

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

A. 510(k) Number:

k042477

B. Purpose for Submission:

New device

C. Measurand:

Transferrin

D. Type of Test:

Quantitative, immunoturbidimetry

E. Applicant:

Ortho-Clinical Diagnostics, Inc.

F. Proprietary and Established Names:

VITROS Chemistry Products TRFRN Reagent

VITROS Chemistry Products Calibrator Kit 20

VITROS Chemistry Products Protein Performance Verifiers I, II and III

G. Regulatory Information:

1. Regulation section:

21 CFR 866.5880, Transferrin immunological test system

21 CFR § 862.1150, Calibrator

21 CFR § 862.1660, Quality control material (assayed and unassayed)

2. Classification:

Class II, Transferrin reagent and calibrator

Class I, Quality control material

3. Product Code:

DDG, Transferrin, antigen, antiserum, control

JIT, Calibrator, secondary

JJX, Single (specified) analyte controls (assayed and unassayed)

4. Panel:

Immunology (82)

H. Intended Use:

1. Intended Use

VITROS Chemistry Products TRFRN Reagent is used to quantitatively measure transferrin (TRFRN) concentration in human serum and plasma.

VITROS Calibrator kit 20 is used to calibrate VITROS 5,1 FS Chemistry System for quantitative measurement of transferrin, C3, C4, IgA and IgM.

VITROS Chemistry Products Protein Performance Verifiers I, II and III are assayed controls used to monitor the performance of transferrin, C3, C4, IgA and IgM Reagents on the FS 5,1 Chemistry Systems.

2. Indication(s) for use:
Same as intended use.
3. Special condition for use statement(s):
The devices are for prescription use only.
4. Special instrument Requirements:
VITROS 5,1 FS Chemistry System (k031924).

I. Device Description:

The VITROS Chemistry Products TRFRN Reagent is a dual-chambered package containing ready to use liquid reagents, Reagents 1 and 2. Reagent 1 consists of preservative, polymer, buffers and inorganic salt whereas Reagent 2 consists of goat anti-sera to human transferrin, preservative, buffer and inorganic salt.

The VITROS Chemistry Products Calibrator kit 20 contains 5 levels of calibrators prepared from processed human serum supplemented with inorganic salts, buffers and preservatives.

Protein performance verifiers contain three levels of assayed controls (low, medium and high) prepared from processed human serum supplemented with inorganic salts buffers and preservatives are added. The transferrin concentrations are: 119 mg/dL (level I), 236 mg/dL (level II) and 478 mg/dL (level III).

J. Substantial Equivalence Information:

1. Predicate device name(s):
Beckman IMMAGE Transferrin Assay and VITROS Performance Verifiers I and II.
2. Predicate K number(s):
Beckman IMMAGE Transferrin (k963427) and VITROS Performance Verifiers (k041720)

3. Comparison with predicate:

DEVICE		PREDICATE
A. Similarities		
Intended Use. Used to quantitatively measure transferrin concentration in human serum and plasma. Assay Format – Quantitative Performance Verifiers – assayed controls for monitoring performance of transferrin, C3, C4, IgA, IgG and IgM reagents		Quantitative determination of transferrin in human serum Same Same
B. Differences		
Assay type – Immunoturbidimetric Instrument - VITROS 5,1 FS Chemistry Systems Sample Type – Serum and plasma Reportable range – 80 – 750 mg/dL Control levels – low, medium and high Matrix of Performance Verifiers – human serum		Rate nephelometric Beckman IMAGE Immunochemistry Systems Serum 75 – 750 mg/dL Low and high Freeze-dried human serum

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

NCCLS Guide line EP5-A, EP7-A, EP9-A, C28.

L. Test Principle:

Samples, calibrators and controls are automatically diluted in saline and mixed with Reagent 1 containing a polymer. Addition of antisera specific for human transferrin (Reagent 2) produces antibody/antigen complexes. The antibody/antigen complexes increase solution turbidity which is proportional to transferrin concentration in the sample. The turbidity is measured spectrophotometrically at 340 nm. The transferrin concentration in each unknown sample is determined using the stored calibration curve and the measured absorbance of the sample.

M. Performance Characteristics (if/when applicable):1. Analytical performance:a. Precision/Reproducibility:

Within-day and within laboratory precision – Three samples with different transferrin concentrations were assayed in duplicate in two runs on each of 23 days on the VITROS 5,1FS System. Testing was performed on two lots of TRFRN Reagent. One set of the five level calibrators was run once weekly and results were used to generate a calibration curve for determining results for that week. Results of the test samples were analyzed using NCCLS EP5-A Guideline. Within-day precision was determined using two runs per day with two replications per run and within-lab precision was determined using a single lot of reagent.

Transferrin reagent (mg/dL)			%CV (mean)	#observed	#days
Mean Conc	Within-Day (SD)	Within-Lab (SD)			
138.08	0.952	6.354	4.6	91	23
269.88	1.463	7.077	2.6	92	23
547.07	6.542	24.491	4.5	92	23

b. Linearity/assay reportable range:

Linearity of the VITROS TRFRN Reagent assay was evaluated according to NCCLS EP6-A. The high pool was Level 5 of the VITROS Calibrator Kit 20 and had a transferrin concentration of 753 mg/dL and the low pool was Level 1 and had a transferrin concentration of 78.3 mg/dL. Thirteen levels spanning the assay reportable range were created by mixing the high and low pools. Three determinations of each of the 13 levels were made together with 3 determinations of the VITROS Performance Protein Verifiers. Linear regression analysis indicated that the assay is linear across the range tested (78.3mg/dL to 753 mg/dL) with $y = 6.8728x + 75.747$ where x is dilution in % high pool. Correlation coefficient (r^2) was 0.999. The product claim for linearity over the reportable range is 80 to 750 mg/dL.

Dilution Study - A total of 5 patient samples, one high calibrator and one concentrated patient pool at the high end of the assay range were evaluated. Recoveries were calculated based on undiluted values measured on the same samples run on the VITROS 5,1 FS Chemistry System. For out of range samples, recoveries were calculated from neat results predicted from an off-board calculation using the initial absorbance results. Recovery of each sample was determined as a % of the neat sample concentration. The two lots tested showed the mean % recovery value of 101% with individual sample recoveries ranged from 96.1% to 104.5% (acceptance criteria was set at 91%-109%). Results also showed that samples with values greater than the reportable range may be diluted up to 1 part sample with 1 part diluent (saline).

The assay reportable range is 80 to 750 mg/dL or 0.8 to 7.5 g/L.

c. Traceability (controls, calibrators, or method):

Values assigned to the Calibrator Kit 20 for transferrin are traceable to IRMM /IFCC (Institute for Reference Methods and Materials) CRM 470 (RPPHS, Reference Preparation for Proteins in Human Serum) reference material.

Calibrator value assignment for transferrin - a five level set of calibrators are prepared using the VITROS 5,1 FS Chemistry System

on-analyzer dilution of CRM 470. These calibration standards are used to measure and assign values to a Master Lot of working calibrators as well as to calibrate the Manufacturer's Selected Measurement Procedure for the VITROS TRFRN Reagent. The Master Lot and the selected measurement procedure are then used to assign values to subsequent Calibrator Kit 20 production lots.

d. *Detection limit (functional sensitivity):*
Not provided.

e. *Analytical specificity:*
Endogenous and exogenous interfering substances were tested according to NCCLS EP7-A in samples with transferrin level of approximately 183 mg/dL (for bilirubin, hemoglobin and Intralipid, samples had approximately 134 mg/dL transferrin). For each interference substance, a control pool and a spiked-in-pool were analyzed in quadruplicate using three reagent lots.

Substances tested included: Acetaminophen (200 µg/mL), acetyl-L-cystein (100 mg/dL), Amoxicillin (20 µg/mL), ascorbic acid (3 mg/dL), bilirubin (842.9 g/mol), carbamazepine (120 µg/mL), dipyrone (30 mg/dL). Ethamsylate (3 mg/dL), gentamicin sulfate (120 µg/mL), hemoglobin (13647 mg/dL), ibuprofen (400 µg/mL), methotrexate (2 mmol/L), procainamide (100µg/mL), propranolol (5000 ng/mL), rantidine (200 µg/mL), lidocaine (60 µg/mL), simvastatin (16 µg/mL), theophylline (250 µg/mL), salicylic acid (500 µg/mL), intralipid (1000 mg/dL), triglycerides (1000 mg/dL) and valproic acid (500 µg/mL). No interference was observed at the concentrations tested.

f. *Assay cut-off:*
Not provided.

2. Comparison studies:

a. *Method comparison with predicate device:*

A total of 139 serum samples were assayed using VITROS Chemistry Products TRFRN assay and the Beckman IMAGE Transferrin assay for comparison. All samples were analyzed in triplicate on the VITROS 5,1 FS Chemistry System analyzer and in singleton on the Beckman IMAGE using two lots of reagents. Only samples within the reportable range of both devices were analyzed. Two samples were excluded because they were out of the reportable range for one of the devices. Data were screened for statistical outliers and no data were rejected. The mean of the triplicates from the VITROS Chemistry Products TRFRN assay and the single replicate for the Beckman IMAGE Transferrin assay

were compared by least squares linear regression analysis. Results showed (VITROS) = $0.96 \times (\text{IMAGE}) - 0.24$ (mg/dL) with a correlation coefficient (r) of 0.986. The 95% confidence intervals (CI) for slope and intercept were 0.94 to 0.99 and -8.97 to 8.50 respectively.

b. Matrix comparison:

For the serum and plasma comparison study, blood from 6 subjects collected in different collection tubes (red top tubes, lithium heparin (Li heparin), EDTA, serum separator [SST], and plasma separator [PST]) as well as 60 paired serum/lithium plasma samples were analyzed. Serum and plasma were separated within 1 hour of collection. Data analysis was performed according to NCCLS EP5-A. Regression analysis of the 60 paired serum and Li heparin plasma samples yielded [Li heparin] = $1.0172 (\text{Serum}) - 3.9218$ with a correlation coefficient (r) of 0.9781. The results of the other tube tubes were within acceptable limits.

3. Clinical studies:

a. Clinical sensitivity:

Not provided.

b. Clinical specificity:

Not provided.

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 expected values for transferrin were determined by assaying 121 samples from apparently healthy subjects using two lots of reagents. The evaluation was performed using NCCLS C28 guideline. The reference interval for lot 1 was 207.7 to 389.4 mg/dL with a mean of 290.5 mg/dL and a median of 286.7 mg/dL. The 90% confidence intervals of the 2.5th and 97.5th percentile values were 198.5 to 224.9 mg/dL and 358.5 to 398.8 mg/dL respectively. The reference interval for lot 2 was 204.0 to 372.9 mg/dL with a mean of 283.9 mg/dL and a median of 282.6 mg/dL. The 90% confidence intervals of the 2.5th and 97.5th percentile values were 191.2 to 221.0 mg/dL and 352.7 to 397.3 mg/dL respectively. The overall reference interval based on the two lots was determined to be 206 to 381 mg/dL (2.1-3.8 SI Units [g/L]).

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.