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

A. 510(k) Number:
k062862

B. Purpose for Submission
New device

C. Measurand:
Uric acid

D. Type of Test:
Quantitative, enzymatic, colorimetric assay

E. Applicant:
Olympus America Inc.

F. Proprietary and Established Names:
Olympus Uric Acid Reagent

G. Regulatory Information:
1. Regulation Section
   21 CFR §862.1775, uric acid test system
2. Classification:
   Class I, Reserved
3. Product Code:
   KNK
4. Panel
   Clinical Chemistry (75)

H. Intended Use:
1. Intended use(s)
   See Indications for use below.

2. Indication(s) for use:
   Olympus Uric Acid Reagent is for the quantitative determination of Uric Acid in human serum, heparinized plasma and urine on OLYMPUS analyzers.

   Measurements of Uric Acid are used in the diagnosis and treatment of numerous renal and metabolic disorders, including renal failure, gout, leukemia, psoriasis, starvation or other wasting conditions, and of patients receiving cytotoxic drugs.
3. Special conditions for use statement(s):
   For Prescription Use only

4. Special instrument requirements:
   AU400/400^{e}, AU600/640/640^{e}, AU2700/5400 system

I. Device Description:

This *in vitro* diagnostic reagent is packaged as two reagents, R1 and R2. The final concentrations of the reactive ingredients are presented in the table below:

Phosphate buffer (pH 7.5)	42	mmol/L
Peroxidase	≥ 5.9	kU/L
MADB	0.15	mmol/L
4-Aminophenazone	0.30	mmol/L
EDTA	0.44	mmol/L
Uricase	≥ 250	U/L
Preservatives		

J. SUBSTANTIAL EQUIVALENCE INFORMATION

1. Predicate device name(s):
   Olympus Uric Acid Reagents
2. Predicate 510(k) number(s):
   k961274
3. Comparison with predicate:

Similarities		
Item	**Device**	**Predicate**
Method Principle	This Olympus Uric Acid procedure is a modification of the Fossati method. Uric acid is converted by uricase to allantoin and hydrogen peroxide. Hydrogen peroxide reacts with 4-aminoantipyrine (4-AAP) in the presence of N,N-bis(4-sulfobutyl)-3,5-dimethylaniline, disodium salt (MADB) to produce a chromophore which is read bichromatically at 660/800 nm. The amount of dye formed is proportional to the uric acid concentration in the sample.	This Olympus Uric Acid procedure is a modification of the Fossati method. Uric acid is converted by uricase to allantoin and hydrogen peroxide. Hydrogen peroxide reacts with 4-aminoantipyrine (4-AAP) in the presence of N,N-bis(4-sulfobutyl)-3,5-dimethylaniline, disodium salt (MADB) to produce a chromophore which is read bichromatically at 660/800 nm. The amount of dye formed is proportional to the uric acid concentration in the sample.
Calibrator Traceability	National Institute of Standards and Technology (NIST) Standard Reference Material (SRM) 909b	National Institute of Standards and Technology (NIST) Standard Reference Material (SRM) 909b
On-board stability	30 days	30 days

Differences		
Item	**Device**	**Predicate**
Intended Use	System reagent is for the quantitative determination of Uric Acid in human serum, heparinized plasma and urine on OLYMPUS analyzers.	System reagent is for the quantitative determination of Uric Acid in human serum, and urine on OLYMPUS analyzers.
Specimen	Serum, plasma, & urine	Serum, & urine

K. STANDARD/GUIDANCE DOCUMENT REFERENCED (IF APPLICABLE)

CLSI EP5-A2: Evaluation of Precision Performance of Quantitative Measurement Methods;
CLSI EP7-A2: Interference Testing in Clinical Chemistry; Approved Guideline.

L. Test Principle

This Olympus Uric Acid procedure is a modification of the Fossati method. Uric acid is converted by uricase to allantoin and hydrogen peroxide. Hydrogen peroxide reacts with 4-aminoantipyrine (4-AAP) in the presence of N,N-bis(4-sulfobutyl)-3,5-dimethylaniline, disodium salt (MADB) to produce a chromophore which is read bichromatically at 660/800 nm. The amount of dye formed is proportional to the uric acid concentration in the sample.

M. Performance Characteristics (if/when applicable):

1. Analytical Performance:

a. Precision /Reproducibility:

Precision was performed by testing four sample pools two-fold twice a day for twenty days. The within-run and total CVs were calculated according to CLSI EP5-A protocol. The within run precision for serum samples is less than 2% and total precision is less than 3% on the AU400/400e, AU600/640/640e, and AU2700/5400 instruments. The within run precision for urine samples is less than 3% and total precision is less than 5% on the AU400/400e, AU600/640/640e, and AU2700/5400 instruments. The results are shown in the table below:

AU400/400^{e} Serum

N = 80	**Within run**		**Total**	
Mean, mg/dL	**SD**	**CV%**	**SD**	**CV%**
3.9	0.02	0.53	0.05	1.31
7.3	0.05	0.64	0.07	0.98
9.8	0.06	0.59	0.12	1.17

AU600/640/640^{e} Serum

N = 80	**Within run**		**Total**	
Mean, mg/dL	**SD**	**CV%**	**SD**	**CV%**
3.8	0.01	0.38	0.03	0.80
7.2	0.03	0.43	0.06	0.89
9.7	0.05	0.53	0.08	0.85

AU2700/5400 Serum

N = 80	Within run		Total	
Mean, mg/dL	SD	CV%	SD	CV%
3.8	0.02	0.48	0.06	1.49
7.3	0.02	0.34	0.11	1.52
9.8	0.05	0.50	0.16	1.60

AU400/400^{e} Urine

N = 80	Within run		Total	
Mean, mg/dL	SD	CV%	SD	CV%
21.5	0.23	1.09	0.36	1.66
58.0	1.06	1.84	1.37	2.36
88.4	1.80	2.03	1.91	2.16

AU600/640/640^{e} Urine

N = 100	Within run		Total	
Mean, mg/dL	SD	CV%	SD	CV%
21.8	0.24	1.12	0.35	1.61
58.4	0.95	1.63	1.33	2.28
89.3	1.78	2.00	2.01	2.25

AU2700/5400 Urine

N = 80	Within run		Total	
Mean, mg/dL	SD	CV%	SD	CV%
21.5	0.25	1.17	0.37	1.73
58.2	0.76	1.31	1.27	2.19
88.8	1.71	1.93	1.98	2.23

b. Linearity/ Assay reportable range.

A linearity study was conducted on the Olympus Uric Acid reagent using prepared standard solutions. Samples were prepared by diluting a high pool containing 33.49 mg/dL with a 0 mg/dL sample and assayed. The linearity was established for serum as 1.5 to 30 mg/dL. For urine linearity, samples were prepared by diluting a high pool containing 123 mg/dL with a 0 mg/dL sample. The linearity was established for urine as 0.7 to 100 mg/dL.

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

The frequency of calibration is every 30 days. Calibration of the Olympus Uric Acid reagent is accomplished by use of the Olympus Chemistry Calibrator (Cat # DR0070 or DR0071), which is traceable to the National Institute of Standard and Technology (NIST) Standard Reference Material (SRM) 909b for serum and plasma specimens. For urine specimens the calibration is established using the Olympus Urine Calibrator (Cat # DR0090).

A stability study was conducted on the Olympus Uric Acid reagent whereby both fresh reagent and reagent at the end of its on-board stability (30 days) were assayed for uric acid recovery on prepared control material and to confirm that the linearity of the reagent was maintained after 30 days on-board,

The manufacturer recommends in the labeling that during operation of the Olympus analyzer at least two levels of an appropriate quality control material should be tested a minimum of once a day. In addition, these controls should be performed after calibration, with each new lot of reagent, and after specific maintenance or troubleshooting steps described in the appropriate Olympus User's Guide. Quality control testing should be performed in accordance with regulatory requirements and each laboratory's standard procedure.

d. Detection Limit

The lowest detectable level represents the lowest measurable level of uric acid that can be distinguished from zero. It is calculated as the absolute mean plus three standard deviations of 20 replicates of an analyte free sample.

The lowest detectable level using serum settings was estimated as follows:

Analyzer	Lowest Detectable Level (mg/dL)
AU600/640/640e	0.02
AU400/400e	0.02
AU2700/5400	0.02

Functional Sensitivity:

Serum:

Precision results (40-fold determination) for a level <0.8 mg/dL are shown below with a CV of <20% for each application.

Analyzer	Mean Concentration (mg/dL)	SD	CV%
AU600/640/640e	0.24	0.013	5.5
AU2700/5400	0.24	0.015	6.2
AU400/400e	0.23	0.012	5.4

Urine:

Precision results (40-fold determination) for a level <3 mg/dL are shown below with a CV of <20% for each application.

Analyzer	Mean Concentration (mg/dL)	SD	CV%
AU600/640/640e	0.64	0.058	9.0
AU2700/5400	0.64	0.038	5.9
AU400/400e	0.63	0.053	8.5

e. Analytical Specificity

A study of common interfering substances was conducted. The results of the study were evaluated following the recommendations of CLSI EP7-A on the AU400/400e, AU600/640/640e, and AU2700/5400. The following substances interfere with this uric acid method:

AU400/400e
Ascorbic Acid: Interference less than 5% up to 20 mg/dL Ascorbate
Bilirubin:Interference less than 5% up to 40 mg/dL Bilirubin
Hemolysis:Interference less than 5% up to 500 mg/dL Hemolysate
Lipemia:Interference less than 5% up to 1000 mg/dL Intralipid

AU600/640/640[e]
Ascorbic Acid: Interference less than 5% up to 20 mg/dL Ascorbate
Bilirubin:Interference less than 5% up to 40 mg/dL Bilirubin
Hemolysis:Interference less than 5% up to 500 mg/dL Hemolysate
Lipemia:Interference less than 5% up to 1000 mg/dL Intralipid

AU2700/5400
Ascorbic Acid: Interference less than 5% up to 20 mg/dL Ascorbate
Bilirubin:Interference less than 5% up to 40 mg/dL Bilirubin
Hemolysis:Interference less than 5% up to 500 mg/dL Hemolysate
Lipemia:Interference less than 5% up to 1000 mg/dL Intralipid

f. Assay Cut-off
Not applicable

2. Comparison Studies:

a. Method comparison with predicate device:

Serum

Patient samples were used to compare the Olympus Uric Acid on the AU600 to another Olympus analyzer Uric Acid method (Method 2). Further studies were conducted as outlined below:

Y Method	AU600/640/640[e]	AU400/400[e]	AU2700/5400
X Method	Method 2	AU600/640/640[e]	AU600/640/640[e]
Slope	1.014	0.973	0.980
Intercept	-0.226	0.250	0.253
Correlation Coeff. (r)	1.000	1.000	1.000
No. of Samples (n)	122	122	122
Range (mg/dL)	1.9 – 29.4	1.7 - 29.4	1.7-29.4

Urine

Urine samples were used to compare this Olympus Uric Acid on the AU640 to another Olympus analyzer Uric Acid method (Method 2). Further studies were conducted as outlined below:

Y Method	AU600/640/640[e]	AU400/400[e]	AU2700/5400
X Method	Method 2	AU600/640/640[e]	AU600/640/640[e]
Slope	0.981	1.034	1.014
Intercept	0.496	-0.199	- 0.195
Correlation Coeff. (r)	0.998	0.999	0.999
No. of Samples (n)	159	159	159
Range (mg/dL)	0.9 – 98.6	0.8 - 96.7	0.8 – 96.7

b. Matrix comparison

Matched serum and heparinized plasma samples were assayed on the AU640 Olympus analyzer to demonstrate that no matrix effect exists for this Olympus Uric acid reagent, between serum and heparinized plasma samples.

Slope	1.018
Intercept	-0.241
Correlation Coeff. (r)	1.000
No. of Samples (n)	47
Range (mg/dL)	1.51 – 29.1

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 Ranges:
   In the labeling the expected values are provided from Teitz, Guide to Laboratory Tests, 4th Edition, Saunders, 2006 as follows:

Serum:	Adults:
Female:	2.3 - 6.6 mg/dL
Male:	4.4 - 7.6 mg/dL
Urine:	
Female:	250 – 750 mg/24 hours
Male:	250 – 800 mg/24 hours

Excretion may decrease by 20 to 25% on a purine-free diet to less than 400 mg/24 hours. Expected values may vary with age, sex, diet and geographical location. Each laboratory should determine its own expected values as dictated by good laboratory practice.

N. Proposed Labeling:

The labeling is sufficient to and 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.