510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE

A. 510(k) Number:

k162399

B. Purpose for Submission:

New Device

C. Measurand:

Magnesium

D. Type of Test:

Quantitative, photometric assay

E. Applicant:

Siemens Healthcare Diagnostics, Inc.

F. Proprietary and Established Names:

Atellica CH Magnesium (Mg)

G. Regulatory Information:

1. Regulation section:

   CFR 862.1495, Magnesium test system

2. Classification:

   Class I, reserved

3. Product code:

   JGJ

4. Panel:

   Clinical Chemistry

H. Intended Use:

1. Intended use(s):

   See Indications for use below.

2. Indication(s) for use:

   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).

3. Special conditions for use statement(s):

   For *in vitro* diagnostic use.

   For Professional use.

4. Special instrument requirements:

   Atellica CH Analyzer

I. Device Description:

The Atellica CH Magnesium (Mg) reagents are liquid packaged in two separate reagent packs with two wells each. The saleable package contains 3 of each of the 2 packs described. These packs include a preserved Tris buffer and a preserved Xylidyl blue (0.84 mmol/L) reagent.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Dimension Magnesium Flex Reagent Cartridge

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

   k861700

3. Comparison with predicate:

Similarities		
Item	**Candidate Device** Atellica CH Magnesium (Mg)	**Predicate Device** Dimension Magnesium Flex Reagent Cartridge (k861700)
Intended Use	The Atellica CH Magnesium (Mg) assay is for in vitro diagnostic use in the quantitative determination of magnesium	Same
Sample Type	Serum, Lithium Heparin plasma, and urine	Same
Expected Values	Urine : 24-255 mg/24 hr	Urine: Same
Traceability	NIST SRM 929	Same

Differences		
Item	**Candidate Device** Atellica CH Magnesium (Mg)	**Predicate Device** Dimension Magnesium Flex Reagent Cartridge (k861700)
Device Technology	Xylidyl blue reaction	Methylthymol blue (MTB) complexometric procedure
Expected Values	Serum/plasma 1.60 to 2.60 mg/dL	Serum/Plasma 1.8 – 2.4 mg/dL
Calibration Frequency	60 Days	90 Days
Analytical Measuring Interval	Serum/Plasma: 0.50 to 5.00 mg/dL	Serum/Plasma: 0.0 – 20.0 mg/dL
	Urine: 1.00 to 14.00 mg/dL	Urine: 0.0 – 20.0 mg/dL

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

- CLSI Guideline, EP07-A2 (7-127): Interference Testing in Clinical Chemistry; Approved Guideline
- CLSI Guideline, EP09-A3 (7-245): Measurement Procedure Comparison And Bias Estimation Using Patient Samples; Approved Guideline - Third Edition
- CLSI Guideline, EP05-A3 (7-251): Evaluation of Precision Performance of Quantitative Measurement Methods: Approved Guideline
- CLSI Guideline, EP06-A (7- 93): Evaluation of the Linearity Of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline
- CLSI Guideline, EP17-A2 (7-233): Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures
- CLSI Guideline, 25-A (7-235): Evaluation of Stability of In Vitro Diagnostic

Reagents; Approved Guideline
- CLSI Guideline, EP28-A3 (7-224): Defining, Establishing, And Verifying Reference Intervals In The Clinical Laboratory; Approved Guideline- Third Edition

L. Test Principle:

The Atellica CH Mg assay is based on the modified xylidyl blue reaction. 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.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Precision testing was performed in accordance with CLSI EP05-A3. Precision was tested in 2 replicates per run, two runs per day for 20 days for a total of 80 results with controls, serum and lithium-heparin plasma pools on one instrument. The data are summarized in the following table.

Sample Type	N	Mean mg/dL	Within Run		Within-Lab Precision	
			SD, mg/dL	%CV	SD, mg/dL	%CV
Serum	80	0.78	0.23	3.0	0.31	3.9
Plasma	80	1.51	0.034	2.3	0.051	3.4
Serum QC	80	2.53	0.044	1.7	0.050	2.0
Serum	80	4.22	0.024	0.6	0.0477	1.1
Urine QC1	80	4.61	0.047	0.8	0.097	2.1
Urine QC2	80	11.19	0.108	1.0	0.141	1.3

b. Linearity/assay reportable range:

Linearity was evaluated with 10 samples which spanned the assay measuring interval for serum specimens (0.42-5.61 mg/dL) and 10 samples which spanned the assay measuring interval for urine specimens (0.65-16.08 mg/dL). Each was prepared by mixing high and low concentration samples across the measurement interval as described in CLSI 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 regression analysis, as summarized below.

Sample Type	Serum	Urine
Linear regression equation	0.999x – 0.022	Y = 1.001x + 0.020
Correlation Coefficient (r)	0.999	1.000
Mean values of samples tested:	0.42, 0.75, 1.07, 1.72, 2.37, 3.02, 3.67, 4.32, 4.96, 5.61	0.65, 1.61, 2.58, 4.51, 6.43, 8.36, 10.29, 12.22, 14.15, 16.08

This study demonstrated linearity across the claimed measuring ranges: 0.50 to 5.00 mg/dL for serum and plasma specimens and 1.00 to 14.00 mg/dL for urine specimens.

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

Traceability:
The Atellica CH Magnesium calibrators were previously cleared in k050374 and are traceable to the Atomic Absorption reference method, which is calibrated with NIST SRM 929 reference material.

Stability:
Real time stability protocols and acceptance criteria for the Atellica CH Magnesium reagents were reviewed and appear to support a closed vial storage claim of 12 months at 2-8 C^o and an onboard shelf life claim of 14 days at 2-8 C^o. Stability studies are ongoing.

d. *Detection limit:*

The Limit of Blank (LoB), Limit of Detection (LoD), and Limit of Quantitation (LoQ) were evaluated in accordance with CLSI EP17-A2. Studies were performed in the following manner.

To calculate the Limit of Blank (LoB), four samples with no analyte were measured in replicates of five for three days using three reagent lots. To estimate the Limit of Detection (LoD), four samples containing low levels of magnesium were measured in replicates of five for three days using three reagent lots. To estimate the Limit of Quantitation (LoQ), four samples containing low levels of magnesium were measured in replicates of five for three days using three reagent lots on one instrument.

The detection limit study results are summarized below:

Sample Type	Serum, mg/dL	Urine, mg/dL
LoB	0.00	0.00
LoD	0.02	0.04
LoQ	0.46	0.57

The detection limit studies support the claimed measuring range of 0.50 – 5.0 mg/dL for serum and plasma samples, and 1.00 – 14.0 mg/dL for urine samples.

e. *Analytical specificity:*

The Atellica CH Magnesium (Mg) reagent cartridge was evaluated for interferences according to CLSI EP7-A2. Potential interfering compounds were spiked into fresh serum or urine sample pools containing either low or high levels of magnesium. Bias was defined as the difference in the results between the control sample (without the interferent) and the test sample (contains the interferent) expressed in percent. The sponsor considered interference as bias exceeding 10%.

The highest concentration of substances tested that did not cause significant interference is summarized in the tables below:

Interference Testing for Serum:

Substance	Highest concentration tested that did not show significant interference
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	Highest concentration tested that did not show significant interference
6 N HCl	0.01% HCl
Ascorbate	50 mg/dL
Hemoglobin	150 mg/dL
Calcium	20 mg/dL
Conjugated Bilirubin	30 mg/dL
Unconjugated Bilirubin	15 mg/dL
Copper	0.5 mg/dL
Iron	0.5 mg/dL
Zinc	0.25 mg/dL

The sponsor has stated the following limitations in the labeling*:*

- Do not use hemolyzed samples. Because Mg concentrations are 3 times higher in red blood cells than in serum, hemolyzed samples may give spuriously elevated magnesium results. Bias from hemolysis may vary due to individual sample variations in intracellular magnesium.
- Hemoglobin concentrations above 500 mg/dL may result in a positive bias in serum/plasma specimens. Hemoglobin at 750 mg/dL increases the magnesium result in serum/plasma at 1.60 mg/dL by 13%.
- Unconjugated bilirubin concentrations above 15 mg/dL may result in a positive bias in urine specimens. Unconjugated bilirubin at 30 mg/dL increases the magnesium result in urine at 2.00 mg/dL by 11%.
- EDTA concentrations above 12.5 mg/dL may result in a negative bias in serum/plasma specimens. EDTA at 25 mg/dL decreases the magnesium result in serum/plasma at 1.60 mg/dL and 2.60 mg/dL by -15%.
- Zinc concentrations above 0.25 mg/dL may result in a positive bias in serum/plasma specimens. Zinc at 0.5 mg/dL increases the magnesium result in serum/plasma at 1.60 mg/dL by 19%. Zinc at 0.5 mg/dL increases the magnesium result in serum/plasma at 2.60 mg/dL by 14%.

2. Comparison studies:

a. Method comparison with predicate device:

The comparator device selected for the method comparison study was the Dimension Magnesium Flex Reagent Cartridge. Serum, lithium heparin plasma, and urine samples were tested. The study included native and diluted samples spanning the claimed assay intervals. For serum, 8 samples were diluted and the remainder were native. For lithium heparin plasma, 8 samples were diluted and the remainder were native. For urine, no samples were diluted; all were native. For all tests, native samples made up more than 90% of the sample pool.

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	N	R	Regression Equation	Sample Range Dimension Magnesium Flex (mg/dL)
Serum	108	0.996	Y = 0.94x + 0.09	0.48-5.16
Lithium Heparin Plasma	109	0.998	Y = 0.97x + 0.09	0.50-5.05
Urine	100	0.998	Y = 0.96x – 0.06	1.10-13.22

b. Matrix comparison:

Not applicable. Please see sections M.1.a, M.1.b,M.1.d, M.1.e, and M.1.2.a, demonstrating the performance of the claimed sample types (serum, lithium

heparin plasma, and urine) for this device.

3. Clinical studies:

   Not Applicable.

4. Clinical cut-off**:**

   Not applicable

5. Expected values/Reference range:

   Reference intervals are based on literature (see table below). In addition, the reference intervals were verified using 20 healthy adults 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]	1.6 - 2.6 mg/dL (0.66 to 1.07 mmol/L)
Adults	Urine[2]	24 - 255 mg/24 hour (0.99 - 10.45 mmol/24 hour)

1. Wu AHB. *Tietz Clinical Guide to Laboratory Tests*. 4th ed. Philadelphia, PA: WB Saunders Co; 2006:706.
2. Pesce, A.J. and Kaplan, L.A., Methods in Clinical Chemistry, C.V. Mosby Co., St. Louis, 1987.

N. Proposed Labeling:

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

O. Conclusion:

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