510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:
k063150

B. Purpose for Submission:
New devices

C. Measurand:
Complement C3 and complement C4

D. Type of Test:
Quantitative, PEG enhanced immunoturbidimetric assay

E. Applicant:
Thermo Electron Oy

F. Proprietary and Established Names:
Complement C3, code 981664
Complement C4, code 981665
Specical (C3 and C4 calibrator)
Specitrol and Specitrol High (C3 and C4 QC materials)

G. Regulatory Information:

1. Regulation sections:
   21 CFR 866.5240 Complement components immunological test system
   21 CFR 862.1150 Calibrator
   21 CFR 862.1660 Quality control (assayed and unassayed)
2. Classification:
   Class II, Immunology Panel (82)
   Class II, Chemistry Panel (75)
   Class I, reserved, Chemistry Panel (75)
3. Product code:
   CZW Complement C3, Antigen, Antiserum, Control
   DBI Complement C4, Antigen, Antiserum, Control
   JIX Calibrator, Multi-Analyte Mixture
   JJY Multi-Analyte Controls, All Kinds (Assayed and Unassayed)
4. Panel:
   See Classifications section above

H. Intended Use:

1. Intended use(s):
   The Complement C3 is for *in vitro* diagnostic use in the quantitative determination of the complement C3 concentration in human serum on the T60 analyzer.

   The Complement C4 is for *in vitro* diagnostic use in the quantitative determination of the complement C4 concentration in human serum on the T60 analyzer.

   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 excel 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 assayed control serum to monitor precision of specific protein tests on the T60 analyzer 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 on the T60 analyzer defined by Thermo Electron Oy.

2. Indication(s) for use:
   C3 and C4 measurements may aid in the diagnosis of immunologic disorders, especially those associated with deficiencies of complement components.
3. Special conditions for use statement(s):
   For prescription use
4. Special instrument requirements:
   DPC T60 analyzer

I. Device Description:

The Complement C3 and Complement 4 assays consists of C3 or C4 antiserum from rabbit, Tris/PEG buffer with sodium azide, and specimen diluent (PBS with sodium azide). The calibrator contains assigned levels of C3 and C4. The two controls contain established values of C3 and C4: Specitrol in the normal range and Specitrol High at a higher level.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   Bayer ADVIA 1650 Complement C3 and Complement C4 reagents
2. Predicate 510(k) number(s):
   k991907
3. Comparison with predicate:

Similarities		
Item	Device	Predicate
	Thermo Electron Oy Complement C3/C4	**Bayer ADVIA 1650 Complement C3/C4**
Indications for Use	May aid in the diagnosis of immunologic disorders, especially those associated with deficiencies of complement disorders.	Same
Assay method	PEG enhanced immunoturbidimetric	Same
Sample matrix	Serum	Serum
Traceability	CRM 470	Same

Differences		
Item	Device	Predicate
	Thermo Electron Oy Complement C3/C4	**Bayer ADVIA 1650 Complement C3/C4**
Instrument	DPC T60	Bayer ADVIA 1650
Reference range	C3: 90-180 mg/dL C4: 10-40 mg/dL Performance not established in pediatric populations	C3: 82-170 mg/dL C4: 12-36 mg/dL Age specific break outs for pediatric patients in the package insert
Measuring range	C3: 28-513 mg/dL 15-940 mg/dL* C4: 6-103 mg/dL 2-410 mg/dL* *with secondary dilution	C3: 0.46 to value of highest calibrator C4: 0.36 to value of highest calibrator

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

CLSI EP5-A2: Evaluation of Precision Performance of Clinical Chemistry Devices
CLSI EP6-A: Evaluation of the 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:

For both C3 and C4 Assays, the method is immunoturbidimetry enhanced by polyethylene glycol (PEG). Specific antiserum is added in excess to buffered samples. The increase in absorbance caused by immunoturbidimetry is recorded when the reaction has reached its endpoint. The change in absorbance at 340 nm is proportional to the amount of C3 or C4 in solution.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

The Precision studies were performed using CLSI Document EP5-A as a guideline.

C3

The precision studies were done during 21 days, with two runs per day, two replicates per run, 1 reagent lot (sample Levels 5 and 6) and 2 reagent lots (sample Levels 1-4), total 84 results per level, including 2 operators (sample Levels 5, 6) and 6 operators (sample Levels 1-4), 3 T60 instruments at one site, and 6 calibrations.

	Mean	Within run		Between run		Total	
Sample	mg/dl	SD	CV%	SD	CV%	SD	CV%
Level 1	42	0.6	1.3	0.6	1.5	1.3	3.0
Level 2	33	0.5	1.4	0.4	1.2	1.2	3.7
Level 3	406	3.4	0.8	4.3	1.1	7.4	1.8
Level 4	441	2.4	0.5	5.2	1.2	9.0	2.0
Level 5	89	0.7	0.8	0.9	1.0	2.1	2.3
Level 6	216	2.0	0.9	1.2	0.6	5.3	2.4

C4:

Sample levels 1-4

The precision study was done during 21 days with two runs per day, two replicates per run, 2 reagent lots, total 84 results per level including 6 operators, 3 T60 instruments at one site, and 6 calibrations.

Sample Levels 5-6

The precision study was done during 16 days with two runs per day, two replicates per run, 1 reagent lot, total 64 results per level including 1 operator, 2 T60 instruments at one site, and 3 calibrations.

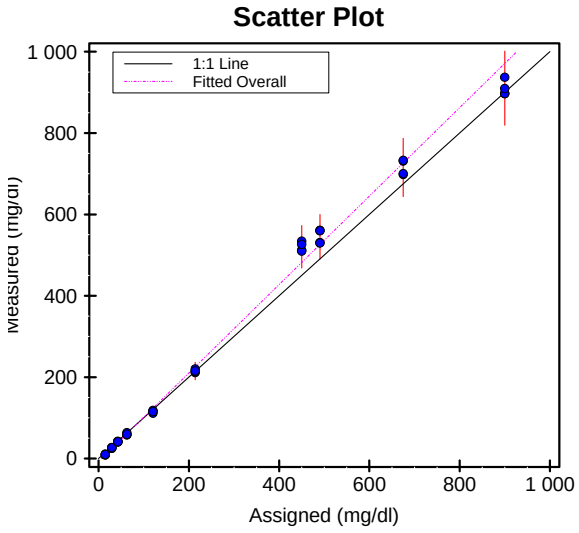
	Mean	Within run		Between run		Total	
Sample	mg/dl	SD	CV%	SD	CV%	SD	CV%
Level 1	8	0.1	1.3	0.1	1.6	0.2	2.8
Level 2	8	0.1	1.5	0.1	1.6	0.2	2.7
Level 3	78	0.8	1.0	0.6	0.7	1.4	1.7
Level 4	88	0.7	0.8	0.7	0.8	1.5	1.7
Level 5	16	0.3	1.7	0.3	1.5	0.6	3.5
Level 6	46	1.0	2.2	0.9	1.9	2.0	4.4

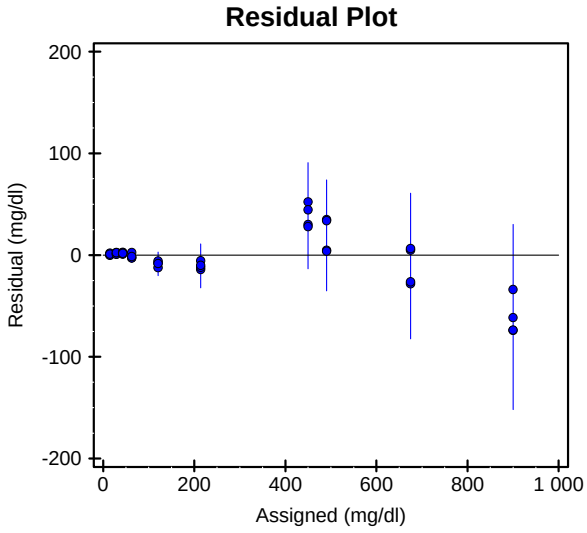
b. *Linearity/assay reportable range:*

The linearity study was performed using CLSI EP6-A as a guideline. Four parallel measurements were made in random order on the DPC T60 analyzer. A dilution series was made from C3 or C4 spiked normal level human serums.

C3:

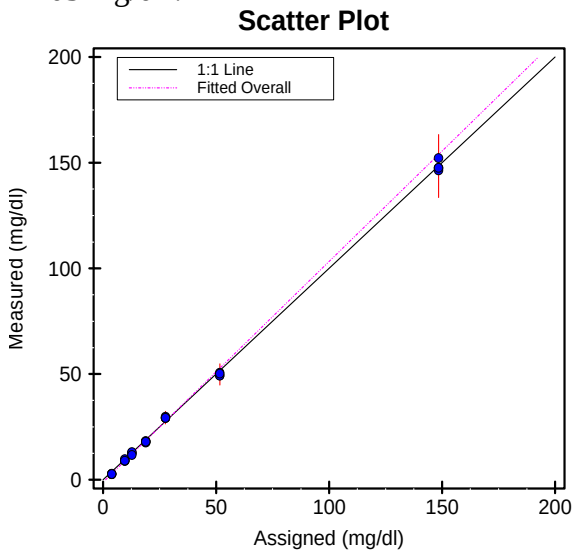
The samples ranged from 9.6 – 910 mg/dL. The maximum bias allowed from the estimated straight line was ± 10%. The claimed measuring range is 28 – 513 mg/dL.

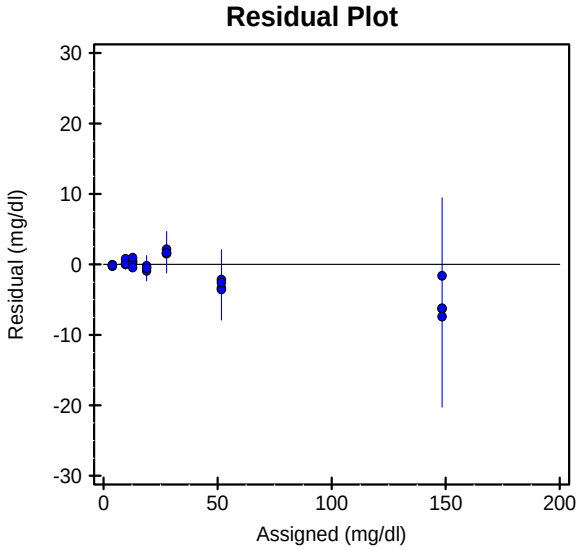




C4:

The samples ranged from 2.7 – 148.4 mg/dL. The maximum bias allowed from the estimated straight line was ± 10%. The claimed measuring range is 6 – 103 mg/dL.





c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
The Specical calibrator is standardized against the primary reference material CRM 470 – CAP/IFCC (International Federation of Clinical Chemistry).

d. *Detection limit:*
The "determination limit" was defined as the lowest concentration that can be measured quantitatively. Additional linearity studies were performed to determine the lowest levels that could be measured with a maximum bias of ± 10%. For C3 it was determined to be 15 mg/dL and for C4 it was 2 mg/dL.

e. *Analytical specificity:*
The interference studies were performed using CLSI document EP7-A as a guideline. In paired-difference testing, both control and test pools were analyzed, with four replicates from each pool, within one analytical run.

Samples for C3 and C4:
Three levels of analyte.
Low level sample: normal human sera diluted with Specimen Diluent.
Medium level sample: normal human sera.
High level sample: normal human sera spiked with C3 or C4 preparate.

Results for **C3** from paired different testing:

Interfering substance		**C3 – mg/dL**					
		Low	Deviation (%)	Medium	Deviation (%)	High	Deviation (%)
Hemoglobin	0 mg/dL	38	-	103	-	204	-
	1000 mg/dL	39	1.89 %	108	4.14 %	207	1.32 %

Interfering substance		C3 – mg/dL					
		Low	Deviation (%)	Medium	Deviation (%)	High	Deviation (%)
Bilirubin conjugated	0 mg/dl	40	-	105	-	201	-
	58.8 mg/dl	42	3.66 %	107	2.00 %	203	0.74 %
Bilirubin unconjugated	0 mg/dl	41	-	109	-	202	-
	58.8 mg/dl	41	1.48 %	109	-0.18 %	204	1.08 %

Results for **C4** from paired different testing:

Interfering substance		C4 – mg/dL					
		Low	Deviation (%)	Medium	Deviation (%)	High	Deviation (%)
Hemoglobin	0 mg/dL	9	-	24	-	46	-
	1000 mg/dL	10	9.94 %	23	-1.06 %	47	1.62 %
Bilirubin conjugated	0 mg/dl	9	-	24	-	46	-
	58.8 mg/dl	9	0.29 %	24	-1.03 %	47	0.54 %
Bilirubin unconjugated	0 mg/dl	9	-	24	-	46	-
	58.8 mg/dl	9	-1.06 %	24	-1.03 %	47	1.09 %

C3 and C4 lipemia (Intralipid®) interference studies were performed using a dose response method.

C3:

Three samples containing different levels of C3 were tested by adding a series of lipid concentrations from 0 – 1000 mg/dL. The clinically significant bias (mg/dL) was established for each level of C3. The claim for the assay is "No interference found up to 500 mg/dL of Intralipid®.

Level of C3 mg/dL	Clinically significant bias (mg/dL) at:	Interference bias result at 500 mg/dL of lipid	95% Confidence Interval
39.9	> 8.0	3.953	3.027-4.880
83.6	>8.4	4.740	1.737-7.743
186.3	>18.6	12.142	8.415-15.869

C4:

Three samples containing different levels of C4 were tested by adding a series of lipid concentrations from 0 – 300 mg/dL. The clinically significant bias (mg/dL) was established for each level of C4. The claim for the assay is "No interference found up to 300 mg/dL of Intralipid®.

Level of C4 mg/dL	Clinically significant bias (mg/dL) at:	Interference bias result at 500 mg/dL of lipid	95% Confidence Interval
9.7	> 2.0	-0.640	(-1.050)-(-0.230)
27.8	> 2.8	-0.167	(-1.061)-(-0.728)
48.9	> 4.9	-2.627	(-3.261)-(-1.993)

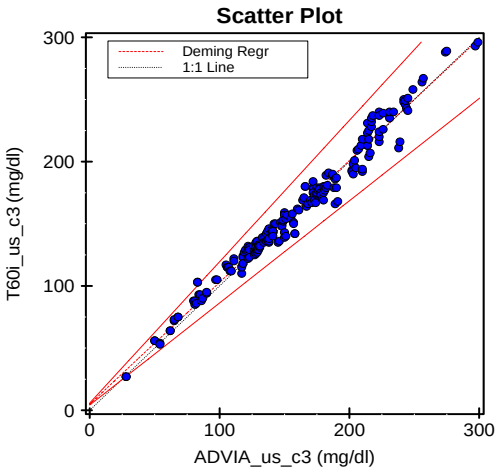
f. *Assay cut-off:*
See Expected values/Reference range

g. *Hook effect (antigen excess):*
Four parallel measurements were made in random order. The test sample series were made from C3 or C4 spiked normal level human serum. The values of the highest samples were 949 mg/dL for C3 (upper end of the measuring range 513 mg/dL) and 419 mg/dL for C4 (upper end of the measuring range 103 mg/dL). Primary and secondary dilutions are automatically made by the instrument. Results for sample concentrations greater than the secondary dilution limit are shown to the user as 'Test limit high' and the user may manually request a further dilution. Whenever manual acceptance is required, the result will not be printed or transmitted via LIS if not accepted by the user.

2. Comparison studies:

a. *Method comparison with predicate device:*
The method comparison studies were performed using CLSI EP9-A as a guideline.

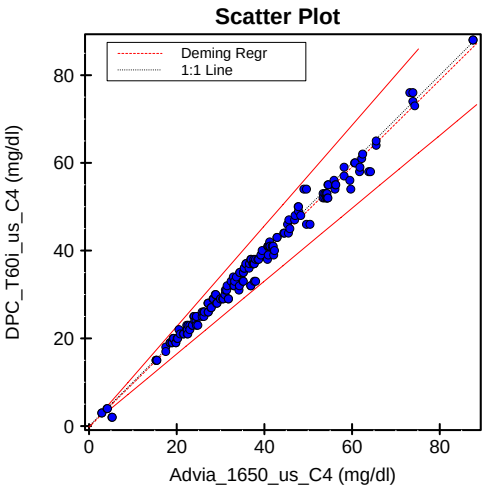
C3:



Deming regression analysis:
y = 0.980x + 4.989
R = 0.989
Range 28 to 299 mg/dL

N = 102
Slope 95% CI: 0.959 - 1.000
Intercept 95% CI: 1.614 – 8.364

C4:



Deming regression analysis
y = 0.989x – 0.184
R = 0.995
Range 2.9 to 87.6 mg/dL
N = 88
Slope 95% CI: 0.973 - 1.004
Intercept 95% CI: -0.800 – 0.432

b. *Matrix comparison:*
Both the new and the predicate devices use serum as the required matrix.

3. Clinical studies:
   a. *Clinical Sensitivity:*
   Not determined
   b. *Clinical specificity:*
   Not determined
   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:
   Expected value ranges (adults) are based on literature.*
   C3: 90-180 mg/dL
   C4: 10-40 mg/dL
   The performance of the assays was not established in pediatric populations.

*Eur J Clin Chem Clin Biochem 1996; 34:517-520. *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).*

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.