510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K240987

B Applicant

Beckman Coulter, Inc.

C Proprietary and Established Names

Access sTfR

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:

Modification of a previously cleared device – the change of substrate and updated analytical measuring interval of the assay on the DxI 9000 Access Immunoassay Analyzer

B Measurand:

Transferrin

C Type of Test:

Quantitative, Chemiluminescent Immunoassay

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

The Access sTfR assay is a paramagnetic particle, chemiluminescent immunoassay for the quantitative determination of soluble transferrin receptor (sTfR) levels in human serum and plasma (heparin) using the Access Immunoassay Systems. This assay is intended as an aid in the diagnosis of Iron Deficiency Anemia (IDA), and for the differential diagnosis of IDA and Anemia of Chronic Disease (ACD).

This assay may also be used in conjunction with an Access Ferritin measurement to provide a calculated sTfR/log ferritin index. This index is intended as an aid in the diagnosis of IDA, and for the differential diagnosis of IDA and ACD.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

D Special Instrument Requirements:

DxI 9000 Access Immunoassay Analyzer (K221225)

IV Device/System Characteristics:

A Device Description:

Each Access sTfR reagent kit contains two reagent packs (50 tests/pack). Each pack contains the following:

- R1a: Paramagnetic particles coated with streptavidin: biotinylated soluble transferrin receptor monoclonal antibody, proteins (mouse, goat, bovine), BSA, 0.1% sodium azide and 0.17% ProClin* 300.
- R1b: Monoclonal mouse anti-human soluble transferrin receptor alkaline phosphatase (bovine) conjugate, BSA, 0.1% sodium azide and 0.17% ProClin 300.

<u>Materials needed but not supplied:</u>

- Access sTfR Calibrators: six levels (0, 3, 10, 30, 80 and 150 nmol/L)
- Quality Control (QC) materials:
  - Access sTfR QC1 (10 nmol/L)
  - Access sTfR QC2 and QC3 (25 and 90 nmol/L)
  - Commercial control materials
- Substrate: Lumi-Phos PRO
- UniCel DxI Wash Buffer II
- Access Wash Buffer II (optional material for dilution)

The modification of the Access sTfR includes:

(a) a new substrate replacement (Lumi-Phos PRO)
(b) run on DxI 9000 Access Immunoassay Analyzer with an updated analytical measuring interval of 0.05 – 150 nmol/L.

B Principle of Operation:

The Access sTfR assay is a sequential two-step immunoenzymatic ("sandwich") assay. A sample is added to a reaction vessel along with paramagnetic particles coated with anti-sTfR antibody. During incubation, the sTfR antigen in the sample binds to the immobilized anti-sTfR antibody on the solid phase. Alkaline phosphatase conjugated anti-sTfR antibody is then added and reacts with a different antigenic site on the sTfR molecule. After incubation, materials bound to the solid phase are held in a magnetic field while unbound materials are washed away. Then, the chemiluminescent substrate is added to the vessel and light generated by the reaction is measured with a luminometer. The light production is directly proportional to the concentration of analyte in the sample. Analyte concentration is automatically determined from a stored calibration.

V Substantial Equivalence Information:

A Predicate Device Name(s):

Access sTfR, Access sTfR Calibrators, and Access sTfR QC

B Predicate 510(k) Number(s):

K080634

C Comparison with Predicate(s):

Device & Predicate Device(s):	K240987 (Candidate)	K080634 (Predicate)
Device Trade Name	Access sTfR	Access sTfR
General Device Characteristic Similarities		
Intended Use/ Indications For Use	The Access sTfR assay is a paramagnetic particle, chemiluminescent immunoassay for the quantitative determination of soluble transferrin receptor (sTfR) levels in human serum and plasma (heparin) using the Access Immunoassay Systems. This assay is intended as an aid in the diagnosis of Iron Deficiency Anemia (IDA), and for the differential diagnosis of IDA	Same

	and Anemia of Chronic Disease (ACD). This assay may also be used in conjunction with an Access Ferritin measurement to provide a calculated sTfR/log ferritin index. This index is intended as an aid in the diagnosis of IDA, and for the differential diagnosis of IDA and ACD.	
Analyte	Soluble Transferrin Receptor	Same
Technology	2-site (sandwich) chemiluminescent	Same
Format	Chemiluminescent	Same
Method	Automated	Same
Calibration	Stored multi-point calibration curve	Same
Sample Type	Serum and plasma (heparin)	Same
Capture Antibody	Monoclonal anti-human sTfR	Same
Detection Antibody	Alkaline phosphatase conjugated mouse monoclonal anti-human sTfR	Same
Stability	28 days after opening, 2-10°C	Same
General Device Characteristic Differences		
Substrate	Lumi-Phos PRO substrate	Access Substrate
Instrument	DxI 9000 Access Immunoassay Analyzer	Access, Access 2, SYNCHRON LXi 725, UniCel DxI 800, UniCel DxC 600i and UniCel DxI 600
Measuring Range	0.05 – 150 nmol/L	3.0 – 150 nmol/L

VI Standards/Guidance Documents Referenced:

The following Clinical and Laboratory Standards Institute (CLSI) guidelines were used:

- CLSI EP05-A3: Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline
- CLSI EP06 2nd Edition: Evaluation of the Linearity of Quantitative Measurement Procedures
- CLSI EP09c 3rd Edition: Measurement Procedure Comparison and Bias Estimation Using Patient Samples
- CLSI EP17-A2: Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

All results presented below met the manufacturer's pre-determined acceptance criteria.

1. Precision/Reproducibility:

   Precision testing was performed in accordance with CLSI Guideline EP05-A3.

   a) Within-Laboratory Precision:

   The studies were performed by testing six levels of human serum samples in a minimum of two replicates per run, two runs per day for 20 days, resulting a minimum of 80 datapoints for each sample. Three reagent lots of the modified Access sTfR and three instruments were used in the study. The data were analyzed for repeatability (within-run), between-run, between-day, and within-laboratory precision. The mean (nmol/L), standard deviation (SD) (nmol/L) and percent coefficient of variation (%CV) were calculated for each sample. The representative data of within-laboratory precision using one lot of reagents on one instrument are summarized in table below.

Sample	Mean (nmol/L)	N	Within-Run (Repeatability)		Between-Run		Between-Day		Within-Laboratory	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
1	9.1	80	0.2	1.6	0.1	1.1	0.2	1.7	0.2	2.6
2	17	80	0.3	1.8	0.3	1.7	0.1	0.8	0.5	2.6
3	20	80	0.4	2.0	0.0	0.0	0.3	1.3	0.5	2.4
4	33	80	0.4	1.2	0.4	1.1	0.2	0.7	0.6	1.8
5	67	80	0.7	1.1	0.4	0.6	1.1	1.6	1.4	2.0
6	118	80	1.5	1.3	1.2	1.0	1.6	1.4	2.6	2.2

   b) Lot-to-Lot Precision:

   The lot-to-lot precision of Lumi-Phos PRO Substrate was assessed in K223921.

   The lot-to-lot precision of the modified Access sTfR was evaluated using three lots of reagents on the DxI 9000 Access Immunoassay Analyzer. Six serum samples at different concentrations were tested in five replicates per run, one run per day over five days, resulting N=75 datapoints per sample on one instrument. The same study was also performed on two additional instruments. The %CV for between-lot imprecision is ≤1.1% for all samples.

   c) Instrument-to-Instrument Precision:

   The instrument-to-instrument reproducibility was evaluated by testing six serum samples at different concentrations on three DxI 9000 Access Immunoassay Analyzers. Each sample was tested in five replicates per run, one run per day over five days, resulting N=75 datapoints using one lot of reagents. The same study was also repeated using two additional reagent lots. The representative data of instrument-to-instrument reproducibility using one lot of reagents are summarized in the table below.

Sample	Mean (nmol/L)	N	Within-Run (Repeatability)		Between-Day		Between-Instrument		Reproducibility	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
1	8.9	75	0.2	1.9	0.1	0.6	0.2	2.4	0.3	3.1
2	19	75	0.3	1.7	0.5	2.5	0.2	1.3	0.6	3.3
3	20	75	0.2	1.1	0.7	3.5	0.3	1.5	0.8	4.0
4	34	75	0.4	1.1	1.0	3.0	0.0	0.0	1.1	3.2
5	68	75	0.7	1.0	0.4	0.6	0.4	0.6	0.9	1.3
6	118	75	1.6	1.3	2.6	2.2	2.0	1.7	3.6	3.1

2. Linearity:

Linearity of the modified Access sTfR on the DxI 9000 Access Immunoassay Analyzer was performed in accordance with CLSI Guideline EP06, 2nd Edition. Three dilution series were prepared by mixing one High serum sample with a Low serum sample. One dilution series included eight dilution levels covering the analytical measuring interval (AMI) of the modified Access sTfR (0.03 – 133.2 nmol/L). The second dilution series included dilution samples covering low end of AMI (0.02 – 28 nmol/L). The third dilution series included dilution samples covering high end of AMI (72.8 – 184.8 nmol/L). For all dilution series, the lowest samples were run in replicates of eight, and all other dilution levels were run in replicates of four on the DxI 9000 Access Immunoassay Analyzer using one lot of reagents. For each level, the 'measured value' (mean sTfR nmol/L) was compared to its predicted value for deviation percentage using a weighted linear regression analysis. This deviation was then compared to the allowable deviation from linearity (ADL). The data showed the linearity interval from 0.02 – 184.8 nmol/L with the deviations from linearity within ±10%.

The results support the linearity of the claimed analytical measuring interval (AMI): 0.05 – 150 nmol/L.

3. Analytical Specificity/Interference:

Refer to K080634

4. Assay Reportable Range:

The reportable range is the same as the claimed analytical measuring interval (AMI): 0.05 – 150 nmol/L.

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

a) Traceability:

The traceability was established in K080634. There is no change to the traceability of the modified Access sTfR.

b) Stability:

The Access sTfR and the Lumi-Phos PRO substrate are packaged separately. Access sTfR kit stability was established in K080634. The proposed change is to replace substrate (Lumi-Phos 530) of the Access sTfR with a new substrate (Lumi-Phos PRO) for the assay run on DxI 9000 Access Immunoassay Analyzer. The shelf-life claims and on-board stability claims of Lumi-Phos PRO substrate were established in K221225.

6. Detection Limit:

CLSI guideline EP17-A2 was followed to determine the Limit of Blank (LoB), Limit of Detection (LoD) and Limit of Quantitation (LoQ) for the Access Ferritin.

a) LoB:

Five analyte depleted ultrafiltered samples (prepared from five unique native serum samples) were tested in five replicates per run, one run per day over three days using two modified Access sTfR reagent lots on two DxI 9000 Access Immunoassay Analyzers (N=75 datapoints for each reagent lot and each instrument). The LoB was determined based on the 95% nonparametric percentile of the replicates for each of the two reagent lots. The claimed LoB for the modified Access sTfR on DxI 9000 Access Immunoassay Analyzer is 0.04 nmol/L.

b) LoD:

Eight serum samples containing low levels of sTfR were tested in nine replicates per run, one run per day for five days using three modified Access sTfR on three DxI 9000 Access Immunoassay Analyzers. LoD was calculated from LoB + "SD multiplied by the 95th percentile of the standard normal distribution". The claimed LoD for the modified Access sTfR on DxI 9000 Access Immunoassay Analyzer is 0.05 nmol/L.

c) LoQ:

Thirteen serum samples containing low levels of sTfR were tested in replicates of nine per run, one run per day, over five total days on each reagent lot and instrument using three reagent lots and three instruments for a minimum of 40 total datapoints for each sample on each lot. A variance components model was used to estimate the within-run and within-laboratory (total) %CV for each sample on each instrument and reagent lot combination. The estimated LoQ of the modified Access sTfR was set to be the sTfR concentration which met the within-laboratory imprecision of 20% CV. The claimed LoQ for the modified Access sTfR on DxI 9000 Access Immunoassay Analyzer is 0.05 nmol/L.

7. Assay Cut-Off:

Not applicable

B Comparison Studies:

1. Method Comparison with Predicate Device:

CLSI Guideline EP09c, 3rd Edition was followed to compare the modified Access sTfR on DxI 9000 Access Immunoassay Analyzer to the predicate device, the Access sTfR on the Access 2 Immunoassay System. A total of 200 deidentified serum samples were tested with three lots of modified Access sTfR on three DxI 9000 Access Immunoassay Analyzers and three predicate reagent lots on three Access 2 instruments. Patient samples falling within the analytical measuring interval (0.05 – 150 nmol/L) were evaluated using Passing-Bablok method. The results are summarized in the following table:

N	Range (nmol/L)	Slope (95% CI)	Intercept (95% CI)	R^2
200	0.10 − 139	1.00 (0.99 − 1.01)	-0.016 (-0.14 − 0.15)	1.00

2. Matrix Comparison:

Refer to K080634

C Clinical Studies:

Refer to K080634

D Clinical Cut-Off:

Refer to K080634

E Expected Values/Reference Range:

Refer to K080634

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.