

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

A. 510(k) Number:

k120236

B. Purpose for Submission:

New device

C. Measurand:

Transferrin

D. Type of Test:

Quantitative Immunoturbidimetric

E. Applicant:

The Binding Site Group, Ltd.

F. Proprietary and Established Names:

Human Transferrin Kit for use on the SPAPlus™

G. Regulatory Information:

1. Regulation section:
21 CFR §866.5880 Transferrin Immunological Test System
2. Classification:
Class II
3. Product code:
DDG, Transferrin, Antigen, Antiserum, Control
4. Panel:
Immunology (82)

H. Intended Use:

1. Intended use(s):
The Binding Site Human Transferrin Kit is intended for the quantitative determination of

human transferrin using the Binding Site SPAPlus™ turbidimetric analyzer in human serum. The measurement of transferrin levels aids in the diagnosis of malnutrition, acute inflammation, infection and iron deficiency anemia. This test should be used in conjunction with other laboratory and clinical findings.

2. Indication(s) for use:

Same as Intended Use

3. Special conditions for use statement(s):

For prescription use only

4. Special instrument requirements:

SPAPlus™ turbidimetric analyzer

I. Device Description:

The Human Transferrin Kit for use on SPAPlus™ consists of the following:

- Human transferrin antiserum: mono-specific antiserum for transferrin and supplied in stabilized liquid form containing 0.099% sodium azide, 0.1% EACA, 0.1% EDTA and 0.01% benzamidine, as preservatives.
- Calibrator and Controls: consisting of pooled human serum and supplied in stabilized liquid form containing 0.099% sodium azide, 0.1% EACA and 0.01% benzamidine, as preservatives.
- Reaction Buffer: containing 0.099% sodium azide, as preservative.

J. Substantial Equivalence Information:

1. Predicate device name (s) and 510(k) numbers:

Dade Behring N Antisera to Human Transferrin, k053075

2. Comparison with predicate:

Similarities		
Item	Human Transferrin Kit for use on the SPAPlus™ (New Device)	N Antisera to Human Transferrin (Predicate)
Intended Use/Indication for Use	For <i>in vitro</i> diagnostic use in the measurement of human transferrin in serum as an aid in the diagnosis of iron deficiency anemia.	Same
Storage Temperature	2 – 8°C	Same

Differences		
Item	Human Transferrin Kit for use on the SPAPlus™ (New Device)	N Antisera to Human Transferrin (Predicate)
Instruments	SPAPlus™	BN systems
Assay Principle	Turbidimetric	Nephelometric
Antibody	Sheep, anti-human transferrin	Rabbit, anti-human transferrin
Sample Type	Serum	Serum, heparinized or EDTA plasma
Measuring range	0.14 – 5.6 mg/L	0.35 – 5.6 mg/L
Open Vial Stability	Three months, 2 – 8°C	4 weeks, 2 – 8°C
On Board Stability	30 days	5 days with 8 hours per day

K. Standard/Guidance Document Referenced:

CLSI EP5-A2: Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline – Second Edition.

CLSI EP6-A: Evaluation of the Linearity of Quantitative Measurement Procedures: a Statistical Approach; Approved Guideline.

CLSI EP17-A: Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline.

CLSI C28-A3: Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline – Third Edition

CLSI EP9-A2: Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline – Second Edition.

L. Test Principle:

Transferrin present in serum reacts with anti-transferrin specific antiserum to form insoluble complexes. When light is passed through the suspension, a portion of the light is transmitted and focused onto a photodiode by an optical lens system. The amount of transmitted light is indirectly proportional to the transferrin concentration in the test sample. Concentrations are automatically calculated by reference to a calibration curve within the instrument.

M. Performance Characteristics:

1. Analytical performance:

a. Precision/Reproducibility:

A precision study was conducted in accordance with CLSI document EP05-A2. Four serum pools (one high transferrin-spiked serum pool, two mid sample serum pools and one low sample serum pool) spanning a large portion of the measuring range (0.14 g/L to 5.60 g/L) were used for this study. All samples were analyzed in duplicate per run, with 2 runs per day for 21 days, using 3 reagent lots and 3

analyzers with one operator, for a total of 84 replicates per sample. The results are summarized below:

Serum Sample	Mean Spiked Transferrin (g/L)	Within Run		Between Run		Between Day		Total	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV
Low	0.261	0.0036	1.6	0.0037	1.7	0.0143	6.5	0.0152	6.9
Mid	1.988	0.0280	1.4	0.0329	1.7	0.0677	3.5	0.0803	4.1
Mid	3.752	0.0690	1.8	0.0569	1.5	0.1489	4.0	0.1737	4.6
High	4.210	0.0956	2.2	0.1946	4.4	0.1027	2.3	0.2399	5.5

Lot-to-lot data:

Sample	Mean g/L Inter-batch	Lot-to-lot	
		SD	%CV
Low	0.221	0.014	6.19
Mid	1.941	0.035	1.79
Mid	3.742	0.076	2.04
High	4.399	0.046	1.05

b. *Linearity/assay reportable range:*

A linearity study was performed following CLSI document EP-6-A, Evaluation of the Linearity of Quantitative Measurement Procedures; Approved Guideline. Serum linearity across the assay range (0.123 to 6.095 g/L) was evaluated by testing thirteen samples with concentrations of transferrin evenly distributed throughout the assay range. The high serum pool (6.095 g/L) was established by spiking with pure transferrin. The series of thirteen serum samples were prepared by dilution of the high serum pool with the low serum pool (0.123 g/L) to give the following thirteen samples: 100, 90, 80, 70, 60, 50, 40, 30, 20, 20, 5, 2.5, 0 (g/L). Each sample was tested in triplicate. The % recovery was calculated as the difference of the expected values and the observed values. The % recovery ranged from 80 to 120%. Linear regression of observed values versus expected values showed that the slope, intercept and r^2 were 0.9791, 0.1235 (g/L) and 0.9965, respectively.

Antigen Excess

In this study a normal sample was aliquotted and then each aliquot was spiked with increasing concentrations of transferrin. All samples were run according to the product insert at standard 1/10 instrument dilution (measuring range 0.14-5.60 g/L).

At this dilution, results were observed to be outside of the measuring range. Samples were then re-diluted to a higher 1/40 dilution and re-tested. The recovery of the samples demonstrated that antigen excess is not observed at concentrations up to at least 3-fold the upper assay range, approximately 17.0 g/L.

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

Traceability:

The values of the calibrator and controls are established by comparison of an internal reference standard to ERM-DA470k.

Stability:

Real time stability studies were performed to support the following stability claims of the Transferrin Kit for use on SPAPlus™. Onboard stability of the Transferrin Antiserum and Reaction buffer is 30 days provided that the reagent carousel is maintained at 8-12°C. Shelf-life stability of the unopened Transferrin Kit stored at 2-8°C is 12 months. Shelf-life stability of the opened Human Transferrin Antiserum, Reaction Buffer, calibrators and controls can be stored up to three months after opening, provided they are capped and stored at 2-8°C. The assay can run for 35 days without recalibration.

d. *Detection limit:*

Testing for limit of detection (LoD) and limit of blank (LoB) was conducted in accordance with CLSI guideline EP-17A. The LoB study was carried out using instrument diluent/saline. Sixty replicates of a blank sample were run on one day using one reagent lot. The LoD study was carried out using a low level sample (non-processed serum diluted with saline to give an analyte concentration of 0.052 g/L). Sixty replicates were run on one day using one reagent lot. The LoQ was determined by assaying 40 replicates of the assay calibrator. The following results were obtained:

LoB = 0.051 g/L

LoD = 0.059 g/L

LoQ = 0.14 g/L

e. *Analytical specificity:*

Interference by endogenous substances were evaluated by addition of hemoglobin (5 g/L), bilirubin (200 mg/L) and chyle (1560 FTU) to test serum samples representing analyte concentrations at the lower end of the reference range (2.100 g/L), just above the upper end of the reference range (3.725 g/L), as well as a supranormal concentration (4.748 g/L), and comparing their recovery to unspiked sample. No significant interference (i.e., sample recovers within ±10% of the unspiked sample)

was observed with the interferences tested at any of the transferrin levels tested.

f. Assay cut-off:

See Expected Value.

2. Comparison studies:

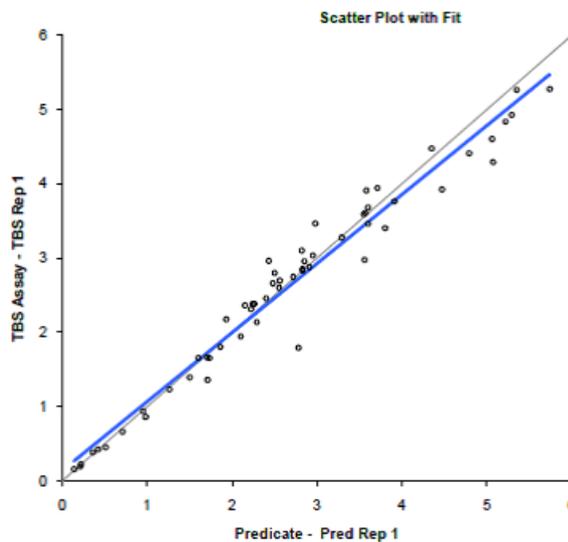
a. Method comparison with predicate device:

Performance of the Human Transferrin Kit for use on SPAPlus™ was evaluated against the predicate using a total of 57 samples, including normal samples (n = 26), as well as samples from patients with conditions such as Goodpasture’s syndrome, glomerulonephritis, iron deficiency anemia and hemochromatosis (n = 31).

Results from least squares linear regression are summarized below:

N	Range (g/L)	Slope (95% Confidence Intervals)	Intercept (95% Confidence Intervals)	r	S _{yx} (g/L)
57	0.140-5.74	0.93 (0.88-0.98)	0.14 (-0.01-0.29)	0.981	0.265

Results from the experiment are shown graphically below:



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 reference interval of 2.0 – 3.5 g/L was transferred from the predicate following CLSI C28-A3. The sponsor added a caution to the labeling that states, “The ranges provided have been obtained from a limited number of samples and are intended for guidance purposes only. Wherever possible it is strongly recommended that local ranges are generated.”

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.