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

A. 510(k) Number:

k073612

B. Purpose for Submission:

The purpose for the submission is to obtain clearance for the addition of uric acid to a multi-constituent calibrator, sCal, multi-constituent controls, Nortrol and Abtrol, and clearance of the Uric Acid assay for the Thermo Fisher T60.

C. Measurand:

Uric Acid

D. Type of Test:

Quantitative, enzymatic, colorimetric assay

E. Applicant:

Thermo Fisher Scientific Oy

F. Proprietary and Established Names:

Uric Acid (AOX)

sCal, Nortrol, Abtrol

G. Regulatory Information:

Regulation Section	Classification	Product Code	Panel
21 § 862.1150, Calibrator	Class II	JIX	Clinical Chemistry (75)
21 § 862.1660, Quality Control Material (assayed and unassayed)	Class I, reserved	JJY	Clinical Chemistry (75)
21 § 862.1775, Uric acid test system	Class I, reserved	KNK	Clinical Chemistry (75)

H. Intended Use:

1. Intended use(s):

   See below

2. Indication(s) for use:

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

   For *in vitro* diagnostic use for quantitative testing on T60 instrument. 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 Instruments using methods defined by Thermo Fisher Scientific Oy.

   For *in vitro* diagnostic use for quantitative testing on T60 instrument. 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 Instruments using methods defined by Thermo Fisher Scientific Oy.

   The Uric Acid test system is intended for quantitative *in vitro* diagnostic measurement of uric acid concentration in human serum or plasma. Such measurements are used in the diagnosis and treatment of numerous renal and metabolic disorders, including renal failure and gout.

3. Special conditions for use statement(s):

   For prescription use only.

4. Special instrument requirements:

   To be used on the T60/T60i Chemistry Analyzer.

I. Device Description:

sCal is a lyophilized multiconstituent calibrator for use on quantitative methods as defined by Thermo Fisher.

Nortrol and Abtrol are lyophilized multiconstituent assayed controls for use on the Thermo Fisher T60 Clinical Chemistry system.

The Uric Acid (AOX) reagent is packaged as two reagents, Reagent A and Reagent B. The constituents and concentrations are:

Reagent A		Reagent B	
Phosphate Buffer pH 7.0	100 mmol/L	Phosphate Buffer pH 7.0	100 mmol/L
TOOS	125 mmol/L	4-Aminoantipyrine	1.5 mmol/L
Ascorbate oxidase (AOX)	> 1.25 kU/L	$K_4[Fe(CN)_6]$	50 µmol/L
Sodium azide	< 0.1%	Peroxidase	> 5 kU/L
		Uricase	> 250 U/L
		Sodium azide	< 1%

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Uric Acid (UA), Advia, Bayer Corp.

2. Predicate K number(s):

   k991576

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Method	Uric acid is oxidized to allantoin by uricase. The generated hydrogen peroxide reacts with 4-aminoantipyrine (4-AAP) and N-ethyl-N-(hydroxy-3-sulfopropyl)-m-toluidin (TOOS) to a blue violet dye.	Same
Reagent Storage	Reagents in unopened vials are stable at 2-8 °C until the expiration date printed on the label, when protected from light	Same
Expected Values	Serum, adult: Male: 3.5 - 7.2 mg/dl (210 - 420 µmol/l) Female: 2.6 - 6.0 mg/dl (150 - 350 µmol/l)	Same
Measuring Range	**Serum:** 0.2 - 20.0 mg/dl (10 - 1200 µmol/l)	Same

Differences		
Item	Device	Predicate
Intended Use	For *in vitro* diagnostic use in the quantitative determination of uric acid concentration in human serum or plasma on T60 instrument.	For *in vitro* diagnostic use in the quantitative determination of uric acid in human serum, plasma and urine on the ADVIA® 1650 Chemistry system.
Traceability/Standardization	The value of Uric Acid has been assigned by using NIST SRM 909b as a primary reference.	The ADVIA 1650 Uric Acid method is traceable to the CDC candidate reference method, which uses reference materials from the National Institute of Standards and Technology (NIST) via patient sample correlation.
Sample Type	Serum, plasma (Li-heparin)	Serum, plasma (Li-heparin) and urine
Limitations	**Lipemia:** No interference found up to 900 mg/dl (9 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 11 mg/dl (200 µmol/l) of conjugated bilirubin **Bilirubin total:** No interference found up to 14 mg/dl (250 µmol/l) of unconjugated bilirubin.	**Triglycerides:** The effect of triglycerides has been measured at analyte concentrations 3.4 mg/dL and 8.9 mg/ dL. The observed interference is expressed as an interference index. **Hemolysate:** No significant interference found up to 525 mg/dl of hemoglobin. **Bilirubin:** No significant interference found up to 30 mg/dl.

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:

Uric acid is oxidized to allantoin by uricase. The generated hydrogen peroxide reacts with 4-aminoantipyrine (4-AAP) and N-ethyl-N-(hydroxy-3-sulfopropyl)-m-toluidin (TOOS) to a blue violet dye. The absorbance of the formed color is measured at 540 nm.

$$\text{Uric acid} + 2\ H_2O + O_2 \xrightarrow{\text{Uricase}} \text{Allantoin} + CO_2 + H_2O_2$$

$$\text{TOOS} + \text{4-AAP} + 2\ H_2O_2 \xrightarrow{\text{POD}} \text{Indamine} + 3\ H_2O$$

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

The Precision study was performed using CLSI EP5-A as a guideline.
The precision study was performed for 21 days, with two runs per day, two replicates per run, for a total of 84 results per level. Levels 1 and 2 included 3 reagent lots, 1 operator, 3 T60 instruments at one site, and 10 calibrations. Level 3 and 4 included 3 reagent lots, 2 operators, 3 T60 instruments at one site, and 9 calibrations. Results are summarized below.

Precision Study							
Sample	Mean	Within run		Between run		Total	
	mg/dl	SD	CV%	SD	CV%	SD	CV%
Level 1	1.2	0.009	0.8	0.015	1.3	0.026	2.3
Level 2	2.3	0.017	0.7	0.020	0.9	0.038	1.7
Level 3	4.4	0.030	0.7	0.030	0.7	0.123	2.8
Level 4	8.9	0.045	0.5	0.039	0.4	0.094	1.1

b. *Linearity/assay reportable range:*

The linearity study was performed using CLSI EP6-A as a guideline. The samples were diluted in 11 steps (from 0% to 100%) by mixing samples with each other 1:1. Two parallel measurements were made in random order using one reagent lot. The extended linearity range was a separate set of samples prepared and measured as above. Six samples were run using an additional secondary dilution of 1:15. Results were as follows:

	Linearity Study	Extended Range
Sample Range	0.07-27.0 mg/dL	6.5-162.9 mg/dL
N	11	11
Slope	0.95	0.96
Intercept	0.007	-0.055
Observer Error	4.9%	4.5%

Based on the linearity study data, the sponsor will claim a measuring range of 0.2-20.0 mg/dL and an extended measuring range of 0.2-40.0 mg/dL after secondary dilution.

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

Traceability for sCal

Traceability is to NIST SRM 909b using a two-fold process. First, the value of the NIST SRM 909b is transferred to a lot of sCal by calibrating the T60 with the NIST material and running the sCal and 5 commercially available controls in triplicate. The measurements are repeated three times on multiple analyzers. Second, the sCal with the newly assigned value is used to calibrate multiple analyzers. The sCal is also run as a sample with 5 commercially available controls in replicates of 10 each.

Traceability of Nortrol and Abtrol

The traceability of controls is determined by calibrating the Uric Acid assay using sCal. The controls together with NIST SRM 909b and five commercially available controls are run as samples with three replicates. The measurements are repeated ten times using several different instruments and ten individual control vials from each control. The control ranges are calculated as median ± 8 %. The expected values for each lot are provided on the value sheet provided with the product.

Stability

The protocols and acceptance criteria for stability studies were reviewed and found to be acceptable. The sponsor claims an open on-board stability of reagents for 32 days. After reconstitution sCal, Abtrol, and Nortrol are stable for 7 days at 2-8 °C.

d. Detection limit:

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 for a total of 60 measurements. The LoB was determined to be 0.01 mg/dL.

The LoD study consisted of five low level samples run in ten replicates with two T60 instruments and two reagent lots during two days for a total of 100 measurements. The LoD was determined to be 0.06 mg/dL.

e. Analytical specificity:

Endogenous and exogenous interference: The interference study was performed according to CLSI EP7-A. Three concentrations of uric acid were run in paired-difference testing with five different levels of interferent against control pools containing no interferent. Three parallel measurements were taken for each level. This protocol was performed for icterus and lipemia. Interference from hemolysis was determined using the same protocol except that control and test pools were tested in four replicates within one run. Interference from ascorbic acid was determined using the same protocol as the hemolysate. The sponsor defined interference as a difference greater than ± 10% or ± 0.8 mg/dL of the initial value.

According to the interference studies, the following claims were established:

Lipemia: No interference found up to 900 mg/dL (9g/L) of Intralipid.

Hemolysate: No interference found up to 1000 mg/dL (10 g/L) of hemoglobin.

Bilirubin conjugated: No interference found up to 11 mg/dL (200 micmol/L) of conjugated bilirubin.

Bilirubin unconjugated: No interference found up to 14 mg/dL (250 micmol/L) of unconjugated bilirubin.

Ascorbic Acid: No interference of ascorbic acid up to 50 mg/L (5 mg/dL).

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

Method comparison studies were performed using CLSI EP9-A as a guide. One hundred thirty-six Li-heparin plasma samples (122 native, 14 contrived) were analyzed using T60i with Uric Acid reagents and Bayer Advia 2400 instrument with Uric Acid reagents to demonstrate the equivalence of the two systems. Samples ranged from 0.27 mg/dL to 18.94 mg/dL. The samples were split in two and run either on the predicate (one replicate) or candidate device (as duplicates). Deming regression analysis resulted in the equation: $y = 1.07x-0.13$, $R = 0.999$

b. Matrix comparison:

Eighty-eight matched serum and plasma (Li-heparin) samples (77 native, 3 diluted and 12 spiked) were run on the T60. Dilutions and spiking were performed in parallel on the matched samples. Samples ranged from 0.8 mg/dL to 19.0 mg/dL. Deming regression analysis resulted in the equation: $y = 1.01x-0.01$, $R = 1.000$.

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:

Male: 3.5-7.2 mg/dL (210-420 micmol/L)

Female: 2.6-6.0 mg/dL (150-350 micmol/L)

Referenced from Burtis, CA and Ashwood, ER (ed.), Tietz Fundamentals of Clinical Chemistry, 5th edition, WB Saunders Company, Philadelphia, 2001, pp. 422-426, 1015. The sponsor recommends that each laboratory determine its own reference range.

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.