510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT COMBINATION TEMPLATE

A. 510(k) Number:

k162698

B. Purpose for Submission:

New device

C. Measurand:

Thyroid stimulating hormone (TSH)

D. **Type of Test:**

Quantitative chemiluminescent immunoassay

E. Applicant:

Shenzhen New Industries Biomedical Engineering Co., Ltd.

F. Proprietary and Established Names:

MAGLUMI 2000 TSH

MAGLUMI 2000 Immunoassay Analyzer

G. Regulatory Information:

Product code	Classification	Regulation section	Panel
JLW	Class II	21 CFR 862.1690, Thyroid stimulating hormone test system	Clinical Chemistry (75)
JJE	Class I	21 CFR 862.2160, Discrete photometric chemistry analyzer for clinical use	Clinical Chemistry (75)

H. Intended Use:

1. Intended use(s):

   See Indication(s) for use below.

2. Indication(s) for use:

   The MAGLUMI 2000 TSH assay is for in vitro diagnostic use in the quantitative determination of thyroid-stimulating hormone (TSH) in human serum. The measurement of TSH is used in the diagnosis of thyroid disorders.

   The MAGLUMI 2000 Immunoassay system is an automated immunoassay analyzer designed to perform in vitro diagnostic tests in clinical serum specimens. The MAGLUMI 2000 Immunoassay system's assay application utilizes chemiluminescents technology for clinical use.

3. Special conditions for use statement(s):

   For prescription use only.

4. Special instrument requirements:

   MAGLUMI 2000 Immunoassay Analyzer

I. Device Description:

The MAGLUMI 2000 TSH kit is available as a 50 test or 100 test kit and consists of the following reagents:

- Magnetic Microbeads coated with anti-TSH monoclonal antibody, phosphate buffer, NaN_3(<0.1%) and ProClin 300.
- Calibrator Low contains TSH antigen (human origin), phosphate buffer bovine serum NaN_3(<0.1%) and ProClin 300. Target Value of 0.129 μIU/mL.
- Calibrator High contains TSH antigen (human origin), phosphate buffer, bovine serum NaN_3(<0.1%) and ProClin 300. Target value of 38.67 μIU/mL.
- Buffer with Tris buffer, HAMA Blocker, BSA, NaN_3(<0.1%) and ProClin 300.
- ABEI labeled with anti-TSH monoclonal antibody (mouse) Tris buffer, containing BSA, NaN_3(<0.1%) and ProClin 300.
- Control 1 - contains TSH antigen (human origin), phosphate buffer, bovine serum NaN_3(<0.1%) and ProClin 300. Target value of 0.6 μIU/mL.
- Control 2 - contains TSH antigen (human origin), phosphate buffer, bovine serum NaN_3(<0.1%) and ProClin 300. Target value of 6.0 μIU/mL.
- Control 3 - contains TSH antigen (human origin), phosphate buffer, bovine serum NaN_3(<0.1%) and ProClin 300. Target value of 18 μIU/mL.

All human sources materials were tests by FDA approved methods and found to be negative for HIV-1, HIV-2, and HBsAg.

The MAGLUMI 2000 Immunoassay Analyzer, is a fully-auto chemiluminescence analyzer used for determination of analytes in serum**.** The MAGLUMI 2000 system is a floor model, fully automated instrument system that utilizes pre-packaged reagent packs to measure a variety of analytes in human body fluids. It is controlled through a combination of custom and off-the-shelf software.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   ADVIA Centaur TSH3-Ultra, Trinidad Immunoassay (IM) System

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

   k083844, k151792

3. Comparison with predicate:

   MAGLUMI 2000 TSH assay:

Similarities /Differences		
Item	Candidate Device MAGLUMI 2000 TSH k162698	Predicate Device ADVIA Centaur TSH3-Ultra k083844
Intended Use	For the quantitative determination of thyroid-stimulating hormone (TSH) in human serum	Same
Measured Analyte	Thyroid-stimulating hormone	Same
Measurement	Quantitative	Same
Test principle	Sandwich chemiluminescent immunoassay	Same
Detection Antibody	anti-TSH monoclonal antibody labeled with N-(amino butyl)-N-(ethylisoluminol) (ABEI)	Monoclonal murine anti-TSH antibody BSA conjugate labeled with acridinium ester
Capture Antibody	Anti-TSH monoclonal antibody bound to magnetic microbeads	Anti-fluorescein labeled monoclonal murine anti-TSH antibody covalently bound to paramagnetic particles
Specimen	Serum	Serum, heparinized plasma, EDTA plasma
Measuring range	0.02 µIU/mL - 91.78 µIU/mL	0.008 µIU/mL – 150 µIU/mL
Sample size	100 µL	Same
Calibration	2 Point	Same

MAGLUMI 2000 Immunoassay Analyzer:

Similarities/Differences		
Item	Candidate Device MAGLUMI 2000 Immunoassay Analyzer k162698	Predicate Device Trinidad Immunoassay (IM) System k151792
Intended Use	Automated, immunoassay analyzer designed to perform in vitro diagnostic tests on clinical specimens	Same
Principles of Assay Operation	Chemiluminescence using magnetic-particle solid phase and chemiluminescent label	Same
Type of System	Random access, Batch, STAT	Random access and Batch
Throughput Rate	Up to 180 tests/hr.	120 to 240 tests/hr.
Optical System	PMT used in photon counting mode	Same
Dispense System	Automated pipetting of samples using precision syringe	Same
Sample Type	Serum	Serum, plasma, urine, whole blood hemolysate, amniotic fluid
Sample Volume	5 to 200 µL	10 to 200 µL

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

- CLSI EP05-A2: Evaluation of Precision Performance of Clinical Chemistry Devices; Approved Guideline-Second Edition.
- CLSI EP06-A: Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline.
- CLSI EP17-A2: Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline-Second Edition.
- CLSI EP07-A2: Interference Testing in Clinical Chemistry; Approved Guideline-Second Edition.
- CLSI EP09-A2: Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline-Second Edition.

L. Test Principle:

The MAGLUMI 2000 TSH assay is a sandwich chemiluminescence immunoassay. Testing is performed by combining the sample with magnetic particles coated with anti-TSH monoclonal antibody, buffer and N-(4-Amino-Butyl)-N-Ethyl-Isoluminol (ABEI) labeled with another monoclonal antibody to TSH, mixing thoroughly, and incubating at 37°C, to form a sandwich of immuno-complexes. After precipitation in a magnetic field, the supernatant is decanted and then a wash cycle is performed. Subsequently, the starters are added to the precipitate to initiate a chemiluminescent reaction. The light signal is measured by a photomultiplier within 3 seconds as relative light units (RLUs), which is indicative of TSH concentration present in samples, calibrators or controls.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

The precision study was performed in accordance with CLSI EP05-A2 guideline. The following sample types were tested: four controls, two calibrators, five spiked patient serum pool samples and four native patient serum pools. Testing was performed using 3 analyzers and 3 different reagent lots, over 20 days in duplicate with 2 runs per day for a total of 80 data points per sample on each analyzer. The combined results for each sample are summarized in the table below:

Sample	Mean µIU/mL (N=240)	Within-Run		Between -Run		Total	
		SD	%CV	SD	%CV	SD	%CV
Control 1	0.221	0.010	4.73	0.005	2.40	0.013	5.95
Control 2	0.620	0.27	1.38	0.013	2.04	0.032	5.12
Control 3	6.546	0.277	4.23	0.233	3.57	0.368	5.62
Control 4	17.961	0.711	3.96	0.354	1.97	0.843	4.70
Calibrator low	0.330	0.015	4.50	0.014	4.38	0.019	5.86
Calibrator high	38.037	1.372	3.61	0.363	0.96	1.478	3.89
Serum pool 1	1.257	0.05	3.95	0.035	2.82	0.067	5.37
Serum pool 2	6.401	0.102	1.60	0.164	2.56	0.157	2.44
Serum pool 3	11.880	0.472	3.97	0.42	3.56	0.66	5.54
Serum pool 4	38.67	1.221	3.24	0.788	2.09	1.533	4.07
Serum pool 5	64.309	2.371	3.69	2.022	3.14	3.109	4.83
Native pool 1	0.5777	0.025	4.33	0.012	2.08	0.029	5.02
Native pool 2	1.137	0.048	4.222	0.032	2.81	0.067	5.89
Native pool 3	5.026	0.201	3.992	0.098	1.95	0.247	4.91
Native pool 4	9.750	0.429	4.401	0.139	1.42	0.460	4.72

b. *Linearity/assay reportable range:*

The linearity for MAGLUMI 20000 TSH was evaluated in a study that followed the CLSI EP6-A guideline. Eleven equally distributed levels samples were prepared by mixing a low TSH serum sample (concentration 0 μIU/mL) and a high TSH serum sample (concentration 105 μIU/mL). All samples were run in quadruplicate on 3 MAGLUMI 2000 Immunoassay Analyzers, with 3 reagent lots. The mean observed value was compared to the expected values, the results obtained are shown in the following table:

Sample	Observed (μIU/mL)	Expected (μIU/mL)	% Recovery
0	0.0	0.0	0.0
1	0.4896	0.5	97.8
2	4.983	5.0	99.6
3	10.691	10.5	101.8
4	21.652	21.0	103.1
5	30.785	30.5	100.9
6	42.555	42.0	101.3
7	52.278	52.5	99.6
8	62.105	63.0	98.6
9	75.052	73.5	102.1
10	83.218	84.0	99.1
11	94.807	94.5	100.3

The expected values were plotted against the observed values and the following regression equation was obtained:

$y= 1.0001x + 0.0474$, $R^2 = 0.9990$

The results of the linearity study support the claimed measuring range of 0.02 μIU/mL to 91.78 μIU/mL .

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

Traceability:
MAGLUMI TSH calibrators are traceable to the TSH WHO 3rd International Standard 81/565.

Stability:
Real-time shelf-life stability testing of the TSH reagent kit (which includes controls and calibrators) is ongoing. The accelerated studies protocols and acceptances criteria were reviewed and found to be acceptable to support a shelf-life of 12 months at 2-8ºC.

Protocols and acceptance criteria for on-board/open vial stability studies for the kit, which includes controls and calibrators, were reviewed and found to be acceptable to support an on-board stability of 28 days at 10ºC ± 3ºC.

d. Detection limit:

The limit of blank (LoB), limit of detection (LoD) and the limit of quantitation (LoQ) of the MAGLUMI 2000 TSH kit were evaluated in accordance with CLSI EP17-A2 guideline.

Limit of Blank (LoB)
To calculate the LoB for the MAGLUMI TSH, 5% BSA diluent was tested in triplicates for 10 consecutive days, 2 runs per day on three different lot reagents to yield 60 data points on the MAGLUMI 2000 Instrument assay. LoB was calculated using the mean of the 57^{th} and 58^{th} highest obtained values and was determined to be 0.001 µIU/mL.

Limit of Detection (LoD)
Four low human serum samples pools with TSH concentrations of 0.005, 0.01, 0.02 and 0. 03 µIU/mL were tested on the MAGLUMI 2000 Immunoassay Analyzer, in duplicates for 10 consecutive days, 2 runs per day on 3 different reagent lots for a total of 60 data sets. LoD was calculated according to the EP17-A2 guideline and determined to be 0.006 µIU/mL .

Limit of Quantitation (LoQ)
Six serum sample pools with TSH concentrations of 0.16, 0.07, 0.03, 0.0017, 0.009 and 0.005 µIU/mL, were used to determine the LoQ. Each level was tested in duplicates for 20 days 2 runs per day using 3 different reagent lots for a total of 60 data points. The sponsor defined LoQ as the lowest concentration that demonstrated an imprecision of 20%, which was determined to be 0.01 µIU/mL.

LoB	LoD	LoQ
0.001 µIU/mL	0.006 µIU/mL	0.01 µIU/mL

The LoB, LoD and LoQ studies support the MAGLUMI TSH assay claimed measuring range of 0.02 to 91.78 µIU/mL.

e. Analytical specificity:

Interference by endogenous and exogenous substances was evaluated in serum samples according to the CLSI EP07-A2 guideline. Two serum samples with TSH concentration of approximately 0.7 µIU/mL and 6.1 µIU/mL were spiked with interfering substances and tested in triplicate with 3 reagent lots on one MAGLUMI 2000 Immunoassay Analyzer. Interference was determined by testing controls (no interfering substance added) and matched test sample (with interfering substance added).

The sponsor defines significant interference as ±10% bias as compared to the control results. The results of the interference study are summarized in the table below:

Substances	Maximum concentration tested that demonstrated no significant interference
Hemoglobin	2000 mg/dL
Conjugated bilirubin	60 mg/dL
Unconjugated bilirubin	40 mg/dL
Rheumatic factor	124 IU/mL
Acetaminophen	20 mg/dL
Ibuprofen	50 mg/dL
Aspirin	50 mg/dL
Biotin	10 ng/mL
Total protein	12.5 mg/mL
Triglycerides	1000mg/dL

Cross-Reactivity Testing:

A cross-reactivity study was performed to evaluate the potential cross-reactivity of the TSH assay. The potential cross-reactants were added at defined concentrations to human serum samples with TSH concentrations of 1.09, 2.1, 5.0 μIU/mL. The control and spiked samples were assayed in triplicates using 3 reagent lots on the MAGLUMI 2000 System. The sponsor defines non-significant interference as ≤5% difference from the of the expected value. The following potentially cross-reacting compounds, at the following concentrations, did not interfere with the performance of the device:

Compound Tested	Highest Concentration	Cross-reactivity (%)
FSH	1,500 mIU/mL	≤ 0.53
LH	600 mIU/mL	≤ 1.39
hCG	200 IU/mL	≤ 1.59

Human Anti-Mouse Antibodies (HAMA):

The effects of human anti-mouse antibodies (HAMA) on the MAGLUMI TSH assay were evaluated. Individual patient serum samples with TSH concentrations of 0.133, 2.56, and 4.71 μIU/mL were mixed with equal volume of HAMA positive samples. The final concentration of HAMA in these samples was 300 ng/mL. The mixed samples were analyzed using the MAGLUMI 2000 Immunoassay Analyzer in triplicate. The results indicate no interference from HAMA up to 300 ng/mL. The following cautionary note has been included in the Limitations of the Procedure section of the product insert: "Patient sample containing human anti-mouse antibodies (HAMA) may give falsely elevated or decreased values. Although HAMA neutralizing agents are added, extremely high HAMA serum concentrations may occasionally influence results".

High Dose Hook Effect:

To evaluate the potential for high dose hook effect on the MAGLUMI TSH assay, six serum samples were spiked with TSH WHO standard to generate concentrations values of 100, 300, 500, 1000, 2000 and 3000 μIU/mL. For each of the six samples, four serial dilutions were created with TSH WHO standard in ratios of 1:10, 1:32, 1:64, and 1:128. Testing was performed for each stock solution and each diluted solution in duplicate using three different reagent lots. The results demonstrate that no hook effect was observed at TSH concentration ≤ 3000 μIU/ml.

f. Assay cut-off:

Not Applicable.

2. Comparison studies:

a. Method comparison with predicate device:

A method comparison study was performed according to the CLSI EP09-A2 guideline. A total of 337 native patient serum samples with TSH values ranging from 0.02 – 91.78 μIU/mL were tested with three lots of MAGLUMI TSH assay on three MAGLUMI 2000 Immunoassay system at three sites. Samples were tested in singlicate on both the MAGLUMI 2000 TSH assay (candidate) and the ADVIA Centaur TSH3-Ultra assay (predicate). The results yielded the following linear regression equation:

$y = 1.0178x - 0.0773$, $R^2 = 0.9974$

b. Matrix comparison:

Not Applicable. Only serum samples are recommended for use with this assay.

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:

   The reference range was determined using the procedure in the CLSI C28-A3 guideline. A total of serum 126 samples from healthy individuals 22 years and older (64 females and 62 males) were tested using three lots of MAGLUMI 2000 TSH reagents on one MAGLUMI 2000 Immunoassay system. The expected normal range of TSH as measured by the MAGLUMI TSH assay is 0.658 – 4.864 μIU/mL based on the central 95% interval of the results from this study (2.5^{th} - 97.5^{th} percentile results).

N. Instrument Name:

MAGLUMI 2000 Immunoassay Analyzer

O. System Descriptions:

1. Modes of Operation:

   Does the applicant's device contain the ability to transmit data to a computer, webserver, or mobile device?

   Yes ___X___ or No _____

   Does the applicant's device transmit data to a computer, webserver, or mobile device using wireless transmission?

   Yes _____ or No___X___

2. Software:

   FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

   Yes___X___or No _____

3. Specimen Identification:

   A barcode scanner is part of the instrument system and is used to identify specimens.

4. Specimen Sampling and Handling:

   The instrument system has automated specimen sampling and handling.

5. Calibration:

   The results are generated using a calibration curve which is instrument specific, generated by 2-point calibration and a master curve provided via the reagent Radio Frequency Identification (RFID) CHIP. Recalibration is needed under the following conditions:

   - Exchange of reagent lot.
   - Every week and/or each time a new reagent is used.
   - After any major service is performed.
   - If the controls are out of the expected range.
   - When the room temperature changes exceeds 5ºC.

6. Quality Control:

   The sponsor recommends the user should follow government regulations or accreditation for quality control frequency. (Three levels of quality control are provided in the kit.)

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above:

A carryover study was performed using a free TSH serum sample (blank), a mid-level pool and a serum pool with a TSH concentration of 90 µIU/mL (high). Testing was performed for five days, according to the following order: Mid, High, Low, Mid, Mid, Low, Low, High, High, Mid. Each sample was analyzed using three instruments and three lots of reagent. Percent carryover was calculated each day and compared to zero. The data obtained in all 5 days showed that the percent carryover is less than 0.01%. The sponsor concluded that the percent carryover is not detectably different from zero.

Q. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

R. Conclusion:

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