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

A. 510(k) Number:

k182072

B. Purpose for Submission:

Adding previously cleared assays to a new instrument platform

C. Measurand:

Chloride, total carbon dioxide (CO2), and glucose

D. Type of Test:

Chloride assay: Potentiometric assay
Total carbon dioxide (CO2) assay: Enzymatic endpoint assay
Glucose assay: Colorimetric assay

E. Applicant:

Ortho-Clinical Diagnostics, Inc.

F. Proprietary and Established Names:

VITROS Chemistry Products Cl- Slides
VITROS Chemistry Products ECO2 Slides
VITROS Chemistry Products GLU Slides

G. Regulatory Information:

Analyte	Product Code	Classification	Regulation Section	Panel
Cl-	CGZ	II	21 CFR 862.1170	Chemistry (75)
CO2	KHS	II	21 CFR 862.1160	
GLU	CGA	II	21 CFR 862.1345	

H. Intended Use:

1. Intended use(s):

   See Indication(s) for use below.

2. Indication(s) for use:

   Chloride: Rx Only. For in vitro diagnostic use only. VITROS Chemistry Products Cl- Slides quantitatively measure chloride (Cl-) concentration in serum, plasma and urine using VITROS 250/350/950/5,1 FS and 4600 Chemistry Systems and the VITROS 5600/ XT 7600 Integrated System. Chloride measurements are used in the diagnosis and treatment of electrolyte and metabolic disorders such as cystic fibrosis and diabetic acidosis.

   CO2: Rx Only. For in vitro diagnostic use only. VITROS Chemistry Products ECO2 Slides quantitatively measure total carbon dioxide (CO2) concentration in serum and plasma using VITROS 250/350/950/5,1 FS and 4600 Chemistry Systems and the VITROS 5600/ XT 7600 Integrated System. Bicarbonate/carbon dioxide measurements are used in the diagnosis and treatment of numerous potentially serious disorders associated with changes in body acid-base balance.

   Glucose: Rx Only. For in vitro diagnostic use only. VITROS Chemistry Products GLU Slides quantitatively measure glucose (GLU) concentration in serum, plasma, urine, and cerebrospinal fluid using VITROS 250/350/950/5,1 FS and 4600 Chemistry Systems and the VITROS 5600/ XT 7600 Integrated System. Glucose measurements are used in the diagnosis and treatment of carbohydrate metabolism disorders including diabetes mellitus, neonatal hypoglycemia, and idiopathic hypoglycemia, and of pancreatic islet cell carcinoma.

3. Special conditions for use statement(s):

   For prescription use only.
   Not for Point-of-Care use.

4. Special instrument requirements:

   Performance characteristics were determined on the VITROS XT 7600 Integrated System

I. Device Description:

VITROS Chemistry Products Cl- Slide:
The VITROS Chemistry Products Cl- Slide is a multilayered, analytical element coated on a polyester support that uses direct potentiometry for measurement of chloride ions. The reactive ingredients per cm^2 are silver 0.4 mg and silver chloride 0.2 mg. Other ingredients: Polymer, plasticizer, surfactant and nickel-chromium.

VITROS Chemistry Products ECO2 Slide:
The VITROS Chemistry Products ECO2 Slide is a multilayered, analytical element coated on a polyester support. The reactive ingredients per cm^2 are phosphoenolpyruvate carboxylase (bacteria) 0.20 U; malate dehydrogenase (porcine heart) 0.26 U; phosphoenolpyruvate 0.39 mg and nicotinamide adenine dinucleotide, reduced 0.44 mg. Other ingredients: binders, buffer, inhibitor, pigment, surfactants, enzyme cofactors, cross-linking agent and filter dye.

VITROS Chemistry Products GLU Slide:
The VITROS Chemistry Products GLU Slide is a multilayered, analytical element coated on a polyester support. The reactive ingredients per cm^2 are glucose oxidase (Aspergillus sp.) 0.77 U; peroxidase (horseradish root) 3.6 U; 1,7-dihydroxynaphthalene (dye precursor) 67 µg and 4-aminoantipyrine hydrochloride (dye precursor) 0.11 mg. Other ingredients: pigment, binders, buffer, surfactants, stabilizers and crosslinking agent.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   VITROS Chemistry Products Cl- Slides
   VITROS Chemistry Products ECO2 Slides
   VITROS Chemistry Products GLU Slides

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

   k162020
   k120765
   k163433

3. Comparison with predicate:

   Chloride:

Similarities and Differences		
Device Characteristic	Candidate Device VITROS Chemistry Products Cl- Slides (k182072)	Predicate Device VITROS Chemistry Products Cl- Slides (k162020)
Intended Use	For the quantitative measure of chloride (Cl-) concentration in serum, plasma and urine.	Same
Measuring range	Serum: 50.0 -175.0 mmol/L Urine: 15-300 mmol/L	Same
Basic principle	Potentiometric; ion-selective electrode (ISE)	Same
Sample type	Serum, plasma, urine	Same

Similarities and Differences		
Device Characteristic	Candidate Device VITROS Chemistry Products Cl- Slides (k182072)	Predicate Device VITROS Chemistry Products Cl- Slides (k162020)
Sample volume	10 µL	Same
Instrumentation	VITROS 250/350/950/5,1 FS and 4600 Chemistry Systems and the VITROS 5600/ XT 7600 Integrated System	VITROS 250/350/950/5,1 FS and 4600 Chemistry Systems and the VITROS 5600 Integrated System

CO2:

Similarities and Differences		
Device Characteristic	Candidate Device VITROS Chemistry Products ECO2 Slides (k182072)	Predicate Device VITROS Chemistry Products ECO2 Slides (k120675)
Intended Use	For the quantitatively measure of total carbon dioxide (CO2) concentration in serum and plasma.	Same
Measuring range	5-40 mmol/L	Same
Basic principle	Enzymatic endpoint	Same
Wavelength	340 nm	Same
Sample type	Serum, plasma	Same
Sample volume	6 µL	Same
Instrumentation	VITROS 250/350/950/5,1 FS and 4600 Chemistry Systems and the VITROS 5600/ XT 7600 Integrated System	VITROS 250/350/950/5,1 FS and 4600 Chemistry Systems and the VITROS 5600 Integrated System

Glucose:

Similarities and Differences		
Device Characteristic	Candidate Device VITROS Chemistry Products GLU Slides (k182072)	Predicate Device VITROS Chemistry Products GLU Slides (k163433)
Intended Use	For quantitatively measure of glucose concentration in serum, plasma, urine, and cerebrospinal fluid.	Same
Measuring range	Serum: 20.0-625.0 mg/dL Urine/CSF: 20.0-650.0 mg/dL	Same
Basic principle	Colorimetric	Same

Similarities and Differences		
Device Characteristic	Candidate Device VITROS Chemistry Products GLU Slides (k182072)	Predicate Device VITROS Chemistry Products GLU Slides (k163433)
Wavelength	540 nm	Same
Sample type	Serum, plasma, urine, CSF	Same
Sample volume	6 µL	Same
Instrumentation	VITROS 250/350/950/5,1 FS and 4600 Chemistry Systems and the VITROS 5600/ XT 7600 Integrated System	VITROS 250/350/950/5,1 FS and 4600 Chemistry Systems and the VITROS 5600 Integrated System

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

CLSI EP05-A3, Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline -Third Edition.

CLSI EP06-A, Evaluation of Linearity of Quantitative Measurement Proceures, Approved Guideline;1st Edition.

CLSI EP07, 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.

L. Test Principle:

VITROS Chemistry Products Cl- Slides (Potentiometric):

A drop of patient sample and a drop of VITROS 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.

VITROS Chemistry Products ECO2 Slides (Enzymatic endpoint):

A drop of patient sample is deposited on the slide and is evenly distributed by the spreading layer to the underlying layers. The high pH in the spreading layer ensures that essentially all CO2 in the sample is in the bicarbonate form. Bicarbonate diffuses to the gel layer and is used to carboxylate phosphoenolpyruvate in the presence of phosphoenolpyruvate carboxylase to form oxalacetate and inorganic phosphate. The final reaction involves the malate dehydrogenase–catalyzed oxidation of NADH and reduction of oxalacetate to produce

NAD+ and malate. The slide is incubated at 37°C. The concentration of CO2 in the sample is determined by measuring the absorbance of the unreacted NADH by reflectance spectrophotometry.

VITROS Chemistry Products GLU Slides (Colorimetric):

A drop of patient sample is deposited on the slide and is evenly distributed by the spreading layer to the underlying layers. The oxidation of glucose in the sample is catalyzed by glucose oxidase to form hydrogen peroxide and gluconate. This reaction is followed by an oxidative coupling catalyzed by peroxidase in the presence of dye precursors to produce a dye. The intensity of the dye is measured by reflected light.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Precision studies were conducted following EP05-A3 guideline. The study was performed by testing a minimum of two quality control fluids and three human based precision pools using the chloride (Cl-), carbon dioxide (ECO2), and glucose (GLU) assays. Samples were analyzed using one VITROS XT 7600 Integrated System over 20 days, with 2 runs per day and 2 replicates per specimen (n=80). The results of the precision study are presented in the tables below:

Cl- Serum (mmol/L):

Sample #	Mean	Repeatability (Within Run)		Within Day		Within Lab (Total)	
		SD	%CV	SD	%CV	SD	%CV
QC-1	86	0.4	0.5	0.5	0.6	1.0	1.2
QC-2	108	0.4	0.4	0.6	0.5	1.2	1.1
Serum Pool 1	66	0.3	0.4	0.4	0.5	0.6	0.9
Serum Pool 4	127	0.4	0.4	0.6	0.4	1.4	1.1
Serum Pool 5	160	0.6	0.4	0.6	0.4	1.8	1.1
Serum Pool (native)	106	0.4	0.3	0.5	0.5	1.2	1.1

Cl- Urine (mmol/L):

Sample #	Mean	Repeatability (Within Run)		Within Day		Within Lab (Total)	
		SD	%CV	SD	%CV	SD	%CV
U QC-1	101	0.4	0.3	0.6	0.6	0.9	0.9
U QC-2	189	0.5	0.3	0.9	0.5	2.3	1.2
Urine Pool 1	22	0.3	1.3	0.5	2.2	0.6	2.6
Urine Pool 3	151	0.4	0.3	0.5	0.4	0.9	0.6
Urine Pool 5	249	0.7	0.3	1.0	0.4	3.9	1.6
Urine Pool (native)	67	0.3	0.4	0.3	0.5	0.6	0.9

ECO2 Serum (mmol/L):

Sample #	Mean	Repeatability (Within Run)		Within Day		Within Lab (Total)	
		SD	%CV	SD	%CV	SD	%CV
QC-1	26	0.3	1.0	0.4	1.4	0.6	2.4
QC -2	16	0.3	1.7	0.4	2.5	0.5	3.1
Serum Pool 1	8	0.3	3.2	0.4	4.5	0.6	7.4
Serum Pool 3	17	0.3	1.5	0.3	2.0	0.4	2.5
Serum Pool 5	33	0.3	0.8	0.4	1.3	0.6	1.9
Serum Pool (native)	26	0.2	0.8	1.1	4.2	1.2	4.4

GLU Serum (mg/dL) :

Sample #	Mean	Repeatability (Within Run)		Within Day		Within Lab (Total)	
		SD	%CV	SD	%CV	SD	%CV
QC -1	89	0.4	0.4	0.6	0.7	0.8	0.9
QC -2	282	1.1	0.4	1.4	0.5	2.6	0.9
Serum Pool 1	27	0.2	0.7	0.3	1.2	0.5	1.8
Serum Pool 3	116	0.5	0.4	0.6	0.5	0.8	0.7
Serum Pool 5	566	1.7	0.3	2.5	0.4	6.1	1.1
Serum Pool (native)	99	0.3	0.3	0.5	0.5	0.8	0.8

GLU Urine (mg/dL):

Sample #	Mean	Repeatability (Within Run)		Within Day		Within Lab (Total)	
		SD	%CV	SD	%CV	SD	%CV
QC -1	29	0.2	0.6	0.4	1.3	0.7	2.2
QC -2	285	1.4	0.5	2.3	0.8	2.6	0.9
Urine Pool 2	1.2	0.4	0.4	0.7	0.7	1.5	1.5
Urine Pool 3	232	1.1	0.5	2.4	1.0	4.3	1.9
Urine Pool 5	593	1.9	0.3	2.7	0.5	10.0	1.7

GLU CSF (mg/dL):

Sample #	Mean	Repeatability (Within Run)		Within Day		Within Lab (Total)	
		SD	%CV	SD	%CV	SD	%CV
QC -1	36	0.2	0.6	0.3	0.9	0.5	1.4
QC -2	84	0.4	0.5	0.5	0.6	0.6	0.8
CSF Pool (native)	41	0.2	0.5	0.3	0.6	0.5	1.2
CSF Pool 1	28	0.1	0.5	0.3	1.1	0.5	1.9
CSF Pool 4	289	1.3	0.5	1.7	0.6	3.1	1.1
CSF Pool 5	563	2.6	0.5	3.7	0.7	5.8	1.0

b. *Linearity/assay reportable range:*

A linearity study was performed following the CLSI EP06-A guideline. A series of eleven proportionally related admixtures of low and high test fluids were tested to verify linearity; each sample was tested in duplicate.

The results of the linear regression analysis support the following claimed measuring ranges for the chloride, total CO2 and glucose assays:

Analyte	Slope	Intercept	r	Range tested	Claimed measuring range
Cl- Serum (mmol/L)	1.00	1.07	1.00	42 - 193	50-175
Cl- Urine (mmol/L)	1.00	4.61	1.00	15 - 326	15-300
ECO2 Serum	0.99	0.61	1.00	3.1 - 44.2	5.0-40.0
Glucose Serum (mg/dL)	1.01	-2.75	1.00	5.3 - 656.6	20.0-625.0
Glucose Urine (mg/dL)	1.02	1.01	1.00	9.0 - 682.4	20.0-650.0
Glucose CSF (mg/dL)	1.01	-0.41	1.00	11.3 - 676.4	20.0-650.0

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

VITROS Chemistry Products Cl- Slides: Values assigned the VITROS Chemistry Products Calibrator Kit 2 for chloride are traceable to the Certified NIST (National Institute of Standards and Technology) Reference Material, SRM (Standard Reference Material) 919.

VITROS Chemistry Products ECO2 Slides: Values assigned to the VITROS Chemistry Products Calibrator Kit2 for carbon dioxide are traceable to the Certified NIST (National Institute of Standards and Technology) Reference Material, SRM (Standard Reference Material) 351.

VITROS Chemistry Products GLU Slides : Values assigned to the VITROS Chemistry Products Calibrator Kit 1 for glucose are traceable to the Certified NIST (National Institute of Standards and Technology) Reference Material, SRM (Standard Reference Material) 917.

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 guideline using the VITROS XT 7600 Chemistry System.

Limit of blank (LoB) studies were performed by testing 4 blank samples in replicates of 6 over 3 days, using 3 lots of reagents, for a total of 216 observations (72 results

per reagent lot). The LoB value for each assay was defined as the highest value achieved using blank samples with the stated probability (i.e. α = 5%). Since the data for all assays were non-gaussian, a non-parametric approach was applied that estimates the LoB using the calculated rank position corresponding to the 95th percentile of the distribution of blank values observed.

Limit of detection (LoD) studies were performed by testing 4 pools of human samples with analyte concentrations close to the expected detection limit for each analyte. Samples were tested in replicates of 6 over 3 days, using 3 lots of reagents, for a total of 216 observations (72 results per reagent lot). The LoD value for the assay is the highest resultant value achieved among the combinations of reagent lots and human pools evaluated, with the stated probability (i.e. β= 5%).

Limit of quantitation (LoQ) studies were performed using 4 pools of low level samples with analyte concentrations close to the expected LoQ of the corresponding assay. Samples were tested in replicates of 4 over 3 days, using 3 lots of reagents, for a total of 144 observations (48 results per reagent lot). Ortho defines LoQ as the lowest concentration with a percent total allowable error < 8% for chloride (serum); percent total allowable error 10% for chloride (urine), percent total allowable error < 30% for carbon dioxide, total allowable error < 30% for glucose in serum, urine, and CSF.

The results of the detection capability studies for each assay are presented in the table below:

	Cl- (mmol/L)		**ECO2 (mmol/L)**	**GLU (mg/dL)**		
	Serum	**Urine**	**Serum**	**Serum**	**Urine**	**CSF**
LoB	9.2202	3.0965	1.9944	4.5753	6.2966	4.0745
LoD	9.9798	4.0417	2.3522	5.2670	6.7212	4.6992
LoQ	49	11	3.7	13	20	19
Claimed LoQ	50	15	5.0	20	20	20
Assay Range	50.0-175.0	15-300	5.0-40.0	20.0-625.0	20.0-650.0	20.0-650.0

e. *Analytical specificity:*

Interference testing was performed in accordance with CLSI EP07-A2 guideline. Testing on the representative assays included known chemical interferents, common chemical substances identified with potential to interfere based upon risk assessment. Testing employed “paired-difference” assessment at a minimum of two analyte levels, as specified by CLSI EP07-A2 guideline. All samples used in the interference testing were pools of human serum, plasma, CSF or urine. For all pools, samples may have been spiked or diluted in order to achieve the appropriate target analyte concentration and was tested at a minimum of two analyte concentration and bias between interferent test and control samples was calculated.

Chloride:

The study was conducted using samples with serum chloride concentrations of 100 and 110 mmol/L. The sponsor defined non-interference as a bias < 1.1 mmol/L (vs. control condition).

The compounds and the highest concentration that don't interfere with serum chloride are listed in the table below:

Compound	Concentration
Acetaminophen	20 mg/dL
Acetylsalicylic Acid	35 mg/dL
Allopurinol	12.5 mg/dL
Alprazolam	20 µg/dL
Para-Aminosalicylic Acid	23 mg/dL
Amitriptyline	1 µg/mL
Amoxicillin	1500 µg/mL
Ascorbic Acid	3 mg/dL
Atenolol	20 µg/mL
Bilirubin	40 mg/dL
Calcium	16 mg/dL
Carbamazepine	60 µg/mL
Cephalexin	11.7 mg/dL
Ciprofloxacin	1 mg/dL
Clarithromycin	20.0 µg/mL
Codeine	4 µg/mL
Dextran	1000 mg/dL
Dextromethorphan	1.0 µg/mL
Digoxin	3 µg/dL
Diltiazem	5 µg/mL
Diphenhydramine	10 µg/mL
Enalapril	1.2 µg/mL
Ethanol	300 mg/dL
Fluoxetine	0.8 mg/dL
Furosemide	10 mg/dL
Gentisic Acid	0.5 mg/dL
Glucose	600 mg/dL
Glyburide	6.4 µg/mL
Guaifenesin	100 mg/dL
Hemoglobin	1000 mg/dL

Compound	Concentration
Hydrochlorothiazide	2 mg/dL
Hydrocodone	250 ng/mL
Ibuprofen	49.5 mg/dL
Isoniazid	0.4 mg/dL
L-Dopa	0.6 mg/dL
Levothyroxine	1 µg/mL
Lithium	1 mEq/L
Loratadine	100 ng/mL
Magnesium	4.5 mg/dL
Meprobamate	2 mg/dL
6-Mercaptopurine	1.5 mg/dL
Nifidepine	0.2 mg/dL
Omeprazole	20 mg/dL
Phenobarbital	3 mg/dL
Phenytoin	10 mg/dL
Phospholipids	500 mg/dL
Prednisone	0.1 mg/dL
Propoxyphene	16.7 ng/mL
Pseudoephedrine	10 µg/mL
Ranitidine	20 µg/mL
Simvastatin	500 mg/L
Sulfamethoxazole	330 mg/dL
Sulfathiazole	6 mg/dL
Tolbutamide	22 mg/dL
Triamterene	886 µg/dL
Trimethoprim	40.1 µg/mL
Tyrosine	24 mg/dL
Urea Nitrogen	100 mg/dL
Warfarin	10.7 mg/dL

The results of substances that interfere with chloride determinations in serum are summarized in the table below:

Interferent	Interferent concentration	Chloride concentration (mmol/L)	Bias (mmol/L)
5-aminosalicylic acid	4 µg/mL	100	-1.5
		109	+6.1
Glutathione	1 mg/dL	104	-1.6
Naproxen	504.5 µg/mL	99	+1.6
Terazosin	3.03 µg/mL	110	-2.4
Triglycerides	600 mg/dL	110	+2.1

The following limitations are listed in the package insert:

- Bromide and iodide from therapeutic drugs and ointments may cause a positive bias. Normal physiological levels of bromide and iodide do not interfere.
- Intralipid at 800 mg/dL may cause a positive bias of approximately 1.5 mmol/L.
- Purines, such as adenine or hypoxanthine, at significantly elevated levels may cause a negative bias of approximately mmol/L.

The sponsor also assessed the effect of potential interference in urine. The study was conducted using samples with urine chloride concentrations of 20 and 180 mmol/L. The sponsor defined non-interference as a bias < 5% (vs. control condition).

The compounds and the highest concentration that don't interfere with urine chloride are listed in the following table:

Substance Tested	Concentration
Acetaminophen	50 mg/dL
Allopurinol	24 mg/dL
Amiloride HCl	1.5 mg/dL
Ascorbic Acid	180 mg/dL
Bilirubin, conjugated	7.25 mg/dL
Boric Acid	670 mg/dL
Boric Acid + Sodium Formate	670 mg/dL + 335 mg/dL
Carbenicillin Disodium	300 mg/dL
Ciprofloxacin	1.16 mg/dL
Furosemide	9 mg/dL
Gentamicin Sulfate	1.5 mg/dL
Glacial Acetic Acid	10 mL/L
Glutathione	1.0 mg/dL
Hemoglobin	1000 mg/dL

Substance Tested	Concentration
Levodopa	67 mg/dL
Lithium Carbonate	236.5 mg/dL
Mannitol	60 mg/dL
N-Acetyl Cysteine	166.2 mg/dL
Ofloxacin	32 mg/dL
pH	4–9
Penicillin G	59.7 mg/dL
Phenazopyridine HCl	19.5 mg/dL
Prednisone	230 µg/dL
Ranitidine HCl	670 µg/dL
Sodium Cefoxitin	340 mg/dL
Sodium Fluoride	500 mg/dL
Sodium Formate	335 mg/dL
Sodium Oxalate	60 mg/dL
Specific Gravity	1.00–1.04

Ibuprofen	50 mg/dL		Tetracycline HCl	70 mg/dL
Intralipid	2524 mg/dL		Toluene	1.3 mL/L

ECO2:

The study was conducted using samples with serum CO2 concentrations of 25 and 35 mmol/L. The sponsor defined non-interference as a bias < 1.9 mmol/L (vs. control condition).

Compound	Concentration
Acetaminophen	20 mg/dL
Acetoacetate	20 mg/dL
Acetylsalicylic acid	50 mg/dL
Alpha-keto-isocaproate	20 mmol/L
5-Aminosalicylate	0.4 mg/dL
4-Aminosalicylate	91 mg/dL
Ammonia	0.5 mmol/L
Argininosuccinate	5 mmol/L
Ascorbic acid	3 mg/dL
Benzamide	20 mmol/L
Benzenesulfonate	2 mmol/L
Benzoic acid	4 mmol/L
Benzyl alcohol	4 mmol/L
Bilirubin	40 mg/dL
Butyric acid	2 mmol/L
Capric acid	4 mmol/L
Caproic acid	2 mmol/L
Cholesterol	390 mg/dL
Dextran	1000 mg/dL
Ethanol	350 mg/dL
Free fatty acids	3 mmol/L
Glutamate	2 mmol/L
Homogentisic acid	2 mmol/L
Hydroclorothiazide	5 mg/dL
Hydroxybutyrate	20 mg/dL
Hydroxyindoleacetate	2 mmol/L
Hydroxyphenylacetate	4 mmol/L

Compound	Concentration
Hydroxyphenyllactate	2 mmol/L
Hydroxyphenylpyruvate	2 mmol/L
Hypaque	500 mg/dL
Ibuprofen	40 mg/dL
Imidazole	20 mmol/L
Imidazoleacetate	20 mmol/L
Indomethacin	50 mg/dL
Intralipid	800 mg/dL
Isovaleric acid	1 mmol/L
Lactate	57 mg/dL
Lactose	3 g/dL
Mannitol	3 g/dL
Methylvaleric acid	2 mmol/L
Naproxen	10 mmol/L
Phenylacetate	1 mmol/L
Phenylpyruvate	2 mmol/L
Phospholipids	400 mg/dL
Propionic acid	2 mmol/L
Propylpentanoic acid	2 mmol/L
Protein	11 g/dL
Pyruvate	1.5 mg/dL
Salicylate	50 mg/dL
Spironolactone	5 mg/dL
Sulfathiazole	5 mg/dL
Triglycerides	900 mg/dL
Urea Nitrogen	322 mg/dL

Known ECO2 interferent:

Interferent	Interferent concentration	CO2 concentration	bias
Hemoglobin	800 mg/dL	25 mmol/L	-2.1

Glucose:

The study was conducted using samples of serum glucose concentrations of 80 mg/dL with non-interference as a bias < 7 mg/dL and serum glucose concentrations of 225 mg/dL with non-interference as a bias < 7 % (vs. control condition).

The compounds and the highest concentration that don't interfere with glucose determinations in serum are listed in the following table:

Compound	Concentration
Acetaminophen	15 mg/dL
Alprazolam	0.2 mg/dL
Amlodipine	10 µg/dL
Amoxicillin	7.53 mg/dL
Ascorbic acid	4.5 mg/dL
Atorvastatin calcium	72.6 mg/dL
Benazepril	2.21 mg/dL
Bilirubin, conjugated	57.64 mg/dL
Bilirubin, unconjugated	40 mg/dL
Cefazolin	125.9 mg/dL
Cefoxitin	69.5 mg/dL
Ceftriaxone	81.0 mg/dL
Chlorpropamide	74.7 mg/dL
Cholesterol	325 mg/dL
Creatinine	15 mg/dL
Diphenhydramine	0.50 mg/dL
Dipyrone (metamizole)	18 mg/dL
Dobutamine	30 µg/dL
Dopamine	90 µg/dL
Ethamsylate (Etamsylate)	3.14 mg/dL
Ethanol	400 mg/dL
Fructose	30 mg/dL
Furosemide	6 mg/dL
Galactose	60 mg/dL
Gentisic acid	1.80 mg/dL
Glipizide	0.20 mg/dL
Glyburide	0.192 mg/dL
Hydralazine HCl	0.046 mg/dL
Hydrochlorothiazide	0.60 mg/dL
Hydroxyurea	7 mg/dL
Ibuprofen	50 mg/dL
Insulin	3.12 µg/dL
Intralipid	800 mg/dL

Compound	Concentration
Isomaltose	0.09 mg/dL
Isoniazid	4 mg/dL
L-Dopa	0.98 mg/dL
Levothyroxine sodium	103 µg/dL
Losartan potassium	0.091 mg/dL
Maltose	75 mg/dL
Metformin HCl	5.1 mg/dL
Methyldopa	2 mg/L
N-Acetylcysteine	15 mg/dL
Naproxen sodium	54.7 mg/dL
Nitrofurantoin	0.4 mg/dL
Omeprazole	0.60 mg/dL
Oxycodone	0.05 mg/dL
Propanolol	0.21 mg/dL
Pseudoephedrine	1 mg/dL
Rifampicin (Rifampin)	6.43 mg/dL
Salicylic acid	60 mg/dL
Sodium	1050 mg/dL
Spironolactone	0.06 mg/dL
Theophylline	4 mg/dL
Tolazamide	28 mg/dL
Tolbutamide	64.1 mg/dL
Tolbutamide	64.1 mg/dL
Total Protein	10 g/dL
Uric acid	23 mg/dL
Vancomycin	10 mg/dL
Warfarin	1 mg/dL
Xylose	100mg/dL
Mannitol	0.09 mg/dL
Sorbitol	0.09 mg/dL
Xylitol	0.09 mg/dL
Lacitol	0.09 mg/dL
Maltitol 578	0.09 mg/dL

The substance that interferes with glucose determinations in serum are summarized in the table below:

Interferent	Interferent concentrations	Glucose concentrations	Bias
Glutathione	61.5 mg/dL	80 mg/dL	-7.4 mg/dL

The following limitations are listed in the package insert:

- When using samples with visible hemolysis (Hb >200 mg/dL), there may be a negative bias due to catalase released from the lysis of red blood cells. On VITROS Systems capable of performing Sample Indices using the MicroSensor, the GLU result will be flagged with H (Hemolysis).
- Elevated lipids may limit diffusion of oxygen to the reactants. Dilute grossly lipemic samples two-fold before analysis.

Glucose – interference testing in urine:

The study was conducted using samples with urine glucose concentrations of approximately 30 mg/dL and found not to interfere, bias <7 mg/dL. The substances were also tested at a glucose concentration of approximately 215 mg/dL and found not to interfere, bias <7% (vs. control condition).
The substances that showed not to interfere in urine are summarized in the following table:

Substances	Highest concentration tested that showed non-significant interference
Boric acid	6.7 mg/mL
Boric acid with Sodium formate	6.7 mg/mL, 3.35 mg/mL
10% Thymol in Isopropanol	3.3 mL/L
Toluene	1.3 mL/L
Sodium fluoride	5 g/L
Sodium formate	3.35 mg/mL
Sodium oxalate	60 mg/dL
Urea nitrogen	100 mg/dL
Magnesium	146 mg/dL
Protein	50 mg/dL

The following substance interferes with glucose determinations in urine:

Interferent	Interferent concentrations	Glucose concentrations	Bias
Ascorbic Acid	50 mg/dL	30 mg/dL	-15.7 mg/dL

The following limitations are listed in the package insert:

- Glacial acetic acid at 10 mL/L results in ~4% negative bias. The magnitude of the bias increases with higher concentrations of glacial acetic acid (60 mL/L). Do not use urine specimens with acetic acid as a preservative.
- 12N Hydrochloric acid (HCl) at 2.5 mL/dL results in a large negative bias, potentially resulting in values less than the measuring range. Do not use urine specimens with HCl as a preservative.

In CSF sample matrix hemoglobin was found not to interfere up to 250 mg/dL at a glucose concentration of 65 mg/dL (bias less than 5.2 mg/dL).

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

A minimum of 125 human serum samples with analyte concentrations within the measuring ranges of chloride, carbon dioxide and glucose assays were tested on the VITROS XT 7600 Integrated System and the VITROS 5600 Integrated System (predicate device).

In addition, 125 human urine samples were tested for chloride and 125 human urine samples and 125 human CSF samples were tested for glucose on the candidate and predicate test systems. The results of the regression analysis are summarized below:

Assay	n	Slope	Intercept	r	Sample Range Tested	Claimed Measuring Range
Cl- Serum (mmol/L)	125	1.00	-0.11	1.00	51.2-167.5	50.0-175.0
Cl- Urine (mmol/L)	123	1.00	-0.11	1.00	15-290	15-300
ECO2 Serum (mmol/L)	124	0.99	0.19	1.00	7.1-38.4	5.0-40.0
GLU Serum (mg/dL)	124	1.00	0.49	1.00	22.1-593.8	20.0-625.0
GLU Urine (mg/dL)	125	1.00	0.28	1.00	25.3-600.4	20.0-650.0
GLU CSF (mg/dL)	125	1.00	0.22	1.00	22.9-649.5	20.0-650.0

b. Matrix comparison:

Based on the sponsor's risk analysis for adding the VITROS Chemistry Products Cl- Slides, VITROS Chemistry Products ECO2 Slides and VITROS Chemistry Products GLU Slides to the VITROS XT 7600 Integrated system and the results of the analytical testing conducted that demonstrated that there was no impact on the assays' performance characteristics, new matrix comparison studies were not performed. FDA found this justification to be acceptable.

The sample types are:

The VITROS Chemistry Products Cl- Slides are suitable for use with serum, lithium heparin plasma, and urine.

VITROS Chemistry Products ECO2 Slides can be used with serum, lithium heparin and sodium heparin plasma.

The VITROS Chemistry Products GLU Slides are suitable for testing serum, plasma samples collected in EDTA, lithium heparin, sodium heparin, and sodium fluoride/potassium oxalate tubes, and also in urine and CSF.

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:

Assay	Range
Serum Chloride	98–107 (mmol/L) [1]
Urine Chloride	Random[2] 18–209 mmol/L

Assay	Range
	24 Hour [4] 110–250 mmol/day*
CO2	22–30 (mmol/L) [3]
Serum Glucose Fasting adults	74–106 mg/dL
Urine Glucose	Random <30 mg/dL
	24 Hour <500 mg/day**
CSF Glucose	40-70 mg/dL

1. This reference interval is the central 95% of serum results from an internal study of 60 apparently healthy individuals from a working population.
2. This reference interval is the central 95% of urine results from an internal study of 135 apparently healthy individuals from a working population.
3. This reference interval is the central 95% of results from a study of 60 apparently healthy adults from a working population (34 females and 26 males).

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

* Chloride concentration (mmol/L) x 24-hour volume (L) = mmol/day

**Glucose concentration (mg/dL) x 24-hour volume (dL) = mg/day.

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.