

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

A. 510(k) Number:

k070835

B. Purpose for Submission:

New Device

C. Measurand:

Creatine Kinase Isoenzyme MB (CK-MB)

D. Type of Test:

Quantitative, enzymatic

E. Applicant:

Olympus Life and Material Science

F. Proprietary and Established Names:

Olympus CK-MB Reagent (OSR6x155)

G. Regulatory Information:

1. Regulation section:

21 CFR 862.1215 Creatine phosphokinase/creatine kinase or isoenzymes test system

2. Classification:

Class II

3. Product code:

JHY

4. Panel:

75 Chemistry

H. Intended Use:

1. Intended use(s):

See indications for use below.

2. Indication(s) for use:

System reagent for the quantitative determination of Creatine Kinase-MB isoenzyme in human serum and heparinized plasma on OLYMPUS analyzers

Measurements of Creatine Kinase are used in the diagnosis and treatment of myocardial infarction and muscle diseases such as progressive, Duchenne-type muscular dystrophy.

3. Special conditions for use statement(s):

For prescription use only

4. Special instrument requirements:

For use on Olympus analyzer AU400/400^e, 600/640/640^e and 2700/5400.

I. Device Description:

The Olympus CK-MB assay is a two step- three reagent quantitative assay. The device uses 3 reagents that contain CK-MB goat antibodies imidoazole, hexokinase and preservatives. Two reagents are mixed before placing them onto the instrument. The second reagent is ready to use.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Olympus CK-MB

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

k971817

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended use	System reagent for the quantitative determination of Creatine Kinase-MB isoenzyme in human serum and heparinized plasma on OLYMPUS analyzers	Same
Instruments	Olympus analyzer AU400/400 ^e , 600/640/640 ^e and	Same

Similarities		
Item	Device	Predicate
	2700/5400	
Specimen	Serum and heparinized plasma	Same
Methodology	Enzymatic	Same
Antibody	Antibody to CK-M subunit	Same
Calibration	Based on theoretical extinction coefficient	Same
Range	10 to 2000 U/L	Same

Differences		
Item	Device	Predicate
Traceability	Procedure is a modification of the IFCC method	Procedure is a modification of the Szasz method
Stability	Open reagents are stable for 30 days when stored in the refrigerated compartment of the analyzer.	Reconstituted reagents are stable for 5 days when stored in the refrigerated compartment of the analyzer.
Antibody	Polyclonal anti CK-M goat antibody	Polyclonal anti CK-M sheep antibody.
Calibration	Calibration of this CK-MB procedure is based upon the theoretical extinction coefficient for NADPH, which has a molar absorptivity of 6300 at 340/660 nm.	Based upon the theoretical extinction coefficient for NADPH, which has a molar absorptivity of 4960 at 340/380 nm

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

EN 14971 ISO Medical Devices-Application of Risk Management to Medical Devices

EP7-A CLSI Interference Testing in Clinical Chemistry

EP5-A2 CLSI Evaluation of Precision Performance of Clinical Chemistry Devices

EP9-A CLSI Method Comparison and Bias Estimation Using Patient Samples

CEN 3640 Stability Testing of In Vitro Diagnostic Reagents

EP15-A CLSI User Demonstration of Performance for Precision and Accuracy

EP6-P2 CSLI Evaluation of the Linearity of Quantitative Analytical Methods: A Statistical Approach

L. Test Principle:

The Olympus Creatine Kinase-MB assay uses 2 steps to determine the presence of creatine kinase MB isoenzyme in human serum or plasma. The R1 reagent contains an antibody which binds the M subunit of CK in the serum sample thereby inhibiting the activity of the M subunit. The B subunit of the enzyme remains free to act on the substrate present in the R2 reagent. CK reversibly catalyzes the transfer of a phosphate group from creatine phosphate to adenosine diphosphate (ADP) to give creatine and adenosine triphosphate (ATP) as products. The ATP formed is used to produce glucose-6-phosphate and ADP from glucose. The glucose-6-phosphate is oxidized to give NADPH and 6-phosphogluconate. The rate of increase of absorbance at 340/660 nm due to the formation of NADPH is directly proportional to the activity of CK/MB in the sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

The sponsor conducted precision studies according to CLSI EP5-A2 guideline. The sponsor tested 2 runs in duplicate for 20 days (n=80) on low, medium and high analyte human plasma pools samples. The within-run and total CVs for each three instrument classes and are shown in the table below. The results met the sponsor's acceptance criteria of within run CV < 5% or SD ≤ 1 U/L and the total precision of < 6.5% or SD ≤ 2 U/L.

AU400/AU400e				
	Within Run		Total	
Mean, U/L	SD	CV%	SD	CV%
17	0.52	2.98	0.74	4.26
87	0.78	0.89	1.14	1.31
197	1.27	0.64	2.16	1.10
AU600/AU640/AU640e				
Mean, U/L	SD	CV%	SD	CV%
17	0.69	4.03	0.86	5.05
86	0.65	0.75	0.99	1.15
194	1.04	0.54	1.76	0.9
AU2700/AU5400				
Mean, U/L	SD	CV%	SD	CV%
17	0.45	2.66	0.59	3.50
83	0.72	0.86	0.94	1.13
187	1.18	0.63	2.26	1.21

b. Linearity/assay reportable range:

The sponsor conducted a linearity study based on CLSI EP6-P2. A high pool sample was serially diluted to cover the sponsor's claimed linear range of 10 to 2000 U/L. Each dilution was assayed in quadruplicate and the mean analytical results were plotted versus the relative analyte concentrations (% dilution). The results met the sponsors' acceptance recovery criteria of 10-2000 U/L \leq 10% or 5 U/L. The results for the diluted samples ranged from 21.91% to 4.48 %. When the percent recovery was greater than 10%, it was with samples that were less than 5 U/L. The values met the sponsor's predetermined acceptance criteria.

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

The sponsor conducted on board stability studies on the Olympus Analyzers by allowing the reagent to degrade based on constant usage. The linearity was checked for all three instruments (AU400, AU640 and AU2700) and the results support the sponsors' on-board stability claim of 30 days.

The sponsor also conducted a closed stability for the AU2700 via a stress model. The results shown below support the sponsors' closed-stability claims of up to 18 months.

d. Detection limit:

The sponsor conducted a limit of quantitation study with the Olympus CK-MB reagent on the Olympus Clinical Chemistry Analyzers. Three patient samples or pools were assayed 40 times at an analyte concentration below the bottom of the measuring range. The level of CK-MB at which a CV is less than 20% for the 40-fold sample is the lowest CK-MB concentration that the assay can measure accurately. The limit of detection of the Olympus CK-MB reagent was determined for the instruments below and supports the sponsor's limit of detection claim of 10 U/L.

	Mean Conc. (U/L)	SD	CV %
AU400/400e	3.705	0.572	15.4
AU600/640/640e	3.951	0.756	19.1
AU2700/5400	3.930	0.716	18.2

The sponsor conducted a limit of blank study with the Olympus CK-MB reagent on the Olympus Clinical Chemistry Analyzers. Analyte-free sample (water) was assayed 20 times on three analyzers. Analytical sensitivity was measured by calculating the absolute mean plus 3 standard deviations. The analytical sensitivity of the Olympus CK-MB reagent was determined for the instruments below and supports the sponsor's limit of blank claim of 5 U/L.

Instrument	Lowest Detectable Limit Limit of Blank (U/L)
AU400	1.88
AU600	1.91
AU2700	3.01

e. Analytical specificity:

The sponsor evaluated common interfering substances on the Olympus Clinical Chemistry Analyzers according to CLSI Guideline EP7-A. One lot (with three reagents) was tested on three instruments to determine the interferences of bilirubin and lipemia. The mean analytical result of the sample containing the interferent is compared with that for the non-spiked sample. The results from bilirubin and lipemia are shown in the tables below. The sponsor has notified users in their package insert to use serum and heparinized plasma samples free from hemolysis because adenylate kinase from red blood cells may react with the reagent to produce spurious results and such specimens should not be used.

^fAU400/AU400^e	
Bilirubin	≤10% up to 40 mg/dL Bilirubin
Lipemia	≤10% up to 900 mg/dL Intralipid
^hAU600/640/640^e	
^s Bilirubin	≤10% up to 40 mg/dL Bilirubin
^s Lipemia	≤15% up to 900 mg/dL Intralipid
^aAU2700/5400	
^y Bilirubin	≤6% up to 40 mg/dL Bilirubin
Lipemia	≤20% up to 900 mg/dL Intralipid

^c

f. Assay cut-off:

Not applicable (N/A)

2. Comparison studies:

a. Method comparison with predicate device:

One hundred and three serum samples were tested with both the Olympus CK-MB OSR6X155 (current) with the sponsors predicate device Olympus CK-MB OSR6X53 on the AU640 instrument using the CLSI Guideline EP9-A. The slope, intercept and correlation coefficient were calculated by linear regression. The samples ranged from 12 to 1860 U/L. The resulting equation

was $y=1.061x + 2.207$ with a correlation coefficient of 1.000.

Additionally the sponsor conducted comparison studies using the other two instruments (AU400 and the AU2700) against the reference instrument AU640. The AU400 equation was $y=1.004x - 3.253$ with a correlation coefficient of 1.000. The AU2700 equation was $y=0.994x - 2.386$ with a correlation coefficient of 1.000.

b. Matrix comparison:

A matrix comparison study between serum and heparin plasma samples was conducted using serum as reference. The study was performed on 40 matched patient samples taken from volunteers. The slope, intercept and correlation coefficient were calculated by linear regression. The samples ranged from 12.83 to 1923.50 U/L. The resulting equation was $y= 1.002x - 0.524$ with a correlation coefficient of 1.000.

3. Clinical studies:

a. Clinical Sensitivity:

N/A

b. Clinical specificity:

N/A

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

N/A

4. Clinical cut-off:

N/A

5. Expected values/Reference range:

The package insert provides expected values from literature as follows:

0 - 10 U/L – Tietz Clinical Guide to Laboratory Tests - 3rd edition, 1995

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.