ARK Diagnostics, Inc.
Dionne Labatore
Director, Regulatory Affairs and Quality Assurance
48089 Fremont Boulevard
Fremont, California 94538

Re: K232522
Trade/Device Name: ARK Levetiracetam II Assay
Regulation Number: 21 CFR 862.3350
Regulation Name: Diphenylhydantoin test system
Regulatory Class: Class II
Product Code: ORI
Dated: January 12, 2024
Received: January 12, 2024

Dear Dionne Labatore:

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 (the 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 available 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.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" (https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

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 Part 803) for devices or postmarketing safety reporting (21 CFR Part 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 Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 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,

Joseph A. Kotarek -S

Digitally signed by Joseph A. Kotarek -S
Date: 2024.02.27 17:40:26 -05'00'

Joseph Kotarek
Branch Chief for Toxicology
Division of Chemistry
and Toxicology Devices
OHT7: Office of In Vitro Diagnostics
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)*
K232522

Device Name
ARK Levetiracetam II Assay

Indications for Use *(Describe)*
ARK Levetiracetam II Assay: The ARK Levetiracetam II Assay is a homogeneous enzyme immunoassay intended for the quantitative determination of levetiracetam in human serum or plasma on automated clinical chemistry analyzers. Levetiracetam concentrations can be used as an aid in management of patients treated with levetiracetam.

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 k232522.

807.92 (a)(1): Name: **ARK Diagnostics, Inc.**

Address: 48089 Fremont Boulevard
Fremont, CA 94538

Owner Operator Number: 10027663
Establishment Registration: 3005755244

Phone: (510) 270-6276
FAX: (510) 270-6298
Contact: Dionne Labatore
Director, Regulatory Affairs and Quality Assurance
Email: dionne@ark-tdm.com
Direct phone: (510) 270-6276

Date prepared: August 18, 2023

807.92 (a)(2): Device name- trade name and common name, and classification

Trade name: ARK Levetiracetam II Assay

Common Name: Homogeneous Enzyme Immunoassay

Classification: 21 CFR 862.3350 ORI Diphenylhydantoin Test System; Class II

807.92 (a)(3): Identification of the legally marketed predicate device

Predicate Device Name: ARK Levetiracetam Assay

Predicate Device 510(k) Number: K091653

807.92 (a)(4): Device Description

The ARK Levetiracetam II Assay is a homogeneous immunoassay based on competition between drug in the specimen and levetiracetam labeled with the enzyme glucose-6-phosphate dehydrogenase (G6PDH) for binding to the antibody reagent. As the latter binds antibody, enzyme activity decreases. In the presence of drug from the specimen, enzyme activity increases and is directly related to the drug concentration. Active enzyme converts the coenzyme nicotinamide adenine dinucleotide (NAD) to NADH that is measured spectrophotometrically as a rate of change in absorbance. Endogenous serum G6PDH does not interfere with the results because the coenzyme NAD functions only with the bacterial enzyme used in the assay.

The ARK Levetiracetam II Assay consists of reagents R1 anti-levetiracetam monoclonal antibody with substrate and R2 levetiracetam labeled with bacterial G6PDH enzyme.

807.92 (a)(5): Intended Use / Indications for Use

ARK Levetiracetam II Assay

The ARK Levetiracetam II Assay is a homogeneous enzyme immunoassay intended for the quantitative determination of levetiracetam in human serum or plasma on automated clinical chemistry analyzers. Levetiracetam concentrations can be used as an aid in management of patients treated with levetiracetam.

807.92 (a)(6): Technological Similarities and Differences to the Predicate

SUBSTANTIAL EQUIVALENCE COMPARATIVE CHART

Comparison between the ARK Levetiracetam Assay and the ARK Levetiracetam II Assay

Characteristic	**Predicate Device** ARK Levetiracetam Assay (K091653)	**Candidate Device** ARK Levetiracetam II Assay
Intended Use	The ARK Levetiracetam Assay is intended for the quantitative determination of levetiracetam in human serum or plasma on automated clinical chemistry analyzers.	Same
Indications for Use	Levetiracetam concentrations can be used as an aid in management of patients treated with levetiracetam.	Same
Sample	Serum or plasma	Same
Methodology	Homogeneous enzyme immunoassay (EIA)	Same
Reagent Components	Two (2) reagent system: Anti-levetiracetam Antibody/Substrate Reagent (R1) containing rabbit polyclonal antibodies to levetiracetam, glucose-6-phosphate, nicotinamide adenine dinucleotide, bovine serum albumin, preservatives, and stabilizers Enzyme Reagent (R2) containing levetiracetam labeled with bacterial G6PDH, buffer, bovine serum albumin, preservatives, and stabilizers	Two (2) reagent system: Anti-levetiracetam Antibody/Substrate Reagent (R1) containing rabbit monoclonal antibodies to levetiracetam, glucose-6-phosphate, nicotinamide adenine dinucleotide, bovine serum albumin, sodium azide, and stabilizers Enzyme Reagent (R2) containing levetiracetam labeled with bacterial G6PDH, buffer, bovine serum albumin, sodium azide, and stabilizers
Platform required	Automated clinical chemistry analyzer	Same
Accessory reagents	Calibrators (six levels) and controls (three levels)	Same
Testing environment	Routine clinical laboratory	Same
Reagent condition and storage	Liquid, 2-8˚ C	Same

807.92 (b)(1) and 807.92 (b)(2): Brief Description of Nonclinical and Clinical Data
The following performance characteristics were obtained on the Beckman Coulter AU680 automated clinical chemistry analyzer.

Limit of Quantitation (LoQ)

The LoQ of the ARK Levetiracetam II Assay was determined to be 2.0 µg/mL and may depend on analyzer specific performance. The LoQ was determined according to CLSI EP17-A2 and is defined as the lowest concentration for which acceptable inter-assay precision (≤20% CV) and recovery (±15%) is observed. Pooled human serum was supplemented with levetiracetam to give concentrations of 1.0, 2.0, and 3.0 µg/mL. Eight (8) replicates of each sample were tested in each of five (5) runs to give a minimum of 40 replicates of each LoQ sample tested.

Nominal Concentration (µg/mL)	N	Grand Mean (µg/mL)	RMS SD	CV
1.0	40	0.9	0.044	4.91
2.0	40	1.9	0.052	2.80
3.0	40	3.0	0.077	2.55

Measurement Range

The measurement range of the ARK Levetiracetam II Assay is 2.0 – 100.0 µg/mL.

Recovery

Analytical recovery throughout the measurement range was performed by adding concentrated levetiracetam drug into human serum negative for levetiracetam. A stock concentrate of highly pure levetiracetam was added volumetrically to human serum negative for levetiracetam, representing drug concentrations across the assay range. Two analytical runs of three replicates of each sample were assayed on an automated clinical chemistry analyzer. The results of the six replicates of each sample were averaged and compared to the target concentration and percent recovery calculated. Recovery at all concentrations tested was ±10% of the expected sample concentration.

Theoretical Concentration Tested (µg/mL)	Mean (µg/mL)	%Recovery
2.0	1.9	95.0
4.0	3.9	97.5
10.0	9.8	98.0
20.0	20.1	100.5
45.0	46.2	102.6
80.0	77.8	97.3
100.0	100.3	100.3

Linearity

Linearity studies were performed as suggested in CLSI Protocol EP06-Ed2. A 120.0 µg/mL levetiracetam serum sample was prepared, and dilutions were made proportionally with human

serum negative for levetiracetam. Levetiracetam concentrations ranged from 2.0 to 100.0 µg/mL. Two analytical runs of three replicates of each sample were assayed on an automated clinical chemistry analyzer. The results of the six replicates of each sample were averaged. A weighted linear regression analysis was performed. Linearity was acceptable if the percent difference (% Deviation) was ±10% between the predicted results and the observed results. The regression equation calculated according to EP06-Ed2 is y=1.003x. A linear relationship was demonstrated between 2.0 to 100.0 µg/mL.

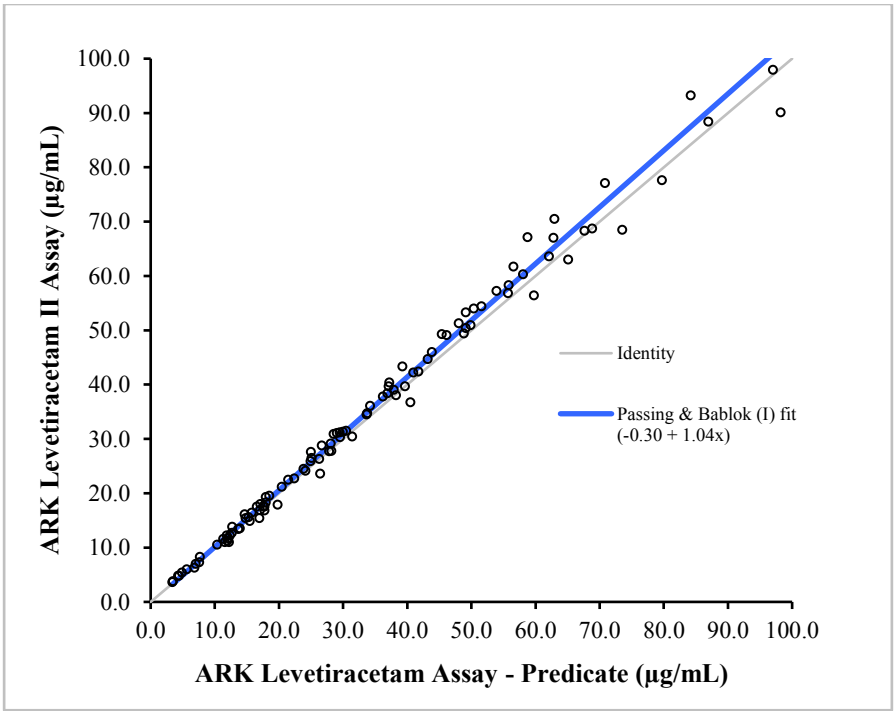
Weighted Linear Regression Analysis

Nominal (Estimated) Value (µg/mL)	Observed Results (µg/mL)	Predicted Results (ug/mL)	% Deviation
0.0	NA	NA	NA
2.0	1.9	2.0	-6.1
3.0	3.2	3.0	4.7
4.0	3.9	4.0	-3.2
6.0	6.1	6.0	1.1
10.0	11.0	10.0	9.5
20.0	20.0	20.1	-0.3
40.0	42.0	40.1	4.7
60.0	62.1	60.2	3.2
80.0	78.9	80.2	-1.7
100.0	105.4	100.3	5.1

Method Comparison

Correlation studies were performed using CLSI Protocol EP9-A3. Results from the ARK Levetiracetam II Assay performed on the Beckman Coulter AU680 were compared with results from the predicate ARK Levetiracetam Assay performed on the Roche/Hitachi 917. Levetiracetam concentrations ranged from 3.4 µg/mL to 98.3 µg/mL. Results of the Passing-Bablok regression analysis for the study are shown below (with 95% confidence limits).

Slope	1.04	(1.03 to 1.06)
y-intercept	-0.30	(-0.78 to 0.11)
Correlation Coefficient (r^2)	0.99	(0.985 to 0.993)
Number of Samples	104	


ARK Levetiracetam II Assay (µg/mL)
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
0.0
10.0
20.0
30.0
40.0
50.0
60.0
70.0
80.0
90.0
100.0
ARK Levetiracetam Assay - Predicate (µg/mL)
Identity
Passing & Bablok (I) fit
(-0.30 + 1.04x)

Precision

Precision was determined as described in CLSI Protocol EP05-A3. Tri-level controls and three samples of levetiracetam in pooled human serum were used in the study. Data were collected on a single analyzer over twenty (20) non-consecutive days. Each level was assayed in quadruplicate twice a day. Each of the runs per day was separated by at least two hours. The within run, between day, total SD, and percent CVs were calculated. Results are shown below. Acceptance criteria: ≤10% total CV.

			Within Run		Between Day		Total	
Sample	**N**	**Mean (µg/mL)**	**SD**	**CV (%)**	**SD**	**CV (%)**	**SD**	**CV (%)**
ARK Levetiracetam II Control								
LOW	160	7.6	0.16	2.1	0.09	1.2	0.18	2.3
MID	160	30.5	0.45	1.5	0.34	1.1	0.60	2.0
HIGH	160	75.7	1.41	1.9	0.99	1.3	2.19	2.9
Human Serum								
LOW	160	7.7	0.11	1.4	0.06	0.8	0.12	1.6
MID	160	32.6	0.47	1.4	0.34	1.1	0.61	1.9
HIGH	160	80.5	1.62	2.0	0.80	1.0	1.79	2.2

Interfering Substances

Interference studies were conducted using CLSI EP07-A3 as a guideline. Clinically high concentrations of the following potentially interfering substances in serum with known levels of levetiracetam (approximately 15 and 50 µg/mL) were evaluated. Two analytical runs of three replicates of each sample (6 replicates total) were assayed using the ARK Levetiracetam II Assay, along with a serum control of levetiracetam. The mean results of levetiracetam were calculated and the percentage recovery relative to the serum control mean result was determined. Measurement of levetiracetam resulted in ≤10% error in the presence of interfering substances at the levels tested.

		Percentage Recovery (%)	
Interfering Substance	**Interferent Concentration**	**15 µg/mL Levetiracetam**	**50 µg/mL Levetiracetam**
Human Albumin	12 g/dL	98.7	99.9
Conjugate Bilirubin	72 mg/dL	100.2	100.9
Unconjugated Bilirubin	72 mg/dL	101.7	97.1
Cholesterol	620 mg/dL	94.9	100.8
Human IgG	12 g/dL	102.7	98.7
Hemoglobin	1050 mg/dL	100.9	95.8
Rheumatoid Factor	1080 IU/mL	98.8	94.5
Triglycerides	1670 mg/dL	98.6	95.9
Uric Acid	30 mg/dL	91.0	98.8

Metabolites

ARK Levetiracetam II Assay serum and plasma results are unlikely to be affected by metabolism of levetiracetam drug, since plasma levels of metabolites are usually not clinically significant. The following metabolite was tested for crossreactivity. Measurement of levetiracetam resulted in ≤ 10% error in the presence of ucb L057 (2-pyrrolidone-*N*-butyric acid) at the level tested.

Metabolite	**ucb L057 (µg/mL)**	**Percent Cross-Reactivity**		**Percent Interference**	
		Levetiracetam 15 µg/mL	**Levetiracetam 50 µg/mL**	**Levetiracetam 15 µg/mL**	**Levetiracetam 50 µg/mL**
ucb L057: 2-pyrrolidone-*N*-butyric acid	250.0	0.0	0.0	0.8	0.1

Drug Interference

Due to structural similarities, brivaracetam (Briviact®) crossreacts substantially in the ARK Levetiracetam II Assay. Measurements of levetiracetam should not be made with the ARK assay when both drugs are present in circulation.

Levetiracetam-selective antibody did not crossreact with other anti-epileptic or coadministered drugs tested. A high concentration of each compound was spiked into normal human serum with known levels of levetiracetam (approximately 15 and 50 µg/mL) and assayed along with a serum control of levetiracetam. Measurement of levetiracetam resulted in ≤ 10% error in the presence of drug compounds at the levels tested.

Compound	Concentration (µg/mL)	Compound	Concentration (µg/mL)
Acetaminophen	500	Nortriptyline	20
Acetylsalicylic acid	1000	Oxcarbazepine	50
Amitriptyline	20	Phenobarbital	200
Caffeine	100	Phenytoin	200
Carbamazepine	120	Primidone	100
Clonazepam	50	Probenecid	600
Cyclosporin A	40	Salicylic Acid	500
Diazepam	50	Sulfamethoxazole	400
Digoxin	40	Sulfisoxazole	400
Erythromycin	200	Theophylline	250
Ethosuximide	250	Tiagabine	200
Felbamate	250	Topiramate	250
Gabapentin	100	Trimethoprim	40
Heparin	200 units/mL	Valproic Acid	500
Hydrochlorothiazide	20	Verapamil	100
Ibuprofen	500	Vigabatrin	150
Lamotrigine	250	Warfarin	250
Naproxen	500	Zonisamide	250

Anticoagulants

Serum and plasma were accepted as equivalent matrices for the measurement of levetiracetam in the predicate submission K091653.

Sample Stability

Serum specimens were shown to be stable for at least forty-eight (48) hours at room temperature (22 °C), forty (40) days when refrigerated (2-8 °C) and after three (3) successive freeze/thaw cycles.

Product Stability

Accelerated stability studies and real time stability studies support a shelf-life stability claim of up to 18 months for the ARK Levetiracetam II Reagents when stored unopened at 2-8°C.

On-Board Stability

Reagents were stable up to 96 days when stored on-board the instrument based on supporting data.

Calibration Curve Stability

A stored calibration curve was effective up to at least 28 days based on supporting data. Calibration curve stability may depend on individual laboratory performance.

807.92 (b)(3): Conclusions from Nonclinical Testing

As summarized above, the ARK Levetiracetam II Assay is substantially equivalent to the ARK Levetiracetam Assay system K091653. The ARK Levetiracetam II Assay system was shown to be safe and effective for its intended use based on performance studies.