

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

A. 510(k) Number:

k080435

B. Purpose for Submission:

New device

C. Measurand:

Direct bilirubin

D. Type of Test:

Quantitative colorimetric

E. Applicant:

Olympus America, Inc.

F. Proprietary and Established Names:

The Olympus Direct Bilirubin Reagent (OSR6X181)

G. Regulatory Information:

1. Regulation section:

21 CFR 862.1110

2. Classification:

Class II

3. Product code:

CIG

4. Panel:

Clinical Chemistry (75)

H. Intended Use:

1. Intended use(s):

See indications for use below.

2. Indication(s) for use:

System reagent for the quantitative determination of Direct Bilirubin in human serum on OLYMPUS analyzers.

Measurements of the levels of bilirubin, an organic compound formed during the normal and abnormal destruction of red blood cells, is used in the diagnosis and treatment of liver, hemolytic hematological, and metabolic disorders, including hepatitis and gall bladder block.

For in vitro diagnostic use.

3. Special conditions for use statement(s):

For prescription use only

4. Special instrument requirements:

Olympus analyzers

I. Device Description:

The device is an in vitro diagnostic assay for the quantitative determination of direct bilirubin in human serum. The assay consists of two ready to use reagents with 3,5-Dichlorophenyl Diazonium (BF)₄ and Hydrochloric acid.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Olympus Direct Bilirubin Reagent

2. Predicate K number(s):

k924963

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Instrument required	Olympus AU400/600/640/2700/5400	Olympus AU400/600/640/2700/5400
Methodology	Photometric Color	Photometric Color
Reagent storage form	Liquid, on-board storage	Liquid, on-board storage

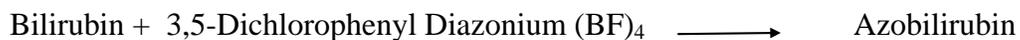
Differences		
Item	Device	Predicate
Sample type	Serum	Serum and plasma
Reagent on-board stability	30 days	20 days
Expected Values	<0.2 mg/dL	0.03 – 0.18 mg/dL

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

- CLSI EP9-A2 Method Comparison and Bias Estimation Using Patient Samples
- CLSI EP5-A2 Evaluation of Precision Performance of Clinical Chemistry Devices
- CLSI C-28 How to Define and Determine Reference Intervals in the Clinical Laboratory

L. Test Principle:

The Olympus Direct Bilirubin Reagent utilizes a variation of the classical method developed by Van den Bergh and Mueller. Direct (conjugated) bilirubin couples directly with a diazonium salt of 3,5-dichloroaniline (DPD) in an acid medium to form azobilirubin. The direct bilirubin in serum is directly proportional to the color development of azobilirubin which is measured bichromatically at 540/600 nm.



M. Performance Characteristics (if/when applicable):

1. Analytical performance:
 - a. *Precision/Reproducibility:*

Precision was evaluated using serum controls in accordance with CLSI EP5-A2 on the Olympus AU400, AU640, and AU2700 analyzers. The results are summarized below.

AU400

N = 80	Repeatability (Within Run)		Within Laboratory (Total)	
	SD	CV%	SD	CV%
Mean, mg/dL				
0.15	0.01	4.33	0.01	5.71
2.15	0.01	0.54	0.06	2.79
5.36	0.04	0.66	0.14	2.69

AU640

N = 80	Repeatability (Within Run)		Within Laboratory (Total)	
	SD	CV%	SD	CV%
Mean, mg/dL				
0.14	0.00	3.18	0.01	5.29
2.17	0.01	0.58	0.07	3.38
5.41	0.04	0.67	0.19	3.46

AU5400

N = 80	Repeatability (Within Run)		Within Laboratory (Total)	
	SD	CV%	SD	CV%
Mean, mg/dL				
0.14	0.00	2.75	0.01	4.11
2.16	0.02	0.72	0.06	2.73
5.33	0.03	0.57	0.14	2.67

b. *Linearity/assay reportable range:*

A series of commercially available linearity panels with bilirubin concentrations ranging from 0.02 mg/dL to 12 mg/dL were analyzed on the Olympus AU400, AU640, and AU2700. Each point was assayed and the mean analytical results were plotted versus the expected concentrations. A linear regression line was calculated and the deviations of the data from linearity were compared to assay specific acceptance criteria of $\pm 15\%$ or 0.05 mg/dL. All data points met the sponsor's acceptance criteria demonstrating that the assay is linear across the claimed reportable range of 0.05 to 10 mg/dL.

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

No information on traceability was provided.

The reagent is stable until the date printed on the vial when stored as directed at 2° - 8°C. On board stability studies demonstrate that the reagent is stable for 30 days when opened and stored in the refrigerated compartment on the analyzer.

d. Detection limit:

The lowest detectable limit was determined by assaying an analyte free sample n=20 on each analyzer and calculating the mean plus three standard deviations. The lowest detectable limit was calculated as 0.03 mg/dL, 0.02 mg/dL, and 0.01 mg/dL on the AU400, AU640, and AU 2700, respectively.

The limit of quantitation (LOQ) was determined by preparing 12 samples with analyte concentrations ranging from 0.006 to 0.25 mg/dL and testing them once per day for 20 days. The mean concentration and %CV for each sample were plotted and a curve fit was performed to model the relationship between the concentration and %CV. The curve fit model was used to determine the LOQ, which was defined as the sample concentration with a 20% CV. The calculated LOQ was below the lowest reportable concentration of the measuring range (0.05 mg/dL) with all three analyzers tested.

e. Analytical specificity:

Interference was evaluated by diluting samples with high interferent concentrations with interferent free samples. Samples were diluted in 10% increments, resulting in 11 sample concentrations tested for each compound, and run in replicates of 4. The mean of each sample is calculated and the Percent recovery of each sample compared to the interferent free sample was determined. Samples showing a difference in recovery of less than 12% or 0.1 mg/dL for samples with <0.8 mg/dL bilirubin compared to the analyte free sample were considered to be free of interference. Each interferent was tested at bilirubin concentrations of approximately 0.25 mg/dL and 1.00 mg/dL. The results demonstrated that there was no interference with up to 25 mg/dL hemoglobin or 500 mg/dL intralipid, which is approximately equivalent to 1500 mg/dL triglyceride. Interference from commonly used drugs was not tested in this assay.

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

A method comparison study was performed by testing individual serum

samples with the Olympus Direct Bilirubin Reagents and the predicate device. For this comparison 50 natural patient samples with concentrations ranging from 0.1 to 7.40 mg/dL were tested. Deming regression was performed with the following results: $y = 1.097x - 0.028$, $R^2 = 0.997$. The following regression equations were obtained in comparing the different analyzers:

Y Method	AU640	AU640	AU2700/5400	AU2700/5400
X Method	Method 2	AU400	AU600//640 ^e	AU400
Slope	1.097	1.018	1.007	1.025
Intercept	-0.028	- 0.010	- 0.005	-0.015
Correlation Coeff. (r)	0.9971	0.9998	0.9996	0.9995
No. of Samples (n)	50	73	73	73
Range (mg/dL)	0.06-8.00	0.05-9.49	0.05-9.49	0.05-9.52

b. Matrix comparison:

Not applicable

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:

Adult:¹ 0.0 - 0.2 mg/dL

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.

1. Burtis. CA & Ashwood. E.R. (eds). Tietz Textbook of Clinical Chemistry, 3rd Edition, WB Saunders, 1999

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.