 911 analyzer. No demographics were provided for samples used in this study due to Privacy Law in Italy. The following results were shown:
Slope = 1.0256 (95% CI 0.948 to 1.085)
Intercept = -1.0205 (95% CI -2.96 to 1.11)
r = 0.9696

A total of 75 patient samples, (one replicate per run) covering the reportable range of the analyte were tested using Sentinel Ceruloplasmin on the AEROSET® analyzer and the ARCHITECT c8000® analyzer. Patient demographics were not provided for samples used in this study due to Privacy Law in Italy. The following results were shown:
Slope = 1.0150 (95%CI 0.930 to 1.073)
Y-intercept = -0.5341 (95%CI -2.17 to 1.81)
r = 0.9723

b. Matrix comparison:

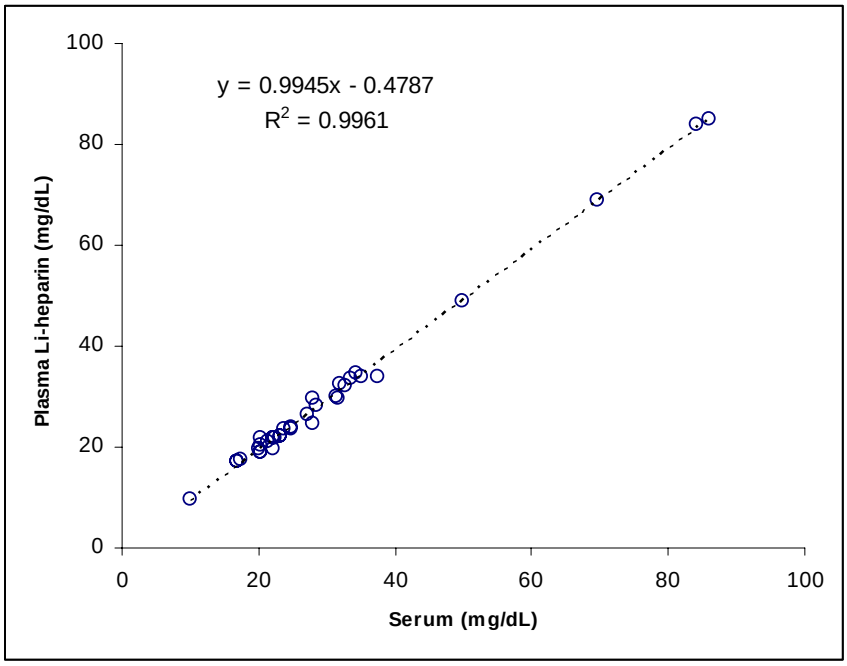
Thirty five (35) fresh samples were collected with no anticoagulant (serum), and in EDTA and Li-heparin plasma. Each three samples of all 35 individuals were analyzed at the same time in one replicate. Criteria of acceptance are slope 1.00± 0.05 and Pearson r≥0.9500. Matrix comparison was performed using Abbott ARCHITECT c8000. Results are as follows :

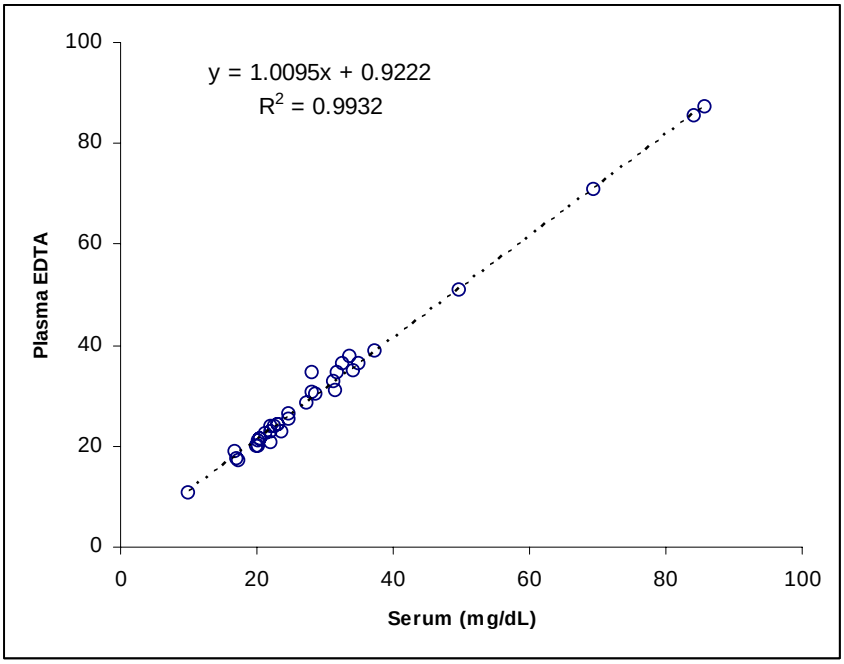
Plasma Li-heparin vs. Serum:

Parameter	Estimation	95% Confidence Interval
Slope	0.9945	0.973 to 1.016
Intercept	-0.4787	-1.24 to 0.28

Plasma EDTA vs. Serum:

Parameter	Estimation	95% Confidence Interval
Slope	1.0095	0.981 to 1.040
Intercept	0.9222	-0.12 to 1.93





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 provided

5. Expected values/Reference range:
   The reference range 20 - 60 mg/dL is from Tietz Textbook of Clinical Chemistry.

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.