

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

A. 510(k) Number:

k063086

B. Purpose for Submission:

This is a new submission.

C. Measurand:

Transferrin

D. Type of Test:

Quantitative, PEG enhanced immunoturbidimetric assay

E. Applicant:

Thermo Electron Oy

F. Proprietary and Established Names:

Transferrin, code 981673

Specitrol and Specitrol High (QC materials)

Specical Calibrator

G. Regulatory Information:

1. Regulation section:

21 CFR§ 866.5880 Transferrin Immunological Test System

21CFR§ 862.1660, Quality Control Material (Assayed and Unassayed)

21CFR§ 862.1150, Calibrator

2. Classification:

Device and calibrator - Class II

Quality control material - Class I

3. Product code:

DDG, Transferrin, Antigen, Antiserum, control

JJY, Multi- Analyte Controls (Assayed and Unassayed)

JIX, Calibrator, Multi-Analyte Mixture

4. Panel:

(82) Immunology

(75) Chemistry

H. Intended Use:

1. Intended use(s):

The transferrin test system is intended for the quantitative in vitro diagnostic determination of transferrin in serum or plasma using T60 Clinical Chemistry Analyzers. Measurement of transferrin levels aid in the diagnosis of malnutrition, acute inflammation, acute infection and iron deficiency anemia.

SpeciCal protein calibrator is for in vitro diagnostic use on T60 analyzer.

SpeciCal protein calibrator is used as a stock calibrator for both quantification of specific proteins in serum and plasma by immunoturbidimetry and for antigen excess detection using methods defined by Thermo Electron Oy.

Specitrol is for in vitro diagnostic use on T60 analyzer. SpeciTrol is intended to

be used as an assayed control serum to monitor precision of specific protein tests defined by Thermo Electron Oy.

Specitrol High is for in vitro diagnostic use on T60 analyzer. Specitrol High is intended to be used as an assayed control serum to monitor precision of specific protein tests defined by Thermo Electron

2. Indication(s) for use:
Same as above.
3. Special conditions for use statement(s):
The device is for prescription use only.
4. Special instrument requirements:
T60 Clinical Chemistry Analyzers (DPC T60i and DPC T60i Kusti Analyzers).
The different names of the T60 analyzer refer to additional modules that can be used on each analyzer and were given FDA clearance under k061107.

I. Device Description:

The device consists of the following: Transferrin Reagent –Anti-human transferrin from swine with <0.1% NaN₃, Transferrin Buffer- a solution of polymers in phosphate-buffered saline and Specimen Diluent with 0.01 mol/L PBS and ,0.1% NaN₃.

The Specical Protein Calibrator, Specitrol Control Serum and the Specitrol High Control are liquid human-based reference preparations for immunoturbidimetric methods which contain <0.1% NaN₃ as a preservative.

Calibrators and controls are sold separately.

J. Substantial Equivalence Information:

1. Predicate device name(s):
Tina-quant Transferrin ver.2 on Roche Hitachi Modular P
Calibrator for Automated Systems (C.f.a.s.) Proteins
Liquichek Immunology Control
2. Predicate 510(k) number(s):
k012371
k011226
k011494
3. Comparison with predicate:

Similarities		
Item	Device	Predicate
	Transferrin	Tina-quant Transferrin ver.2
Intended Use	Quantitation of transferrin	Same
Indications for Use	Aid in the diagnosis of	Same

Similarities		
Item	Device	Predicate
	malnutrition, acute inflammation, acute infection and iron deficiency anemia	
Expected Values	200-360 mg/dL	Same
Sample type	Serum and lithium heparin plasma	Same
Reagent storage	2°C – 8°C until expiration date printed on the label	Same
Assay Principle	Immunoturbidimetry	Same
Components	Controls and calibrators are sold separately	Same

Differences		
Item	Device	Predicate
Instrument	T60 Clinical Chemistry Analyzers	Roche Hitachi Modular P
Source of antibody	Swine	Rabbit
Measuring range	50-980 mg/dL (related to transferrin concentration of the calibrator and are lot dependent)	0.7-520 mg/dL Extended measuring range with rerun (0.7-780 mg/dL)

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

CLSI EP5-A2: Evaluation of Precision Performance of Clinical Chemistry Devices

CLSI EP6-A: Evaluation of Linearity of Quantitative Analytical Methods

CLSI EP7-A2: Interference Testing in Clinical Chemistry

CLSI EP9-A2: Method Comparison and Bias Estimation Using Patient Samples

L. Test Principle:

The method is based on measurement of immunoprecipitation enhanced by polyethylene glycol (PEG) at 340nm. Specific antiserum is added in excess to buffered samples. The increase in absorbance caused by immunoprecipitation is recorded when the reaction has reached its end-point. The change in absorbance is proportional to the amount of transferrin in solution.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

The precision studies were performed using CLSI EP5-A2 as a guideline. Six samples were measured in 2 replicates per run, 2 runs per day during 21 days with 3 T60 instruments; for samples 6 and 7, one reagent lot and 2 operators; for samples 2-5, two reagent lots and six operators. The precision study at the extended low end was done during 5 days, with 2 runs per day, 2

replicates per run, 1 reagent lot, 1 instrument, 1 operator.

The following results are obtained:

Level	N	Mean (mg/dL)	Within-run Mean %CV	Between-run Mean %CV	Total %CV
1	20	42.3	1.4	1.0	4.3
2	84	60	1.6	1.4	2.9
3	84	83	1.7	0.8	2.3
4	84	159	0.9	1.0	2.2
5	84	403	0.9	1.0	2.6
6	84	606	1.2	1.3	2.6
7	84	851	1.3	1.4	2.4

b. Linearity/assay reportable range:

The linearity study was performed using CLSI EP6-A as a guideline. Dilution series were made from transferrin spiked normal human sera over a measured range of 36.2 to 1421.8 mg/dL and analyzed on a DPC T60 analyzer. Four parallel measurements were made in random order. The study was performed with one reagent lot. The maximum bias allowed from the estimated straight line was $\pm 10\%$. Observed error was 3.4%. Claimed measuring range is 50-980 mg/dL. The values are related to the transferrin concentration of the calibrator and are lot dependent.

Studies to determine extended measuring range for low and high ranges were performed using one reagent lot.

Low end extended measuring range. Seven samples (with concentrations 9.6 to 131.6 mg/dL) were diluted using specimen diluent. The maximum bias allowed from the estimated straight line was $\pm 10\%$. The observed error was 4%. The results were linear down to 30 mg/dL.

High end extended measuring range. Eleven samples (with concentrations 38.68 to 3096.57 mg/dL) were diluted using specimen diluent. The maximum bias allowed from the estimated straight line was $\pm 10\%$. The observed error was 3%. The results were linear up to 3000 mg/dL.

Claimed extended measuring range was 30-3000 mg/dL.

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

The Specical calibrator is standardized against CRM 470 – CAP/IFCC (International Federation of Clinical Chemistry).

Calibration stability was tested with initial calibration and running two levels of samples in duplicate. The reagents were left open in the analyzer and the samples were analyzed on days 8 and 15 without recalibration. Acceptance criteria: $\pm 10\%$ of initial value. Results showed calibration curve is stable up to 15 days.

Product stability claims are as follows:

- Open vial: 3 months at 2-8°C.
- Shelf life: 15 months at 2-8°C.

d. Detection limit:

Detection limit was not claimed for this device. Instead, limit of quantitation, lowest concentration that can be measured quantitatively after secondary dilution, was established. This was a fixed value (30 mg/dL) set from the extended measuring range low studies.

e. Analytical specificity:

Interfering substances

The interference studies were performed using CLSI document EP7-A as a guideline. In a paired-difference testing three levels of analyte were analyzed with four replicates from each pool. Potential interfering substances were added in varying concentrations. An acceptance criterion is defined as deviations less than or equal to $\pm 10\%$ of initial value. No significant interference was observed in:

- Bilirubin conjugated and unconjugated up to 58 mg/dL
- Hemoglobin up to 1000 mg/dL
- Intralipid up to 1000 mg/dL

A disclaimer regarding interference of heterophile antibodies and rheumatoid factor was supported by an article, "Interference in Immunoassay by C. Shelby, Ann Clin Biochem, 1999; 36:704-721.

f. Assay cut-off:

See expected value.

2. Comparison studies:

a. Method comparison with predicate device:

A total of 88 patient samples with transferrin concentrations within the reportable range were tested one replicate per run using Thermo Electron Transferrin assay on the T60® analyzer and the predicate device Tina-quant Transferrin ver.2 on Roche Hitachi Modular P. No demographics were provided for samples used in this study. The transferrin concentrations ranged from 43 to 832 mg/dL. Acceptance criteria: $r \geq 0.85$. Deming regression analysis yields a slope of 1.065 (95%CI: 1.050 to 1.079) and a y-intercept of -18.037 mg/dL (95%CI: -22.722 to -13.352). The correlation coefficient (r) is 0.998.

b. Matrix comparison:

Fifty (50) paired samples (serum and Li-heparin plasma) from anonymous donors were run on T60 instrument. The transferrin concentrations ranged from 58 to 922 mg/dL. Each sample was analyzed in duplicates. Linear regression analysis gave a slope of 0.976 (95% CI: 0.965 to 0.986) and a y-

intercept of 0.0310 mg/dL (95% CI: -4.0105 to 4.0726).

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 200 - 360 mg/dL is from “Consensus of a Group of Professional Societies and Diagnostic Companies on Guidelines for Interim Reference Ranges for 14 Proteins in Serum Based on the Standardization against the IFCC/BCR/CAP Reference Material (CRM 470), Eur J Clin Chem Clin Biochem 1996; 34:517-520.

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.