APR 16 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 K083799.

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

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Sunnyvale, CA 94089

Owner Operator Number: 10027663

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Executive Director of Quality and Regulatory Affairs

Date prepared: April 14, 2009

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

Trade name: ARK™ Topiramate Assay
ARK™ Topiramate Calibrator
ARK™ Topiramate 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

Seradyn QMS® Topiramate Assay	K070645
Seradyn QMS® Topiramate Calibrator	K970509 INNOFLUOR
Seradyn QMS® Topiramate Control	K970517 INNOFLUOR

807.92 (a)(4): Device Description

The ARK Topiramate Assay is a homogeneous immunoassay based on competition between drug in the specimen and topiramate epitope 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 Topiramate Assay consists of reagents R1 anti-topiramate polyclonal antibody with substrate and R2 topiramate epitope labeled with bacterial G6PDH enzyme. The ARK Topiramate Calibrator consists of a six-level set to calibrate the assay, and the ARK Topiramate 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™ Topiramate Assay is a homogeneous enzyme immunoassay intended for the quantitative determination of topiramate in human serum or plasma on automated clinical chemistry analyzers. The results obtained are used in the diagnosis and treatment of topiramate overdose and in monitoring levels of topiramate to help ensure appropriate therapy.

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

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

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

SUBSTANTIAL EQUIVALENCE COMPARATIVE CHART

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

Characteristic	**Device** ARK™ Topiramate Assay	**Predicate** Seradyn QMS® Topiramate K070645
Intended Use	The ARK™ Topiramate Assay is intended for the quantitative determination of topiramate in human serum or plasma on automated clinical chemistry analyzers.	The Seradyn QMS® 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 topiramate overdose and in monitoring levels of topiramate 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 particle-enhanced turbidometric immunoassay (particle agglutination) (PETIA)
Reagent Components	Two (2) reagent system: Anti-topiramate Antibody/Substrate Reagent (R1) containing rabbit polyclonal antibodies to 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	Two (2) reagent system: Anti-topiramate Antibody Reagent (R1) in buffers containing protein stabilizers with sodium azide Topiramate-coated Microparticle Reagent (R2) in buffer containing surfactant as stabilizers with sodium azide
Platform required	Automated clinical chemistry analyzer	Automated clinical chemistry analyzer
Accessory reagents	Calibrators (six levels) 0.0 to 60.0 µg/mL and controls (three levels)	Calibrators (six levels) 0.0 to 32.0 µg/mL and controls (three levels)
Testing environment	Routine clinical laboratory	Routine clinical laboratory
Reagent condition and storage	Liquid, 2-8° C	Liquid, 2-8° C
Assay Range	1.5 µg/mL to 54.0 µg/mL	1.5 µg/mL to 32.0 µg/mL
Total Precision (each sample tested 4x/day or 8x/day for 20 days)	Sample N mean SD %CV 1 160 2.4 0.10 4.3 2 160 10.2 0.28 2.7 3 160 40.2 1.29 3.2	Sample N mean SD %CV 1 80 2.94 0.12 4.22 2 80 10.14 0.34 3.37 3 80 25.69 1.14 4.44

Characteristic	Device ARK™ Topiramate Assay	Predicate Seradyn QMS® Topiramate K070645
Accuracy-recovery	Percent recoveries from the testing (in six replicates) of samples spiked between 1.5 and 55.0 µg/mL were all within 10% of their theoretical levels	Percent recoveries from the testing (in triplicate) of samples spiked between 1.28 and 32.00 µg/mL were all within 10% of their theoretical levels
Method Comparison (each assay compared to a commercially-available FPIA immunoassay	No of samples: 113 Range of samples: 1.5 µg/mL to 53.4 µg/mL Slope: 0.99 y-intercept: - 0.17 correlation coefficient (r^2): 0.99	No of samples: 148 Range of samples: 1.56 µg/mL to 30.72 µg/mL Slope: 0.962 y-intercept: 0.228 correlation coefficient (r^2): 0.986
Interfering substances	A series of biological substances and co-administered drugs were tested for potential interference at two levels (approx. 5 and 20 µg/mL) of topiramate. The results demonstrated a ≤ 10% difference between the control samples and the challenged samples.	A series of biological substances and co-administered drugs were tested for potential interference at two levels (approx. 5 and 20 µg/mL) of topiramate. The results demonstrated a ≤ 10% difference between the control samples and the challenged samples.

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 Topiramate 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 (often considered ≤20% CV with ±15% recovery). The LOQ was determined to be 1.5 µg/mL.

Accuracy

Accuracy (analytical recovery) was performed by adding concentrated topiramate drug into human serum negative for topiramate. A stock concentrate of highly pure topiramate was added volumetrically to human serum negative for topiramate, 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
1.5	1.4	95.6
2.0	2.7	106.7
4.0	4.2	104.2
5.0	5.3	106.0
6.0	6.4	106.7
10.0	10.4	103.8
15.0	15.5	103.4
30.0	30.8	102.6
45.0	47.3	105.0
55.0	58.9	107.1

Linearity

Linearity studies were performed as suggested in CLSI/NCCLS Protocol EP6-A. A 60.0 µg/mL serum sample was prepared and dilutions were made proportionally with human serum negative for topiramate. Topiramate concentrations ranged from 0.6 to 60.0 µg/mL. Linearity at specific dilutions was considered acceptable if the percent difference was ±10% between the predicted 1st and 2nd order regressed values. A linear relationship was demonstrated between 1.2 and 54.0 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%)
0.6	0.5	0.56	0.46	-18.14
1.2	1.0	1.19	1.10	-7.42
1.8	1.7	1.83	1.75	-4.16
2.4	2.4	2.46	2.40	-2.60
3.0	3.0	3.09	3.04	-1.68
3.6	3.7	3.73	3.69	-1.09
4.2	4.4	4.36	4.33	-0.68
4.8	4.9	4.99	4.98	-0.38
5.4	5.8	5.63	5.62	-0.15
6.0	6.3	6.26	6.26	0.02
12.0	12.9	12.60	12.68	0.64
18.0	18.9	18.94	19.06	0.66
24.0	25.5	25.28	25.41	0.53
30.0	31.4	31.61	31.72	0.33
36.0	37.9	37.95	37.99	0.11
42.0	44.8	44.29	44.23	-0.14
48.0	50.7	50.63	50.43	-0.39
54.0	56.5	56.96	56.60	-0.65
60.0	62.3	63.30	62.73	-0.91

Assay Range

The range of the assay is 1.5 to 54.0 µg/mL. Report results below this range as <1.5 µg/mL or below the analyzer-specific lower LOQ established in your laboratory. Report results above this range as >54.0 µg/mL or above the analyzer-specific upper LOQ established in your laboratory.

Method Comparison

Correlation studies were performed using CLSI/NCCLS Protocol EP9-A2. Results from the ARK Topiramate assay were compared with results from a commercially available FPIA Immunoassay. The topiramate concentrations ranged from 1.5 µg/mL to 53.4 µg/mL. Results of the Passing-Bablok regression analysis for the study are shown below.

Slope	0.99
y-intercept	-0.17
Correlation Coefficient (r^2)	0.99
Number of Samples	113

Precision

Precision was determined as described in CLSI/NCCLS Protocol EP5-A2. Tri-level controls containing topiramate 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 (%)**
1	160	2.4	0.08	3.4	0.05	2.0	0.10	4.2
2	160	10.2	0.24	2.4	0.14	1.4	0.28	2.7
3	160	40.2	1.19	2.9	0.64	1.6	1.29	3.2

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 topiramate (approximately 5 and 20 µg/mL) were evaluated. Each sample was assayed using the ARK Topiramate Assay, along with a serum control of topiramate. Measurement of topiramate resulted in ≤10% error in the presence of interfering substances at the levels tested.

Interfering Substance	Interferent Concentration
Albumin	12 g/dL
Bilirubin	60 mg/dL
Cholesterol	301 mg/dL
Gamma-Globulin	10 g/dL
Hemoglobin	1000 mg/dL
Heparin	200 units/mL
Rheumatoid Factor	1000 IU/mL
Triglycerides	1105 mg/dL
Uric Acid	25 mg/dL

Metabolites

ARK Topiramate Assay serum and plasma results are unlikely to be affected by metabolism of topiramate drug, since plasma levels of metabolites are usually not clinically significant. The following metabolite was tested for crossreactivity. Measurement of topiramate resulted in ≤ 10% error in the presence of 9-Hydroxy-topiramate at the level tested.

Metabolite	Metabolite Conc. (µg/mL)	Percent Cross-Reactivity		Percent Interference	
		Low Topiramate	High Topiramate	Low Topiramate	High Topiramate
9-Hydroxy-topiramate	40.0	1.2	1.6	8.6	3.2

Drug Interference

Topiramate-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 topiramate (approximately 5 and 20 µg/mL) and assayed along with a serum control of topiramate. Measurement of topiramate resulted in ≤ 10% error in the presence of drug compounds at the levels tested.

Data are representative of performance on automated clinical chemistry analyzers. Each laboratory is responsible for verification of performance using instrument parameters established for their analyzer.

Compound	**Concentration (µg/mL)**	**Compound**	**Concentration (µg/mL)**
Acetaminophen	50	Levitiracetam	200
Acetozolamide	50	Methysergide	100
Alprazolam	20	Metoprolol	100
Amitriptyline	10	Nadolol	150
Acetylsalicylic acid	100	Naproxen	600
Atenolol	50	Nimodipine	100
Caffeine	100	Nortriptyline	10
Carbamazepine	100	Oxcarbazepine	50
Chlorthalidone	100	Phenelzine	15
Clonazepam	50	Phenobarbital	40
Clorazepate	20	Phenytoin	50
Diazepam	50	Primidone	100
Dichlorphenamide	40	Protriptyline	20
Ethosuxamide	500	Salicylic Acid	750
Famotidine	50	Sulfanilamide	2000
Felbamate	500	Tiagabine	200
Flurazepam	20	Tolbutamide	750
Furosemide	10	Valproic Acid	200
Gabapentin	100	Verapamil	100
Hydrochlorothiazide	60	Vigabatrin	150
Ibuprofen	500	Zonisamide	200
Lamotrogine	100		

Anticoagulants

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

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

On-Board Stability

Calibration Curve Stability: A stored calibration was effective up to 49 days based on supporting data.

Reagent on-board stability: Reagents were effective when stored with caps after transfer to analyzer specific reagent containers for up to 60 days based on supporting data.

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

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

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

APR 16 2009

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

Re: k083799
Trade name: ARK Topiramate Assay, ARK Topiramate Calibrator, ARK Topiramate Control
Regulation Number: 21 CFR 862.3350
Regulation Name: Diphenylhydantoin Test System
Regulatory Class: Class II
Product Code: NWM, DLJ, LAS
Dated: April 3, 2009
Received: April 6, 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). This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of

substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

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 (240) 276-0450. 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 (240) 276-3474. For questions regarding the reporting of device adverse events (Medical Device Reporting (MDR)), please contact the Division of Surveillance Systems at (240) 276-3464. For more information regarding the reporting of adverse events, please go to http://www.fda.gov/cdrh/mdr/.

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 (240) 276-3150 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Courtney C. Harper, Ph.D.
Acting 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): K083799

Device Name:

ARK™ Topiramate Assay
ARK™ Topiramate Calibrator
ARK™ Topiramate Control

Indications for Use:

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

The results obtained are used in the diagnosis and treatment of topiramate overdose and in monitoring levels of topiramate to help ensure appropriate therapy.

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

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

Carol C. Benson

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

510(k) K083799