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

A. 510(k) Number:

k181748

B. Purpose for Submission:

Addition of a new matrix (urine) to a previously cleared assay.

C. Measurand:

Magnesium

D. Type of Test:

Quantitative, enzymatic assay

E. Applicant:

Abbott Laboratories

F. Proprietary and Established Names:

Magnesium

G. Regulatory Information:

1. Regulation section:

   CFR 862.1495, Magnesium test system

2. Classification:

   Class I, reserved

3. Product code:

   JGJ

4. Panel:

   Chemistry (75)

H. Intended Use:

1. Intended use(s):

   See indications for use below.

2. Indication(s) for use:

   The Magnesium assay is used for the quantitation of magnesium in human serum, plasma, or urine on the ARCHITECT c8000 System.

   Magnesium measurements are used in the diagnosis and treatment of hypomagnesemia (abnormally low plasma levels of magnesium) and hypermagnesemia (abnormally high plasma levels of magnesium).

3. Special conditions for use statement(s):

   For *in vitro* diagnostic use only.
   For prescription use only.

4. Special instrument requirements:

   ARCHITECT c8000 Analyzer

I. Device Description:

The magnesium assay consists of 2 ready to use reagent solutions (R1 and R2). The R1 reagent contains isocitrate dehydrogenase at a concentration of 2.2 U/mL and D-isocitrate potassium salt with a concentration of 1.47 mg/mL. The R2 reagent contains NADP with a concentration of 8.37 mg/mL.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Roche Magnesium Gen.2

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

   k983416

3. Comparison with predicate:

Similarities		
Item	Candidate Device Magnesium LN 3P68 (k181748)	Predicate Device Roche Magnesium Gen. 2 (k983416)
Intended Use	For the quantitation of magnesium in serum, plasma, or urine.	Same
Analysis Medium	Aqueous solution	Same
Used on Automated Chemistry Analyzers?	Yes	Same
Reference Range - Urine	24-hour 72.9 to 121.5 mg/day	Same
Sample types	Serum, plasma, or urine	Same
Calibrators	Two levels	Same

Differences		
Item	Candidate Device Magnesium LN 3P68 (k181748)	Predicate Device Roche Magnesium Gen. 2 (k983416)
Device Technology	Enzymatic quantitative method	Colorimetric photometric method
Assay Range (urine)	1.81 to 26.35 mg/dL (0.74 to 10.85 mmol/L)	1.36 to 26.7 mg/dL (0.56 11.0 mmol/L)
Traceability	NIST SRM 956	AAS method
Controls	Two levels	Four levels

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

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

- CLSI EP06-A *Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline*

- CLSI EP05-A2 *Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline—Second Edition*

- CLSI EP07-A2, *Interference Testing in Clinical Chemistry; Approved Guideline-Second Edition*

L. Test Principle:

Magnesium present in the sample is a cofactor in an enzymatic reaction with isocitrate dehydrogenase. The rate of increase in absorbance at 340 nm, due to the formation of NADPH, is directly proportional to the magnesium concentration.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

Analytical performance for serum and plasma was cleared under k173294. Analytical performance for urine is presented below.

a. Precision/Reproducibility:

Precision was evaluated according to the CLSI EP05-A2 guideline. Precision testing included 2 commercially available urine-based controls (Control 1 and 2) and 3 contrived urine pools (A, B, and C). Each sample was tested in 2 replicates per run, 2 runs per day for 20 days for a total of 80 replicates per sample. The results from the precision study are summarized in the table that follows:

Sample	n	Mean (mg/dL)	Within Run		Total	
			SD	%CV	SD	%CV
Control 1	80	4.54	0.055	1.2	0.058	1.3%
Control 2	80	11.17	0.114	1.0	0.149	1.3%
Urine Pool A	80	1.89	0.036	1.9	0.045	2.4%
Urine Pool B	80	5.7	0.096	1.7	0.102	1.8%
Urine Pool C	80	22.51	0.394	1.7	0.394	1.8%

b. Linearity/assay reportable range:

Linearity was evaluated according to CLSI EP06-A guideline. The linearity of the Magnesium assay was evaluated by preparing a series of 12 sample pools with analyte concentrations of 0.98, 1.47, 1.97, 3.09, 5.12, 9.27, 13.60, 18.04, 22.51, 27.02, 31.95 and 36.34 mg/dL. Samples were tested in four replicates with 2 reagent lots on 1 ARCHITECT c8000 System. The linear regression results of a representative sample set are as follows:

$y = 1.03 x - 0.20$, $r = 1.00$

The results of the linearity study supports the claimed analytical measuring interval of 1.81 to 26.35 mg/dL.

Automatic dilution:

The sponsor evaluated the automatic dilution (auto-dilution) protocol using a 1:3 dilution factor. Two urine pools were prepared to magnesium concentrations above 26.35 mg/dL and evaluated in replicates of 12 using the on board auto-dilution on the ARCHITECT c8000 System. Results obtained using auto-dilution were found to be less than 10% difference from the expected values. The results of this study support the sponsor's labeling claims that, using the Automated Dilution Protocol, samples with magnesium concentrations above 26.35 mg/dL may be auto-diluted 1:3 on board the analyzer.

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

Traceability:
The assigned values for Magnesium are traceable to NIST SRM 956 reference material.

d. *Detection limit:*

Detection limit studies were carried out in accordance with the CLSI EP17-A2 guideline.

The limit of blank (LoB) was determined by running 4 blank samples in 10 replicates per run and 2 runs per day for 3 days using 2 reagent lots on one ARCHITECT c8000 System. The 95^{th} percentile of the zero-analyte sample concentration was calculated and considered to the estimated LoB.

The limit of detection (LoD) was determined by running ten low level samples in 10 replicates per run and 2 runs per day for 3 days using 2 reagent lots on one ARCHITECT c8000 System. LoD was calculated based on the following equation: $LoD = LoB + Cp \times SD_L$, where Cp is multiplier to give the 95^{th} percentile of a normal distribution and SD_L is the pooled SD).

The limit of quantitation (LoQ) was determined by running ten low level samples in 10 replicates per run and 2 runs per day for 3 days using 2 reagent lots on one ARCHITECT c8000 System. LoQ was defined as the lowest concentration that yielded an estimated total error less than or equal to the total allowable error of 22.0%.

The results for the urine application of the assay (new claim) are summarized in the table below:

	mg/dL
LoB	0.04
LoD	0.09
LoQ	0.75

The detection limit study supports the claimed measuring range of 1.81 mg/dL to 26.35 mg/dL.

e. Analytical specificity:

An interference study was performed based on the CLSI EP07-A2 guideline. Interference effects were assessed by dose response and paired difference methods. For each potentially interfering substance, 2 base pools were prepared using human urine and magnesium chloride at magnesium levels of approximately 5 mg/dL and 14 mg/dL. Bias is defined as the difference in the results between the control sample (without interference) and the test sample (contains interferent) expressed in percent. Difference exceeding 10% is considered significant interference by the sponsor.

The highest concentration of substance tested that did not cause significant interference for magnesium samples is summarized in the table below.

Substance	Highest concentration tested that did not show significant interference
Albumin	64 mg/dL
Ascorbic acid	200 mg/dL
Bilirubin (conjugated)	59.5 mg/dL
Calcium	26 mg/dL
Glucose	1220 mg/dL
Hemoglobin	1200 mg/dL
Phosphorus	307 mg/dL
Boric Acid	1000 mg/dL
Hydrochloric Acid	3.0 mL/dL
Copper	21.6 µg/dL
Zinc	3504 µg/dL
Iron	0.6 mg/dL

The following statements have been included in the Limitations of the Procedure section of the package insert:
- The Magnesium assay is susceptible to interference from hemoglobin.
- Do not use acetic acid, nitric acid, and sodium fluoride as urine preservatives.
- Do not use more than 2.5 mL 6N HCl per 100 mL of urine. Excess hydrochloric acid may cause elevated results with this methodology.
- Do not exceed 10 g/L boric acid.

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

A method comparison study was conducted by testing a total of 118 patient urine samples (106 native and 12 spiked urine samples) with magnesium concentrations from 1.82-23.25 mg/dL, as determined on the predicate device. Three aliquots from each sample were prepared to characterize bias under different testing conditions: (a) without acidification to represent random urine samples with no preservative added, (b) with acidification to pH < 2 (pH 1.8 – 1.9) using 6N HCl to represent samples with added preservative, or (c) with acidification to pH ~1 (pH 0.9 – 1.1) using 6N HCl, as per predicate device instructions. Results obtained for each aliquot (a), (b), and (c) on the candidate device were compared to results obtained for aliquot (c) using the predicate device (Roche Magnesium Gen.2).

The results of the regression analyses are summarized in the tables below:

No acidification

N	Concentration Range Tested	Slope	Intercept	R
118	1.82-23.25 mg/dL (predicate)	1.04	-0.10	1.00

pH < 2

N	Concentration Range Tested	Slope	Intercept	R
118	1.82-23.25 mg/dL (predicate)	1.08	-0.14	1.00

pH ~ 1

N	Concentration Range Tested	Slope	Intercept	R
118	1.82-23.25 mg/dL (predicate)	1.05	-0.13	1.00

b. Matrix comparison:

Serum, plasma, and urine samples are acceptable to be used with this assay. Serum and plasma were previously cleared under k173294. Please refer to the method comparison studies in M.2. a. above for urine.

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:

Reference intervals are based on literature[1] (see table below). The sponsor recommends that each laboratory should determine its own reference range based upon its locale and population characteristics.

Urine

	Range (mg/day)
24 Hour	72.9 to 121.5

[1]Wu AHB. *Tietz Clinical Guide to Laboratory Tests*. 4th ed. Philadelphia, P.A: WB Sauders; 2006: 706 -708.

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Parts 801 and 809, as applicable.

O. Conclusion:

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