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

I Background Information:

A 510(k) Number

K232587

B Applicant

Shenzhen New Industries Biomedical Engineering Co., Ltd

C Proprietary and Established Names

MAGLUMI 25-OH Vitamin D, MAGLUMI X3 Fully-auto chemiluminescence immunoassay analyzer

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
MRG	Class II	21 CFR 862.1825 - Vitamin D Test System	CH - Clinical Chemistry
JJE	Class I	21 CFR 862.2160 - Discrete photometric chemistry analyzer for clinical use	CH - Clinical Chemistry

II Submission/Device Overview:

A Purpose for Submission:

New Device

B Measurand:

Total 25-hydroxyvitamin 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:

The MAGLUMI X3 Fully-auto chemiluminescence immunoassay analyzer is an automated, immunoassay analyzer designed to perform in vitro diagnostic tests on clinical specimens.

The MAGLUMI 25-OH Vitamin D is an in vitro chemiluminescence immunoassay for the quantitative determination of 25-OH Vitamin D (25-OH VD) in human serum and plasma using the MAGLUMI series Fully-auto chemiluminescence immunoassay analyzer, and the assay is used for an aid in assessment of vitamin D sufficiency.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

Not for Point of care (POC) testing

D Special Instrument Requirements:

MAGLUMI X3 Fully-auto chemiluminescence immunoassay analyzer.

IV Device/System Characteristics:

A Device Description:

MAGLUMI X3 Fully-auto chemiluminescence immunoassay analyzer:
The MAGLUMI X3 Fully-auto chemiluminescence immunoassay analyzer is a fully automated instrument system designed to perform in vitro diagnostic tests on clinical specimens. The system utilizes chemiluminescent technology and uses pre-packaged reagent packs for quantitative analysis of the analytes in human samples. The analyzer performs automatic sample pipetting, reagent loading, incubation, washing, measurements, and result calculations.

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

- Magnetic Microbeads- coated with anti-25-OH VD antibody in PBS buffer, NaN3 (<0.1%).
- Calibrator Low- A low concentration of 25-OH VD antigen in Carbonate buffer, NaN3 (<0.1%).
- Calibrator High- A high concentration of 25-OH VD antigen in Carbonate buffer, NaN3 (<0.1%).
- Buffer- Acidic buffer
- ABEI Label- ABEI labeled with anti-25-OH VD antibody (~0.500 μg/mL) in PBS buffer, NaN3 (<0.1%).
- Control 1- A low concentration of 25-OH VD antigen in Carbonate buffer, NaN3 (<0.1%).
- Control 2- A high concentration of 25-OH VD antigen in Carbonate buffer, NaN3 (<0.1%).

B Principle of Operation:

The 25-OH Vitamin D assay is a sandwich chemiluminescence immunoassay for the quantitative determination of total 25-OH vitamin D in human serum and plasma. The sample, magnetic microbeads coated with anti-25-OH VD antibody, and buffer are mixed thoroughly, incubated and a wash cycle is performed after a precipitation in a magnetic field. N-(4-Aminobutyl)-N-ethyl isoluminol (ABEI)-labeled with another anti-25-OH VD antibody is then added, reacting to form sandwich complexes and incubated. After precipitation in a magnetic field, the supernatant is

decanted, and then another wash cycle is performed. Subsequently, the starter 1+2 is added to initiate a chemiluminescent reaction. The light signal is measured by a photomultiplier as relative light units (RLUs), which are proportional to the concentration of 25-OH VD present in the sample.

C Instrument Description Information:

1. Instrument Name: MAGLUMI X3 Fully-auto chemiluminescence immunoassay analyzer

2. Specimen Identification:
   The specimen is in a tube with a barcode label. The system identifies the specimen by scanning the barcode. This is the primary use case for sample identification. For samples that have no barcode, the system also supports manual entry of sample IDs.

3. Specimen Sampling and Handling:

   Specimen sampling and handling procedures are analyte specific and are documented in the specific reagent Instructions for Use (IFU).

4. Calibration: Calibrators are prepared according to the reagent kit instructions. Calibration recommendations are described in the labeling.

5. Quality Control: Recommendations relating to Quality Control procedures are described in the labeling.

V Substantial Equivalence Information:

A Predicate Device Name(s):
MAGLUMI 2000 25-OH Vitamin D, MAGLUMI 2000 Immunoassay Analyzer

B Predicate 510(k) Number(s):
K191499, K162698

C Comparison with Predicate(s):
MAGLUMI 25-OH Vitamin D assay

Device & Predicate Device(s):	K232587	K191499
Device Trade Name	MAGLUMI 25-OH Vitamin D	MAGLUMI 2000 25-OH Vitamin D
General Device Characteristic Similarities		
Intended Use/Indications For Use	Quantitative determination of 25-OH Vitamin D (25-OH VD); used as an aid in assessment of vitamin D sufficiency.	Same
Capture antibody	Magnetic microbeads	Same

	coated with 25-OH Vitamin D monoclonal antibody	
General Device Characteristic Differences		
Sample Type/ Specimen	Serum and K2EDTA Plasma	Serum
Measuring Range	5.371-150 ng/ml	5.371-143 ng/ml
Sample Size	10 µl	100 µl
Traceability	NIST SRM 2972a	ID-LC-MS/MS traceable to NIST RMP 2972

MAGLUMI X3 Fully-auto chemiluminescence immunoassay analyzer

Device & Predicate Device(s):	K232587	K162698
Device Trade Name	MAGLUMI X3 Fully-auto chemiluminescence immunoassay analyzer	MAGLUMI 2000 Immunoassay Analyzer
General Device Characteristic Similarities		
Intended Use/Indications For Use	Automated, immunoassay analyzer designed to perform in vitro diagnostic tests on clinical specimens.	Same
Principle of Assay Operation	Chemiluminescence	Same
General Device Characteristic Differences		
Reagent Volume	10 to 200 µl	10 to 450 µl
Throughput Rate	Up to 200 tests/hr	Up to 180 tests/hr

VI Standards/Guidance Documents Referenced:

Clinical and Laboratory Standards Institute (CLSI) EP05-A3 – Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline-Third Edition

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

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:
   The precision study was performed based upon recommendations in the CLSI EP05-A3 Guideline. The study was conducted using three lots of the MAGLUMI 25-OH VITAMIN D reagent on three different MAGLUMI X3 instruments with two controls, three spiked patient serum pools, and three native patient sample pools. 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 shown in the table below.

Sample	N	Mean (ng/mL)	Repeatability		Between-Run		Between-Day		Total (within instrument)		Reproducibility (across instruments)	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Calibrator Low	240	6.986	0.270	3.86	0.214	3.06	0.398	5.70	0.526	7.53	0.564	8.07
Calibrator High	240	97.698	1.543	1.58	1.976	2.02	0.923	0.94	2.672	2.73	2.692	2.76
Control 1	240	19.962	0.512	2.56	0.706	3.54	0.956	4.79	1.294	6.48	1.306	6.54
Control 2	240	50.181	1.405	2.80	1.150	2.29	1.398	2.79	2.292	4.57	2.292	4.57
Spiked serum pool	240	130.310	0.770	0.59	2.024	1.55	0.508	0.39	2.224	1.71	2.305	1.77
Native Serum Pool 1	240	30.084	1.027	3.41	0.626	2.08	1.294	4.30	1.766	5.87	1.766	5.87
Native Serum Pool 2	240	8.376	0.469	5.60	0.251	3.00	0.299	3.57	0.610	7.28	0.610	7.28
Native Serum Pool 3	240	100.082	1.022	1.02	2.128	2.13	0.517	0.52	2.417	2.42	2.417	2.41

2. Linearity:

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 1.8 to 195 ng/mL. Each sample was measured in 4 replicates on 3 lots of reagent. Linearity was evaluated using regression analysis.

Slope	Intercept	r^2	Sample range tested
1.0016	0.4938	0.9974	1.8 to 195 ng/mL

The results of the linearity study support the claimed reportable range of 5.371-150 ng/mL.

Sample Dilution study

A sample dilution study was conducted to support the claim in the product labeling that 25-OH vitamin D samples with results above the measuring range may be manually diluted with a carbonate buffer, pH 9.2. In the study, five serum samples were spiked with 25-OH vitamin D to prepare concentrations with expected values ranging from 150 - 300 ng/mL. Each of the four samples were diluted 1:2. Each diluted sample was assayed in duplicate and analyzed for recovery after correcting for dilution. The recoveries ranged from 97% to 99%. The dilution study results support the sponsor's labeling claims that samples with 25-OH vitamin D concentrations above 150 ng/mL may be manually diluted 1:2 to obtain results up to 300 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 10, 50 and 100 ng/mL of 25-OH Vitamin D were analyzed. No significant interference was defined as recovery within ± 10% when compared to the control sample. The substances and the highest concentration tested which did not cause 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 potential endogenous interferents was evaluated using human serum samples. Each potential interferent was added to three serum samples containing 10, 50 and 100 ng/mL of 25-OH Vitamin D and these were analyzed using 3 lots of reagents. For all substances tested, no significant interference was defined as recovery within ± 10% when compared to the

control sample. The potential interferents and the highest concentration tested which did not cause 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
Uric Acid	20 mg/dL
Cholesterol	300 mg/dL

Cross-Reactivity Study:
A cross-reactivity study was performed using three base serum samples containing total 25-OH Vitamin D at concentrations of 10 ng/mL, 50 ng/mL, and 100 ng/mL. These samples were spiked with various cross reactants and measured 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 the 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:
   5.371-150 ng/ml

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

The candidate device assay is traceable to the National Institute of Standards and Technology (NIST) Standard Reference Material (SRM) 2972a.

6. Detection Limit:

   The limit of blank (LoB) was determined by testing four 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 57th and 58th highest obtained values and was determined to be 0.923 ng/mL (highest of the 3 lots).

The limit of detection (LoD) was determined by testing four level of low serum samples in 5 replicates per day, over 3 days using 3 lots of reagents. The LoD was calculated using parametric analysis. LOD was determined to be 1.398 ng/mL (highest of the 3 lots).

The limit of quantitation (LoQ) was determined by measuring six low serum samples, in five replicates per run, one run per day, over 3 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 2.289 ng/mL (highest of the 3 lots).

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

LoB	LoD	LoQ
0.923 ng/mL	1.398 ng/mL	2.289 ng/mL

7. Assay Cut-Off:
   Not applicable.

8. Accuracy (Instrument):
   Not applicable?

9. Carry-Over:

Information regarding the potential impact of carry-over on the candidate device was reviewed and determined to be acceptable.

B Comparison Studies:

1. Method Comparison with Predicate Device:
   A comparison study between the MAGLUMI 25-OH VITAMIN D and the MAGLUMI 2000 25-OH VITAMIN D (i.e., the predicate, K191499) assays was conducted at three different intended use sites.
   A total of 329 patient serum samples with 25-OH VITAMIN D values ranging from 5.933 to 142.1 ng/mL were collected and evaluated. The data were analyzed using Passing-Bablok regression and the comparison of the MAGLUMI 25-OH Vitamin D assay (y) with the predicate device, the MAGLUMI 2000 25-OH Vitamin D assay (x), is summarized below:

   Passing-Bablok: y=0.989x+0.248, R=0.997

2. Matrix Comparison:
   A matrix comparison study was conducted to support the use of the MAGLUMI 25-OH VITAMIN D on the MAGLUMI X3 instrument with different sample matrices. Specifically, the study compared values obtained from samples drawn into serum and k2EDTA plasma collection tubes. 78 serum/K2EDTA plasma pair samples, with 25-OH Vitamin D concentrations ranging from 5.3 to 143 ng/mL, were collected from the same donor and tested. The following results were determined using Passing-Bablok regression analysis: y=0.977x-0.0256, R^2=0.9938

The results support the sponsor's claims that the assay is suitable for use with serum and K2EDTA plasma 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:

E Expected Values/Reference Range:

Reference Range
The reference range was evaluated using serum samples from 312 normal apparently healthy individuals (21 years and older), consisting of 131 females and 181 males, and were collected year-round (35% Spring, 25% Summer, 9% Autumn, and 31% Winter) from three regions (Central, Southeast and Northeast) in the US, and evaluated.

The reference range for the total study population using the MAGLUMI 25-OH VITAMIN D assay is summarized below:

N	Mean	Median	2.5^{th} – 97.5^{th} percentile
312	22.5	21.2	7.4 – 45.1 ng/mL

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.