

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

A. 510(k) Number:

K070453

B. Purpose for Submission:

Clearance of a new device

C. Measurand:

D-dimer

D. Type of Test:

Immuno-turbidimetric

E. Applicant:

Olympus Life and Material Science Eurpoa GMBH

F. Proprietary and Established Names:

Olympus D-Dimer Reagent

Olympus D-Dimer Calibrator

Olympus D-Dimer Control

G. Regulatory Information:

1. Regulation section:

21 CFR 864.7320

2. Classification:

Class II

3. Product code:

DAP

4. Panel:

81 Hematology

H. Intended Use:

1. Intended use(s):

For the quantitative determination of D-dimer in human plasma.

2. Indication(s) for use:

Aid in detecting the presence and degree of intravascular coagulation and fibrinolysis and in monitoring therapy for disseminated intravascular coagulation.

3. Special conditions for use statement(s):

4. Special instrument requirements:

OLYMPUS Analyzers

I. Device Description:

The Olympus D-Dimer test system consists of reagents, calibrators, and bi-level controls. The calibrators include a zero calibrator and a d-dimer calibrator that is diluted to make up a series of 6 standards. The assay is intended for use on the Olympus family of automated clinical chemistry analyzers (Olympus AU400/AU400E Clinical Chemistry Analyzer K981743; Olympus AU600/AU640/AU640E Clinical Chemistry Analyzer k961274; Olympus AU2700 Clinical Chemistry Analyzer K003721; Olympus AU5400 Clinical Chemistry Analyzer K011720).

J. Substantial Equivalence Information:

1. Predicate device name(s):

Roche Tina-Quant D-dimer

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

K030740/K002706

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	Quantitative determination of d-Dimer in human plasma	same
Specimen type	Citrate and lithium heparin Plasma	same
Methodology	Latex enhanced immunoturbidimetric	same

Differences		
Item	Device	Predicate
Instrumentation required	Olympus AU400/400e, 600/640/640e, and 2700/5400	Roche Hitachi analyzers

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

- ISO EN 14971 Medical Devices-Application of Risk Management to Medical Devices
- ISO EN 13640 Stability Testing of In Vitro Diagnostic Reagents
- CLSI EP7-A Interference Testing in Clinical Chemistry
- CLSI EP5-A2 Evaluation of Precision Performance of Clinical Chemistry Devices
- CLSI EP9-A Method comparison and Bias Estimation Using Patient Samples
- CLSI C28-A2 How to Define and Determine Reference Intervals in the Clinical Laboratory
- CLSI EP15-A User Demonstration of Performance for Precision and Accuracy
- CLSI EP6-P2 Evaluation of the Linearity of Quantitative Analytical Methods: A Statistical Approach

L. Test Principle:

The Olympus D-Dimer assay system is based on the decrease in transmitted light due

to absorbance by insoluble d-dimer-/anti d-dimer aggregates which form in the reaction mixture when latex particles coated with monoclonal mouse anti-human d-dimer react with d-dimer fragments from the patient sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Precision was assessed according to CLSI EP5-A2 by testing a low, medium, and high analyte human plasma pool. 2 runs of duplicates were assayed each day for 20 days (n=80). All results were within acceptable limits (<10%).

	Within Run (%)	Total (%)
AU400/400e		
0.28	6.12	9.44
0.54	3.21	7.99
5.86	0.55	2.48
AU600/640/AU640e		
0.28	4.6	9.14
0.55	4.22	7.95
5.66	0.69	3.02
AU2700/5400		
0.28	4.42	8.17
0.54	2.06	4.44
6.18	0.42	2.52

b. *Linearity/assay reportable range:*

Linearity was established based on CLSI Guideline EP6-P2. At least 10 serial dilutions of a high sample pool was prepared and assayed in quadruplicate. The mean result of each dilution was plotted against the analyte concentration. The AU400, AU640, and AU2700 instruments were evaluated and the Olympus D-Dimer assay system was determined to be linear from 0.15 to 8.00 µg FEU/mL

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

The Olympus D-Dimer calibrators are bi-level calibrators derived from human serum. Values are based on an in-house master calibrator that is traceable to a gravimetric standard and converted from $\mu\text{g/mL}$ to $\mu\text{g FEU/mL}$. The assignment value protocol is located in Section 8 of the submission.

The Olympus D-Dimer controls are bi-level controls, and are derived from a lyophilized human based matrix. Controls values are assigned per lot for each matched set of reagents, and are based on the mean of ≥ 8 runs of the control serum.

d. *Detection limit:*

An analyte free sample was tested 20X on the AU400, AU640 and AU2700. The analytical sensitivity was determined to be $0.15 \mu\text{g FEU/mL}$ by calculating the absolute mean plus 3 standard deviations.

e. *Analytical specificity:*

To assess analytical specificity, the mean analytical result of the sample containing the interferent is compared with that for the non-spiked sample. The Olympus D-dimer assay demonstrated no significant inference with Bilirubin (up to 40 mg/dL), hemolysis (up to 500 mg/dL hemoglobin), lipemia (up to 1000 mg/dL), rheumatoid factor (up to 100 IU/mL) and heparin (up to 1.5 IU/mL).

f. *Assay cut-off:*

2. Comparison studies:

a. *Method comparison with predicate device:*

The Olympus D-dimer assay was compared to the predicate device and evaluated using linear regression ($n=104$, $y=1.010x + 0.079$, $r = 0.996$). In addition, the performance of the Olympus D-Dimer assay on the AU640 was compared to performance of the assay on the AU400 ($n=104$, $y = 1.014 x - 0.029$, $r = 0.998$) and the AU2700 ($n = 104$, $y = 1.020x - 0.037$, $r=0.997$).

b. *Matrix comparison:*

Matched heparin (y) and citrated samples (x) were tested in single replicates ($n=51$) and the results analyzed using linear regression ($y= 1.167x + 0.48$, $r=0.998$).

Although the results demonstrated good correlation, d-dimer concentrations in citrated samples are generally lower than d-dimer concentrations in heparinized samples by 16%. For harmonization a conversion factor of 0.84

for heparin plasma is recommended. This recommendation is reflected in the device labeling.

3. Clinical studies:

a. *Clinical Sensitivity:*

b. *Clinical specificity:*

c. Other clinical supportive data (when a. and b. are not applicable):

4. Clinical cut-off:

5. Expected values/Reference range:

151 healthy volunteers were assayed. The reference range was established following CLSI C28-A2, and was determined to be 0.01 – 0.5 µg FEU/mL

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.