

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

A. 510(k) Number:

k073295

B. Purpose for Submission:

New Device

C. Measurand:

Blood Urea Nitrogen (BUN)

D. Type of Test:

Quantitative Enzyme Assay

E. Applicant:

Thermo Fisher Scientific Oy

F. Proprietary and Established Names:

Urea / BUN, codes 981818 and 981820

sCal, code 981831

Nortrol, code 981043

Abtrol, code 981044

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
Urea Nitrogen (CDQ)	Class II	21 CFR 862.1770 Urea Nitrogen Test System	75 Clinical Chemistry(CH)
Product Code	Classification	Regulation Section	Panel
eCal Calibrator, Multi-Analyte Mixture (JIX)	Class II	21 CFR 862.1150 Calibrator	75 Clinical Chemistry(CH)
Product Code	Classification	Regulation Section	Panel
Nortrol, Abtrol 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):

Urea/BUN

The Urea / BUN test system is intended for quantitative *in vitro* diagnostic measurement of Urea / BUN (urea nitrogen) concentration in human serum or plasma. Such measurements are used in the diagnosis and treatment of certain renal and metabolic diseases.

sCal

For *in vitro* diagnostic use on T60 instrument. eCal is used as a calibrator for enzyme tests using methods defined by Thermo Fisher Scientific Oy.

Nortrol

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.

Abtrol

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.

2. Indication(s) for use:

See Intended Use above.

3. Special conditions for use statement(s):

Prescription Use Only

4. Special instrument requirements:

To be used with T60 chemistry analyzer system.

I. Device Description:

The BUN test system is supplied as a ready-to-use, liquid IVD reagent kit containing Jack Bean Urease, salts and preservative (two kit sizes, codes 981818 and 981820).

sCal calibrator is a lyophilized bovine serum based reference preparation to be used as a multi-analyte calibrator and does not contain human constituents.

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):
Blood Urea Nitrogen (UN)
2. Predicate K number(s):
k991576
3. Comparison with predicate:

Similarities		
Item	New Device	Predicate (k991576)
Sample Type	Serum, plasma (Li-heparin)	Same
Reagent Storage	Reagents in unopened vials are stable at 2...8 °C until the expiration date printed on the label.	Same
Intended Use	For <i>in vitro</i> diagnostic use in the quantitative determination of Urea / BUN (urea nitrogen) concentration in human serum or plasma on T60 instrument. Such measurements are used in the diagnosis and treatment of certain renal and metabolic diseases.	Same

Differences		
Item	Device	Predicate
Sample Type	Serum, plasma (Li-heparin)	Serum, plasma (Li-heparin) and urine
Instrument	T60 chemistry analyzer system	ADVIA [®] 2400 Chemistry system.
Measuring Range	Serum: Urea nitrogen: 4.2 - 56 mg/dl (1.5 - 20.0 mmol/l) Urea: 4.2 - 360 mg/dl (1.5 - 60.0 mmol/l)	Serum: Urea nitrogen 5 - 150 mg/dL (1.8 - 53.6 mmol/L) Urea: 35 - 1000 mg/dL (12.5 - 357 mmol/L)
Traceability/Standardization	The value of Urea / BUN has been assigned by using NIST SRM 909b as a primary reference	The ADVIA UN method is traceable to the CDC/NIST reference method using patient sample correlation.

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

CLSI EP5-A – Evaluation of Precision Performance of Clinical Chemistry Devices; Approved Guidelines

CLSI EP6-A – Evaluation of Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline

CLSI EP7-A – Interference Testing in Clinical Chemistry; Approved Guideline

CLSI EP9-A – Method Comparison and Bias estimation Using Patient Samples; Approved Guideline

L. Test Principle:

Urea is hydrolysed in the presence of water and urease to produce ammonia and carbon dioxide. In the presence of glutamate dehydrogenase (GLDH) and reduced nicotinamide adenine dinucleotide (NADH), the ammonia combines with alpha - ketoglutarate (α -KG) to produce L-glutamate. The resulting decrease in absorbance at 340 nm, as NADH is converted to NAD, is proportional to the level of urea in the sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

The precision study was done using serum samples during 21/22 days, with two runs per day, two replicates per run, total 84/88 results per level. For levels 1 and 3 the study included 2 reagent lots, 4 operators, 3 T60 instruments at one site, and 9 calibrations. For level 2 the study included 3 reagent lots, 1 operator, 3 T60 instruments at one site, and 9 calibrations. For the level 4 (~5.7 mg/dL) the precision study was done during 5 days, with two runs per day, two replicates per run, 1 reagent lot, 1 instrument and 2 calibrations with the total number of measurements being 20. Results are summarized below:

Precision Study							
Sample	Mean mg/dl	Within run		Between run		Total	
		SD	CV%	SD	CV%	SD	CV%
Level 1 (N=84)	14.7	0.2	1.4	0.1	1.0	0.4	2.7
Level 2 (N=84)	24.7	0.4	1.7	0.4	1.8	0.9	3.6
Level 3 (N=88)	44.8	0.4	0.8	0.4	1.0	1.0	2.2
Level 4 (N=20)	5.7	0.2	3.1	0.4	7.4	0.5	8.1

b. *Linearity/assay reportable range:*

The linearity study was performed per CLSI EP6-A. The serum samples were diluted in 10 steps (from 100% to 0%) by mixing samples with each other 1:1. For example, the 50% sample resulted from a 1:1 mixture of the 100% and 0% samples. Four parallel measurements were made in random order using one reagent lot (fresh and 30 days open on boarded). To generate samples at low level, commercially available human sera pool was used, while the same was spiked with Urea to generate high level samples. In addition, 8 samples were run using an additional secondary dilution of 1:10 to determine the extended linearity range. Results were as follows:

	Linearity study	Extended Linearity study
Sample range	2.3-61.85 mg/dL	8.67-194.02 mg/dL
Slope	1.075	1.09
Intercept	0	0
Obs. Error	7.50%	2.90 %
N	10	8

Based on the linearity study data, the sponsor claims a measuring range of 4.2-56 mg/dL and an extended measuring range of 4.2-168 mg/dL after secondary dilution.

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

Traceability for sCal:

sCal has been cleared earlier for glucose and Carbon Dioxide in the submissions k061107 and k071340 respectively.

sCal is traceable to the NIST SRM 909b reference material. sCal target values are determined using assay specific methods on the DPC T60 and other Thermo analyzer models. The target value is the median of all values obtained by these determinations. The exact calibration values are listed in the separate sCal calibrator sheet. The sponsor recommends that calibration be performed at least once a month or every time a new bottle of reagent is used or whenever control results require recalibration.

Traceability for Nortrol and Abtrol:

Controls Nortrol and Abtrol have been cleared earlier for glucose, AST and Carbon Dioxide in the submissions k061107, k071580 and k071340 respectively.

The target values of the Nortrol and Abtrol are control solutions are determined using assay specific methods on the T60 and other Thermo analyzer models (calibrated by the sCal calibrator). The target value is the median of all values obtained by these determinations.

The sponsor recommends that the quality control samples be used at least once a day and after each calibration and every time a new bottle of reagent is used. Further, the control intervals and limits must be adapted to the individual laboratory requirements. The results of the quality control sample(s) should fall within the limits pre-set by the laboratory. The sponsor further recommends that all local, state and federal guidelines be followed.

Stability:

The protocol and acceptance criteria for stability studies were reviewed and found to be acceptable. The sponsor claims 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 using serum samples. In the Limit of Blank study thirty replicates of a blank sample (0.9% NaCl) were run using two T60 instruments and one reagent lot with the total number of measurements being 60. The results support a claimed LOB of 0.3 mg/dL. In the Limit of Detection study five low level samples were run in ten replicates with two T60 instruments and one reagent lot during two days with the total number of measurements being 100. The results support a claimed LOD of 1.2 mg/dL.

e. Analytical specificity:

Interference Studies: For each interfering substance three parallel measurements of one interfering concentration (including non-interfered sample) were run. There was deemed to be no interference if the observed values were $\pm 10\%$ or ± 7.5 U/L of initial value.

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 unconjugated: 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 sixteen Li-heparin plasma samples were analyzed using T60 instrument with Urea / BUN reagents and Bayer Advia 2400 instrument with Urea Nitrogen reagents to demonstrate the equivalence of the two systems. The samples were split in two and then run each one either on the predicate (as singlets) or Thermo device (as duplicates). Each individual measurement is compared to one individual measurement result of the predicate. From Thermo device only the first results from the duplicate measurements were used. Samples ranged from 4.6 mg/ dL to 55.94 mg/ dL. Data obtained was plotted and the results of the Deming regression analysis were as follows:

$$y = 0.92x + 0.937; r = 0.995.$$

b. *Matrix comparison:*

Twenty-four matched serum and plasma (Li-heparin) samples were run on T60 instrument to demonstrate the use of serum samples. Both serum and plasma samples were run in duplicates but only the first replicate results were used for calculations. Samples ranged from 4.9 to 55.8 mg/dL. Data obtained was plotted and the results of the Deming regression analysis were as follows:

$$y = 1.03x - 0.16; r = 0.999.$$

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 Applicable

5. Expected values/Reference range:

Serum adult:

Urea nitrogen: 6 – 20 mg/dL (2.2 – 7.2 mmol/L)

Urea: 13- 43 mg/dL (2.2 – 7.2 mmol/L)

Source citation: Burtis, CA and Ashwood, E R (ed.), Tietz Fundamentals of Clinical Chemistry, 5th edition, W B Saunders Company, Philadelphia, 2001, pp. 366-367, 1002.

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.