

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

A. 510(k) Number:

k080094

B. Purpose for Submission:

New device

C. Measurand:

Total beta human chorionic gonadotrophin (intact β hCG and free β)

D. Type of Test:

Quantitative chemiluminescent immunoassay

E. Applicant:

Olympus Life and Material Science Research Europa, GmbH

F. Proprietary and Established Names:

Olympus Total β hCG Test System

G. Regulatory Information:

1. Regulation section:

21 CFR §862.1155 Human chorionic gonadotropin test system

21 CFR §862.1150 Calibrators

21 CFR §862.1660 Quality control material (assayed and unassayed)

2. Classification:

Class II

Class I (reserved)

3. Product code:

DHA Human chorionic gonadotropin (HCG) test system

JIT Calibrator

JJX Control material

4. Panel:

Chemistry (75)

H. Intended Use:

1. Intended use(s):

See Indications for Use below.

2. Indication(s) for use:

The Olympus β hCG assay is a paramagnetic particle, chemiluminescent immunoassay for the quantitative determination of total beta human chorionic gonadotropin (intact β hCG and free β) levels in human serum using the Olympus

AU3000i Immunoassay System. Total β hCG is used for the early detection of pregnancy. For in vitro diagnostic use only.

The Olympus β hCG Calibrator is for calibrating the quantitative Olympus β hCG assay on the Olympus AU3000i Immunoassay System.

The Olympus β hCG Control is used for quality control of the Olympus β hCG assay on the Olympus AU3000i Immunoassay System.

3. Special conditions for use statement(s):
For prescription use only.
4. Special instrument requirements:
For use on the Olympus AU3000i clinical chemistry system.

I. Device Description:

The Olympus β hCG test system consists of Reagent 1, Reagent 2, one calibrator, one control and a septum. The Reagent 1, Reagent 2, calibrator and control display bar codes. When a new reagent is added, the system recognizes it from the barcode. The one dimensional barcode on Reagent 1, QC sample and calibrator links the kit components to the corresponding Reagent 2. The Reagent 2 includes a two dimensional barcode that contains information on the lot specific counts of the master curve and the values for calibrators and QC samples.

J. Substantial Equivalence Information:

1. Predicate device name(s):
ADVIA Centaur total hCG
2. Predicate K number(s):
k925277 and k971418
3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	The Olympus β hCG assay is a paramagnetic particle, Chemiluminescent immunoassay for the quantitative determination of total beta human chorionic gonadotropin (intact β hCG and free β) levels in human serum using the Olympus AU3000i Immunoassay System. Total β hCG is used for the early detection of pregnancy. For <i>in vitro</i> diagnostic use only.	For the in vitro use in the quantitative determination of human chorionic gonadotropin in serum using the ADVIA Centaur system. The results obtained from hCG specimens are used as an aid in the assessment of pregnancy status. This assay detects the intact hCG molecule and the free beta subunit of the hCG molecule.

Similarities		
Item	Device	Predicate
Assay Principle	Competitive immunoassay	Same
Sample Type	Serum	Same
Reagent Form	Liquid ready-to-use	Same
Calibration	Master curve provided via barcode	Same
Calibration Interval	28 days	Same
Control Matrix	Human matrix with added antigen	Same

Differences		
Item	Device	Predicate
Traceability/Standardization	4 th WHO reference standard 75/589.	3 rd WHO reference standard 75/537
Control Levels	1	3
Open Stability	28 days	various
Measuring Range (mIU/mL)	0.53 – 1000	2.0 - 1000
Antibody	Monoclonal anti- β hCG antibody	Monoclonal and polyclonal anti-hCG antibody

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

CLSI - EP05-A2 - *Evaluation of Precision Performance of Clinical Chemistry Devices*

CLSI - EP09-A2 - *Method Comparison and Bias Estimation Using Patient Samples*

CLSI - C28-A2 - *How to Define and Determine Reference Intervals in the Clinical Laboratory; Approved Guideline Second edition*

L. Test Principle:

The Olympus β hCG assay is a two step paramagnetic particle enzyme immunoassay based on the sandwich principle. Samples are incubated with monoclonal anti- β hCG antibody bound to paramagnetic particles. After a wash step, a second monoclonal anti- β hCG antibody conjugated with alkaline phosphatase is added. The β hCG reacts with the paramagnetic particles and the conjugated antibody to form a sandwich complex. Washing steps remove the unbound material. The chemiluminescent substrate is added to the assay cuvette and reacts with the alkaline phosphatase; the resulting light emission is proportional to the quantity of β hCG in the sample. Results are calculated from a pre-defined calibration curve. The Olympus AU3000i system

automatically calculates the β hCG concentration of each sample in IU/L or mIU/mL.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

A precision study was conducted using pooled human sera according to CLSI protocol EP5-A. Samples were run twice a day in duplicate for 20 days (n=80) on the Olympus AU 3000i analyzer. The precision results are shown below:

Olympus Total β hCG Assay: Precision

Sample	Within run			Total	
	Mean [mIU/mL]	SD [mIU/mL]	CV [%]	SD [IU/mL]	CV [%]
1	6.48	0.19	2.9	0.21	3.3
2	33.18	0.74	2.2	1.05	3.2
3	569.07	11.64	2.0	16.81	3.0

b. *Linearity/assay reportable range:*

The reportable range for this assay is 0.53-1000 mIU/mL. This claim was supported by a study that measured dilutions of a high sample across the range following CLSI EP-6A. The eleven dilutions, each measured in quadruplicate, all recovered within $\pm 5\%$ of the expected value.

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

Reagent stability is claimed as 12 months based on an accelerated stability study; real time studies are underway. The assay components (i.e. reagent, calibrator, and control) were shown to be stable for 28 days on-board the instrument.

The lot-specific calibrator is prepared by addition of β hCG to a bovine calf serum matrix. The concentration of the calibrator is verified by using one instrument calibrated with the master calibrators testing 45 replicates. The calibrator master lot is made by adding quantities of purified β hCG into bovine calf serum with preservatives. The master lot is traceable to the WHO standard for HCG, 4th IS, 75/589.

d. *Detection limit:*

The limit of detection (LoD) was determined by measuring a blank sample 20 times and a low sample five times with three different lots of reagents. The LoD was calculated by multiplying the standard deviation of the mean of the samples by two and adding it to the absolute value of the mean. The LoD determined for all three lots 0.05 mIU/mL.

The Limit of Quantitation (LoQ) was determined to be 0.53 mIU/mL as determined by the lowest concentration at which samples had a CV<20%.

e. Analytical specificity:

Cross reactivity: Thyroid stimulating hormone (TSH), luteinizing hormone (LH), follicle stimulating hormone (FSH), and human growth hormone (hGH) were spiked into serum to evaluate cross-reactivity. No detectable cross-reactivity was observed for 2500 µIU/mL TSH, 1000 mIU/mL LH, 2000 mIU/mL FSH, and 1000 ng/mL hGH.

Interference: The assay was evaluated for interference. Hemoglobin (5 g/L), Bilirubin (unconjugated at 40 mg/dL) and Lipids (1000 mg/dL) did not affect the performance of the assay when samples containing various concentrations of BhCG were tested. The sponsor defines interference as results exceeding +/-10% of the expected value. Other substances, including various prescription and over-the-counter drugs, were tested and shown not to interfere with this assay. No hook effect was seen up to 100,000 mIU/mL. Sera containing Rheumatoid Factor (RF) or human anti-mouse antibodies (HAMA) were shown not to interfere with the assay. The sponsor includes a discussion of these factors in the product labeling.

f. Assay cut-off:

Not applicable; this is a quantitative assay.

2. Comparison studies:

a. Method comparison with predicate device:

118 patient serum samples were used to compare the results of the Olympus Total BhCG assay run on the Olympus AU3000i analyzer to those of the Advia Centaur total hCG assay; the experiment was based on the CLSI protocol EP9-A. Results of regression by Passing-Bablok analysis are shown below:

N	Range of sample concentrations [mIU/mL]	Intercept [mIU/mL] (95% CI)	Slope	Correlation Coefficient
118	2.2 – 969.3	0.175 (0.91, 0.96)	0.93	0.988

b. Matrix comparison:

Not applicable. This assay is indicated for serum only.

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:
The sponsor used procedures in CLSI C28-A2 to bridge the transference of a reference range established with the predicate method in Snyder *et al.* (Clinical Chemistry 51:1830 – 1835, 2005) to the Olympus AU3000i Total β hCG assay. Snyder *et al.* established a hCG range in 240 women in the same age group as < 2.0 to 4.6 mIU/mL where the 97.5 percentile value was 2.5 mIU/mL (2.0 mIU/mL was the LoD of the predicate method). In the sponsor's bridging study, serum from 86 women 18 – 40 years of age was tested; all samples tested were below the LoQ of the device (i.e., below 0.53 mIU/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.