Food and Drug Administration
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510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

I Background Information:

A 510(k) Number

K190495

B Applicant

BioSystems S.A.

C Proprietary and Established Names

Transferrin

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
DDG	Class II	21 CFR 866.5880 - Transferrin immunological test system	IM - Immunology

II Submission/Device Overview:

A Purpose for Submission:

New Device

B Measurand:

Transferrin

C Type of Test:

Quantitative, Turbidimetry

III Intended Use/Indications for Use:

A Intended Use(s):
See Indications for Use below.

B Indication(s) for Use:
Reagents for the measurement of transferrin concentration in human serum or plasma. The obtained values are useful as an aid in the diagnosis of iron deficiency anemia and hemochromatosis. This reagent is for use in the BioSystems BA analyzers.

C Special Conditions for Use Statement(s):
Rx - For Prescription Use Only

D Special Instrument Requirements:

BioSystems BA400 analyzer

IV Device/System Characteristics:

A Device Description:

The Transferrin assay consists of the following reagents:
A Reagent: 60 mL/vial, imidazole buffer 0.05 mol/L, sodium azide 0.95 g/L, pH 7.5.
B Reagent: 15 mL/vial, goat anti-human transferrin antibodies, sodium azide 0.95 g/L

Additional materials required but not provided are protein calibrators (BioSystems cod. 31075). The set contains 5 different levels and it should be used to prepare the calibration curve. The calibrators are supplied ready to use.

These reagents are intended to be used with the BioSystems BA analyzers.

B Principle of Operation:

The Transferrin reagent is a turbidimetric assay in which the transferrin in the sample precipitates in the presence of anti-human transferrin antibodies. The light scattering of the antigen-antibody complexes is proportional to the transferrin concentration and can be measured by turbidimetry.

V Substantial Equivalence Information:

A Predicate Device Name(s):
Tina-quant Transferrin Ver.2

B Predicate 510(k) Number(s):
K012393

C Comparison with Predicate(s):

Device & Predicate Device(s):	K190495 Device	K012393 Predicate
Device Trade Name	**Transferrin**	**TRSF2 Tina-quant Transferrin ver.2**
General Device Characteristic Similarities		
Intended Use/Indications For Use	Reagents for the measurement of transferrin concentration in human serum or plasma. The obtained values are useful as an aid in the diagnosis of iron deficiency anemia and hemochromatosis. This reagent is for use in the BioSystems BA analyzers.	In vitro test for the quantitative determination of transferrin in human serum and plasma on Roche/Hitachi cobas c systems.
Measurand	Transferrin	Same
Method	Immunological agglutination	Same
Assay type	Quantitative	Same
Traceability	ERM-DA470k/IFCC	Same
Sample Type	Serum and Li-heparin plasma	Same
General Device Characteristic Differences		
Analyzer	BioSystems BA400	Cobas c 311, 501/502
Antibody soruce	Goat anti-human transferrin	Rabbit anti-human transferrin
Measuring range	12 – 520 mg/dL	10 – 520 mg/dL

VI Standards/Guidance Documents Referenced:

CLSI EP05-A3, Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline-Third Edition
CLSI EP06-A, Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline
CLSI EP17-A2, Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline-Second Edition
CLSI EP09-A3, Measurement Procedure Comparison and Bias Estimation Using Patient Samples; Approved Guideline - Third Edition
CLSI EP07-A3 Interference Testing in Clinical Chemistry

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

Precision of the Ferritin assay was evaluated according to CLSI EP05-A3. Five different levels of human serum patient samples where used to carry out precision, with concentrations of 20.4 mg/dL, 123 mg/dL, 225 mg/dL, 402 mg/dL and 466 mg/dL. The study was conducted over 20 days, with two runs per day and two replicates per specimen, for a total of 80 measurements. The same five samples were used to assess lot-to-lot and instrument-to-instrument imprecision. For the lot-to-lot imprecision assessment, the study was conducted over five days, with two runs per day and with two replicates per one, using three reagent lots and one analyzer. For the instrument-to-instrument imprecisions assessment, the study was conducted over five days, with two runs per day and with two replicates per run, using three analyzers and one reagent lot. The results are summarized in the table below:

Sample	Mean (mg/dL)	Within-Run		Between-Run		Between-Day		Total	
		SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
1	20.4	0.52	2.6	1.3	6.2	1.4	6.7	0.73	3.6
2	123	1.1	0.9	2.3	1.9	2.6	2.1	1.3	1.1
3	225	1.5	0.7	4.5	2.0	4.7	2.1	2.9	1.3
4	402	7.2	1.8	8.9	2.2	11.4	2.8	7.4	1.8
5	466	8.1	1.7	9.3	2.0	12.3	2.7	7.0	1.5

Sample	Mean (mg/dL)	Between-lot		Between-Instrument	
		SD	CV (%)	SD	CV (%)
1	20.4	2.2	6.6	1.2	6.3
2	123	4.2	7.2	1.5	1.3
3	225	6.2	4.3	7.7	3.6
4	402	7.1	2.3	19.2	5.2
5	466	11.6	2.4	22.0	5.0

2. Linearity:

Linearity was evaluated according to CLSI guideline EP6-A. A dilution series with nine levels was prepared by diluting a high sample with a concentration of 641 mg/dL with the low concentration sample of 0 mg/dL to cover the measuring range. The results are summarized as follows:

Analyte	Test Range	Slope (95% CI)	Intercept (95% CI)	R^2
Transferrin	0–641 mg/dL	1.01 (0.999–1.029)	-0.83 (-5.50–3.84)	0.999

3. Analytical Specificity/Interference:

An interference study was performed in accordance with CLSI EP07-A3 guideline. Two human serum samples with two different analyte concentrations (178 mg/dL and 425 mg/dL) were spiked with increasing concentrations of potential endogenous and exogenous interferents and analyzed in duplicate.

No significant assay interference effects were observed in serum when tested with hemoglobin (500 mg/dL), unconjugated bilirubin (30 mg/dL), conjugated bilirubin (30 mg/dL), triglycerides (1625 mg/dL), rheumatoid factor (300 IU/mL), acetaminophen (20 mg/dL), ascorbic acid (30 mg/dL), N-acetyl-L-cysteine (10 mg/L), heparin (3000 U/L), deferoxamine (250 mg/L), dobesilate (200 mg/L), ampicillin (152 µmol/L), levodopa (20 mg/L), acetylsalicylic acid (3.62 mmol/L), ferrous sulfate (1.0 mmol/L), rifampicin (60 mg/L), EDTA (3.4 µmol/L), valproic acid (3467 µmol/L), phenylbutazone (400 mg/L), theophylline (222 µmol/L), cholesterol (13 mmol/L), metronidazole (701 µmol/L), prednisone (0.84 µmol/L), and methotrexate (2 mmol/L).

Antigen Excess/Prozone Effect:

A study was performed to verify the prozone performance on the BioSystems BA400 analyzer. A total of 11 samples with different analyte concentrations were evaluated. No prozone effect was observed up to 3000 mg/dL.

4. Assay Reportable Range:

   Transferrin: 12–520 mg/dL

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

   Traceability:

   The calibration of the assay is traceable to ERM-DA470k/IFCC.

   Stability:

   Real-time stability testing was conducted using human serum level samples with concentrations of 200 mg/dL and 400 mg/dL. Eight time points were tested, 0, 1, 3, 6, 10, 14, 20, 26 and 41 months. The results from this study support a shelf-life of 26 months when stored at the recommended storage temperature of 2–8°C.

   Real-time stability study was carried out with open-vial reagents. Therefore, the results support the open-vial reagent shelf-life of 26 months when stored at the recommended storage temperature of 2–8°C.

   On-board stability study supports reagent stability of up to 2 months when kept in the refrigerated compartment of the analyzer.

6. Detection Limit:

   Detection capabilities studies for each analyte were evaluated based upon CLSI EP17-A2 guideline.

   Limit of blank (LoB) study was performed by testing five blank samples comprised of albumin matrix. Samples were tested in replicates of four per run, one run per day for three days using two reagent lots, for a total of 60 observations per reagent lot, and for a total of 120 observations.

Limit of detection (LoD) study was performed by testing five native serum samples with analyte concentrations close to expected detection limit for each analyte. Samples were tested in replicates of four per run, one run per day for three days using two reagent lots, for a total of 60 observations per reagent lot, and for a total of 120 observations.

Limit of Quantitation (LoQ) study was performed using five native serum samples. Samples were tested in replicates of four per run, one run per day for three days using two reagent lots, for a total of 60 observations per reagent lot, and for a total of 120 observations.

The results are as follows:

Detection Limit Parameter	Transferrin (mg/dL)
LoB	0.49
LoD	1.18
LoQ	12.0

7. Assay Cut-Off:

Not applicable

B Comparison Studies:

1. Method Comparison with Predicate Device:

A total of 84 human serum samples with transferrin concentrations across the assay measuring range were tested compared to the predicate device. Another study was conducted using a total of 69 human Li-heparin plasma samples with transferrin concentration covering the measuring range compared to the predicate device.

Passing Bablok regression analysis was performed to evaluate the analytical equivalence of the transferrin assay when compared to the predicate. The results are summarized as follows:

Matrix	N	Range	Slope (95% CI)	Intercept (95% CI)	R^2
Serum	84	75.4–504	0.95 (0.92–0.98)	7.91 (1.48–14.33)	0.993
Li-heparin plasma	69	61.1–494.0	0.97 (0.95–0.99)	-0.01 (-4.81–4.31)	0.997

2. Matrix Comparison:

Matrix comparison study was carried out using 40 paired specimens of serum and lithium-heparin plasma, across the assay measuring range. The results of the Passing-Bablok regression analysis support the equivalency of the two matrices, and are as follows:

N	Slope (95% CI)	Intercept (95% CI)	R^2
40	0.94 (0.93–0.95)	2.18 (0.42–5.63)	0.999

C Clinical Studies:

1. Clinical Sensitivity:

   Not applicable

2. Clinical Specificity:

   Not applicable

3. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

   Not applicable

D Clinical Cut-Off:

Not applicable

E Expected Values/Reference Range:

Transferrin (serum or plasma): 200–360 mg/dL

The reference range was verified by testing 20 apparently healthy subjects.

This range is given for orientation only, and each lab should establish their own reference range.

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.