

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE**

A. 510(k) Number:

k073355

B. Purpose for Submission:

New device

C. Measurand:

Calcium

D. Type of Test:

Quantitative assay

E. Applicant:

Thermo Fisher Scientific

F. Proprietary and Established Names:

Calcium

sCal, code 981831

Nortrol, code 981043

Abtrol, code 981044

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
Azo Dye, Calcium (CJY)	Class II	21 CFR 862.1145 Calcium test system	75 Clinical Chemistry(CH)
Product Code	Classification	Regulation Section	Panel
Calibrator, Multi- Analyte Mixture (JIX)	Class II	21 CFR 862.1150 Calibrator	75 Clinical Chemistry(CH)
Product Code	Classification	Regulation Section	Panel
Control (JJY)	Class I, reserved	21 CFR§ 862.1660 Quality control material (assayed and unassayed)	75 Clinical Chemistry(CH)

H. Intended Use:

1. Intended use(s):

See Indications for use.

2. Indication(s) for use:

Calcium:

The Calcium test system is intended for quantitative in vitro diagnostic measurement of calcium concentration in human serum or plasma. Calcium measurements are used in the diagnosis and treatment of parathyroid disease, a variety of bone diseases, chronic renal disease and tetany.

sCal:

For in vitro diagnostic use on T60 analyzer. sCal is used as a multicalibrator for quantitative measurements using methods defined by Thermo Fisher Scientific Oy.

Nortrol:

For in vitro diagnostic use for quantitative testing on T60 analyzer. Nortrol is a control serum to monitor trueness and precision of the analytes listed in the separate Nortrol value sheet. The given values are valid for T60 Clinical Chemistry Analyzers using methods defined by Thermo Fisher Scientific Oy.

Abtrol:

For in vitro diagnostic use for quantitative testing on T60 analyzer. Abtrol is a control serum to monitor trueness and precision of the analytes listed in the separate Abtrol value sheet. The given values are valid for T60 Clinical Chemistry Analyzers using methods defined by Thermo Fisher Scientific Oy.

3. Special conditions for use statement(s):

For Prescription use only.

4. Special instrument requirements:

To be used with T60 chemistry analyzer systems.

I. Device Description:

The assay is supplied as a liquid, ready-to-use single reagent kit containing Arsenazo-III dye at a concentration of 0.2 mmol/L.

Nortrol and Abtrol are freeze-dried products prepared from human serum with added constituents of purified biochemicals (tissue extracts of human and animal origin), chemicals, therapeutic drugs, preservatives and stabilizers. The control is provided in lyophilized form for increased stability.

All human materials included in the calibrators and controls were tested by FDA approved methods and found to be negative for the presence of antibodies to HIV-1, HIV-2, HBsAg, and HCV.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Bayer ADVIA Calcium

2. Predicate 510(k) number(s):

k991576

3. Comparison with predicate:

Similarities		
Characteristics	Thermo Fisher Calcium	Bayer ADVIA Calcium
Indications for Use	same	same

Differences		
Characteristics	Thermo Fisher Calcium	Bayer ADVIA Calcium
Assay Protocol	Calcium ions form a highly colored complex with Arsenazo III at neutral pH. The amount of the complex is measured at 660 nm.	Calcium ions form a violet complex with <i>o</i> -cresolphthalein complexone in an alkaline medium. The reaction is measured at 545/658 nm.
Sample Type	Serum, plasma (Li-heparin)	Serum, plasma (Li-heparin) and urine
Expected Values	Serum/ plasma 8.6 - 10.3 mg/dl (2.15 - 2.57 mmol/l)	Serum/Plasma: 8.3 – 10.6 mg/dL (2.08 – 2.65 mmol/L) Urine: 100 – 300 mg/day (2.50 – 7.50 mmol/day)
Instrument	T60 and DPC T60i, DPC T60i Kusti	ADVIA [®] 2400 Chemistry system.
Measuring Range	Serum/ plasma 2.8 - 16.0 mg/dl (0.70 - 4.00 mmol/l)	Serum/ Plasma: 1.0 – 15.0 mg/dL (0.25 – 3.75 mmol/L) Urine: 1.0 – 30.0 mg/dL (0.25 – 7.50 mmol/L)

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

CLSI EP5-A: Evaluation of Precision Performance of Clinical Chemistry Devices; Approved Guideline. Vol. 19 No.2, 2/1999

CLSI EP6-A: Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline. Vol. 23 No. 16, 4/2003

CLSI EP7-A: Interference Testing in Clinical Chemistry; Approved Guideline. Vol. 22 No. 27, 12/2002

CLSI EP9-A: Method Comparison and Bias estimation Using Patient Samples; Approved Guideline. Vol. 15, No. 17, 12/1995

CLSI EP17-A: Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline. Vol. 24 No. 34, 10/2004

L. Test Principle:

Calcium ions form a highly colored complex with Arsenazo III at neutral pH. The amount of the complex is measured at 660 nm.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

The Precision study was performed according to CLSI EP5-A. The precision study was done during 20 to 21 days using three levels of controls, with two runs per day, two replicates per run, total 80 to 84 results per level, including 3 reagent lots, 1 operator, 3 T60 instruments at one site, and 10 calibrations.

			Within run		Between run		Total	
Level	N	Sample Mean	SD	%CV	SD	%CV	SD	%CV
Level 1	84	4.0 mg/dL	0.04	1.0	0.02	0.6	0.06	1.6
Level 2	84	8.4 mg/dL	0.07	0.8	0.03	0.4	0.12	1.5
Level 3	80	11.9 mg/dL	0.08	0.7	0.08	0.7	0.18	1.5

b. Linearity/assay reportable range:

The linearity study was performed based on CLSI EP6-A. The samples were diluted in steps from 0% to 100% by mixing samples with each other 1:1. Four parallel measurements were made in random order using one reagent lot.

	Linearity Study	Extended Linearity Study
Sample Range	2.1 – 17.7 mg/dL	9.3 – 56.5 mg/dL
N	8	11
Slope	1.012	0.970
Intercept	-0.07	0.292
Observer Error	2.4%	5.0%

Based on the linearity study data, the sponsor will claim a measuring range of 2.8 – 16.0 mg/dL and an extended range of 2.8 – 48.0 mg/dL after secondary dilution.

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

The sponsor's protocols indicate that each calibrator (sCal), and control (Nortrol and Abtrol) lot is traceable to NIST SRM 909b. The values are assigned based on multi determinations performed using T60 instruments. The assigned value is the median of all the values generated for each calibrator and control. Additionally, control range is calculated as the target value ± 2 standard deviations. The expected values for each lot are provided on the value sheet provided with the product.

The sponsor supports a claim of an open on-board stability of reagents for 30 days. After reconstitution sCal, Abtrol, and Nortrol are stable for 7 days at 2-8 °C.

d. Detection limit:

The Limit of Blank (LoB) and Limit of Detection (LoD) studies were performed according to CLSI EP17-A. In the LoB study, thirty replicates of a blank sample (0.9% NaCl) were run using two T60 instruments and two reagent lots with the total number of measurements being 60. The LoB was determined to be 0.02 mg/dL.

In the Limit of Detection study five low level samples were run in ten replicates with two T60 instruments and two reagent lots during two days with the total number of measurements being 100. The LoD was determined to be 0.08 mg/dL.

e. Analytical specificity:

The interference study was performed according to CLSI EP7-A. In a paired-difference testing using with three levels of analyte both control and test pools were analyzed, with four replicates from each pool, within one analytical run. The sponsor defined interference as a difference exceeding $\pm 10\%$ of the test value compared to control value. According to the interference studies the following claims were established:

Lipemia: No interference found up to 1000 mg/dl (10 g/l) of Intralipid.

Hemolysate: No interference found up to 1000 mg/dl (10 g/l) of hemoglobin

Bilirubin conjugated: No interference found up to 58 mg/dl (1000 $\mu\text{mol/l}$) of conjugated bilirubin

Bilirubin total: No interference found up to 58 mg/dl (1000 $\mu\text{mol/l}$) of unconjugated bilirubin.

f. Assay cut-off:

Not Applicable.

2. Comparison studies:

a. Method comparison with predicate device:

One hundred and twelve Li-heparin plasma samples (104 clinical, 2 diluted) were analyzed using T60i instrument with Calcium reagents and Bayer Advia 2400 instrument with Calcium reagents to demonstrate the equivalence of the two systems. Samples ranged from range from 3.2 to 14.6 mg/dL. The samples were split in two and then run each one either on the predicate or Thermo device. Each individual measurement was compared to one individual measurement result of the predicate. Deming regression analysis resulted in the equation, $y = 1.03x + 0.096$, $r = 0.987$.

b. Matrix comparison:

Ninety-seven matched serum and plasma (Li-heparin) samples (94 clinical, 3 contrived) were run on T60 instrument to demonstrate the use of serum samples. Samples ranged from range from 6.3 to 15.0 mg/ dL. Both serum and plasma samples were run in duplicates and each individual measurement was compared to one individual measurement. Deming regression analysis resulted in the equation, $y = 0.95x + 0.373$, $r = 0.990$.

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):

4. Clinical cut-off:

Not Applicable.

5. Expected values/Reference range:

The expected values of Calcium referenced by the sponsor is 8.6 - 10.3 mg/dl (2.15 - 2.57 mmol/l). The sponsor recommends that each laboratory determine its own reference range.

Referenced from: Burtis, CA and Ashwood, E R (ed.), Tietz Fundamentals of Clinical Chemistry, 5th edition, W B Saunders Company, Philadelphia, 2001, pp. 797-799, 968.

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.