Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002
www.fda.gov

510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

k192547

B Applicant

Shenzhen New Industries Biomedical Engineering Co., Ltd

C Proprietary and Established Names

MAGLUMI 2000 HCG/ β-HCG

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
DHA	Class II	21 CFR 862.1155 - Human Chorionic Gonadotropin (HCG) Test System	CH - Clinical Chemistry

II Submission/Device Overview:

A Purpose for Submission:

New device

B Measurand:

Total beta human chorionic gonadotropin (intact hCG and free β-hCG) in human serum

C Type of Test:

Quantitative immunoassay

III Intended Use/Indications for Use:

A Intended Use(s):
See Indications for Use below.

B Indication(s) for Use:
MAGLUMI 2000 HCG/β-HCG is an in vitro chemiluminescence immunoassay for the quantitative determination of total beta human chorionic gonadotropin (total β-hCG) in human serum. The measurement of total β-hCG is used as an aid in the early detection of pregnancy.

C Special Conditions for Use Statement(s):
Rx - For Prescription Use Only

D Special Instrument Requirements:
Performance characteristics studies were conducted on the MAGLUMI 2000 Immunoassay Analyzer

IV Device/System Characteristics:

A Device Description:

MAGLUMI 2000 HCG/β-HCG assay kit consists of the following:

Magnetic microbeads coated with anti-hCG monoclonal antibody, containing bovine serum albumin (BSA) and sodium azide.

Buffer containing BSA and sodium azide for sample dilution.

Anti-hCG monoclonal antibody labeled with N-(4-aminobutyl)-N-ethylisoluminol (ABEI), containing BSA and sodium azide.

Calibrator Low- HCG antigen, containing BSA and sodium azide.

Calibrator High- HCG antigen, containing BSA and sodium azide.

Control 1- hCG antigen, containing BSA and sodium azide.

Control 2- hCG antigen, containing BSA and sodium azide.

B Principle of Operation:

The MAGLUMI 2000 HCG/β-HCG assay is an immunoassay run on the MAGLUMI 2000 Immunoassay Analyzer (cleared under k162698). The assay methodology is a sandwich chemiluminescence immunoassay. The sample is mixed with magnetic microbeads coated with anti-hCG monoclonal antibody, and then incubated at 37°C. The microbead bound immunocomplex is washed to separate the unbound phase. Labeled anti-hCG monoclonal

antibody is added to form a sandwich complexes. A second wash step is conducted, and followed by addition of a reagent to initiate the chemiluminescent reaction. The light signal is measured by a photomultiplier tube and is proportional to the concentration of total β-hCG (intact hCG and free β-hCG) present in the sample.

V Substantial Equivalence Information:

A Predicate Device Name(s):
Access Total βhCG (5th IS)

B Predicate 510(k) Number(s):
k130020

C Comparison with Predicate(s):

Device & Predicate Device(s):	k192547	k130020
Device Trade Name	**MAGLUMI 2000 HCG/β-HCG**	**Access Total βhCG (5th IS) Assay**
General Device Characteristic Similarities		
Intended Use/Indications For Use	Early detection of pregnancy.	Same
Measurand	Total β-hCG (intact hCG and free β -hCG subunit)	Same
Standardization	WHO 5th International Reference Standard, 07/364	Same
General Device Characteristic Differences		
Measurement Range	1.13 - 4680 mIU/mL	0.6 - 1350 mIU/mL; up to 270,000 mIU/mL with sample dilution.
Specimen types	Serum	Serum and plasma

VI Standards/Guidance Documents Referenced:

Clinical and Laboratory Standards Institute (CLSI) EP05-A3 Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline—Third Edition.

CLSI EP06-A Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline.

CLSI EP07 Interference Testing in Clinical Chemistry; Approved Guideline —Third Edition.

CLSI EP17-A2 Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline—Second Edition.

CLSI EP28-A3: Defining, Establishing and Verifying Reference Intervals in the Clinical Laboratory

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

The precision performance of the MAGLUMI 2000 HCG/β-HCG was established in a reproducibility study. In the study, 2 controls, 2 calibrators, and 6 native patient sample pools were assayed in replicates of 2 per run, with 2 runs per day for 20 days on each of three MAGLUMI 2000 Immunoassay Analyzers; for a total of 240 measurements. Each instrument used a different reagent lot. Three different operators performed tests on each of the instruments for a total of 9 operators. The results are summarized as follows:

Sample	Mean hCG conc. (mIU/mL)	Within-run		Between-Run		Between-Day		Total (within instrument)		Reproducibility (across instruments)	
		SD	CV%	SD	CV%	SD	CV%	SD	CV%	SD	CV%
Control 1	5.0	0.22	4.5	0.10	2.0	0.20	4.1	0.32	6.4	0.33	6.5
Control 2	37.1	1.53	4.1	0.81	2.2	1.28	3.4	2.16	5.8	2.25	6.1
Control 3	300	10.7	3.5	7.67	2.6	10.3	3.4	16.8	5.6	17.7	5.9
Calibrator	2.9	0.20	6.9	0.05	1.8	0.15	5.4	0.26	8.9	0.28	9.6
Calibrator	1722	47.2	2.7	43.6	2.5	53.8	3.1	83.8	4.9	92.8	5.4
Serum 1	1.9	0.14	7.2	0.04	2.1	0.10	5.4	0.17	9.3	0.18	9.8
Serum 2	13.6	0.57	4.2	0.37	2.7	0.53	3.9	0.86	6.3	0.87	6.4
Serum 3	104	3.80	3.7	2.7	2.6	3.71	3.6	5.94	5.7	6.38	6.2
Serum 4	771	25.8	3.4	21.3	2.8	19.6	2.6	38.8	5.0	42.9	5.6
Serum 5	2443	80.5	3.3	53.3	2.2	64.9	2.7	116.3	4.8	126.7	5.2
Serum 6	4555	107.0	2.4	96.6	2.1	102.4	2.2	176.9	3.9	198.3	4.4

2. Linearity:

A linearity study was conducted following the recommendations in CLSI EP6-A.

Low range linearity was established by assaying 11 samples of varying concentration (0.33 to 280 mIU/mL) that were each prepared by a dilution scheme of mixing known volumes of reference material (WHO 5th International Standard) and hCG free serum.

High range linearity was established by assaying 10 samples of varying concentration (260 to 4680 mIU/mL) that were each prepared by a dilution scheme of mixing known volumes of reference material (WHO 5th International Standard) and hCG free serum.

Each sample was measured in replicates of 4 using three instruments and three reagents lots. The recovery at each concentration was calculated relative to the expected concentration based on the dilution. All recoveries ranged from 90.1% to 109%. A regression analysis was conducted with the following linear regression lines supporting the claimed analytical measurement range of 1.13 - 4680 mIU/mL.

High Dose Hook Effect

A high dose hook effect study was conducted to assess the highest hCG concentration along the dose response curve where the reported results are not impacted by conditions of antigen excess. In the study, six samples with total β-hCG concentrations from 5,000 to 1,000,000 mIU/mL were prepared by spiking reference material (WHO 5th International Standard) into hCG free serum. Each sample was measured in duplicates across each of 3 lots. The study found no evidence of a high dose hook effect for total β-hCG concentrations up to 1,000,000 mIU/mL.

Dilution study

A dilution study was conducted to establish a range in hCG concentrations which are accurately reported following dilution. The product labeling identifies that samples with hCG concentrations above the measuring range can be diluted either automatically by the analyzer or manually using diluent (buffer containing BSA and sodium azide from the kit) and the recommended dilution is 1:50. After dilution by the analyzer, the analyzer software automatically takes the dilution into account when reporting the hCG concentration. In the study, 12 serum samples were prepared by spiking reference material (WHO 5th International Standard) into hCG free serum and covering an hCG concentration from 4475 mIU/mL to 223,750 mIU/mL. Each of the 12 sample was individually diluted (manually and automated) samples 5 times and then assayed using 3 reagent lots on 3 instruments in two replicates for each lot and instrument. The results demonstrated that all individual dilution recoveries for both manual and automated dilution were between 90.0% and 110.0%.

3. Analytical Specificity/Interference:

The analytical specificity performance of the MAGLUMI 2000 HCG/β-HCG assay was established by conducting interference testing. Interference from potentially cross reacting substances, certain exogenous and endogenous substances were assessed using serum samples spiked to three total hCG concentrations of 6.0, 100, and 2000 mIU/mL. Each sample was divided into two aliquots: test (with added interferent) and control (with no added interferent), and measured in triplicates across each of 3 lots. Bias in the results was analyzed by comparing the test sample quantitation to the control. The sponsor defined no significant interference as a bias within ± 10%. The following table lists the concentration of each substance at which no significant interference was found in the study.

Substances	Highest concentration tested without significant interference
Bilirubin, conjugated	60 mg/dL
Bilirubin, unconjugated	42.5 mg/dL
Hemoglobulin	1000 mg/dL
Triglyceride	2000 mg/dL
Rheumatoid factor	1745 IU/mL
HAMA	401 ng/mL
Total protein	15,000 mg/dL
Acetaminophen	15.6 mg/dL
Ascorbic Acid	16.95 mg/dL
Biotin	5 mg/dL
Cefoxitin	680 mg/dL
Cyclosporine	0.6 mg/dL
Doxycycline	3.2 mg/dL
Ethanol	790 mg/dL
EDTA-Na2	4 mg/dL
Ibuprofen	50 mg/dL
Levodopa	3.25 mg/dL
Metronidazole	12.3 mg/dL
Rifampicin	6.5 mg/dL
Theophylline	11.4 mg/dL
TSH	1000 mIU/L
LH	500,000 mIU/L
FSH	500,000 mIU/L
hGH	25,000 mIU/L
hCG α-subunit	500,000 mIU/L

4. Assay Reportable Range:

   See section VII.A.2 - Linearity.

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

   Traceability
   The MAGLUMI 2000 HCG/β-HCG method has been standardized against WHO 5th International Standard 07/364.

6. Detection Limit:

   The detection limit of the MAGLUMI 2000 HCG/β-HCG was established by evaluation of the Limit of Blank (LoB), Limit of Detection (LoD) and Limit of Quantification (LoQ).

   LoB
   The LoB was estimated following the recommendations in CLSI EP17-A2 and derived from the 95th percentile from non-parametric distribution of replicate measurements of a blank sample. In the study, a blank sample comprised of hCG negative serum was measured using 3 reagent lots and one instrument. For each lot, the sample was measured in replicates of 16

per run over 5 days for a total of 80 measurements per lot. The higher of the three LoB values from each lot is taken as the LoB concentration; 0.30 mIU/mL.

LoD
The LoD was estimated following the recommendations in CLSI EP17-A2. In the study four low concentration samples (0.5 mIU/mL to 1.6 mIU/mL) were prepared near the expected LoD by spiking reference material (WHO 5th International Standard) into hCG free serum. Each of the four samples was measured using three reagents lots. For each lot, the samples were measured in replicates of 16 per run over 5 days using one instruments for a total of 80 measurements per lot. The higher of the three LoD values from each lot is taken as the LoD concentration; 0.47 mIU/mL.

LoQ
The LoQ was estimated following the recommendations in CLSI EP17-A2. In the study six low concentration samples (0.5 mIU/mL to 5.0 mIU/mL) were prepared near the expected LoQ by spiking reference material (WHO 5th International Standard) into hCG free serum. Each of the six samples was measured using three reagents lots. For each lot, the samples were measured in replicates of 6 per run over 5 days using one instruments for a total of 30 measurements per lot. The LOQ of each reagent lot was derived as the lowest concentration of which percent bias is less than 15% and CV% is less than 20%. The higher of the three LoQ values from each lot was taken as the LoQ; 1.13 mIU/mL.

The results of the detection limit studies are summarized as follows:

LoB	LoD	LoQ	Analytical Measurement Range
0.30 mIU/mL	0.47 IU/mL	1.13 mIU/mL	1.13 to 4680 mIU/mL

7. Assay Cut-Off:

Not applicable.

B Comparison Studies:

1. Method Comparison with Predicate Device:
A method comparison study was conducted to establish the accuracy performance for agreement between the MAGLUMI 2000 HCG/β-HCG assay and the predicate device. In the study, unaltered serum samples were assayed in singlicate on the candidate device and predicate method at each of the three intended use sites. Samples were maintained under validated storage conditions prior to testing. The results from one representative site of the three sites were analyzed by Deming regression and for bias, as provided in the below tables.

Deming regression analysis

Slope	Intercept	R	Range Tested (predicate)	Number
0.997	7.6	0.993	1.2 to 4934 mIU/mL	201

Individual bias

Within ±10%	Within ±15%	Within ±20%
108/201 (54%)	150/201 (75%)	185/201 (92%)

Min = -24%, Max = +31%

2. Matrix Comparison:

Not applicable. This assay is intended to be used only with serum samples.

C Clinical Studies:

1. Clinical Sensitivity:

Not applicable.

2. Clinical Specificity:

Not applicable.

3. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

Not applicable.

D Clinical Cut-Off:

Not applicable.

E Expected Values/Reference Range:

To determine the hCG reference range for the MAGLUMI 2000 HCG/β-HCG assay, serum samples from 431 non-pregnant, apparently healthy females, consisting of 138 females of 20-39 years of age, 149 females pre-menopausal of 40 years of age or older, and 144 females post-menopausal of 50 years of age or older were assayed on three reagent lots. The reference range was determined using the procedure in CLSI EP28-A3. The expected normal range MAGLUMI 2000 HCG/β-HCG assay is the following:

Age range, females	Number	Median (mIU/mL)	95th Percentile (mIU/mL)
20 to 39 years old	138	< 1.1	< 1.1
≥ 40 years old, Pre-menopausal	149	< 1.1	1.6
≥ 50 years old, Post-menopausal	144	2.4	7.8

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.