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

December 16, 2016

ORTHO CLINICAL DIAGNOSTICS
MARLENE HANNA
SR. MANAGER REGULATORY AFFAIRS
100 INDIGO CREEK DRIVE
ROCHESTER, NY 14626

Re: K162020
Trade/Device Name: VITROS Chemistry Products Cl- Slides
Regulation Number: 21 CFR 862.1170
Regulation Name: Chloride test system
Regulatory Class: II
Product Code: CGZ
Dated: November 9, 2016
Received: November 10, 2016

Dear Marlene Hanna:

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,

Courtney H. Lias -S

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)*
k162020

Device Name
VITROS Chemistry Products Cl- Slides

Indications for Use *(Describe)*

Rx. For in vitro diagnostic use only.
VITROS Chemistry Products Cl- Slides quantitatively measure chloride (Cl-) concentration in serum, plasma, and urine using VITROS Chemistry and Integrated Systems. Chloride measurements are used in diagnosis and treatment of electrolyte and metabolic disorders such as cystic fibrosis and diabetic acidosis.

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: k162020

VITROS Chemistry Products Cl- Slides: A summary of 510(k) safety and effectiveness information in accordance with the requirements of 21 CFR 807.92.

Submitter Information	
Name	Ortho-Clinical Diagnostics, Inc.
Address	100 Indigo Creek Drive Rochester, New York 14626
Phone number	585-453-4041
Fax number	585-453-3368
Email	Marlene.hanna@orthoclinicaldiagnostics.com
Establishment Registration	1319809
Name of contact person	Marlene Hanna , RAC
Date prepared	December 12, 2016
Name of devices	
Trade or proprietary name	VITROS Chemistry Products Cl^- Slides
Common or usual name	Chloride test
Classification name	Chloride test system
Classification panel	Chemistry
Regulation	21 CFR 862.1170
Product Code(s)	CGZ
Legally marketed device to which equivalence is claimed	The VITROS Chemistry Products Cl^- slides are substantially equivalent to the Siemens ADVIA® Chloride (CL) assay, cleared on May 21, 1999 (k990346).
Device description	The VITROS® Chemistry Products Cl^- Slide assay is performed using the VITROS® Chemistry Products Cl^- Slide and the VITROS® Chemistry Products Calibrator Kit 2 on the VITROS Chemistry Systems. The VITROS® Cl- Slide is a multilayered, analytical element coated on a polyester support that uses direct potentiometry for measurement of chloride ions. All reactions necessary for a single quantitative measurement of chloride take place within the multi-layered analytical element of a VITROS® Chemistry Products Cl^- slide. The slide consists of two ion-selective electrodes, each containing a protective layer, a silver layer and a silver chloride layer coated on a polyester

	support. The protective layer inhibits interference from normal levels of bromide and uric acid.
Indications For Use	Rx. For *in vitro* diagnostic use only .VITROS® Chemistry Products Cl^- Slides quantitatively measure chloride (Cl^-) concentration in serum, plasma, and urine using VITROS® Chemistry Systems. Chloride measurements are used in the diagnosis and treatment of electrolyte and metabolic disorders such as cystic fibrosis and diabetic acidosis.

Comparison with Predicate Device:

Characteristic	**Predicate Device Siemens ADVIA Chloride (CL) assay (k990346)**	**New/Modified Device VITROS Chemistry Products Cl^- Slides**
Indications for Use	For in vitro diagnostic use in the quantitative determination of chloride in human serum, plasma and urine on the ADVIA Chemistry systems.	Rx. For *in vitro* diagnostic use only .VITROS® Chemistry Products Cl^- Slides quantitatively measure chloride (Cl^-) concentration in serum, plasma, and urine using VITROS® Chemistry Systems. Chloride measurements are used in the diagnosis and treatment of electrolyte and metabolic disorders such as cystic fibrosis and diabetic acidosis.
Sample Types	Serum, Plasma, Urine	Same
Reaction type	Potentiometric	Same
Method Principle	Ion Selective Electrode (ISE), Indirect (diluted)	Ion Selective Electrode (ISE), Direct (undiluted)
Measuring Range for Urine	15-400 mmol/L	15-300 mmol/L
Expected Values for Urine	110 – 250* mmol/day	Same

*Wu, Alan H.B. Tietz Clinical Guide to Laboratory Tests. 4th ed. Saunders Elsevier, St. Louis, MO: 2006, 234-241.

Performance Summary:

Substantial Equivalence was demonstrated by testing several performance characteristics including method comparison, precision, detection limits, linearity, measuring range, expected values, and interfering substances.

Method Comparison:

Method Comparison testing followed CLSI Protocol EP09-A3, *Measurement Procedure Comparison and Bias Estimation Using Patient Samples (2013)*[1]. A total of 130 human urine samples were tested. The 130 samples were measured with VITROS Cl^- Slides and a predicate method, Siemens Chloride (CL) method for ADVIA® Chemistry Systems. Of the 130 samples tested 125 were within the measuring range of both the VITROS Cl^- assay (15-300 mmol/L) and the Siemens Chloride assay (15 – 400 mmol/L).

The relationship between the VITROS Cl^- Slides method and the Predicate method (Siemens Chloride) based on data from 125 samples using slide lot 4005-0626-9198 on the VITROS 5,1 FS Chemistry System is as follows:

VITROS Cl^- Slides = 0.996 x [Siemens] - 4.7 mmol/L with a correlation coefficient (r) of 0.998.

Precision:

The evaluation was performed according to CLSI protocol EP05-A: *Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline – Third Edition* [2] . The data generated for the reported claims are pooled estimates of two reagent lots. Precision results for each slide lot were evaluated independently, but data from two lots were pooled per the procedure described in CLSI EP05-A3[2]. Two runs were performed on each of 20 non-consecutive days. Each run consisted of four precision samples run in duplicate. Two of the evaluation samples were commercially available control materials in a human urine matrix, and two samples were prepared in a polyvinylpyrrolidone (PVP) matrix to challenge the ends of the proposed measuring range. Runs within day were separated by at least two hours. A fresh sample aliquot was used for each run. Data were screened for gross outliers according to the statistical outlier test in CLSI EP05-A3[2]. No outlier data points were observed.

Precision for VITROS Cl^- Slides for use with Urine

	Conventional and SI Units (mmol/L)								
	Mean	Repeatability		Within-Day		Within Lab		No.	No.
System	(mmol/L)	SD	CV%	SD	CV%*	SD	CV%**	Observ.	Days
5,1 FS	18	0.2	1.2	0.6	3.3	0.8	4.2	80	20
	105	0.5	0.4	0.5	0.5	0.7	0.6	80	20
	191	0.6	0.3	0.7	0.4	1.2	0.6	80	20
	282	0.9	0.3	1.1	0.4	2.6	0.9	80	20

* Within Day precision was determined using two runs per day with two replications.
** Within Lab precision was determined using a single lot of slides and calibrating weekly.

Limit of Blank (LoB), Limit of Detection (LoD), Limit of Quantitation (LoQ):

The Limit of Blank (LOB), Limit of Detection (LOD), and Limit of Quantitation (LOQ) of the VITROS Cl^- assay were determined according to CLSI EP17-A2: *Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures*[3]. The following limits were determined:

LoB* (mmol/L)	LoD** (mmol/L)	LoQ*** (mmol/L)
1.1	2.2	5

* Limit of Blank, or the highest value likely to be observed with a sample containing no analyte, replaces the term "analytical sensitivity."
** Proportions of false positives (α) and false negatives (β) were less than 5%; based on 180 determinations, with 4 blank and 6 low-level samples.
*** The level of imprecision used to accept the LoQ was within 5%

Linearity:

The linearity evaluation was performed following CLSI EP06-A, *Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approac*h*; Approved Guideline*[4], across one slide lot on one VITROS 5,1 FS Chemistry System. A commercial urine linearity panel was used to evaluate linearity of the VITROS Cl^- Slides for urine. The low pool had an estimated concentration near 0 mmol/L. The high pool had an estimated concentration of 320 mmol/L. The commercial panel contained 5 additional levels prepared from admixtures of the high and low pools. An additional four levels targeting lower chloride concentrations were prepared from the intermediate levels for a total of 11 levels. Analysis by linear regression indicated that the assay is linear across the determined range of 12 to 320 mmol/L, which supports the proposed measuring range of 15 to 300 mmol/L.

Results of linearity study:

Linear Regression Equation	**Correlation Coefficient, R^2**
Y= 1.0044x -1.37	0.9995

Measuring Range and Expected Results:

The measuring range of the VITROS Cl^- Slides assay for urine was determined by assessing the limit of quantitation and linearity results obtained from three slide lots, and was limited by the lower measuring range of the predicate method, 15 mmol/L. The measuring range for the VITROS Cl^- Slides assay for urine is 15 to 300 mmol/L. The expected values for random urine samples were established for VITROS Cl^- Slides per CLSI EP28-A3c. *Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline—Third Edition*[5]. An in-house collection of 135 normal patient samples were evaluated using two slide

lots on one VITROS 5,1 FS Chemistry System. The expected values for random urine are 17 to 209 mmol/L.

The expected value for 24 hour urine samples, 110- 250 mmol/day, was based on a literature reference, Wu, Alan H.B. *Tietz Clinical Guide to Laboratory Tests*. 4th ed. Saunders Elsevier, St. Louis, MO: 2006, 234-241[6].

Interfering Substances:

The VITROS Chemistry Products Cl^- Slides assay was screened for interfering substances following CLSI Protocol EP07-A2 *Interference Testing in Clinical Chemistry; Approved Guideline – Second Edition*[7].

Specimens Not Recommended

Urine with the following preservatives:

- Hydrochloric acid (12N HCl)
- 10% Thymol in isopropanol

Known Interferences

Bromide and iodide from therapeutic drugs and ointments may cause a positive bias of approximately 5 mmol/L and 6 mmol/L, respectively, for each mmol of halide. Normal physiological levels of bromide and iodide do not interfere.

Interference claims were cited when the observed bias exceeded the acceptance criteria for bias. Substances exhibiting bias less than the stated acceptance criteria have been cited as substances that do not interfere. It is possible that other interfering substances may be encountered. These results are representative; however results may differ somewhat due to test-to-test variation. The degree of interference at concentrations other than those listed may not be predictable.

Specificity

Substances that Do Not Interfere

The substances listed in the table below were tested with the VITROS Cl^- Slides for urine according to CLSI Protocol EP07-A2[7], and found not to interfere at the test concentrations shown. The substances were tested at chloride concentrations of approximately 20 and 180 mmol/L and found not to interfere, bias < 5%.

Substance Tested	Highest Concentration with no Significant Interference	
	Conventional Units	SI Units
Acetaminophen	50 mg/dL	3.31 mmol/L
Allopurinol	24 mg/dL	1.8 mmol/L
Amiloride HCl	1.5 mg/dL	56 µmol/L
Ascorbic Acid	180 mg/dL	10 mmol/L
Bilirubin, conjugated	7.25 mg/dL	91 µmol/L
Boric Acid	670 mg/dL	108 mmol/L
Boric Acid + Sodium Formate	670 mg/dL + 335 mg/dL	108 mmol/L + 49 mmol/L
Carbenicillin Disodium	300 mg/dL	7.1 mmol/L
Ciprofloxacin	1.16 mg/dL	35 µmol/L
Furosemide	9 mg/dL	0.27 mmol/L
Gentamicin Sulfate	1.5 mg/dL	10 µmol/L
Glacial Acetic Acid	10 mL/L	175 mmol/L
Glutathione	1.0 mg/dL	33 µmol/L
Hemoglobin	1000 mg/dL	0.16 mmol/L
Ibuprofen	50 mg/dL	2.42 mmol/L
Intralipid	2524 mg/dL	2.524 g/L
Levodopa	67 mg/dL	3.4 mmol/L
Lithium Carbonate	236.5 mg/dL	29.6 mmol/L
Mannitol	60 mg/dL	3.3 mmol/L
N-Acetyl Cysteine	166.2 mg/dL	10 mmol/L
Ofloxacin	32 mg/dL	0.89 mmol/L
pH	4 - 9	N/A
Penicillin G	59.7 mg/dL	1.7 mmol/L
Phenazopyridine HCl	19.5 mg/dL	0.91 mmol/L
Prednisone	230 µg/dL	6.4 µmol/L
Ranitidine HCl	670 µg/dL	19 µmol/L
Sodium Cefoxitin	340 mg/dL	7.57 mmol/L
Sodium Fluoride	500 mg/dL	119 mmol/L
Sodium Formate	335 mg/dL	49 mmol/L
Sodium Oxalate	60 mg/dL	4.5 mmol/L
Specific Gravity*	1.00 - 1.04	N/A
Tetracycline HCl	70 mg/dL	1.58 mmol/L
Toluene	1.3 mL/L	12 mmol/L

* Specific gravity was evaluated using three patient samples with chloride concentrations of 50 - 67 mmol/L

Conclusion:

The conclusions drawn from the nonclinical tests (discussed above) demonstrate the VITROS Chemistry Products Cl^- Slides are as safe, effective, and perform as well as the predicate device. The information submitted in the premarket notification is complete and supports a substantial equivalence decision.

References

1. CLSI. *Measurement Procedure Comparison and Bias Estimate Using Patient Samples; Approved Guideline – Third Edition*. CLSI document EP09-A3-IR [ISBN 1-56238-887-8]. Clinical and Laboratory Standards Institute, 950 West Valley Road, Suite 2500, Wayne, PA 19087 USA, 2013.
2. *Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline – Third Edition.* CLSI document EP05-A3 [ISBN 1-56238-968-8]. CLSI, 950 West Valley Road, Suite 2500, Wayne, PA 19087 USA, 2014.
3. CLSI. *Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline-Second Edition*. CLSI document EP17-A2 (IBSN 1-56238-796-0). Clinical and Laboratory Standards Institute, 950 West Valley Road, Suite 2500, Wayne Pennsylvania 19087 USA, 2012.
4. CLSI. *Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline*. CLSI document EP06-A. Wayne, PA: Clinical and Laboratory Standards Institute; 2003.
5. *CLSI. Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline—Third Edition.* CLSI document EP28-A3c [ISBN 1-56238-682-4]. Clinical and Laboratory Standards Institute, 950 West Valley Road, Suite 2500, Wayne, PA 19087 USA, 2010.
6. Wu, Alan H.B. Tietz, *Clinical Guide to Laboratory Tests*. 4th ed. Saunders Elsevier, St. Louis, MO: 2006, 234-241.
7. Clinical and Laboratory Standards Institute (CLSI). *Interference Testing in Clinical Chemistry; Approved Guideline – Second Edition*, CLSI document EP07-A2 (ISBN 1-56238-584-4), Clinical and Laboratory Standards Institute, 950 West Valley Road, Suite 2500, Wayne, Pennsylvania 19087 USA, 2005.