August 13, 2021

Ortho-Clinical Diagnostics, Inc.
Darlene Phillips
Manager, Regulatory Affairs
100 Indigo Creek Drive
Rochester, New York 14626-5101

Re: K210858
Trade/Device Name: VITROS Chemistry Products PHBR Slides
Regulation Number: 21 CFR 862.3660
Regulation Name: Phenobarbital Test System
Regulatory Class: Class II
Product Code: DLZ
Dated: March 22, 2021
Received: March 23, 2021

Dear Darlene Phillips:

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/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); 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 https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). 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 (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Marianela Perez-Torres, Ph.D.
Deputy Director
Division of Chemistry
and Toxicology Devices
OHT7: Office of In Vitro Diagnostics
and Radiological Health
Office of Product Evaluation and Quality
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: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
k210858

Device Name
VITROS Chemistry Products PHBR Slides

Indications for Use *(Describe)*
Rx Only
For in vitro diagnostic and laboratory professional use.
VITROS Chemistry Products PHBR Slides quantitatively measure phenobarbital (PHBR) concentration in serum and plasma (lithium heparin) using the automated VITROS 5600 Integrated System.

Measurements obtained by this device are used as an aid in the diagnosis and treatment of phenobarbital use or overdose and in monitoring levels of phenobarbital to help ensure appropriate therapy.

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

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**:** K210858

Submitter's Information

Ortho-Clinical Diagnostics, Inc.
100 Indigo Creek Drive
Rochester, New York 14626-5101
Phone: (585) 453-4253
Fax: (585) 453-4110

Contact Person:

Darlene J Phillips, RAC
Manager, Regulatory Affairs

Date of Preparation:

22-March-2021

Device Proprietary Name(s):

VITROS Chemistry Products PHBR Slides

Common Names:

Phenobarbital assay

Classification Names

Product Code	Class	Regulation Section	Panel
DLZ	II	21 CFR 862.3660 Phenobarbital test system	Clinical Chemistry (75)

Predicate Device(s)

Predicate Device	FDA 510(k) Number
ARCHITECT *i*Phenobarbital Assay	K081231

Intended Use Statement(s)

VITROS Chemistry Products PHBR Slides

Rx Only

For in vitro diagnostic and laboratory professional use.

VITROS Chemistry Products PHBR Slides quantitatively measure phenobarbital (PHBR) concentration in serum and plasma(lithium heparin) using the automated VITROS 5600

Integrated Systems. Measurements obtained by this device are used as an aid in the diagnosis and treatment of phenobarbital use or overdose and in monitoring levels of phenobarbital to help ensure appropriate therapy.

Device Description

The VITROS PHBR Slide is a multilayered, analytical element coated on a polyester support. The phenobarbital assay is based on an enzymatic heterogeneous, competitive immunoassay format. Immobilized anti-phenobarbital antibody and phenobarbital-peroxidase conjugate are present in the spreading layer.

A drop of patient sample is deposited on the slide and is evenly distributed by the spreading layer to the underlying layers. Phenobarbital in the sample competes with the phenobarbital-peroxidase conjugate for a limited number of antibody binding sites during Incubation 1. The subsequent addition of 12 µL of VITROS Immuno-Wash Fluid to the slide removes unbound phenobarbital-peroxidase conjugate from the read area, while also providing a substrate for the enzyme mediated oxidation of leuco dye.

The rate of dye formation, as monitored by reflectance spectrophotometry for Incubation 2, is inversely proportional to the phenobarbital concentration in the sample. To determine if an adequate wash has occurred, a wash detection dye is read at 540 nm during Incubation 2.

Comparison to Predicate Devices

Indications for use/intended use of candidate and predicate devices are the same. The following tables show similarities and differences between the new and predicate devices.

Summary of the technological characteristics of the device compared to the predicate device		
Device Characteristic	**New Device** **VITROS PHBR Slide** **(New)**	**Predícate Device** **ARCHITECT *i*Phenobarbital Assay [k081231]**
Intended Use	For *in vitro* diagnostic use only. Same	For *in vitro* diagnostic use only. Quantitative measurement of phenobarbital in human serum or plasma
Device Description	Multilayered, analytical element coated on a polyester support	Two ready-to-use solutions
Basic Principle	Multi-point immunorate assay	Chemiluminescent Microparticle Immunoassay (CMIA)
Sample type	Serum and lithium heparin plasma	Serum and plasma
Sample Volume	11 µL	20 µL
Assay Range	3.0 – 80.0 µg/mL	1.10 – 80.00 µg/mL
Calibrators	VITROS Chemistry Products Calibrator Kit 9	ARCHITECT *i*Phenobarbital Calibrator Kit
Controls	VITROS Chemistry Products TDM Performance Verifiers	Abbott Immunoassay-MCC (Liquid) or other commercial controls
Instrumentation	VITROS 5600 Integrated System	ARCHITECT i System

Non-Clinical Testing Analytical Performance

Method Comparison

Method Comparison testing followed CLSI Protocol EP09-A3, *Measurement Procedure Comparison and Bias Estimation Using Patient Samples.* Serum samples were evaluated on the VITROS Chemistry Products PHBR Slides using the VITROS 5600 Integrated System and the ARCHITECT *i*Phenobarbital assay. Passing-Bablok Regression was performed to determine the correlation.

N	Slope	Correlation Coefficient	Range of Samples µg/mL	Intercept µg/mL	Sy.x
142	0.92	0.983	5.6 - 76.1	-2.0	2.6

Precision

Precision was evaluated with patient pools and quality control materials following CLSI Protocol EP05-A3, *Evaluation of Precision Performance of Quantitative Methods; Approved Guideline—Third Edition*, using the VITROS Chemistry Products PHBR Slides on the VITROS 5600 Integrated System. The test included 88 observations (2 replicates per run, 2 runs per day over 22 days).

The data presented are a representation of test performance and are provided as a guideline. Variables such as sample handling and storage, reagent handling and storage, laboratory environment, and system maintenance can affect reproducibility of test results.

Mean PHBR Conc.	Conventional Units (µg/mL)				No. of Days	No. of Obs.
	Repeatability*		Within Lab**			
	SD	%CV	SD	%CV		
5.0	0.20	3.9%	0.25	5.0%	22	88
9.1	0.27	2.9%	0.33	3.6%	22	88
11.0	0.30	2.7%	0.44	4.0%	22	88
23.0	0.50	2.2%	0.65	2.8%	22	88
25.1	0.59	2.4%	0.81	3.2%	22	88
38.1	0.79	2.1%	1.09	2.9%	22	88
59.3	1.50	2.5%	2.11	3.6%	22	88

*Repeatability was determined using two replicates per run.

**Within Lab precision was determined using a single lot of slides and a single calibration

Detection Limits

The Limit of Detection (LoD) and Limit of Quantitation (LoQ) were determined for the VITROS PHBR Slides assay consistent with CLSI document EP17.: Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures. The total allowable error goal used to accept the LoQ was ≤ 1.5 µg/mL.

The limit of detection (LoD) for the VITROS PHBR Slides assay is 1.3 µg/mL.

The claimed limit of quantification (LoQ) is 3.0 µg/mL. The Total Error goal used to accept the LoQ was ≤ 1.5 µg/mL.

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 PHBR Slides were tested on the VITROS 5600 Integrated System. A series of fourteen proportionally related admixtures of low and high concentration fluids were tested to verify linearity of the VITROS PHBR Slides test; each sample was tested in duplicate.

Lower Limit of Linearity Interval (LLLI)	Upper Limit of Linearity Interval (ULLI)
0.5 µg/mL	83.5 µg/mL

The deviation from linearity was within the allowable deviation of ± 1.3 µg/mL at phenobarbital concentrations ≤10 µg/mL and within a maximum concentration-dependent allowable deviation of ± 11.5 µg/mL at phenobarbital concentrations > 10 µg/mL.

The VITROS Chemistry Product PHBR Slides assay is linear over the measuring range of 3.0 – 80.0 µg/mL.

Serum and plasma samples with values greater than the VITROS PHBR Slides test measuring range may be diluted with 1part sample and 1part diluent. VITROS Chemistry Products Specialty Diluent is an acceptable diluent for the VITROS PHBR Slides test.

Expected Values

The expected values of the VITROS PHBR Slides are based on the therapeutic range* of 10.0 to 40.0 µg/mL.

*Burtis CA, Bruns DE. Tietz Fundamentals of Clinical Chemistry and Molecular Diagnostics. 7th ed. St. Louis, MO: Elsevier Saunders; 2015:pg 545.

Each laboratory should confirm the validity of these intervals for the population it serves.

Specificity

The VITROS Chemistry Products PHBR Slide test was screened for interfering substances following CLSI document EP07-A3, Interference Testing in Clinical Chemistry. The supplemental tables in CLSI document EP37 were referenced for recommended testing concentrations for analytes and endogenous substances that may interfere in clinical chemistry measurement procedures.

Point estimates of the effects of potential interferents on the VITROS PHBR Slides were made using the paired difference method. Dose-response analysis was conducted to characterize the degree of interference for each substance that exceeded the acceptance criterion in the initial screening test, and expected bias was reported at the lowest test level which did not meet acceptance criteria for bias as shown in the product claims.

Nine (9) substances were found to interfere with the VITROS Chemistry Products PHBR Slides, bias > 1.8 µg/mL at a phenobarbital concentration of approximately 15 µg/mL or bias > 5.2 µg/mL at a phenobarbital concentration of approximately 50 µg/mL.

The substances listed in the table, when tested at the concentrations indicated, caused the bias shown. The bias is an estimate of the maximum bias observed.

Interferent	Conventional Units		
	PHBR Conc. (µg/mL)	Interferent Concentration	Bias (µg/mL)
Conjugated bilirubin	15	13.7 mg/dL	2.1
Ethamsylate		4.5 mg/dL	3.4
Hemoglobin		300 mg/dL	-2.3
Mephobarbital		0.79 mg/dL	2.6
Thiamylal		7.4 mg/dL	3.1
Thiopental		2.5 mg/dL	4.2
Total protein		13.0 g/dL	-2.8
Valproic acid		18.4 mg/dL	2.3

Interferent	Conventional Units		
	PHBR Conc. (µg/mL)	Interferent Concentration	Bias (µg/mL)
Conjugated Bilirubin	50	27.4 mg/dL	6.3
Ethamsylate		3.0 mg/dL	7.2
Ethanol		6.0 mg/mL	7.7
Hemoglobin		225 mg/dL	-8.9
Mephobarbital		0.79 mg/dL	6.6
Thiamylal		7.4 mg/dL	8.5
Thiopental		10.1 mg/dL	9.1
Total protein		13.0 g/dL	-13.5

These results are representative. It is possible that other interfering substances may be encountered in the patient population. The degree of interference at concentrations other than those listed might not be predictable.

Sixty-one (61) test substances, when tested at the concentrations indicated, were found not to interfere with the VITROS PHBR Slides, not to cause bias > 1.8 µg/mL at a phenobarbital concentration of approximately 15 µg/mL or bias > 5.2 µg/mL at a phenobarbital concentration of approximately 50 µg/mL. These will be listed in the customer instructions for use.

Cross-Reactivity

The most common drugs concurrently prescribed with anti-convulsant therapies were reviewed for selection for testing, as well as compounds structurally related to phenobarbital. Substances tested included amobarbital, aprobarbital, barbital, butabarbital, butalbital, hexobarbital, mephobarbital, pentobarbital, phenylethyl-malonamide (pema), phenytoin, primidone, secobarbital, thiamylal, and thiopental. The cross-reactivity of the VITROS Chemistry Products PHBR Slides method was evaluated by adding the substances to serum samples containing phenobarbital concentrations of approximately 15 and 50 µg/mL. Results are provided for reference in the customer instructions for use.

Other Limitations

Certain drugs and clinical conditions are known to alter phenobarbital concentrations in vivo.

Conclusion

The conclusions drawn from the nonclinical tests (discussed above) demonstrate the VITROS Chemistry Products PHBR Slides for use on the VITROS 5600 Integrated System is as safe, effective, and performs as well as the predicate device. The information submitted in the premarket notification is complete and supports a substantial equivalence decision.