

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

A. 510(k) Number:

k063804

B. Purpose for Submission:

Modification to existing device: New formulation, new indicator and addition of plasma to Indications for Use,

C. Measurand:

Triglyceride

D. Type of Test:

Quantitative

E. Applicant:

Olympus America, Inc.

F. Proprietary and Established Names:

Olympus Triglyceride Test System

G. Regulatory Information:

1. Regulation section:

21 CFR 862.1705 Triglyceride test system

21 CFR 862.9 (c)(4), Limitations of exemptions, For assessing risk of cardiovascular diseases

2. Classification:

Class I, meets limitations of exemptions, 21 CFR 862.9(c)(4)

3. Product code:

CDT

4. Panel:

75

H. Intended Use:

1. Intended use(s):

System reagent for the quantitative determination of triglyceride concentrations in human serum and plasma on OLYMPUS analyzers.

Measurements of triglyceride are used in the diagnosis and treatment of patients with diabetes mellitus, nephrosis, liver obstruction, other diseases involving lipid metabolism, or various endocrine disorders.

2. Indication(s) for use:

See Intended Use

3. Special conditions for use statement(s):

Prescription use only

4. Special instrument requirements:

Olympus AU400/AU400E, Olympus AU600/AU640/AU640E, Olympus AU2700, Olympus AU5400

I. Device Description:

Olympus Triglyceride Test System is an *in vitro* diagnostic reagent. The reagent is supplied as a two-liquid ready to use test system.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Olympus triglyceride reagent

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

k961274

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Measurement method	Enzymatic	same
Reagents	Liquid – ready to use	same

Differences		
Item	Device	Predicate
Specimen types	Serum and plasma	serum
Indicator	N,N bis (4-sulfobutyl) - 3,5-dimethylaniline, disodium salt (MADB)	4-chlorophenol
Methodology	Enzymatic endpoint at 660 nm	Enzymatic endpoint at 520 nm

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

CLSI EP5-A2, CLSI EP9-A, CLSI EP7-A, CLSI EP14-A

L. Test Principle:

Olympus Triglyceride procedure is based on a series of coupled enzymatic reactions. The triglycerides in the sample are hydrolyzed by a combination of microbial lipases to give glycerol and fatty acids. The glycerol is phosphorylated by adenosine triphosphate (ATP) in the presence of glycerol kinase (GK) to produce glycerol-3-phosphate. The glycerol-3-phosphate is oxidized by molecular oxygen in the presence of glycerol phosphate oxidase (GPO) to produce hydrogen peroxide (H₂O₂) and dihydroxyacetone phosphate. The formed H₂O₂ reacts with 4-aminophenazone and N, N-bis (4-sulfobutyl) -3,5 dimethylaniline, disodium salt (MADB) in the presence of peroxidase (POD) to produce a chromophore, which is read at 660/800 nm. The increase in absorbance at 600/800 nm is proportional to the triglyceride content of the sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Estimates of precision were based on CLSI EP5-A2 guidelines by testing a low, medium and high human serum pool, in duplicate twice a day for 20 days. Assays of serum pools were analyzed on the Olympus AU400, Olympus AU600,

and Olympus AU2700 instruments. The results of the studies are displayed in the tables below:

AU400/AU400E

n = 80	Within run		Total	
Mean, mg/dL	SD	CV%	SD	CV%
89	1.09	1.22	2.30	2.58
190	1.72	0.90	4.84	2.54
439	4.64	1.06	10.60	2.41

AU 600/640/640E

n = 80	Within run		Total	
Mean, mg/dL	SD	CV%	SD	CV%
89	0.57	0.64	1.48	1.65
191	0.95	0.49	2.69	1.41
442	2.28	0.51	6.45	1.46

AU2700/5400

n = 80	Within run		Total	
Mean, mg/dL	SD	CV%	SD	CV%
90	0.54	0.60	1.81	2.00
192	0.85	0.44	3.30	1.72
443	3.11	0.70	7.90	1.78

b. Linearity/assay reportable range:

The linearity studies performed support the sponsor's claimed measuring range of 10 to 1000 mg/dL. Studies were performed on the Olympus AU400, Olympus AU640, and Olympus AU2700 analyzers. A series of analyte concentrations covering the entire measuring range (sample range was 0 – 1098 mg/dL) were prepared by dilution of a high pool sample. The best fit line was calculated using a validated excel template by linear regression and the deviations of the data from linearity were examined. The results all met the sponsor's acceptance criteria of $\pm 5\%$ for the range of 10-1000 mg/dL or ± 6 mg/dL below 248 mg/dL.

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

NIST Standard Reference Material (SRM) 1951b

d. Detection limit:

The limit of the blank was determined by testing an analyte-free sample twenty times each on the AU400, AU640 and AU2700 analyzers. The value was determined by calculating the absolute mean plus 3 standard deviations. The lowest detectable levels are 0.31 mg/dL for AU400, 0.31 mg/dL for AU640 and 0.26 mg/dL for AU2700.

The limit of quantitation was determined by testing 3 pools of patient samples with values below the lower point of the measuring range of 10 mg/dL 40 times over a one month period of time. The lowest level of triglyceride was determined to be 3.47 mg/dL for AU400, 4.07 mg/dL for AU640 and 4.09 mg/dL for AU2700 at which the CV was less than 20%. The results support the limit of quantitation claim of 5mg/dL.

e. Analytical specificity:

Analytical specificity studies were performed based on CLSI Guideline EP7-A. Studies performed on the AU400, AU 600 and AU2700 demonstrated $\leq 3\%$ interference from bilirubin up to 40 mg/dL, $\leq 3\%$ interference from hemolysate up to 500 mg/dL and $\leq 5\%$ interference from ascorbate up to 20 mg/dL.

The labeling contains the limitation that when using enzymatic methodologies for triglyceride, samples which are extremely lipemic with triglyceride levels typically exceeding 1700 mg/dL, results can be erroneously reported as being within the linear range of the assay. In order to identify grossly lipemic samples, Data Check Parameters are provided. If the reaction kinetics of a test exhibits the characteristics of an elevated triglyceride sample, the result will be flagged. The labeling states that grossly lipemic samples may, under rare circumstance, evade the Data Check Parameters and should routinely be diluted 1 part sample to 4 parts saline prior to analysis and the results multiplied by 5.

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

Method comparison studies were performed based on CLSI EP9-A using 148 serum samples with values ranging from 13 – 953 mg/dL. The samples were run with the predicate Olympus Triglyceride Reagent (k961274) on the Olympus AU640 analyzer. The same samples were run on the Olympus AU640, AU400, and AU2700 analyzers using the Olympus Triglyceride Test System (k063804). The results are displayed in the table below.

Y method	AU600/AU640	AU400/AU400E	AU2700/5400
X method	Predicate method on AU640	Predicate method on AU640	Predicate method on AU640
Slope	1.011	1.023	0.970
Intercept	-0.871	-2.232	+2.783
R	1.000	1.000	1.000
N	148	148	148
Range (mg/dL)	14 - 939	13 - 953	13 - 953

b. *Matrix comparison:*

Matrix comparison studies were performed on the AU640 analyzer based on CLSI EP14-A using matched patient samples for EDTA plasma vs. serum and for Lithium-Heparin plasma vs. serum. The results of the studies are displayed in the table below.

Y method	EDTA plasma	Heparin plasma
X method	Serum	Serum
Slope	1.004	0.999
Intercept	-2.987	-3.215
r	1.000	0.999
n	41	40
Range (mg/dL)	12 - 903	12 - 811

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:

Expected values are from the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) Guidelines.

ATP III Classification of Serum Triglycerides (mg/dL)

<150 Normal

150-199 Borderline high

200-499 High

≥ 500 Very high

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.