

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY**

A. 510(k) Number:

k073489

B. Purpose for Submission:

Addition of plasma (Li heparin/EDTA) matrix claim to the predicate device

C. Measurand:

Immunoglobulin A (IgA)

D. Type of Test:

Quantitative immunoturbidimetric assay

E. Applicant:

Olympus America, Inc.

F. Proprietary and Established Names:

Olympus IgA reagent (OSR6X171)

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
CFN Method, Nephelometric, Immunoglobulins (G, A, M)	Class II	21 CFR 866.5510 Immunoglobulins A, G, M, D, E Immunological Test System	Immunology (IM82)

H. Intended Use:

1. Intended use(s):

System reagent for the quantitative determination of IgA immunoglobulins in human serum and plasma on OLYMPUS analyzers

2. Indication(s) for use:

The spectrum of abnormalities in serum immunoglobulin concentration is broad. Abnormal concentrations range from a virtual absence of one or more of the three major classes of immunoglobulins (IgA, IgG and IgM) to polyclonal increases in one or more immunoglobulins. Measurement of these immunoglobulins aids in the diagnosis of abnormal protein metabolism and the body's lack of ability to resist infectious agents.

3. Special conditions for use statement(s):

For prescription use only

4. Special instrument requirements:

OLYMPUS analyzers: AU400/400^e, 600/640/640^e and 2700/5400

I. Device Description:

The device consists of two reagents: R1 buffer (Tris buffer pH 7.2, polyethylene glycol 6000) and R2 (goat anti-IgA antiserum). The reagents contain sodium azide as preservative.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Olympus IgA reagent (OSR6X44)

2. Predicate 510(k) number(s):
k951055
3. Comparison with predicate:

Similarities		
Item	Device	Predicate
	Olympus IgA reagent (OSR6X171)	Olympus IgA reagent (OSR6X44)
Intended Use	System reagent for the quantitative determination of IgA immunoglobulins in human serum and plasma on Olympus analyzers	Same but in serum only
Indications for Use	Aid in the diagnosis of abnormal protein metabolism and the body's lack of ability to resist infection	Same
Test principle	Immunturbidimetric	Same
Antibody	Goat anti-IgA	Same
Reagent form and storage	Liquid, on-board storage	Same
On-board stability	90 days	Same
Calibrator	Olympus Serum Protein Multi-calibrator	Same
Calibrator traceability	International Reference Preparation CRM 470	Same
Expected values	66-433 mg/dL	Same

Differences		
Item	Device	Predicate
	Olympus IgA reagent (OSR6X171)	Olympus IgA reagent (OSR6X44)
Matrix	Serum, plasma (Li heparin or EDTA)	Serum only
Calibration frequency	90 days	7 days

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

EN14971 (2000) *ISO Medical Devices – Application of Risk Management to Medical Devices*; EP7-A2 (2005) *CLSI Interference Testing in Clinical Chemistry*; EP5-A2 (2004) *CLSI Evaluation of Precision Performance of Clinical Chemistry Devices*; EP9-A2 (2002) *CLSI Method Comparison and Bias Estimation Using Patient Samples*; CEN 13640 (2002) *Stability Testing of In Vitro Diagnostic Reagents*; C28-A2 (2000) *CLSI How to Define and Determine Reference Intervals in the Clinical Laboratory*; EP6-A (2003) *CLSI Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach*; FDA: *Draft Guidance document for 510(k) Submission of Immunoglobulins A, G, M, D and E Immunoglobulin Test System In Vitro Devices*

L. Test Principle:

When a sample is mixed with R1 buffer and R2 antiserum solution, human IgA reacts specifically with anti-human IgA antibodies to yield insoluble aggregates. Immune complexes formed in solution scatter light in proportion to their size, shape and concentration. The Olympus analyzer measures the decrease in intensity of light transmitted (increase in absorbance) through particles suspended in solution as a result of complexes formed during the antigen-antibody reaction.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Assays of three human serum pools (low, medium and high) sera were performed in duplicate 2 runs per day for 20 days (n=80) on the AU400/400^e, AU600/640/640^e, and AU2700/5400. The acceptance criteria for within-run and total precision were <4.2% and <10% respectively. The within-run precision covering the platforms ranged from 1.05–2.18% and the total precision ranged from 1.50-4.01%.

AU400/400^e

N=80 Mean (mg/dL)	Within-run		Total	
	SD	%CV	SD	%CV
102	1	1.20	2	2.43
244	4	1.48	6	2.52
504	11	2.18	15	2.95

AU600/640/640^e

N=80 Mean (mg/dL)	Within-run		Total	
	SD	%CV	SD	%CV
102	1	1.41	3	3.39
240	4	1.52	9	3.85
479	10	2.18	19	4.01

AU2700/5400

N=80 Mean (mg/dL)	Within-run		Total	
	SD	%CV	SD	%CV
102	1	1.05	2	1.50
237	4	1.56	5	1.91
486	10	1.20	9	1.83

Auto dilution:

To validate the accuracy and precision of automated sample dilution protocol, three auto-dilution samples were diluted manually and run on the instrument.

The same samples were diluted automatically by the AU640. Accuracy (%difference) and precision (%CV) were determined.

Accuracy 1:5

Level	Automatic dilution (mg/dl)	Manual dilution (mg/dl)	% Difference
1	996	948	-5.1
2	817	805	-1.5
3	522	512	-2.0

Accuracy 1:10

Level	Automatic dilution (mg/dl)	Manual dilution (mg/dl)	% Difference
1	970	961	-0.9
2	767	780	1.7
3	577	584	1.2

Precision (within run) 1:5

Level	Mean (mg/dL)	SD (mg/dL)	CV (%)	Essential Specification	
1	93	1	1.38	≤4.2% CV	Pass
2	125	1	0.91		
3	157	2	1.42		

Precision (within run) 1:10

Level	Mean (mg/dL)	SD (mg/dL)	CV (%)	Essential Specification	
1	42	1	1.24	≤4.2% CV	Pass
2	58	1	1.12		
3	75	1	1.29		

b. *Linearity/assay reportable range:*

The measuring range for the assay is 10-700 mg/dL. The procedure used to demonstrate linearity was based on CLSI EP6-A. A series of at least ten analyte concentrations, covering the linear dynamic range were prepared by dilution of a high pool sample. Each dilution was assayed in quadruplicate and the mean analytical results were plotted versus the relative analyte concentrations (% dilution). Studies were performed on the AU400, AU640 and AU2700 analyzers. The acceptance criteria for deviation from the regression line for the 10-40 mg/dL and 40-700 mg/dL ranges were ± 4 mg/dL and $\pm 10\%$ respectively. The studies showed the assay was linear from 10-700 mg/dL. There was no high dose hook effect up to 10,000 mg/dL.

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

The calibrator is traceable to the International Reference Preparation CRM470 (US designation RPPHS lot 91/0619).

Calibration frequency:

The calibration stability period change from 7 days to 90 days was validated during the on-board reagent stability studies. Linearity and in-house control recovery were checked after 90 days of reagent storage. The linearity is displayed at day 90 and the %drift from Day 0 from control recovery (with calibration at day 0) was calculated. Results were acceptable.

Reagent on-board stability was demonstrated according to internal procedures where the linearity displayed at day 90 and the % drift from Day 0 from control recovery were calculated. A change of $\leq 10\%$ was demonstrated over the 90 days.

d. *Detection limit:*

The Limit of Quantitation (LoQ) for the new assay was determined by testing

3 patient pools, 40 fold at an analyte concentration below the lower end of the measuring range on the AU400, AU640 and AU2700. The analyte level at which a CV of less than 20% was determined to be <10 mg/dL. This was determined using a method based on the CLSI protocol EP17-A.

	Mean Concentration (mg/dL)	SD	CV (%)
AU400	6.3	1.1	18.0
AU640	3.2	0.21	6.4
AU2700	2.9	0.26	8.8

The Limit of Detection (LoD) or the concentration of analyte which is significantly different from zero was determined by testing an analyte free sample twenty-fold on the AU400, AU640 and AU2700. LoD was calculated as the absolute mean + 3SD. The lowest detectable level was determined to be ≤ 1 mg/dL.

	Mean Concentration (mg/dL)	SD	LoD (mg/dL)
AU400	0.0	0.0	0.00
AU640	-0.02	0.162	0.51
AU2700	-0.02	0.107	0.34

e. *Analytical specificity:*

The impact of bilirubin, lipids and hemoglobin were assessed in accordance with CLSI EP7-A2. The RF interference studies were carried out following in-house procedures.

Substance	Levels up to	% Interference		
		AU400/400 ^c	AU600/640/640 ^c	AU2700/5400
Bilirubin	40 mg/dL	$\leq 2\%$	$\leq 3\%$	$\leq 3\%$
Lipids	1000 mg/dL	$\leq 10\%$	$\leq 6\%$	$\leq 4\%$
Hemoglobin	500 mg/dL	$\leq 1\%$	$\leq 5\%$	$\leq 4\%$
RF	600 IU/mL	$\leq 8\%$	$\leq 8\%$	$\leq 4\%$

f. *Assay cut-off:*

See reference range

2. Comparison studies:

a. *Method comparison with predicate device:*

Y method (new)	AU2700	AU2700/5400	AU2700/5400
X method (predicate)	AU2700	AU400	AU640/640 ^c
Slope	0.923	1.029	0.948
Intercept	15.1	-2.8	9.1
Correlation coefficient (r)	0.999	0.998	0.999
Number of samples	111	115	115
Range (mg/dL) Y method	38-672	21-672	21-672
Range (mg/dL) X method	32-684	23-659	21-697

b. *Matrix comparison:*

Studies were performed based on CLSI EP9-A2.

Y method	Li-heparin plasma	EDTA plasma
X method	Serum	Serum
Slope	0.944	0.942
Intercept	+3.984	+2.227
Correlation coefficient	1.000	0.999
Number of samples	45	45
Patient mean value – serum mg/dL	245.14	245.14
Patient mean value – plasma mg/dL	235.50	233.05
Reference range – serum mg/dL	42.88 – 614.44	42.88 – 614.44
Reference range - plasma mg/dL	40.61 – 581.67	40.54 – 598.41

3. Clinical studies:
 - a. *Clinical Sensitivity:*
Not determined
 - b. *Clinical specificity:*
Not determined
 - 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:

Expected values may vary with age, sex, diet and geographical location. The reference range of 66-433 mg/dL established for the predicate device was re-verified according to CLSI C28-A2 on the Olympus AU400, 600 and 5400.

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.