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

K191499

B Applicant

Shenzhen New Industries Biomedical Engineering Co., Ltd

C Proprietary and Established Names

MAGLUMI 2000 25-OH Vitamin D

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
MRG	Class II	21 CFR 862.1825 - Vitamin D Test System	CH - Clinical Chemistry

II Submission/Device Overview:

A Purpose for Submission:

New device

B Measurand:

Total 25-hydroxyvytamin D (25-OH Vitamin D)

C Type of Test:

Quantitative, chemiluminescent immunoassay

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

MAGLUMI 2000 25-OH Vitamin D is an in vitro chemiluminescence immunoassay for the quantitative determination of 25-OH Vitamin D in human serum using Maglumi 2000 Fully-auto chemiluminescence immunoassay analyzer. The measurement of 25-OH Vitamin D is to be used as an aid in the assessment of vitamin D sufficiency.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

D Special Instrument Requirements:

MAGLUMI 2000 Immunoassay Analyzer

IV Device/System Characteristics:

A Device Description:

The MAGLUMI 2000 25-OH Vitamin D assay consists of the following reagents:

- Magnetic Microbeads - coated with 25-OH Vitamin D monoclonal antibody, containing BSA, NaN3 (<0.1%)
- Calibrator Low- Containing BSA and 25-OH Vitamin D antigen, NaN3(<0.1%)
- ABEI Label- 25-OH Vitamin D antigen labeled with ABEI
- Control 1- Containing BSA and 25-OH Vitamin D antigen, NaN3 (<0.1%)
- Control 2- Containing BSA and 25-OH Vitamin D antigen, NaN3 (<0.1%)

B Principle of Operation:

The 25-OH VITAMIN D assay is a competitive chemiluminescence immunoassay using FDA previously cleared MAGLUMI 2000 instrument (k162698).

The 25-OH Vitamin D assay is a two-incubation chemiluminescence immunoassay for the quantitative determination of total 25-OH vitamin D in human serum. In the first incubation, the 25-OH vitamin D is dissociated from its binding protein by the displacing reagent and binds to the 25-OH vitamin D antibody on the magnetic microbeads forming an antibody-antigen complex. Following a second incubation, the 25-OH Vitamin D labeled ABEI are added. The rest unbound material is removed during a wash cycle. Subsequently, the Starter 1+2 are added to initiate a flash chemiluminescent reaction. The resulting chemiluminescent reaction is measured as relative light units (RLUs), which is inversely proportional to the concentration of 25-OH Vitamin D present in the sample.

V Substantial Equivalence Information:

A Predicate Device Name(s):

Liaison 25 Oh Vitamin D Total Assay

B Predicate 510(k) Number(s):

K112725

C Comparison with Predicate(s):

Device & Predicate Device(s):	K191499	K112725
Device Trade Name	**MAGLUMI 2000 25-OH Vitamin D Assay**	**Liaison 25 OH-Vitamin D Total Assay**
General Device Characteristic Similarities		
Intended Use/Indications For Use	For the quantitative determination of total 25-hydroxyvitamin D in human serum. The measurement of 25-OH Vitamin D is to be used as an aid in the assessment of vitamin D sufficiency.	Same
Specimen	Serum	Same
Measurement	Quantitative	Same
Automated	Yes	Same
Calibration	2 points	Same
General Device Characteristic Differences		
Test principle	Two-step competitive chemiluminescence immunoassay (CLIA)	Direct competitive chemiluminescence immunoassay (CLIA)
Measuring range	5.371-143.000 ng/ml	4-150 ng/ml
Capture antibody	Magnetic microbeads coated with 25- OH Vitamin D monoclonal antibody	Magnetic particles coated with antibody against 25-OH Vitamin D
Detection	ABEI-labeled 25-OH Vitamin D antigen	25-OH Vitamin D conjugated to an isoluminol derivative
Sample size	100 µL	25 µL

Device & Predicate Device(s):	K191499	K112725
Traceability	ID-LC-MS/MS traceable to NIST RMP 2972	Calibrators are traceable to concentrations determined by UV spectrophotometric analysis.

VI Standards/Guidance Documents Referenced:

CLSI EP05-A2 – Evaluation of Precision Performance of Clinical Chemistry Devices-Approved Guideline-Second Edition.
CLSI EP06-A – Evaluation of the Linearity of Quantitative Analytical
CLSI EP07-A2 – Interference Testing in Clinical Chemistry
CLIS EP17-A2: Evaluation of detection Capability for Clinical Laboratory Measurement Procedures

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:
   The precision was determined using the CLSI EP5-A3 guideline. The study was conducted by testing three controls, two calibrators, three spiked patient serum pools and three native patient sample pools on three different instruments using 3 reagent lots. The data was collected over 20 days in duplicate with 2 runs per day with a total of 80 samples analyzed per level on each instrument. The results are summarized on the table below.

Sample	N	Mean (ng/mL)	Repeatability		Between Run		Between Day		Within instrument		Reproducibility	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Control 1	240	30.077	1.039	3.45	0.389	1.29	1.546	5.14	1.903	6.33	1.944	6.46
Control 2	240	60.362	1.625	2.69	0.487	0.81	2.590	4.29	3.096	5.13	3.096	5.13
Control 3	240	119.953	1.741	1.45	1.842	1.54	3.971	3.31	4.711	3.93	4.930	4.11
Calibrator Low	240	7.635	0.385	5.04	0.177	2.32	0.408	5.34	0.588	7.70	0.602	7.89
Calibrator High	240	97.863	1.529	1.56	0.938	0.96	3.585	3.66	4.009	4.10	4.278	4.37
Spiked Serum Pool l	240	56.361	1.850	3.28	0.576	1.02	1.788	3.17	2.637	4.68	2.764	4.90
Spiked Serum Pool 2	240	80.795	1.800	2.23	0.705	0.87	1.972	2.44	2.762	3.42	2.812	3.48
Spiked Serum Pool 3	240	130.363	1.530	1.17	1.960	1.50	3.572	2.74	4.353	3.34	4.701	3.61
Native Serum Pool 1	240	8.387	0.458	5.46	0.235	2.80	0.578	6.89	0.774	9.23	0.778	9.28
Native Serum Pool 2	240	30.512	1.092	3.58	0.682	2.24	1.330	4.36	1.851	6.07	2.220	7.27

Sample	N	Mean (ng/mL)	Repeatability		Between Run		Between Day		Within instrument		Reproducibility	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Native Serum Pool 3	240	106.049	1.353	1.28	1.971	1.86	2.068	1.95	3.161	2.98	3.313	3.12

2. Linearity:

The linearity of the MAGLUMI 25-OH VITAMIN D method was determined following the CLSI EP6-A guideline. A low serum sample pool and a high serum sample pool were mixed in different proportions to create eleven linearity samples with 25-OH vitamin D concentrations from 4.600 to 145.800 ng/mL. Each sample was measured in quadruple on 3 lots of reagent. Linearity was evaluated using regression analysis.

Slope	Intercept	r^2	Sample range tested
0.9885	0.1192	0.9986	4.600 -145.800 ng/mL

The results of the linearity study support the sponsor claimed that the candidate assay is linear from 5.371 to 143 ng/mL.

3. Analytical Specificity/Interference:

The effect of common drugs and interference substances were evaluated using human serum pools. For each substance, three serum samples containing 20, 30 and 60 ng/mL concentration of 25-OH Vitamin D were analyzed. No significant interference was defined as recovery ± 10% when compared to the control sample. The substances and the highest concentration tested which did not caused significant interference are listed below.

Potential Interferent	**Highest concentration tested at which no significant interference is observed (mg/dL)**
Cefoxitin	340
Levodopa	3.25
Metronidazole	12.3
Ascorbic Acid (Vitamin C)	16.95
Acetaminophen	15.6
Biotin	5
Cyclosporine	0.6
Rifampicin	6.5
Doxycycline	3.2
Theophylline	11.4

The effect of conjugated/unconjugated bilirubin, hemoglobin, triglyceride, uric acid, cholesterol, human anti-mouse antibodies (HAMA), rheumatoid factor (RF) and human serum total protein was evaluated using human serum samples. Each potential interferent was added to 25-OH Vitamin D human serum samples and tested using 3 lots of reagents. For all substances tested, no significant interference was defined as recovery ± 10% when compared to control sample.
The potential interferents and the highest concentration tested which did not caused significant interference are listed below.

Potential Interferent	**Highest concentration tested at which no significant interference is observed (mg/dL)**
Conjugated Bilirubin	60
Unconjugated Bilirubin	42.5
Triglyceride	500
Hemoglobin	250
HAMA	401 ng/mL
RF	1745 IU/mL
Total protein	6.25 g/dL

Cross-Reactivity Study:
A cross-reactivity study was performed using two base serum samples containing total 25-OH Vitamin D 30 ng/mL and 60 ng/mL respectively. These samples were spiked with various cross reactants and measured for these solutions using 3 lots of reagents. The cross-reactivity was determined using the following formula: % cross reactivity = [(mean recovery of test samples in ng/mL) – (mean recovery of control sample in ng/mL) / (concentration of cross reactant in ng/mL)] * 100.

The following table shows cross-reactivity of potential cross reactant.

Cross Reactant	**%Cross-reactivity**
25-OH Vitamin D2	98.10%
25-OH Vitamin D3	96.13%
Vitamin D2	1.04%
Vitamin D3	1.98%
1,25-(OH)2-Vitamin D3	8.12%
1,25-(OH)2-Vitamin D2	8.77%
3-epi-25OH D3	2.04%

4. Assay Reportable Range:

5.371 – 143.000 ng/mL

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

The MAGLUMI 2000 25-OH Vitamin D assay is traceable to the National Institute of Standards and Technology (NIST) Standard Reference Material (SRM) 2972a reference material.

6. Detection Limit:

Detection limit studies were performed following CLSI EP17-A guideline.

The limit of blank (LoB) was determined by testing 25-OH Vitamin D-depleted serum samples in 12 replicates per day, over 5 days using 3 different reagent lots. The LoB was calculated using the mean of the 57^{th} and 58^{th} highest obtained values and was determined to be 1.990 ng/mL (highest of the 3 lots).

The limit of detection (LoD) was determined by testing four level of low samples in 60 replicates of 12 per day over 5 days using 3 lots of reagents. The LoD was calculated using parametric analysis. LOD was determined to be 3.800 ng/mL (highest of the 3 lots).

The limit of quantitation (LoQ) was determined by measuring six low serum samples, in six replicates per run, one run per day, over 5 days, using 3 lots of reagents. LoQ is defined as the lowest analyte concentration that can be reproducibly measured with an intermediate precision CV of ≤ 20 % and was determined to be 5.371 ng/mL (highest of the 3 lots).

The results of the LoB, LoD, and LoQ are summarized below:

LoB	LoD	LoQ
1.990 ng/mL	3.800 ng/mL	5.371 ng/mL

The sponsor claimed that the candidate assay has a measuring range from 5.371 to 143 ng/mL.

7. Assay Cut-Off:

Not applicable.

B Comparison Studies:

1. Method Comparison with Predicate Device:

A method comparison study was performed by testing 241 human serum samples with concentrations ranging from 5.371 to 143.000 ng/mL, as determined by the predicate device. The comparison of the MAGLUMI 25-OH VITAMIN D assay with the predicate device, LIAISON 25-OH VITAMIN D total assay (x), produced the following linear regression equation:

N	Slope (95% CI)	Intercept (95% CI)	Correlation Coefficient (r)	Sample Range Tested (ng/mL)
241	1.013	-0.504	0.9739	5.371- 143.000

2. Matrix Comparison:

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

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:

The study was conducted following CLSI EP28-A3c guideline. Three hundred and two (302) samples from apparently healthy donors including 169 males ranging in age from 20 to 89 and 133 females ranging in age from 21 to 89 were collected from three regions (Northern, Central, and Southern) in the US. The 302 samples from apparently healthy donors met the following inclusion/exclusion criteria as follows:

- Age from 21 to 90
- Roughly 50% female and 50% male
- 20% from Northern, 20% from Central and 60% from Southern region
- 40% collected in spring, 30% in summer and 30% in winter
- Study included at least 30% African Americans and 30% Caucasians
- Subject did not have a history of kidney, GI, parathyroid or calcium regulatory disease and did not take vitamin D supplements.

Samples were tested with the MAGLUMI 25-OH VITAMIN D assay in singlicate. The observed median, mean, and range between 2.5^{th} to 97.5^{th} percentile are summarized below:

N	Mean	Median	2.5^{th} – 97.5^{th} percentile
302	25.403 ng/mL	24.885 ng/mL	9.99 – 49.3 ng/dL

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.