October 30, 2018

Ortho-Clinical Diagnostics, Inc.
Marlene Hanna
Director, Regulatory Affairs
100 Indigo Creek Drive
Rochester, NY 14626

Re: K182063
Trade/Device Name: VITROS Chemistry Products CRBM Slides
VITROS Chemistry Products CREA Slides
VITROS Chemistry Products TBIL Slides
VITROS XT 7600 Integrated System
Regulation Number: 21 CFR 862.1225
Regulation Name: Creatinine test system
Regulatory Class: Class II
Product Code: JFY, KLT, CIG, JJE
Dated: July 30, 2018
Received: August 1, 2018

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. 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)*
k182063

Device Name
VITROS Chemistry Products CRBM Slides
VITROS Chemistry Products CREA Slides
VITROS Chemistry Products TBIL Slides VITROS XT 7600 Integrated System

Indications for Use *(Describe)*

1. VITROS Chemistry Products CRBM Slides: Rx Only. For in vitro diagnostic use only. VITROS Chemistry Products CRBM Slides quantitatively measure carbamazepine (CRBM) 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. Measurements obtained are used in monitoring levels of carbamazepine to help ensure appropriate therapy.

2. VITROS Chemistry Products CREA Slides: Rx Only. For in vitro diagnostic use only. VITROS Chemistry Product CREA Slides quantitatively measure creatinine (CREA) 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. Creatinine measurements are used in the diagnosis and treatment of renal diseases, in monitoring renal dialysis, and as a calculation basis for measuring other urine analytes.

3. VITROS Chemistry Products TBIL Slides: Rx Only. For in vitro diagnostic use only. VITROS Chemistry Products TBIL Slides quantitatively measure total bilirubin (TBIL) 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. Measurements of the levels of bilirubin are used in the diagnosis and treatment of liver, hemolytic hematological and metabolic disorders, including hepatitis and gall bladder block.

4. VITROS XT 7600 Integrated System: Rx Only. For in vitro diagnostic use only. The VITROS XT 7600 Integrated System is intended for use in the measurement of a variety of analytes of clinical interest.

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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5 510(k) Summary Information

This summary of 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: k182063

Submitter's Information
Ortho-Clinical Diagnostics, Inc.
100 Indigo Creek Drive
Rochester, New York 14626-5101
Phone: (585) 453-4041
Fax: (585) 453-3368

Contact Person:
Marlene Hanna, RAC
Director, Regulatory Affairs

Date of Preparation: July 30, 2018

Device Proprietary Name(s):

VITROS Chemistry Products CRBM Slides
VITROS Chemistry Products CREA Slides
VITROS Chemistry Products TBIL Slides
VITROS XT 7600 Integrated System

Common Names:
Carbamazepine assay
Creatinine assay
Total bilirubin assay
Clinical chemistry analyzer

Classification Names

VITROS	Product Code	Class	Regulation Section	Panel
CRBM	KLT	Class II	21 CFR 862.3645 Neuroleptic drugs radioreceptor assay test system.	Clinical Toxicology
CREA	JFY	Class II	21 CFR 862.1225 creatinine test system	Clinical Chemistry
TBIL	CIG	Class II	21 CFR 862.1110 Bilirubin (total or direct) test system.	Clinical Chemistry
XT 7600	JJE	Class I	21 CFR 862.2160 Discrete photometric chemistry analyzer for clinical use	Clinical Chemistry

Predicate Device(s)

No.	New Devices	Predicate Devices	Predicate Device FDA 510(k) Number
1	VITROS Chemistry Products CRBM Slides	VITROS Chemistry Products CRBM Slides	k160495
2	VITROS Chemistry Products CREA Slides	VITROS Chemistry Products CREA Slides	k063591
3	VITROS Chemistry Products TBIL Slides	VITROS Chemistry Products TBIL Slides	k840880
4	VITROS XT 7600 Integrated System	VITROS 5600 Integrated System	k081543

Intended Use Statement(s)

1. VITROS Chemistry Products CRBM Slides
Rx Only. For *in vitro* diagnostic use only. VITROS Chemistry Products CRBM Slides quantitatively measure carbamazepine (CRBM) 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. Measurements obtained are used in monitoring levels of carbamazepine to help ensure appropriate therapy.

2. VITROS Chemistry Products CREA Slides

Rx Only. For *in vitro* diagnostic use only. VITROS Chemistry Product CREA Slides quantitatively measure creatinine (CREA) 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. Creatinine measurements are used in the diagnosis and treatment of renal diseases, in monitoring renal dialysis, and as a calculation basis for measuring other urine analytes.

3. VITROS Chemistry Products TBIL Slides
Rx Only. For *in vitro* diagnostic use only. VITROS Chemistry Products TBIL Slides quantitatively measure total bilirubin (TBIL) 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. Measurements of the levels of bilirubin are used in the diagnosis and treatment of liver, hemolytic hematological and metabolic disorders, including hepatitis and gall bladder block.

4. VITROS XT 7600 Integrated System
Rx Only. For *in vitro* diagnostic use only. The VITROS XT 7600 Integrated System is intended for use in the measurement of a variety of analytes of clinical interest.

Device Description

The VITROS XT 7600 Integrated System is a fully automated, computer controlled, clinical chemistry and immunodiagnostic analyzer intended for the in vitro determination of a variety of general chemistries, therapeutic drugs, drugs of abuse, proteins, infectious diseases, as well as cardiac, metabolic, thyroid, anemia, and oncology markers in biological fluids such as serum, plasma, urine and cerebral spinal fluid. The System operates in conjunction with reagents, calibrators and controls designed for use with the System in the MicroSlide, MicroTip or MicroWell format.

The VITROS Chemistry MicroSlide range of products (in this case VITROS Chemistry Products CRBM Slides, VITROS Chemistry Products CREA Slides, and VITROS Chemistry Products TBIL Slides), are combined with the VITROS XT 7600 Integrated System to perform the VITROS CRBM, CREA, and TBIL assays.

Comparison to Predicate Devices

The following tables show similarities and differences between the new and predicate devices.

Table 1 VITROS Chemistry Products CRBM Slides

Similarities		
Device Characteristic	**Candidate VITROS CRBM Slides**	**Predicate Device VITROS CRBM Slides k160495**
Intended Use	Rx Only. For in vitro diagnostic use only. VITROS Chemistry Products CRBM Slides quantitatively measure carbamazepine (CRBM) concentration in serum and plasma.	Same
Basic principle	Multiple-point Immunorate	Same
Reactive Ingredients per cm^2	Immobilized mouse monoclonal anti-carbamazepine antibody 0.02 mg; carbamazepine-horseradish peroxidase conjugate 1.6 ng; and 2-(3,5-dimethoxy-4-hydroxyphenyl)-4,5-bis(4-dimethylaminophenyl) imidazole (leuco dye) 0.02 mg.	Same
Wavelength	670 nm, 540 nm is also used for wash detection	Same
Sample type	Serum and plasma	Same
Sample volume	11 µL	Same

Differences		
Device Characteristic	**Candidate VITROS CRBM Slides**	**Predicate Device VITROS CRBM Slides k160495**
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

Table 2 VITROS Chemistry Products CREA Slides

Similarities		
Device Characteristic	**Candidate VITROS CREA Slides**	**Predicate Device VITROS CREA Slides k063591**
Intended Use	Rx Only. For in vitro diagnostic use only. VITROS Chemistry Product CREA Slides quantitatively measure creatinine (CREA) concentration in serum, plasma, and urine.	Same
Basic principle	Two-point rate	Same
Reactive Ingredients per cm^2	Creatinine amidohydrolase (*Flavobacterium sp.*) 0.20 U; creatine amidinohydrolase (*Alcaligenes sp.*) 3.6 U; sarcosine oxidase (*Bacillus sp.*) 0.55 U; peroxidase (horseradish root) 1.6 U and 2- (3,5-dimethoxy-4-hydroxyphenyl)-4,5-bis(4-dimethylaminophenyl) imidazole (leuco dye) 32 µg.	Same
Wavelength	670 nm	Same
Sample type	Serum, plasma, urine	Same
Sample volume	6 µL	Same

Differences		
Device Characteristic	**Candidate VITROS CREA Slides**	**Predicate Device VITROS CREA Slides k063591**

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

Table 3 VITROS Chemistry Products TBIL Slides

Similarities		
Device Characteristic	**Candidate VITROS TBIL Slides**	**Predicate Device VITROS TBIL Slides K840880**
Intended Use	Rx Only. For *in vitro* diagnostic use only. VITROS Chemistry Products TBIL Slides quantitatively measure total bilirubin (TBIL) concentration in serum and plasma.	Same
Basic principle	Dual wavelength endpoint	Same
Reactive Ingredients per cm^2	Dyphylline 0.5 mg and 4-(N-carboxymethylaminosulfonyl) benzene diazonium hexafluorophosphate 57 µg.	Same
Wavelength	measured at 2 wavelengths, 460 and 540nm	Same
Sample type	Serum and plasma	Same
Sample volume	10 µL	Same

Differences		
Device Characteristic	**Candidate VITROS TBIL Slides**	**Predicate Device VITROS TBIL Slides k840880**
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

Table 4 VITROS XT 7600 Integrated System

Similarities		
Device Characteristic	**Candidate VITROS XT 7600 System**	**Predicate Device VITROS 5600 System k081543**

Similarities		
Device Characteristic	**Candidate VITROS XT 7600 System**	**Predicate Device VITROS 5600 System k081543**
System Features		
Intended use	For use in the in vitro quantitative, semi-quantitative, and qualitative measurement of a variety of analytes of clinical interest, using VITROS Chemistry Products Slides, VITROS Chemistry Products MicroTip Reagents and VITROS Immunodiagnostic Products Reagents.	No change
Fundamental scientific technology	MicroSlides - Colorimetric, Potentiometric, enzymatic endpoint and Immunorate assays. MicroTip and MicroWell reagents The analyzer uses four main detection systems: 1) Reflection densitometry for colorimetric and Immunorate VITROS MicroSlides. 2) Transmission spectrophotometry for VITROS MicroTip assays. 3) Enhanced chemiluminescent detection for VITROS MicroWell assays. 4) Electrometer for VITROS MicroSlide ion-selective electrode (ISE) assays.	No change
Operating principle	Sample programming, sampling processing, result calculation, result reporting	No change
Modes of operation	Continuous, Random, STAT	No change
Throughput	845 tests per hour	No change
User interface	Touch screen (17 inch monitor), keyboard, ADD	No change
Sample and reagent volume verification	Verification to ensure sufficient quantity of sample and reagent to run requested assays	No change
On-Board Dilution Range	Dilution factor of 1: 400	No change
Predictive alerts through eConnectivity	The predictive alerts are logged and are electronically sent to the equipment service group real time for monitoring.	No change
e-Connectivity	Yes	No change

Similarities		
Device Characteristic	**Candidate VITROS XT 7600 System**	**Predicate Device VITROS 5600 System k081543**
(remote access)		
Lab Information System (LIS)	Enabled	No change
VAS Lab Automation System (LAS)	Enabled	No change
Specimen Sampling and Handling		
Specimen type	Serum, Plasma, Urine, CSF, Whole Blood	No change
Specimen containers	Cups, Primary Sample Collection Tubes	No change
Identification	Manual entry or Bar Code	No change
Specimen handling	Universal Sample Tray	No change
Specimen processing	Auto-dilution, repeat and reflex capabilities	No change
Automation capabilities: 10.25 mm tube for pediatric samples	Supported	No change
Sample Quality Monitoring (hemolysis, icterus and turbidity)	Yes	No change
Calibration		
Calibrators	MicroSlide and MicroTip: analyte specific and multiple analytes MicroWell: analyte specific	No change
Identification	MicroSlide and MicroWell: Bar Code or manual entry MicroTip: Manual entry	No change
Calibration Programming	Sample tray can contain Calibrators, QC samples and/or patient samples	No change
Frequency	According to the assay Instructions for Use	No change
Calibration Completion Time Monitoring	Tracking time until calibration completion is displayed to the operator.	No change
Quality Control		

Similarities		
Device Characteristic	**Candidate VITROS XT 7600 System**	**Predicate Device VITROS 5600 System k081543**
Controls	MicroSlide and MicroTip: analyte specific and multiple analyte performance verifiers MicroWell: analyte specific and multiple analyte selling controls and range verifiers	No change
Review Mode	Review Data by Assay and by Event (scroll through multiple assays' QC results which were run at the same time)	No change
Identification	Manual entry or Bar Code	No change
Frequency	According to the assay Instructions for Use. User configurable QC expiration interval.	No change
QC Programming	Programmed by assay	No change

Differences		
Device Characteristic	**Candidate VITROS XT 7600 System**	**Predicate Device VITROS 5600 System K081543**
The following subsystems of the VITROS 5600 Integrated System will be modified	REFL – Reflectometer SLIN – Slide Incubator SLSU – Slide Supply SAIN – Sample Integrity SRME – Sample and Reagent Metering SWCT - System Control and Sample Processing Software SWIN – Software Infrastructure SWUI – Graphical User Interface Software ADDI – Assay Data Disk.	All modifications pertain solely to the MicroSlide processing center. There are no changes being made to the MicroTip and MicroWell processing centers.

Method Comparison

Method Comparison testing was designed and conducted in accordance with CLSI EP09-A3, "*Measurement Procedure Comparison and Bias Estimation Using Patient Samples; Approved Guideline – Third Edition" (2013*).

Method comparison studies were conducted by testing a minimum of 116 human serum samples with analyte concentrations across the analytical ranges of carbamazepine, creatinine and total bilirubin assays on the VITROS XT 7600 Integrated System and the VITROS 5600 Integrated System (predicate device). In addition, 125 human urine samples were tested for creatinine on the

candidate and predicate test systems. The results of the regression analyses for each of the assays are summarized below:

VITROS assay	N	Regression Analysis	Slope	Intercept	Test range	Claimed Measuring Range
CRBM Serum (ug/mL)	118	Deming	1.00	0.12	3.1-17.8	3.0-20.0
CREA Serum (mg/dL)	116	Passing Bablock	0.99	0.00	0.25-13.4	0.15-14.0
CREA Urine (mg/dL)	122	Passing Bablock	0.99	-0.45	3.7-331.0	3.2-346.5
TBIL Serum (mg/dL)	125	Passing Bablok	0.99	0.01	0.14-23.65	0.10-27.00

In addition to the above mentioned method comparison studies, testing was performed to determine the precision, linearity, LoB, LoD, LoQ, and Interfering substances of the representative VITROS assays on the VITROS XT 7600 System.

Precision

Precision studies were conducted following EP05-A3, *Evaluation of Precision of Quantitative Measurement Procedures, Approved Guidelines* – Third Edition (2014). The study was performed by testing a minimum of two Quality control fluids and three human based precision fluids using the Carbamazepine (CRBM), Creatinine (CREA), and Total Bilirubin (TBIL) 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).

CRBM Precision Table (Conventional units)

			Repeatability (Within Run)		Within Day		Between Day		Between Cal		Within Lab (Total)	
Fluid ID	Mean (ug/mL)	N	SD (ug/mL)	%CV	SD (ug/mL)	%CV	SD (ug/mL)	%CV	SD (ug/mL)	%CV	SD (ug/mL)	%CV
CRBM-PP1	3.9	80	0.13	3.30	0.13	3.30	0.08	2.08	0.03	0.77	0.16	3.98
CRBM-6155-1	4.7	80	0.14	2.97	0.14	3.02	0.00	0.00	0.07	1.40	0.16	3.32
CRBM-6156-2	10.1	80	0.24	2.38	0.25	2.46	0.00	0.00	0.13	1.25	0.28	2.76
CRBM-PP3	11.6	80	0.30	2.57	0.35	2.98	0.00	0.00	0.18	1.56	0.39	3.37
CRBM-5896-3	13.1	80	0.29	2.19	0.35	2.67	0.00	0.00	0.22	1.64	0.41	3.14
CRBM-PP5	17.6	80	0.33	1.86	0.37	2.10	0.10	0.57	0.18	1.03	0.42	2.41

CREA Serum Precision Table (Conventional units)

			Repeatability (Within Run)		Within Day		Between Day		Between Cal		Within Lab (Total)	
Fluid ID	Mean (mg/dL)	N	SD (mg/dL)	%CV	SD (mg/dL)	%CV	SD (mg/dL)	%CV	SD (mg/dL)	%CV	SD (mg/dL)	%CV
CREAS-5903-1	0.82	80	0.006	0.713	0.009	1.050	0.003	0.364	0.009	1.121	0.013	1.579
CREAS-PP1	0.88	80	0.006	0.642	0.007	0.743	0.008	0.954	0.012	1.400	0.016	1.850
CREAS-SRM	0.99	80	0.007	0.697	0.008	0.829	0.006	0.568	0.014	1.396	0.017	1.720
CREAS-5905-2	5.39	80	0.039	0.716	0.049	0.914	0.058	1.075	0.043	0.804	0.088	1.624
CREAS-PP2	9.63	80	0.057	0.594	0.070	0.729	0.049	0.513	0.104	1.079	0.135	1.400
CREAS-PP5	12.65	80	0.109	0.865	0.109	0.865	0.071	0.563	0.108	0.850	0.169	1.337

CREA Urine Precision Table (Conventional units)

			Repeatability (Within Run)		Within Day		Between Day		Between Cal		Within Lab (Total)	
Fluid ID	Mean (mg/dL)	N	SD (mg/dL)	%CV	SD (mg/dL)	%CV	SD (mg/dL)	%CV	SD (mg/dL)	%CV	SD (mg/dL)	%CV
CREAU-66791-1	55.6	80	0.58	1.05	0.67	1.20	0.43	0.77	0.96	1.72	1.24	2.23
CREAU-PP1	78.4	80	1.10	1.40	1.13	1.44	0.35	0.45	0.68	0.86	1.36	1.73
CREAU-URN	88.0	80	0.69	0.79	0.98	1.11	0.29	0.33	0.97	1.10	1.41	1.60
CREAU-66792-2	131.2	80	1.67	1.27	1.89	1.44	0.76	0.58	1.78	1.36	2.71	2.06
CREAU-PP4	251.8	80	1.99	0.79	2.12	0.84	1.01	0.40	3.11	1.24	3.90	1.55
CREAU-PP5	320.9	80	2.99	0.93	3.49	1.09	1.49	0.46	3.99	1.24	5.51	1.72

TBIL Precision Table (Conventional units)

			Repeatability (Within Run)		Within Day		Between Day		Between Cal		Within Lab (Total)	
Fluid ID	Mean (mg/dL)	N	SD (mg/dL)	%CV	SD (mg/dL)	%CV	SD (mg/dL)	%CV	SD (mg/dL)	%CV	SD (mg/dL)	%CV
TBIL-PP1	0.3	80	0.01	4.54	0.02	5.20	0.01	4.25	0.00	0.00	0.02	6.72
TBIL-5903-1	1.6	80	0.03	1.68	0.04	2.88	0.01	0.51	0.03	1.84	0.05	3.45
TBIL-PP3	6.5	80	0.03	0.52	0.06	0.87	0.06	0.88	0.04	0.64	0.09	1.40
TBIL-5905-2	15.3	80	0.10	0.67	0.16	1.05	0.10	0.68	0.15	0.99	0.24	1.60
TBIL-PP5	21.6	80	0.17	0.77	0.20	0.92	0.28	1.29	0.00	0.00	0.34	1.58

Linearity

Linearity studies were performed according to CLSI EP06-A, *Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach Approved Guideline (2003).* VITROS CRBM Slides, VITROS CREA Slides, and VITROS TBIL Slides were tested on the VITROS XT 7600 Integrated System. A series of eleven proportionally related admixtures of low and high test fluids were tested to verify linearity; each sample was tested in triplicate, a minimum of two replicates was acceptable for analysis.

The linearity studies support the claimed measuring ranges for the VITROS CRBM, VITROS CREA, and VITROS TBIL assays.

Detection Limits

Detection capability studies for each analyte were evaluated based upon CLSI EP17-A2, *Evaluation of Detection Capability for Clinical Laboratory Measurements Procedures: Approved Guidelines – Second Edition (2012*).

Limit of blank (LoB) studies were performed by testing 4 blank samples. Samples were tested in replicates of 6 over 3 days, using 3 lots of reagents, 4 samples every day, 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, with the 4 human sample pools every day, for a total of 216 observations (72 results per reagent lot). The data were analyzed according to CLSI EP17-A2, using CLSI-approved statistical software Analyse-it version 4.95.4, Method Validation Edition (Analyse-it Software Limited, Leeds UK). The software calculated LoD using a pooled SD from the low level fluid results and the input LoB value for the assay, determined as described above. 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 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, 4 samples every day, for a total of 144 observations (48 results per reagent lot). Ortho defines LoQ as the lowest concentration with an imprecision of ≤20% and percent total allowable error ≤ 19% for carbamazepine; imprecision of ≤20% and percent total allowable error ≤ 30% for creatinine in serum and urine, and imprecision of ≤25% and total allowable error ≤ 0.09 mg/dL for total bilirubin in serum.

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

	CARB (µg/mL)	**TBIL mg/dL**	**Creatinine (mg/dL)**	
			Serum/plasma	**Urine**
LoB	0.6108	0.0378	0.0933	1.9973
LoD	0.6821	0.0722	0.0991	2.1986
LoQ	2.6860	0.0616	0.1119	2.0060
Claimed LoQ	3.0	0.10	0.15	3.2
Assay Range	3.0-20.0	0.10-27.00	0.15-14.0	3.2-346.5

Specificity

Interference Testing was performed in accordance with CLSI EP07-A2, *Interference Testing in Clinical Chemistry, Approved Guidance—Second Edition. Clinical and Laboratory Standards Institute. November 2005,* using VITROS CRBM, VITROS CREA and VITROS TBIL assays.

Assays were tested on one VITROS XT 7600 Integrated System ('VITROS XT 7600, Test System) and one VITROS 5600 Integrated System (VITROS 5600, Predicate/Control System). Testing on the representative assays included known chemical interferents, common chemical substances identified with potential to interfere based upon risk assessment, as well as several claimed non-interferents. If hemoglobin, bilirubin, and/or intralipid were not previously identified as known interferents for the representative assays, Hemolysis, Icterus and/or Turbidity (HIT) indices, respectively, were evaluated during testing. Testing employed "paired-difference" assessment at a minimum of two analyte levels, as specified by CLSI EP07-A2.

*****VITROS Chemistry Products MicroSensor™: Sub-system of analyzer that performs automated semi-quantitative sample quality index determinations on serum/plasma and cerebrospinal fluid samples. The sample quality index determinations performed are hemolysis, icterus, and turbidity; also referred to as 'HIT indices' or 'sample integrity indices'.

Results were evaluated as follows:

Known Interferents: The observed bias was compared to predetermined acceptance criteria (the Maximum Allowable Interference (MAI)) per product design input, and the Claimed Bias derived from product claims.

- If the observed bias was within the MAI criteria (either in a positive or negative direction) and/or less than the Claimed Bias, performance was acceptable.
- If the observed bias was greater than the Claimed Bias, the bias was compared to the 95% Confidence Limit (one-sided) per CLSI EP07-A2. If the Claimed Bias fell within the 95% Confidence Limit, performance was acceptable.

Potential Interferents and Non-Interfering Substances: The observed bias was compared to the Maximum Allowable Interference (MAI).

- If the observed bias was within the MAI criteria (either in a positive or negative direction), performance was acceptable.
- If the observed bias was greater than the MAI the bias was compared to the 95% Confidence Limit (two-sided) per CLSI EP07-A2. If the Claimed Bias fell within the 95% Confidence Limit, performance was acceptable.

Results demonstrate acceptable bias on the VITROS XT 7600 versus the VITROS 5600 for currently claimed interferents. The following previously untested analyte/interferent levels yielded new information for currently claimed interferent compounds as a result of testing:

- 3.0 ug/mL CRBM/ 20 mg/dL Bilirubin on CRBM MicroSlides
- 3.0 ug/mL CRBM/ 3.0 mg/dL Ethamsylate on CRBM MicroSlides

- 3.0 ug/mL CRBM/ 394 mg/dL Ethanol on CRBM MicroSlides
- 3.0 ug/mL CRBM/ 5.0 mg/dL Gentisic Acid on CRBM MicroSlides
- 3.0 ug/mL CRBM/ 100 mg/dL N-Acetylcysteine on CRBM MicroSlides

One new interfering substance was identified as a result of testing:

- Tolazamide on CREA(s) MicroSlides

For the above, bias profiles on the VITROS XT 7600 demonstrated equivalent magnitudes to those using the VITROS 5600, using the noted substances. The Instructions for Use (IFU) for the VITROS CRBM and CREA assays have been updated to claim the additional interfering levels.

Conclusion

The data presented in this pre-market notification demonstrate that the performance of the VITROS XT 7600 Integrated System and the VITROS Chemistry Products assays are substantially equivalent to the cleared predicate devices. The VITROS Chemistry Products CRBM Slides, VITROS Chemistry Products CREA slides, and VITROS Chemistry Product TBIL Slides analyzed on the VITROS XT 7600 Integrated System are substantially equivalent to the VITROS Chemistry Products CRBM Slides (k160495), VITROS Chemistry Products CREA Slides (k063591), and VITROS Chemistry Products TBIL Slides (k840880) analyzed on the VITROS 5600 Integrated System.

Equivalence to predicates was demonstrated using commercially available reagents along with human serum, plasma, and urine samples.

The data presented in the premarket notification provide a reasonable assurance that the VITROS XT 7600 Integrated System and the VITROS assays are safe and effective for the stated intended uses.