K091653

510(k) SUMMARY

NOV - 2 2009

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 **K091653**.

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

Address: 1190 Bordeaux Drive
Sunnyvale, CA 94089

Owner Operator Number: 10027663
Establishment Registration: 3005755244

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Executive Director of Quality and Regulatory Affairs

Date prepared: October 23, 2009

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

Trade name: ARK™ Levetiracetam Assay
ARK™ Levetiracetam Calibrator
ARK™ Levetiracetam Control

Common Name: Homogeneous Enzyme Immunoassay

Classification: 21 CFR 862.3350 NWM Diphenylhydantoin Test System; Class II
(21 CFR 862.3200 DLJ, 21 CFR 862.3280 LAS)

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

ARK™ Topiramate Assay	K083799 (bundled)
ARK™ Topiramate Calibrator	
ARK™ Topiramate Control	

807.92 (a)(4): Device Description

The ARK Levetiracetam 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 proportional 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 coenyzme NAD functions only with the bacterial enzyme used in the assay.

The ARK Levetiracetam Assay consists of reagents R1 anti-levetiracetam polyclonal antibody with substrate and R2 levetiracetam labeled with bacterial G6PDH enzyme. The ARK Levetiracetam Calibrator consists of a six-level set to calibrate the assay, and the ARK Levetiracetam Control consists of a three-level set used for quality control of the assay.

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

The ARK™ Levetiracetam 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.

The ARK™ Levetiracetam Calibrator is intended for use in calibration of the ARK Levetiracetam Assay.

The ARK™ Levetiracetam Control is intended for use in quality control of the ARK Levetiracetam Assay.

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

SUBSTANTIAL EQUIVALENCE COMPARATIVE CHART

Comparison between the ARK™ Levetiracetam Assay and the ARK™ Topiramate Assay

Characteristic*	Device ARK™ Levetiracetam Assay	Predicate ARK™ Topiramate Assay K083799
Intended Use	The ARK™ Levetiracetam Assay is intended for the quantitative determination of levetiracetam in human serum or plasma on automated clinical chemistry analyzers.	The ARK™ Topiramate Assay is intended for the quantitative determination of topiramate in human serum or plasma on automated clinical chemistry analyzers.
Indications for Use	The results obtained are used in the diagnosis and treatment of levetiracetam overdose and in monitoring levels of levetiracetam to help ensure appropriate therapy.	The results obtained are used in the diagnosis and treatment of topiramate overdose and in monitoring levels of topiramate to help ensure appropriate therapy.
Sample	Serum or plasma	Serum or plasma
Methodology	Homogenous enzyme immunoassay (EIA)	Homogenous enzyme immunoassay (EIA)
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-topiramate Antibody/Substrate Reagent (R1) containing rabbit polyclonal antibodies to an epitope of topiramate, glucose-6-phosphate, nicotinamide adenine dinucleotide, bovine serum albumin, preservatives, and stabilizers Enzyme Reagent (R2) containing topiramate epitope labeled with bacterial G6PDH, buffer, bovine serum albumin, preservatives, and stabilizers
Platform required	Automated clinical chemistry analyzer	Automated clinical chemistry analyzer
Accessory reagents	Calibrators (six levels) and controls (three levels)	Calibrators (six levels) and controls (three levels)
Testing environment	Routine clinical laboratory	Routine clinical laboratory
Reagent condition and storage	Liquid, 2-8° C	Liquid, 2-8° C

807.92 (b)(1) and 807.92 (b)(2):
Brief Description of Nonclinical and Clinical Data

Limit of Quantitation (LOQ)

The LOQ of the ARK Levetiracetam Assay was determined according to CLSI EP17-A and is defined as the lowest concentration for which acceptable inter-assay precision and recovery is observed (≤20% CV with ±15% recovery). The LOQ was determined to be 2.0 µg/mL.

Accuracy

Accuracy (analytical recovery) 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. Six replicates of each sample were assayed on an automated clinical chemistry analyzer. The results were averaged and compared to the target concentration and percent recovery calculated. Results are shown below.

$$\% \text{ Recovery} = 100 \times \frac{\text{Mean recovered concentration}}{\text{Theoretical concentration}}$$

Theoretical Concentration (µg/mL)	Mean Recovered Concentration (µg/mL)	Percent Recovery
2.0	1.9	95.8
4.0	3.8	94.6
10.0	10.0	100.0
20.0	19.2	95.9
45.0	44.1	98.0
80.0	79.3	99.1
100.0	105.3	105.3

Linearity

Linearity studies were performed as suggested in CLSI/NCCLS Protocol EP6-A. A 100.0 µg/mL serum sample was prepared and dilutions were made proportionally with human serum negative for levetiracetam. Levetiracetam concentrations ranged from 1.0 to 100.0 µg/mL. Linearity at specific dilutions was considered acceptable if the percent difference was ±10% between the predicted 1st and 2nd order regressed values or ±15% below 3.0 µg/mL. A linear relationship was demonstrated between 2.0 and 100.0 µg/mL. Results are shown below.

Estimated Value (µg/mL)	Results (µg/mL)	1st Order Predicted Results	2nd Order Predicted Results	% Difference (Acceptance Criteria: ±10%)
2.0	1.9	2.1	2.4	13.2
3.0	3.2	3.1	3.4	7.6
4.0	4.1	4.2	4.3	4.8
5.0	5.3	5.2	5.3	3.1
6.0	6.4	6.2	6.3	2.0
7.0	7.6	7.2	7.3	1.3
8.0	8.4	8.3	8.3	0.7
9.0	9.5	9.3	9.3	0.3
10.0	10.7	10.3	10.3	-0.1
20.0	20.7	20.6	20.4	-1.3
30.0	31.0	31.0	30.5	-1.4
40.0	41.3	41.3	40.8	-1.2
50.0	51.9	51.6	51.1	-0.9
60.0	60.3	61.9	61.6	-0.5
70.0	71.2	72.2	72.1	-0.1
80.0	81.4	82.5	82.8	0.3
90.0	93.7	92.8	93.5	0.7
100.0	104.6	103.1	104.3	1.2

Assay Range

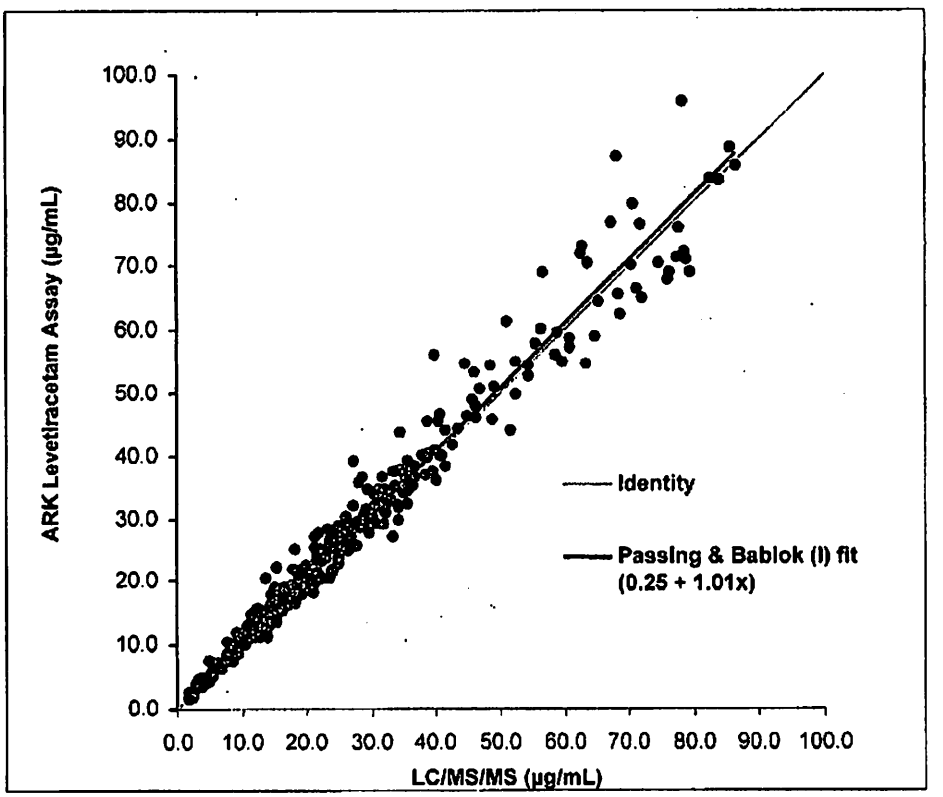
The range of the assay is 2.0 to 100.0 µg/mL. Report results below this range as <2.0 µg/mL or below the analyzer-specific lower LOQ established in your laboratory. Report results above this range as >100.0 µg/mL or above the analyzer-specific upper LOQ established in your laboratory.

Specimens testing initially above the assay range may be diluted in Calibrator A and retested. Multiply the assay result by the dilution factor to obtain the concentration of levetiracetam in the undiluted specimen.

Method Comparison

Correlation studies were performed using CLSI/NCCLS Protocol EP9-A2. Results from the ARK Levetiracetam assay were compared with results from a reference LC/MS/MS method. The levetiracetam concentrations ranged from 2.0 µg/mL to 86.4 µg/mL. Results of the Passing-Bablok regression analysis for the study are shown below (with 95% confidence limits).

Slope	1.01	(0.99 to 1.03)
y-intercept	0.25	(- 0.24 to 0.63)
Correlation Coefficient (r^2)	0.97	(0.96 to 0.97)
Number of Samples	305	



Precision

Precision was determined as described in CLSI/NCCLS Protocol EP5-A2. Tri-level controls and three human serum pooled specimens containing levetiracetam were used in the study. Each level was assayed in quadruplicate twice a day for 20 days. 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 Control								
LOW	160	7.5	0.25	3.4	0.23	3.2	0.34	4.5
MID	160	29.4	0.85	2.9	0.83	2.8	1.08	3.7
HIGH	160	73.4	2.14	2.9	2.03	2.8	3.08	4.2
Human Serum								
LOW	160	6.9	0.26	3.8	0.22	3.1	0.33	4.8
MID	160	30.2	0.87	2.9	1.10	3.7	1.23	4.1
HIGH	160	75.5	2.19	2.9	2.35	3.1	3.31	4.4

Interfering Substances

Interference studies were conducted using CLSI/NCCLS Protocol EP7-A2 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. Each sample was assayed using the ARK Levetiracetam Assay, along with a serum control of levetiracetam. Measurement of levetiracetam resulted in ≤10% error in the presence of interfering substances at the levels tested.

Interfering Substance	Interferent Concentration
Albumin	12 g/dL
Bilirubin	70 mg/dL
Cholesterol	535 mg/dL
Gamma-Globulin	12 g/dL
Hemoglobin	1000 mg/dL
Intralipid®	1500 mg/dL
Rheumatoid Factor	1100 IU/mL
Triglycerides	1033 mg/dL
Uric Acid	30 mg/dL

Metabolites

Levetiracetam is hydrolyzed to its major metabolite 2-pyrrolidone-*N*-butyric acid (ucb L057) and two minor metabolites.[3] The metabolite ucb L057 was tested for cross-reactivity.

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	-0.2	1.3	-3.0	6.6

Drug Interference

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	Conc. Tested (µg/mL)	Percentage Recovery	
		15 µg/mL Levetiracetam	50 µg/mL Levetiracetam
Acetaminophen	200	99.3	97.5
Acetyl Salicyclic acid	1000	103.2	98.9
Amitriptyline	20	98.4	100.7
Caffeine	100	95.4	97.7
Carbamazepine	120	101.1	99.7
Clonazepam	50	100.2	100.4
Cyclosporin A	40	99.9	98.4
Diazepam	50	100.3	98.6
Digoxin	40	92.9	100.2
Erythromycin	200	99.0	97.9
Ethosuxamide	250	98.1	101.1
Felbamate	250	100.8	97.9
Gabapentin	100	101.3	96.3
Heparin	200 units/mL	97.0	97.2
Hydrochlorothiazide	20	98.2	98.9
Ibuprofen	500	98.5	99.2
Lamotrigine	250	94.3	102.4
Naproxen	500	99.0	101.3
Nortriptyline	20	99.3	97.8
Oxcarbazepine	50	95.5	100.4
Phenobarbital	200	98.8	99.4
Phenytoin	200	97.8	96.8
Primidone	100	97.7	97.3
Probenecid	600	100.5	101.5
Salicylic Acid	500	95.1	98.4

Compound	Conc. Tested (µg/mL)	Percentage Recovery 15 µg/mL Levetiracetam	50 µg/mL Levetiracetam
Sulfamethoxazole	400	97.9	96.3
Sulfisoxazole	400	100.6	100.4
Theophylline	250	96.6	101.1
Tiagabine	200	99.0	97.5
Topiramate	250	94.7	99.2
Trimethoprim	40	102.0	99.3
Valproic Acid	500	98.7	96.2
Verapamil	100	100.3	96.4
Vigabatrin	150	94.0	97.1
Warfarin	250	96.6	102.3
Zonisamide	250	100.3	101.7

Anticoagulants

Studies were conducted to determine the performance characteristics of the assay for both serum and plasma samples containing levetiracetam.

The results indicate that there is no significant difference between the recovery of levetiracetam in serum or plasma.

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.

On-Board Stability

Calibration Curve Stability: A stored calibration was effective up to 40 days based on supporting data.

Reagent on-board stability: Reagents were effective when stored after transfer to analyzer specific reagent containers for up to at least 40 days based on supporting data. In-use stability of calibrator and controls was also demonstrated.

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

As summarized above, the ARK Levetiracetam Assay, the ARK Levetiracetam Calibrator and the ARK Levetiracetam Control are substantially equivalent to the ARK™ Topiramate Assay system. The ARK Levetiracetam Assay system was shown to be safe and effective for its intended use based on performance studies.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
10903 New Hampshire Avenue
Document Mail Center – WO66-0609
Silver Spring, MD 20993-0002

JUN 09 2010

ARK Diagnostics
C/O Mr. Johnny Valdez
1190 Bordeaux Drive
Sunnyvale, CA 94089

Re: k091653
Trade/Device Name: ARK Levetiracetam Assay, ARK Levetiracetam Calibrators and ARK Levetiracetam Controls
Regulation Number: 21 CFR 862.3350
Regulation Name: Diphenylhydantoin Test System
Regulatory Class: Class II
Product Code: ORI, LAS, DLJ
Dated October 20, 2009
Received October 21, 2009

Dear Mr. Valdez:

This letter corrects our substantially equivalent letter of November 2, 2009.
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 (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. 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.

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); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (301) 796-5450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding postmarket surveillance, please contact CDRH's Office of Surveillance and Biometric's (OSB's) Division of Postmarket Surveillance at (301) 796-5760. 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 the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-5680 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Courtney C. Harper, Ph.D.
Director
Division of Chemistry and Toxicology
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

Indication for Use

510(K) Number (if known): K091653

Device Name:

ARK™ Levetiracetam Assay
ARK™ Levetiracetam Calibrator
ARK™ Levetiracetam Control

Indications for Use:

The ARK™ Levetiracetam 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.

The ARK™ Levetiracetam Calibrator is intended for use in calibration of the ARK Levetiracetam Assay.

The ARK™ Levetiracetam Control is intended for use in quality control of the ARK Levetiracetam Assay.

Prescription Use ___X___ (21 CFR Part 801 Subpart D) And/Or Over the Counter Use ____. (21 CFR Part 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE; CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD)

Division Sign-Off
Office of In Vitro Diagnostic Device
Evaluation and Safety

510(k) K091653

Indication for Use

510(K) Number (if known): K091653

Device Name:

ARK™ Levetiracetam Assay
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Division Sign-Off
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Evaluation and Safety

510(k) K091653