DEC - 9 2009

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 **K091884**.

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: November 24, 2009

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

Trade name: ARK™ Zonisamide Assay
ARK™ Zonisamide Calibrator
ARK™ Zonisamide 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

K051211
QMS® Zonisamide Assay, QMS® Zonisamide Calibrator Set, QMS® Zonisamide Control Set

807.92 (a)(4): Device Description

The ARK Zonisamide Assay is a homogeneous immunoassay based on competition between drug in the specimen and zonisamide 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 Zonisamide Assay consists of reagents R1 anti-zonisamide polyclonal antibody with substrate and R2 zonisamide labeled with bacterial G6PDH enzyme. The ARK Zonisamide Calibrator consists of a six-level set to calibrate the assay, and the ARK Zonisamide 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™ Zonisamide Assay is a homogeneous enzyme immunoassay intended for the quantitative determination of zonisamide in human serum or plasma samples on automated clinical chemistry analyzers. Zonisamide concentrations can be used as an aid in management of patients treated with zonisamide.

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

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

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

SUBSTANTIAL EQUIVALENCE COMPARATIVE CHART

Comparison between the ARK™ Zonisamide Assay and the Seradyn QMS® Zonisamide Assay

Characteristic	**Device** ARK™ Zonisamide Assay	**Predicate** QMS® Zonisamide Assay K051211
Intended Use	The ARK™ Zonisamide Assay is intended for the quantitative determination of zonisamide in human serum or plasma on automated clinical chemistry analyzers.	The QMS® Zonisamide Assay is intended for the quantitative determination of zonisamide in human serum or plasma samples.
Indications for Use	Zonisamide concentrations can be used as an aid in management of patients treated with zonisamide.	Zonisamide concentrations can be used as an aid in management of patients treated with zonisamide.
Sample	Serum or plasma	Serum or plasma
Methodology	Homogenous enzyme immunoassay (EIA)	Homogenous particle-enhanced turbidimetric immunoassay
Reagent Components	Two (2) reagent system: Anti-zonisamide Antibody/Substrate Reagent (R1) containing rabbit polyclonal antibodies to zonisamide, glucose-6-phosphate, nicotinamide adenine dinucleotide, bovine serum albumin, preservatives, and stabilizers Enzyme Reagent (R2) containing zonisamide labeled with bacterial G6PDH, buffer, bovine serum albumin, preservatives, and stabilizers No special handling required. Reagents do not contain azide.	Two (2) reagent system: The device consists of ready-to-use reagents containing rabbit polyclonal zonisamide antibodies in buffer (R1), and zonisamide-coated microparticles with (R2), both with azide preservative.
Platform required	Automated clinical chemistry analyzer Validated on Hitachi 917	Automated clinical chemistry analyzer Validated on Hitachi 717
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 Zonisamide 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.

Recovery

Analytical recovery was performed by adding concentrated zonisamide drug into human serum negative for zonisamide. A stock concentrate of highly pure zonisamide was added volumetrically to human serum negative for zonisamide, representing drug concentrations across the assay range. Twenty replicates of each sample were assayed. 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	1.7	85.3
3.0	3.0	100.0
5.0	5.5	110.0
15.0	15.7	104.5
25.0	25.3	101.0
35.0	35.0	100.0
50.0	49.1	98.1

Linearity

Linearity studies were performed as suggested in CLSI/NCCLS Protocol EP6-A. An 80.0 µg/mL serum sample was prepared and dilutions were made proportionally with human serum negative for zonisamide. Zonisamide concentrations ranged from 0.8 to 80.0 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 between 2.4 and 48.0 µg/mL is shown below.

Estimated Value (µg/mL)	Results (µg/mL)	1st Order Predicted Results	2nd Order Predicted Results	% Difference
2.4	2.3	2.5	2.3	-7.0
3.2	3.2	3.3	3.2	-3.8
4.0	4.1	4.1	4.0	-1.8
4.8	4.8	4.8	4.8	-0.6
5.6	5.8	5.6	5.6	0.3
6.4	6.7	6.4	6.5	1.0
7.2	7.4	7.2	7.3	1.4
8.0	8.2	8.0	8.1	1.8
16.0	16.2	15.7	16.2	2.7
24.0	23.4	23.5	24.0	2.3
32.0	32.0	31.3	31.7	1.4
40.0	39.7	39.1	39.2	0.4
48.0	45.8	46.8	46.5	-0.7

Assay Range

The range of the assay is 2.0 to 50.0 µg/mL. Report results below this range as <2.0 µg/mL. Report results above this range as >50.0 µg/mL.

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 zonisamide in the undiluted specimen. The concentration after dilution must exceed the limit of quantitation and fall within the measuring range.

Method Comparison

Correlation studies were performed using CLSI/NCCLS Protocol EP9-A2. Results from the ARK Zonisamide Assay were compared with results from a turbidimetric immunoassay. The zonisamide concentrations ranged from 6 µg/mL to 45 µg/mL. Results of the Passing-Bablok regression analysis for the study are shown below with 95% confidence limits shown in parentheses.

Slope	1.00	(0.96 to 1.00)
y-intercept	- 1.00	(- 1.00 to - 0.46)
Correlation Coefficient (r^2)	0.93	(0.91 to 0.95)
Number of Samples	176	

Precision

Precision was determined as described in CLSI/NCCLS Protocol EP5-A2. Tri-level controls containing zonisamide and pooled human serum specimens were used in the study. Each level of control 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 Zonisamide Control								
LOW	160	5.0	0.21	4.1	0.16	3.2	0.25	5.1
MID	160	24.4	0.96	3.8	0.56	2.3	1.12	4.5
HIGH	160	50.6	1.97	3.9	1.33	2.6	2.63	5.3
Human Serum								
LOW	160	7.0	0.29	4.0	0.21	3.0	0.36	4.9
MID	160	22.6	0.81	3.5	0.59	2.6	1.01	4.4
HIGH	160	51.6	2.47	4.9	1.66	3.2	2.96	5.9

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 zonisamide (approximately 15 and 45 µg/mL) were evaluated. Each sample was assayed using the ARK Zonisamide Assay, along with a serum control of zonisamide. Measurement of zonisamide resulted in ≤10% error in the presence of interfering substances at the levels tested.

		Percentage Recovery	
Interfering Substance	**Interferent Concentration**	**15 µg/mL Zonisamide**	**45 µg/mL Zonisamide**
Albumin	12 g/dL	103.3	97.9
Bilirubin - conjugated	70 mg/dL	102.8	101.0
Bilirubin - unconjugated	70 mg/dL	100.1	98.8
Cholesterol	651 mg/dL	98.5	97.0
Gamma-Globulin	12 g/dL	97.3	101.4
Hemoglobin	1000 mg/dL	96.6	104.1
Intralipid®	1500 mg/dL	94.8	94.7
Rheumatoid Factor	1100 IU/mL	98.4	100.2
Triglycerides	1204 mg/dL	96.5	96.9
Uric Acid	30 mg/dL	98.5	99.4

Metabolites

N-acetyl zonisamide (NAZ) and the non-glucuronidated 2-sulfamoylacetyl phenol (SMAP) were evaluated. Metabolites NAZ and SMAP-glucuronide are found primarily in urine of patients administered zonisamide therapy. They have not been detected in plasma. Crossreactivity was evaluated in the presence of Low (15 µg/mL) and High (45 µg/mL) zonisamide.

Metabolite	**Metabolite Conc (µg/mL)**	**Percentage Cross-Reactivity**		**Percentage Interference**	
		Low Zonisamide	**High Zonisamide**	**Low Zonisamide**	**High Zonisamide**
NAZ	50.0	1.7	5.5	5.4	6.1
	10.0	5.3	3.3	3.3	0.7
SMAP	50.0	18.2	19.5	57.1	20.6
	10.0	14.8	27.3	8.8	5.8

Drug Interference

Zonisamide-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 zonisamide (approximately 15 and 45 µg/mL) and assayed along with a serum control of zonisamide. Measurement of zonisamide resulted in ≤ 10% error in the presence of drug compounds at the levels tested.

Compound	Concentration (µg/mL)	Percentage Recovery	
		15 µg/mL Zonisamide	45 µg/mL Zonisamide
2-Ethyl-2-phenylmalonamide	1000	98.4	100.2
Acetaminophen	200	98.7	98.7
Acetyl Salicylic Acid	1000	100.3	102.3
Caffeine	100	97.0	97.5
Carbamazepine-10, 11-epoxide	120	99.9	100.9
Carbamazepine	120	101.7	100.8
10-Hydroxy Carbamazepine	100	96.6	93.5
Clonazepam	50	100.0	99.1
Cyclosporin A	40	101.2	104.9
Diazepam	20	98.0	100.8
Erythromycin	200	101.4	103.9
Ethosuximide	1000	99.9	100.5
Felbamate	1000	94.3	102.4
Gabapentin	100	100.9	105.3
Heparin	200 units/mL	104.1	102.7
Ibuprofen	500	101.3	105.9
Lamotrigine	300	100.0	99.8
Levetiracetam	400	95.6	97.9
L-Tryptophan	50	102.9	104.7
Oxcarbazepine	50	99.1	105.2
Phenobarbital	400	98.6	101.9
Phenytoin	200	105.1	106.7
Primidone	100	98.3	98.8
Salicylic Acid	500	104.7	106.6
Sulfamethoxazole	400	102.0	105.2
Sulfisoxazole	1000	95.8	98.3
Theophilline	250	101.7	100.3
Tiagabine	200	102.2	103.5
Topiramate	250	101.7	105.0
Trimethoprim	40	101.1	96.3
Valproic Acid	1000	99.8	101.2

Anticoagulants

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

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

Sample Stability

Serum specimens were shown to be stable for at least twenty-four (24) hours at room temperature (22°C), twenty-eight (28) days when refrigerated (2-8°C), fifty six (56) days frozen, and after three (3) successive freeze/thaw cycles.

On-Board Stability

Calibration Curve Stability: A stored calibration was effective up to 46 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 32 days uncapped and 46 days capped 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 Zonisamide Assay, the ARK Zonisamide Calibrator and the ARK Zonisamide Control are substantially equivalent to the QMS® Zonisamide assay system. The ARK Zonisamide 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

ARK Diagnostics, Inc.
c/o Mr. Johnny Valdez
President
1190 Bordeaux Drive
Sunnyvale, CA 94089

DEC - 9 2009

Re: k091884
Trade name: ARK Zonisamide Assay, Zonisamide Calibrator, ARK Zonisamide Control
Regulation Number: 21 CFR 862.3350
Regulation Name: Diphenylhydantoin Test System
Regulatory Class: Class II
Product Code: NWM, DLJ, LAS
Dated: November 11, 2009
Received: November 12, 2009

Dear Mr. Valdez:

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. 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 such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. 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 Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

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): K091884

Device Name:

ARK™ Zonisamide Assay
ARK™ Zonisamide Calibrator
ARK™ Zonisamide Control

Indications for Use:

The ARK™ Zonisamide Assay is a homogeneous enzyme immunoassay intended for the quantitative determination of Zonisamide in human serum or plasma on automated clinical chemistry analyzers.

Zonisamide concentrations can be used as an aid in management of patients treated with zonisamide.

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

The ARK™ Zonisamide Control is intended for use in quality control of the ARK Zonisamide 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) K091884