September 12, 2018

Abbott Laboratories
Mark Littlefield
Assoc. Director, Regulatory Affairs
1921 Hurd Drive
Irving, TX 75038

Re: K181748
Trade/Device Name: Magnesium
Regulation Number: 21 CFR 862.1495
Regulation Name: Magnesium test system
Regulatory Class: Class I, reserved
Product Code: JGJ
Dated: June 28, 2018
Received: July 2, 2018

Dear Mark Littlefield:

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. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. 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 Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/CombinationProducts/GuidanceRegulatoryInformation/ucm597488.htm); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

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 comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/) and CDRH Learn (http://www.fda.gov/Training/CDRHLearn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (http://www.fda.gov/DICE) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Kellie B. Kelm -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: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
k181748

Device Name
Magnesium

Indications for Use *(Describe)*
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).

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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510(k) Summary (Summary of Safety and Effectiveness)

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

The assigned 510(k) number is: k181748.

1. Applicant Name

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Date Summary prepared: August 28, 2018

2. Device Name

Trade Name: Magnesium
Device Classification: Class I Reserved
Classification Name: Magnesium Reagent
Governing Regulation: CFR 862.1495
Product Code: JGJ

3. Predicate Device

Roche Magnesium Gen.2 (510(k) number k983416)

4. Description of Device

The Magnesium reagent kit contains:

Component	3P68-22	3P68-32
Number of Tests	670* (urine)	2540* (urine)
Reagent 1 (R1)	5 × 39 mL	10 × 71 mL
Reagent 2 (R2)	5 × 11 mL	10 × 18 mL

* Calculation is based on the minimum reagent fill volume per kit and may vary depending on the mix of urine samples.

Reagent	Reactive Ingredients	Concentration
Reagent 1	Isocitrate dehydrogenase	2.2 U/mL
	D-Isocitrate potassium salt	1.47 mg/mL
Reagent 2	NADP	8.37 mg/mL
Inactive Ingredients: R1 and R2 contain sodium azide (0.1%) as a preservative.		

Principles of the Procedure

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.

$$\text{D-isocitric acid} + \text{NADP} \xrightarrow[Mg^{2+}]{\text{Isocitrate dehydrogenase}} \text{2-oxoglutarate} + CO_2 + \text{NADPH}$$

Methodology: Enzymatic

5. Intended Use of the Device

The Magnesium assay is used for the quantitation of magnesium in human serum, plasma, or urine on the ARCHITECT *c*8000 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).

6. Comparison of Technological Characteristics

The Magnesium assay is used for the quantitation of magnesium in human serum, plasma, or urine on the ARCHITECT *c*8000 System.

A comparison of the candidate assay (Magnesium, List No. 3P68) and the predicate assay (Roche Magnesium Gen.2 REF 06407358 190) is presented in the table on page 4.

Comparison of Magnesium (LN 3P68) to Roche Magnesium Gen.2

Assay Characteristics	Magnesium LN 3P68	Roche Magnesium Gen.2
Analyte Measured	Magnesium	Same
Intended Use	The Magnesium assay is used for the quantitation of magnesium in human serum, plasma, or urine on the ARCHITECT *c*8000 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).	In vitro test for the quantitative determination of magnesium in human serum, plasma and urine on Roche/Hitachi cobas c systems.
Assay 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.	Colorimetric endpoint method. In alkaline solution, magnesium forms a purple complex with xylidyl blue, diazonium salt. The magnesium concentration is measured photometrically via the decrease in the xylidyl blue absorbance.
Detection of Analyte	Rate-up Enzymatic	Endpoint
Samples	Urine	Serum, plasma or urine
Assay Range - Urine	1.81 mg/dL to 26.35 mg/dL (0.74 mmol/L to 10.85 mmol/L)	1.36 to 26.7 mg/dL (0.56‑11.0 mmol/L)
Reference Range - Urine	<u>Range (mg/day)</u> 24 hour 72.9 to 121.5	Same
Analysis Medium	Aqueous solution	Same
Use of Calibrators	Yes	Yes
Use of Controls	Yes	Yes

7. Summary of Performance Testing

Limit of Blank, Limit of Detection, and Limit of Quantitation

The study was performed based on guidance from the Clinical and Laboratory Standards Institute (CLSI) document EP17-A2. LoB was determined using 4 obtained saline samples (zero-analyte samples). LoD and LoQ were determined using low-level analyte samples prepared from a magnesium standard. Two low-analyte level samples were gravimetrically prepared at each of the following 5 target concentration levels: 0.390, 0.780, 1.285, 1.560, 3.130 mg/dL. The zero-analyte samples were tested in replicates of 10. The low-analyte samples were tested in replicates of 10. Testing was performed over 3 days, two runs per day, using 2 lots of reagent, 1 lot of calibrators, and 1 lot of commercially available controls on 1 ARCHITECT *c*8000 System.

The urine application of the Magnesium assay, had an LoB of 0.04 mg/dL, an LoD of 0.09 mg/dL, and an LoQ of 0.75 mg/dL.

Within-Laboratory Precision (20-Day)

Precision was evaluated using the following control materials.

- Level 1: Bio-Rad Liquichek Urine Chemistry Control Level 1
- Level 2: Bio-Rad Liquichek Urine Chemistry Control Level 2
- LoQ Urine Pool -Low Mg[*]
- Human Urine Pool - Normal Mg[#]
- Human Urine Pool - Abnormal Mg[$]

[*] LoQ Urine Pool - Low Mg was prepared by diluting Bio-Rad Liquichek Urine Chemistry Control Level 1 with normal saline.
[#] Human Urine Pool – Normal Mg is a pool of human urine specimens.
[$] Human Urine Pool - Abnormal Mg were prepared by spiking normal human urine with a $MgCl_2$ stock solution.

The levels were tested in 2 replicates, 2 times per day (separated by a minimum of 2 hours) for a total of 20 testing days. Testing was performed using 1 lot of reagents, 1 lot of calibrators and 1 lot of commercially available controls on 1 ARCHITECT *c*8000 System.

The evaluation was performed by instrument based on guidance from CLSI document EP05-A2.

The within-laboratory imprecision (within-run, between-run, and between-day) for Magnesium urine was as follows:

- 1.3 %CV for Bio-Rad Level 1
- 1.3 %CV for Bio-Rad Level 2
- 2.4 %CV for LoQ Urine Pool -Low Mg
- 1.8 %CV for Human Urine Pool - Normal Mg
- 1.8 %CV for Human Urine Pool - Abnormal Mg

Interference

The interference study for endogenous substances (albumin, ascorbic acid, bilirubin (conjugated), calcium, glucose, hemoglobin, and phosphorous) and urine preservatives (acetic acid, boric acid, 6N hydrochloric acid, nitric acid, and sodium fluoride) was performed based on guidance from CLSI document EP07-A2. Interference effects were assessed by comparing test samples containing potentially interfering albumin, ascorbic acid, bilirubin (conjugated), calcium, glucose, hemoglobin, phosphorous, acetic acid, boric acid, 6N hydrochloric acid, nitric acid, and sodium fluoride to control level samples.

The control and test level samples were tested in a minimum of 7 replicates using 1 lot of reagents,1 lot of Multiconstituent Calibrator (LN 1E65) and 1 lot commercially available controls on 1 ARCHITECT *c*8000 System. The control and test level samples for a given potential interferent/magnesium level combination were tested in the same run.

Additionally, a cation interference study was performed for copper and zinc.

For the copper and zinc study, solutions of each potential interferent were prepared by spiking urine with stock solutions in order to generate copper and zinc samples with concentrations of approximately 21.6 µg/dL and 3504 µg/L respectively. A control sample (urine) and test level samples were tested in 12 replicates using 1 lot of reagents,1 lot of Multiconstituent Calibrator (LN 1E65) and 1 lot commercially available controls on 1 ARCHITECT *c*8000 System.

For magnesium samples targeted to 5 mg/dL, the assay showed no more than ± 10% interference for the listed substances at the interferent levels indicated in the following table.

Interferent	Interferent Level
Albumin	≤ 64.0 mg/dL
Ascorbic Acid	≤ 200 mg/dL
Bilirubin (Conjugated)	≤ 59.9 mg/dL
Calcium	≤ 26.0 mg/dL
Glucose	≤ 1220 mg/dL
Hemoglobin	≤ 1200 mg/dL
Phosphorous	≤ 307 mg/dL
Boric Acid	≤ 1000 mg/dL
6N Hydrochloric Acid	≤ 3.0 mL/dL
Copper	≤ 21.6 µg/dL
Zinc	≤ 3504 µg/L
Iron	≤ 0.6 mg/dL

For magnesium samples targeted to 14 or 15 mg/dL, the assay showed no more than ± 10% interference for the listed substances at the interferent levels indicated in the following table.

Interferent	Interferent Level
Albumin	≤ 64.0 mg/dL
Ascorbic Acid	≤ 200 mg/dL
Bilirubin (Conjugated)	≤ 59.5 mg/dL
Calcium	≤ 27.0 mg/dL
Glucose	≤ 1237 mg/dL
Hemoglobin	≤ 1200 mg/dL
Phosphorous	≤ 313 mg/dL

Boric Acid	≤ 1000 mg/dL
6N Hydrochloric Acid	≤ 3.0 mL/dL
Copper	≤ 21.6 µg/dL
Zinc	≤ 3504 µg/L
Iron	≤ 0.6 mg/dL

Acetic acid, nitric acid, and sodium fluoride did not meet the evaluation criteria of having a difference within or equal to ± 10% at a target of 5 mg/dL or 15 mg/dL levels of magnesium and will be included in the limitations of the procedure section of the package insert.

Linearity

Linearity was determined based on guidance from Clinical and Laboratory Standards Institute (CLSI) document EP06-A. Three sets of linearity standards were prepared using a magnesium standard and saline (diluent). For each sample set, a low and high sample pool was prepared.

- the low sample pool (Level 1) had a concentration greater than 0.0 mg/dL but below the LoQ and
- the high sample pool (Level 12) was 20 to 30% beyond the highest expected measurement concentration.

A sample set was prepared for each combined magnesium pool. Each sample set consisted of 12 levels at the following magnesium target concentrations: 0.90, 1.43, 1.97, 3.03, 5.16, 9.43, 13.69, 17.95, 22.21, 26.48, 30.74 and 35.00 mg/dL. Levels 1 through 12 for each sample set were tested in a random order in a minimum of 4 replicates using 2 lots reagents and 1 lot each of Multiconstituent Calibrator (LN 1E65) and commercially available controls on 1 ARCHITECT *c*8000 System. All levels in a sample set were tested in the same run.

The urine application of the Magnesium assay was demonstrated to be linear across the range of 1.04 to 36.24 mg/dL, which spans the analytical measuring interval of 1.81 to 26.35 mg/dL.

Measuring Interval

The measuring interval was determined based on the results from 3 studies: Within Laboratory Precision (20-Day); Linearity; and Limit of Blank, Limit of Detection, and Limit of Quantitation.

The analytical measuring interval for the Magnesium assay was determined to be from 1.81 to 26.35 mg/dL.

Method Comparison

The study was performed based on guidance from CLSI document EP09-A3. A total of 118 patient urine specimens were evaluated with the Magnesium (LN 3P68) and Roche Magnesium Gen.2 (REF 06407358 190) assays. Of these samples, 12 of the samples were normal urine specimens spiked with magnesium stock to achieve samples with magnesium concentrations in the range of 15.5 to 26 mg/dL. Three aliquots were prepared and tested:

a) No acidification
b) Acidified using 6N HCl to pH <2 (1.8 to 1.9)
c) Acidified using 6N HCl to pH ~1 (0.9 to 1.1)

Two replicates of each aliquot (a), (b) and (c) were run using the Magnesium (LN 3P68) reagent kit where the first valid replicate was used in the analysis. One replicate of each aliquot (c) was run at UT Southwestern Medical Center (UTSW, Dallas) using Roche Magnesium Gen.2 (REF 06407358 190) reagent.

The urine application of the Magnesium (LN 3P68) assay, which had a regression slope of 1.08 and correlation coefficient (r-value) of 1.00 for urine samples at pH <2 across the measuring interval of the assay, a regression slope of 1.04 and correlation coefficient (r-value) of 1.00 for urine samples with no acidification across the measuring interval of the assay, and a regression slope of 1.05 and correlation coefficient (r-value) of 1.00 for urine samples at pH ~1 across the measuring interval of the assay demonstrated acceptable correlation to the predicate device.

Automated Dilution Protocol

One sample was prepared targeting magnesium concentration of 75 mg/dL and evaluated in replicates of 10 using the autodilution protocol. All samples were tested in the same run using 1 lot of reagents and 1 lot each of commercially available calibrators and controls on one ARCHITECT *c*8000 System.

Magnesium assay results were impacted by not more than ±10% for analyte concentration of 75 mg/dL.

Manual Dilution

Three urine pools were prepared targeting magnesium concentrations of 15, 25, and 40 mg/dL. Endogenous magnesium concentrations were measured in random urine specimens which were then spiked using a concentrated $MgCl_2$ stock to the target concentrations. Each analyte pool was evaluated after 1:2 manual dilution. Dilutions were performed using 0.85% and 0.90% (NaCl) saline. Samples were tested in a minimum of 12 replicates using 1 lot of reagent, 1 lot of Multiconstituent Calibrator (LN 1E65), and 1 lot of commercially available controls on 1 ARCHITECT *c*8000 System. Diluted samples at a given magnesium level were tested in the same run.

Magnesium assay results were impacted by not more than ±10% for analyte concentrations 15, 25, and 40mg/dL when evaluated with a 1:2 manual dilution (using 0.85% or 0.90% saline).

8. Conclusion Drawn from Performance Testing

The results presented in this 510(k) premarket notification demonstrate that the candidate assay (Magnesium, List No. 3P68) performance is substantially equivalent to the predicate assay (Roche Magnesium Gen.2 (REF 06407358 190)).

The similarities and differences between the candidate assay and the predicate assay are presented in the table on page 4. The results presented in this 510(k) provide reasonable assurance that the Magnesium assay is safe and effective for the stated intended use. Any differences between the candidate assay and the predicate assay shown in the tables do not affect the safety and effectiveness of the candidate assay.

There is no known potential adverse effect to the operator when using this device according to the Magnesium package insert instructions.