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

A. 510(k) Number:

k162020

B. Purpose for Submission:

This submission is for the addition of urine as a matrix for cleared VITROS Chemistry Products Cl- Slides (k071801), which is currently available for use with serum and plasma

C. Measurand:

Chloride

D. Type of Test:

Quantitative, Potentiometry

E. Applicant:

Ortho-Clinical Diagnostics, Inc.

F. Proprietary and Established Names:

VITROS Chemistry Products Cl- Slide

G. Regulatory Information:

Product Code	Regulation Name	Classification	Regulation Section	Panel
CGZ	Chloride test system	II	21CFR 862.1170	Chemistry (75)

H. Intended Use:

1. Intended use(s):

   See Indications for Use below

2. Indication(s) for use:

   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.

3. Special conditions for use statement(s):

   In vitro diagnostic use only
   For prescription use only

4. Special instrument requirements:

   VITROS 5,1 FS Chemistry System

I. Device Description:

The VITROS Chemistry Products Cl- slide was previously cleared via k071801for use with serum and plasma. This submission is to add a claim for use with urine samples.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Siemens ADVIA Chloride (Cl) Assay

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

   K990346

3. Comparison with predicate:

Similarities		
Device Characteristic	**Predicate Device Siemens ADVIA Chloride (CL) (k990346)**	**Candidate Device VITROS Cl- assay (k162020)**
Indications for Use	For in vitro diagnostic use in the quantitative determination of chloride in human serum, plasma and urine	Same
Reaction Type	Potentiometric	Same

Sample Types	Serum, Plasma (lithium heparin), Urine	Same
Differences		
Device Characteristic	**Predicate Device Siemens ADVIA Chloride (CL) (k990346)**	**Candidate Device VITROS Cl- assay (k162020)**
Method Principle	Ion Selective Electrode (ISE), Indirect (diluted)	Ion Selective Electrode (ISE), Indirect (undiluted)
Measuring Range for Urine	15-400 mmol/L	15-300 mmol/L

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

CLSI-EP5-A3: "Evaluation of Precision of Quantitative Measurement Procedures" Approved Guideline- Third Edition"

CLSI-EP6-A: "Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach" Approved Guideline"

CLSI-EP9-A3: "Measurement Procedure Comparison and Bias Estimation Using Patient Samples" Approved Guideline- Third Edition"

CLSI- EP7-A2: "Interference Testing in Clinical Chemistry: Approved Guideline- Second Edition"

CLSI- EP17-A2: "Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures: Approved Guideline-Second Edition"

CLSI- EP28-A3c: "Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory: Approved Guideline-Third Edition"

L. Test Principle:

The VITROS Cl- Slide assay is performed using the VITROS Cl- Slides and the VITROS Chemistry Products Calibrator Kit 2 on 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.

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. A drop of patient sample and a drop of VITROS Electrode Reference Fluid on separate halves of the slide results in migration of both fluids toward the center of the paper bridge. A stable liquid junction is formed connecting the reference electrode to the sample indicator electrode. Each electrode

produces an electrical potential in response to the activity of chloride ions applied to it. The potential difference poised between the two electrodes is proportional to the chloride concentration in the sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Precision studies were performed in accordance with CLSI document EP05-A3. The precision study was performed with two VITROS Cl- Slide lots on the VITROS 5,1 FS Chemistry System. Two runs were performed on each of 20 non-consecutive days. Each run consisted of four samples run in duplicate (N=80). Runs within day were separated by at least two hours. A fresh sample aliquot was used for each run.

The summary of the precision study results are presented below:

Mean (mmol/L)	Repeatability		Within Day		Within Lab	
	SD (mmol/L)	CV (%)	SD (mmol/L)	CV (%)	SD (mmol/L)	CV (%)
18	0.2	1.2	0.6	3.3	0.8	4.2
105	0.5	0.4	0.5	0.5	0.7	0.6
191	0.6	0.3	0.7	0.4	1.2	0.6
282	0.9	0.3	1.1	0.4	2.6	0.9

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

b. Linearity/assay reportable range:

A linearity study was performed following the CLSI EP06-A guideline. Eleven equally spaced samples (12-320 mmol/L) covering the measuring range were prepared by mixing high and low concentration patient samples. Six replicates were measured for each sample and the mean of these replicates was compared to the expected values. Linear regression summary results are presented below and support the claimed measuring range of the device (15-300 mmol/L):

Analyte	**Slope**	**Intercept**	**r^2**	**Linear Range Tested (mmol/L)**	**Claimed Measuring range**
Urine Cl-	1.0044	-1.37	0.9995	12-320 mmol/L	15-300 mmol/L

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

Traceability

The VITROS chloride slides are traceable to the NIST Reference Material, SRM 919.

d. *Detection limit:*

The Limit of Blank (LoB), Limit of Detection (LoD) and Limit of Quantification (LoQ) were evaluated in accordance with CLSI EP17-A2 Guideline using the VITROS 5,1 FS Chemistry System.

LoB was determined by testing four chloride-depleted formulations of surrogate urine samples designed for use in electrolyte calibrator materials using three VITROS Cl- Slide lots. Six replicates were run once per day for three days. A total of 72 measurements were obtained per Cl- Slide lot. LoB was determined non-parametrically using the worst case from the three slide lots.

LoD was determined by testing six low level human urine pools using three Cl- Slide lots. Six replicates were run once per day for three days. A total of 108 measurements were obtained per Cl- Slide lot. The LoD was calculated parametrically using the worst case from three slide lots.

Results from the LoD test samples were used to estimate imprecision at the low analyte level according to the protocol in CLSI EP17-A2. The LoQ is determined as the lowest concentration at which the assay demonstrates an imprecision of ≤5% for each slide lot. The claimed LoQ is representative of the worst case from three slide lots.

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

e. *Analytical specificity:*

Interference studies were performed according to CLSI EP7-A2 guideline to determine the effects of exogenous and endogenous substances on the performance of the VITROS Chemistry Products Cl- Slides assay for urine.

Two human urine pools containing approximately 20 and 180 mmol/L of chloride were used as the base pools for all evaluations via paired difference testing.

Test pools were spiked with test substances at the target test levels and the VITROS Cl- Slides results were compared to matched control pools prepared with no test substance added. Six replicates of each test substance were tested on three Cl- Slide lots.

There was no significant interference (defined by the sponsor as ≤ 5% bias between the test pool and control pool) when these substances were tested in the concentrations indicated below:

Test Substances	Highest Concentration tested with no Significant Interference (mg/dL)
Acetaminophen	50
Allopurinol (Zyloprim)	24
Amiloride HCl	1.5
Ascorbic Acid	180
Bilirubin, Taurine Conjugate	7.3
Boric Acid	670
Boric Acid + Sodium formate	670+335
Carbenicillin Disodium Salt	300
Ciprofloxacin	1.2
Furosemide	9
Gentamicin Sulfate	1.5
Glacial Acetic Acid	10 mL/L
Glutathione	1.0
Hemoglobin	1000
Ibuprofen	50
Intralipid (Lipemia)	2524
Levodopa	67
Lithium Carbonate	236.5
Mannitol	60
N-Acetyl Cysteine	166
Ofloxacin	32
Penicillin G	59.7
Phenazopyridine HCl	19.5
Prednisone	230 ug/dL
Rantidine HCl	670 ug/dL
Sodium Cefoxitin	340
Sodium Fluoride	500
Sodium Formate	335
Sodium Oxalate	60
Tetracycline	70
Toluene	1.3 mL/L

Effect of pH: The sponsor evaluated the effect of pH on the test results using two human urine pools with chloride concentrations of 20 and 180 mmol/L, and demonstrated that pH values of 4.0 and 9.0 did not interfere with test results.

Effect of specific gravity: The sponsor evaluated the effect of specific gravity on the test results using three human urine pools with chloride concentrations of 50, 67, and 50 mmol/L. The specific gravity of these pools was adjusted using sucrose and demonstrated that Specific Gravity values of 1.00-1.04 did not interfere with test results.

The sponsor added the following limitations to their labeling:

- Specimens Not Recommended: Urine with the following preservatives:
  - Hydrochloric acid (12N HCl)
  - 10% Thymol in isopropanol
- 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/L of halide. Normal physiological levels of bromide and iodide do not interfere.

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

Method comparison studies were performed according to CLSI document EP9-A3. A total of 125 random catch human urine samples covering the claimed measuring range were assayed in triplicate on the VITROS 5,1 FS Chemistry System and in singleton using the Siemens Chloride (CL) method for ADVIA Chemistry Systems (predicate device; k990346) over four test days. Only the first replicate from each sample tested on the VITROS system and Siemens ADVIA was used in the analysis. Ten of the 125 samples tested were spiked with sodium chloride to cover the upper end of the measuring range. Samples were assayed with the VITROS Cl- Slides and comparative method within 8 hours of each other.

The linear regression analysis results are shown in the table below.

N	Slope	Intercept	Correlation Coefficient	Sample Range Tested (mmol/L)
125	0.996	-4.7	0.998	17-302

b. Matrix comparison:

Not applicable

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:

The method for expected values determinations was based on CLSI EP28-A3c.

Random Catch Reference Range:

135 human urine samples were collected from normal healthy subjects and were analyzed in triplicate using the VITROS Cl- Slides assay. Two slide lots were tested on one VITROS 5,1 FS Chemistry System. Determination of expected values for random urine samples was performed using a non-parametric approach. The inner 95th% percentile for random urine samples was determined as 17-209 mmol/L.

24 Hour Reference Range:

The expected values for 24 hour urine samples are cited from literature[1]: 110-250 mmol/L.

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

P. Proposed Labeling:

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

Q. Conclusion:

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