DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
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Silver Spring, MD 20993-0002

January 19, 2017

SIEMENS HEALTHCARE DIAGNOSTICS, INC.
LAURA DUGGAN
REGULATORY TECHNICAL SPECIALIST
500 GBC DRIVE, PO BOX 6101 MS 514
NEWARK DE 19711

Re: K162399
Trade/Device Name: Atellica Ch Magnesium (Mg)
Regulation Number: 21 CFR 862.1495
Regulation Name: Magnesium Test System
Regulatory Class: I, reserved
Product Code: JGJ
Dated: December 14, 2016
Received: December 15, 2016

Dear Dr. Duggan:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Katherine Serrano -S

For: Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
k162399

Device Name
Atellica CH Magnesium (Mg)

Indications for Use *(Describe)*

The Atellica™ CH Magnesium (Mg) assay is for in vitro diagnostic use in the quantitative determination of magnesium in human serum, plasma (lithium heparin), and urine using the Atellica™ CH Analyzer. Magnesium measurements are used in the diagnosis and treatment of hypomagnesemia (abnormally low levels of magnesium) and hypermagnesemia (abnormally high levels of magnesium).

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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10. 510(K) SUMMARY

This summary of 510(k) safety and effectiveness information is submitted in accordance with the requirements of SMDA 1990 and 21 CFR §807.92.

ASSIGNED 510(K) NUMBER

The assigned 510(k) number is k162399.

APPLICANT AND DATE

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January 19, 2017

MANUFACTURER

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Registration Number: 2432235

REGULATORY INFORMATION

Regulatory Submission for the Atellica™ CH Magnesium (Mg)

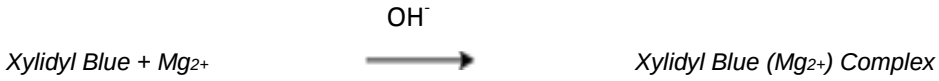
Common Name:	Photometric Method, Magnesium
Proprietary Name:	Atellica CH Magnesium (Mg)
Classification Name:	Magnesium Test System
Regulation Number:	21CFR862.1495
Classification:	Class I
Product Code:	JGJ
Panel:	Clinical Chemistry
Predicate Device:	Dimension Magnesium Flex Reagent Cartridge (k861700)

DEVICE DESCRIPTION

ATELLICA CH MAGNESIUM (MG)

The Atellica CH Mg assay is based on the modified xylidyl blue reaction, which was first described by C.K. Mann and J.H. Yoe.[1,2] The reagent was modified to eliminate the use of organic solvents. Magnesium ions react with xylidyl blue in an alkaline medium to form a water-soluble purple-red complex. The increase in absorbance of xylidyl blue at 505/694 nm is proportional to the concentration of magnesium in the sample. Calcium is excluded from the reaction by complexing with EGTA.

Reaction Equation



Serum, lithium heparin plasma and urine specimens may be used. The reagent is stored unopened at 2 – 8 °C and is stable for use on system for 14 days. Calibration is performed every 60 days for a reagent lot or every 3 days for an individual pack.

INTENDED USE/INDICATIONS FOR USE

ATELLICA CH MAGNESIUM (MG)

The Atellica™ CH Magnesium (Mg) assay is for in vitro diagnostic use in the quantitative determination of magnesium in human serum, plasma (lithium heparin), and urine using the Atellica™ CH Analyzer. Magnesium measurements are used in the diagnosis and treatment of hypomagnesemia (abnormally low levels of magnesium) and hypermagnesemia (abnormally high levels of magnesium).

COMPARISON OF TECHNOLOGICAL CHARACTERISTICS

Below is a features comparison for the Atellica CH Magnesium (Mg) assay and the predicate device:

Feature	**Predicate Device:** Dimension Magnesium Flex Reagent Cartridge (k861700)	**New Device:** Atellica CH Magnesium (Mg)
Intended Use :	The MG method used on the Dimension® clinical chemistry system is an *in vitro* diagnostic test intended for the quantitative determination of magnesium in human serum, heparinized plasma and urine.	The Atellica™ CH Magnesium (Mg) assay is for *in vitro* diagnostic use in the quantitative determination of magnesium in human serum, plasma (lithium heparin), and urine using the Atellica™ CH Analyzer.
Indications for Use:		Magnesium measurements are used in the diagnosis and treatment of hypomagnesemia (abnormally low levels of magnesium) and hypermagnesemia (abnormally high levels of magnesium).
Device Technology:	Methylthymol blue (MTB) complexometric procedure	Xylidyl blue reaction
Sample Type:	Serum, plasma and urine	Serum, Lithium Heparin plasma, and urine
Expected Values:	Serum/Plasma 1.8 – 2.4 mg/dL Urine 24 – 255 mg/24hr	Serum/plasma 1.60 to 2.60 mg/dL Urine : Same
Standardization:	NIST SRM 929	Same

Calibration Frequency:	90 days	60 days
Analytical Measuring Interval:	Serum/Plasma: 0.0 – 20.0 mg/dL Urine: 0.0 – 20.0 mg/dL	Serum and plasma: 0.50 to 5.00 mg/dL Urine: 1.00 to 14.00 mg/dL
Interferences:	Bilirubin (Unconjugated) – 40 mg/dL Lipemia (Intralipid®) – 1000 mg/dL Hemoglobin – 200 mg/dL	Bilirubin (Unconjugated) – 30 mg/dL Bilirubin (Conjugated) – 30 md/dL Lipemia (Intralipid®) – 500 mg/dL Hemoglobin – 500 mg/dL

SUMMARY OF PERFORMANCE TESTING

Assay performance comparison results for the Atellica CH Magnesium (Mg) were obtained by processing the appropriate body fluids. Summary statistics for each are provided. These data demonstrate substantial equivalency of the Atellica CH Magnesium (Mg) compared to the predicate device. The following data represent typical assay performance.

DETECTION LIMIT

The Limit of Blank (LoB) and Limit of Detection (LoD) were evaluated in accordance with CLSI EP17-A2 Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline.

Assessment of LoB was the 95th percentile of all values (sorted from lowest to highest), using non-parametric approach.

LoB Rank Position = 0.5 +0.95*B, where B=total reps=60; Rank = 57.5

Atellica CH Magnesium (Mg) – Detection Capability		
Limit	Protocol	Result

LoB	4 samples with no analyte were tested (N=5) for 3 days, one run per day, 3 reagent lots	0.00 mg/dL
LoD	4 low analyte samples were tested (N=5) for 3 days, one run per day, 3 reagent lots	0.02 mg/dL serum 0.04 mg/dL urine

LOQ

The Limit of Quantitation (LoQ) for serum was determined as described in CLSI Document EP17-A2. The mean, SD, %CV and bias relative to the reference values were calculated for each sample per reagent lot. The lowest sample concentration that met the maximum allowable imprecision and maximum allowable bias acceptance criteria was taken as the LoQ estimate for each reagent lot.

For both serum/plasma and urine fluids, 4 low samples were processed on three reagent lots for three days, on one instrument for a total of 60 measurements per lot. For serum LoQ estimate is 0.46 mg/dL (0.19 mmol/L) with maximum allowable imprecision of 5% CV and maximum allowable bias of 15%. For Urine LoQ estimates is 0.57 mg/dL (0.23 mmol/L) with maximum allowable imprecision of 5% CV and maximum allowable bias of 15%. For serum, the measured LoQ was 0.46 mg/dL in support of the low end of the measuring interval of 0.50 mg/dL for serum and plasma samples. For urine, the measured LoQ was 0.57 mg/dL in support of the low end of the measuring interval of 1.00 mg/dL for urine samples.

LINEARITY STUDY

Linearity was evaluated with 10 samples which spanned the assay measuring interval for serum specimens and 10 samples which spanned the assay measuring interval for urine specimens. Each was prepared by mixing high and low concentration samples across the measurement interval as described in CLSI Evaluation of the Linearity of Quantitative Measurement Procedure (EP06-A). The high sample was prepared by spiking native serum or urine pools with magnesium acetate. Low pools were created by diluting serum and urine samples with saline solution. Four replicates were measured for each sample. The mean of these replicates was used for the calculations.

The assay was considered linear across the measuring interval if the p values of nonlinear terms in the quadratic and cubic fit equations are nonsignificant ($p \leq 0.05$). If

the p-value is > 0.05, then the allowable bias is ≤ 5% or 0.10 mg/dL, whichever is greater. Linearity of the Atellica CH Magnesium (Mg) was demonstrated with both serum and urine specimens to encompass the measuring intervals of 0.50 to 5.00 mg/dL for serum and plasma specimens and 1.00 to 14.00 mg/dL for urine specimens.

PRECISION STUDIES

Precision testing was performed in accordance with CLSI EP05-A3 Evaluation of Precision Performance of Quantitative Measurement Methods: Approved Guideline – Third Edition. Precision was tested n = 2 replicates, two times a day for at least 20 days for a total of 80 replicates with controls, serum and plasma pools on one instrument. Analysis of variance (ANOVA) was used to evaluate the data consistent with the recommendations of EP05-A3. The data are summarized in the following table.

			Repeatability		**Within-Lab Precision**	
Sample Type	**n**	**Mean mg/dL (mmol/L)**	**SD[a] mg/dL (mmol/L)**	**CV[b] (%)**	**SD[a] mg/dL (mmol/L)**	**CV[b] (%)**
Serum	80	0.78 (0.32)	0.023 (0.009)	3.0	0.031 (0.013)	3.9
Plasma	80	1.51 (0.62)	0.034 (0.014)	2.3	0.051 (0.021)	3.4
Serum QC	80	2.53 (1.04)	0.044 (0.018)	1.7	0.050 (0.021)	2.0
Serum	80	4.22 (1.74)	0.024 (0.010)	0.6	0.047 (0.019)	1.1
Urine QC1	80	4.61 (1.89)	0.037 (0.015)	0.8	0.097 (0.040)	2.1
Urine QC2	80	11.19 (4.60)	0.108 (0.044)	1.0	0.141 (0.058)	1.3

[a] SD = standard deviation

[b] CV = coefficient of variation

INTERFERENCES

CLSI EP7-A2 was followed for the interference testing. The interference study was conducted using a “paired difference worst case scenario” approach where these compounds were spiked into fresh sample pools containing either low or high levels of measurand in serum and urine pools.

Bias is the difference in the results between the control sample (without the interferent) and the test sample (contains the interferent) expressed in percent. Bias exceeding 10% is considered interference. Dilution studies were conducted to determine the level at which the spiked substance no longer displayed significant interference. Dilution studies were conducted at two analyte concentrations, if both sample pools show significant interference. This study was conducted as needed for both serum pools.

Approximate Concentration (within 15%) of Analytes in Test Pools			
Analyte	Matrix	Low	High
Magnesium	Serum	1.60 mg/dL	2.60 mg/dL
Magnesium	Urine	2.00 mg/dL	6.00 mg/dL

No interference was detected at the following analyte concentrations.

Interference Testing for Serum

Substance	Substance Test Concentration Common Unit
Hemoglobin	500 mg/dL
Bilirubin, conjugated	30 mg/dL
Bilirubin, unconjugated	30 mg/dL
Lipemia (Intralipid®)	500 mg/dL
EDTA	12.5 mg/dL
Copper	0.50 mg/dL
Calcium	20 mg/dL
Iron	0.50 mg/dL
Zinc	0.25 mg/dL
Acetaminophen	200 mg/dL
Ibuprofen	500 mg/dL

Interference Testing for Urine

Substance	Substance Test Concentration Common Unit
6N HCl	0.01% HCl
Ascorbate	50 mg/dL
Hemoglobin	150 mg/dL
Calcium	20 mg/dL
Conjugated Bilirubin	30 mg/dL
Copper	0.50 mg/dL
Iron	0.50 mg/dL
Zinc	0.25 mg/dL

METHOD COMPARISON

The predicate device selected for the method comparison study was the Dimension Magnesium Flex Reagent Cartridge. Remnant de-identified samples were tested. No patient history information was obtained on these samples. Inclusion/exclusion data criteria are not applicable. The study included native and diluted samples to properly span the assay intervals.

These studies were conducted internally by Siemens Healthcare Diagnostic Inc. R&D organization personnel. The personnel conducting the study were laboratory technicians with training similar to personnel who would conduct the tests in a hospital laboratory setting. They were trained on the operation of both the device and the predicate device. A split sample method comparison, following EP09-A3, demonstrated good agreement between the Atellica CH Magnesium (Mg) and the predicate Dimension Magnesium Flex Reagent Cartridge (Mg) assay with patient samples.

The results across the full assay intervals were analyzed using Deming regression. One replicate of each sample was tested and used in the analysis.

Specimen Type	Comparison Assay (x)	N	r	Regression Equation	Sample Range (on the Dimension RxL)
Serum	Dimension RxL Mg	108	0.996	y = 0.94x + 0.09 mg/dL (0.04 mmol/L)	0.48-5.16 mg/dL (0.20 - 2.12 mmol/L)
Urine	Dimension RxL Mg	100	0.998	y = 0.96x – 0.06 mg/dL (0.02 mmol/L)	1.10-13.22 mg/dL (0.45 - 5.43 mmol/L)

MATRIX EQUIVALENCY

Due to the difficulty with obtaining matched serum and plasma magnesium samples across the measuring interval, an additional method comparison study was conducted with lithium heparin plasma samples on Atellica CH Magnesium (Mg) and Dimension Magnesium Flex Reagent Cartridge. Some samples were diluted to obtain samples spanning the assay measuring interval. The table below summarizes the Deming linear regression statistics. One replicate of each sample was tested and used in the analysis.

Specimen Type	Comparison Assay (x)	N	r	Regression Equation	Sample Range (on the Dimension RxL)
Lithium heparin plasma	Dimension RxL Mg	109	0.998	y = 0.97x + 0.09 mg/dL (0.04 mmol/L)	0.50-5.05 mg/dL (0.21 – 2.08 mmol/L)

EXPECTED VALUES

Reference intervals for healthy adults were verified on the Atellica CH Analyzer in accordance with CLSI Document EP28-A3c. As with all in vitro diagnostic assays, each laboratory should determine its own reference interval for the diagnostic evaluation of patient results. Consider these values as guidance only.

Group	**Specimen type**	**Reference Interval common unit (SI unit)**
Adults	Serum/plasma[1]	1.60 to 2.60 mg/dL (0.66 to 1.07 mmol/L)
Adults	Urine[2]	24 to 255 mg/24 hour (0.99 to 10.45 mmol/24 hour)

Wu AHB. *Tietz Clinical Guide to Laboratory Tests*. 4th ed. Philadelphia, PA: WB Saunders Co; 2006:706.

1. Pesce, A.J. and Kaplan, L.A., Methods in Clinical Chemistry, C.V. Mosby Co., St. Louis, 1987.

EXTENDED MEASURING INTERVAL

The Mg assay parameters support both serum/plasma and urine extended ranges 2x the upper measuring intervals. Two-fold manual dilutions of 5 serum pools and 5 urine pools were made with CH Diluent, and both the undiluted and diluted pools were processed with N=5 replicates. The serum/plasma extended measuring interval is up to 10 mg/dL. The urine extended measuring interval up to 28 mg/dL.

STANDARDIZATION

Magnesium values are traceable to Atomic Absorption reference method which is calibrated with NIST SRM 929 reference material. SRM909 reference material from the National Institute of Standards and Technology (NIST) was processed with N=5 replicates with 3 reagent lots of Atellica CH Magnesium (Mg) and the mean results were compared to the target value. All results recover within ± 5.0% of the expected value.

CONCLUSION

The Atellica CH Magnesium (Mg) is substantially equivalent to the Dimension Magnesium Flex Reagent Cartridge in principle and performance based on the similarity of device designs and function demonstrated through method comparison and other performance attributes.