August 5, 2021

ARK Diagnostics, Inc.
Thomas Houts
Director, Quality Regulatory and Planning
48089 Fremont Boulevard
Fremont, CA 94538

Re: K201089
Trade/Device Name: ARK Lacosamide Assay
Regulation Number: 21 CFR 862.3350
Regulation Name: Diphenylhydantoin test system
Regulatory Class: Class II
Product Code: NWM
Dated: October 28, 2020
Received: November 19, 2020

Dear Thomas Houts:

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)*
k201089

Device Name
ARK Lacosamide Assay

Indications for Use *(Describe)*
ARK Lacosamide Assay:
The ARK Lacosamide Assay is a homogeneous enzyme immunoassay intended for the quantitative determination of lacosamide in human serum on automated clinical chemistry analyzers. The measurements obtained are used in monitoring levels of lacosamide 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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Section 5: 510(k) SUMMARY

This 510(k) Summary of Safety and Effectiveness information is being submitted in accordance with the requirements of Safe Medical Device Act of 1990 and 21 CFR 807.92.

The assigned 510(k) number is K201089.

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

Address: 48089 Fremont Blvd
Fremont, CA 94538 USA

Owner Operator Number: 10027663
Establishment Registration: 3005755244

Phone: (510) 270-6270
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Director, Quality, Regulatory and Planning
Email: tom@arkt-dm.com
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Date Prepared: April 22, 2020

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

Trade Name: ARK Lacosamide Assay

Common Name: Homogeneous Enzyme Immunoassay

Classification:

Product Code	Classification	Regulation Section	Panel
NWM	Class II	862.3350 Diphenylhydantoin Test System	Toxicology (91)

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

Predicate Device Name: ARK™ Topiramate Assay

Predicate 510(k) Number: K083799

807.92 (a)(4): Device Description

The ARK Lacosamide Assay is a homogeneous enzyme immunoassay based on competition between drug in the specimen and lacosamide 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 Lacosamide Assay consists of reagents R1 anti-lacosamide polyclonal antibody with substrate and R2 lacosamide labeled with bacterial G6PDH enzyme.

Summary and Explanation of Test

Lacosamide (Vimpat®, UCB, Inc.) [(R)-2-acetamido-N-benzyl-3-methoxypropionamide] is indicated for adjunctive therapy of partial-onset seizures in patients ≥17 years.

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

ARK Lacosamide Assay

The ARK Lacosamide Assay is a homogeneous enzyme immunoassay intended for the quantitative determination of lacosamide in human serum on automated clinical chemistry analyzers. The measurements obtained are used in monitoring levels of lacosamide to help ensure appropriate therapy.

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

SUBSTANTIAL EQUIVALENCE COMPARATIVE TABLES

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

Characteristic	**Predicate Device** ARK™ Topiramate Assay (K083799)	**Candidate Device** ARK™ Lacosamide Assay
Intended 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 ARK Lacosamide Assay is a homogeneous enzyme immunoassay intended for the quantitative determination of lacosamide in human serum 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 measurements obtained are used in monitoring levels of lacosamide to help ensure appropriate therapy.
Sample Matrix	Human serum or plasma	Human serum
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-lacosamide Antibody/Substrate Reagent (R1) containing rabbit polyclonal antibodies to lacosamide, glucose-6-phosphate, nicotinamide adenine dinucleotide, bovine serum albumin, sodium azide, and stabilizers Enzyme Reagent (R2) containing lacosamide labeled with bacterial G6PDH, buffer, bovine serum albumin, sodium azide, and stabilizers
Methodology	Homogeneous Enzyme Immunoassay (EIA)	Same
Platform Required	Automated Clinical Chemistry Analyzer	Same
User Environment	Clinical Laboratories; Prescription Use Only	Same
Reagents Form	Liquid – Ready to use	Same
Storage	2-8˚ C until expiration date	Same
Analyte	Topiramate	Lacosamide

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 for the ARK Lacosamide Assay was determined to be 0.40 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 lacosamide to give concentrations of 0.30, 0.40 and 0.50 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 (µg/mL)	Mean (µg/mL)	SD	% CV	% Recovery	N
0.30	0.25	0.013	5.0	83.2	40
0.40	0.35	0.012	3.4	88.1	40
0.50	0.47	0.016	3.5	94.1	40

Measurement Range

The measurement range of the ARK Lacosamide Assay is 0.40 – 24.00 µg/mL. Specimens containing lacosamide in higher concentrations (>24.00 µg/mL) may be assayed by dilution of the specimen into the measurement range for a quantitative result or otherwise reported as detected above the measurement range. Multiply the assay result by the dilution factor to obtain the concentration of lacosamide in the undiluted specimen.

Recovery

Analytical recovery throughout the measurement range was performed by adding concentrated lacosamide drug into human serum negative for lacosamide. A certified stock concentrate of highly pure lacosamide was added volumetrically to human serum negative for lacosamide, 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 samples tested was within ±10% of the expected sample concentration.

Theoretical Concentration (µg/mL)	Mean Recovered Concentration (µg/mL)	Percent Recovery (%)
0.40	0.36	90.4
0.50	0.47	93.3
1.00	1.04	104.2

Theoretical Concentration (µg/mL)	Mean Recovered Concentration (µg/mL)	Percent Recovery (%)
3.00	3.07	102.3
6.00	6.15	102.6
9.00	8.92	99.1
15.00	14.42	96.1
20.00	21.15	105.8

Linearity

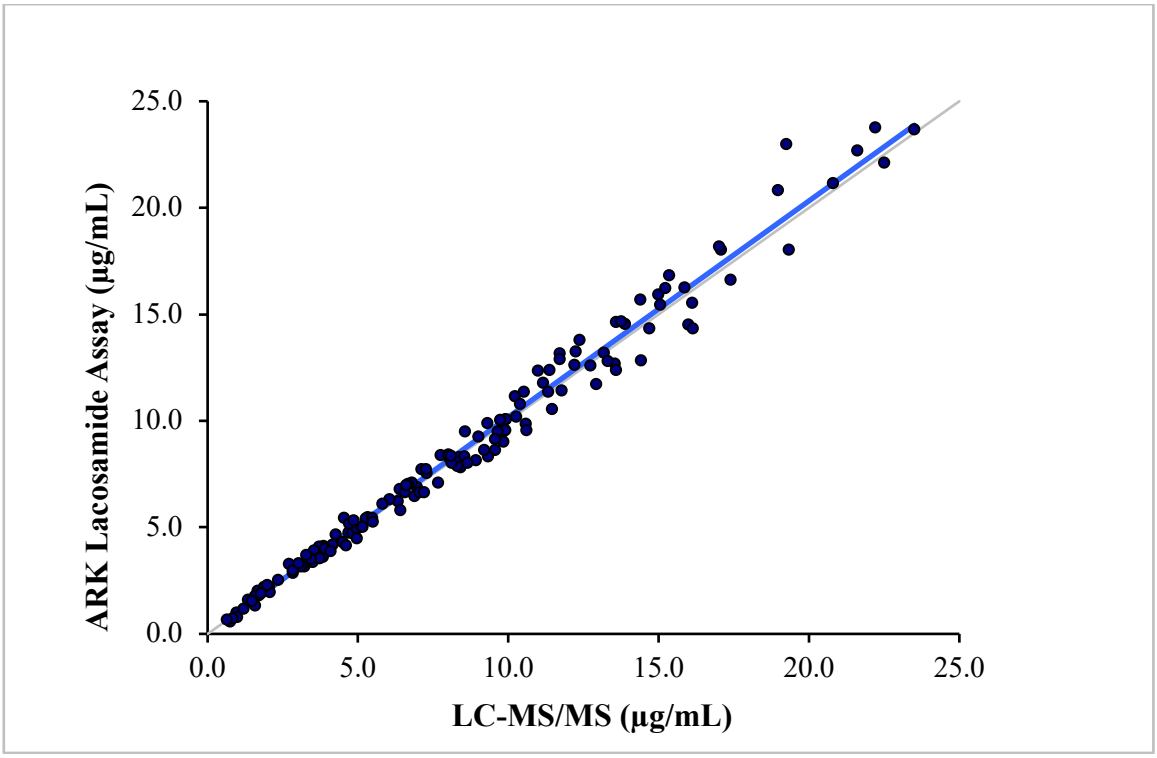
Linearity studies were performed as suggested in CLSI EP06-A. A 30.00 µg/mL lacosamide serum sample was prepared and dilutions were made proportionally with human serum negative for lacosamide. Two analytical runs of three replicates of each sample were assayed on an automated clinical chemistry analyzer. The results of the six replicates of each sample were averaged. The data were analyzed using linear regression as well as non-linear fitted polynomial regression. Linearity at specific dilutions was considered acceptable if the percent difference was ±10% between the predicted 1st and 2nd order regressed values at concentrations >1.00 µg/mL, or ≤0.20 µg/mL at concentrations ≤1.00 µg/mL. A linear relationship was demonstrated between 0.40 and 25.00 µg/mL ($y = 0.9998x - 0.0170$).

Nominal (µg/mL)	Measured Results (µg/mL)	1st Order Predicted Results	2nd Order Predicted Results	Difference
0.00	0.00	-0.02	-0.08	NA
0.40	0.36	0.38	0.33	-0.05 µg/mL
1.50	1.55	1.48	1.45	-2.0 %
3.00	2.95	2.98	2.98	0.0 %
6.00	5.83	5.98	6.02	0.7 %
9.00	8.91	8.98	9.05	0.7 %
12.00	12.01	11.98	12.05	0.6 %
15.00	15.02	14.98	15.04	0.4 %
18.00	18.11	17.98	18.01	0.2 %
21.00	21.41	20.98	20.97	-0.1 %
25.00	24.55	24.98	24.87	-0.4 %

Method Comparison

Method comparison studies were performed using CLSI EP09-A3 as a guideline. Method comparison was conducted with 150 unaltered, human serum specimens that are not individually identifiable. Results from the ARK Lacosamide Assay were compared with results from LC-MS/MS. The lacosamide concentrations ranged from 0.65 µg/mL to 23.50 µg/mL. Results of the Passing-Bablok regression analysis are shown below (with 95% confidence limits).

Slope	1.01	(0.99 to 1.04)
y-intercept	0.03	(-0.10 to 0.15)
Correlation Coefficient (r^2)	0.98	(0.98 to 0.99)
Number of Samples	150	



Precision

Precision was determined as described in CLSI EP05-A3. Tri-level controls and three samples of lacosamide in pooled human serum were used in the study. Data were collected on a single analyzer over twenty (20) non-consecutive days. Two (2) calibrations were performed according to requirements for quality control. 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.

Sample	N	Mean (µg/mL)	Within Run		Between Day		Total	
			SD	CV (%)	SD	CV (%)	SD	CV (%)
ARK Lacosamide Control								
LOW	160	1.55	0.049	3.1	0.049	3.1	0.070	4.5
MID	160	7.13	0.202	2.8	0.204	2.9	0.287	4.0
HIGH	160	14.94	0.450	3.0	0.445	3.0	0.664	4.4
Human Serum								
LOW	160	1.49	0.045	3.0	0.037	2.5	0.058	3.9
MID	160	7.10	0.175	2.5	0.217	3.1	0.283	4.0
HIGH	160	15.18	0.456	3.0	0.432	2.8	0.657	4.3

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 lacosamide (2.0 and 15.0 µg/mL) were evaluated. Two analytical runs of three replicates of each sample (6 replicates total) were assayed using the ARK Lacosamide Assay, along with a serum control of lacosamide. The mean results of lacosamide were calculated and the percentage recovery relative to the serum control mean result was determined. Measurement of lacosamide resulted in ≤10% error in the presence of interfering substances at the levels tested.

		Percentage Recovery (%)	
Interfering Substance	**Interferent Concentration**	**2.0 µg/mL Lacosamide**	**15.0 µg/mL Lacosamide**
Albumin	12 g/dL	99.8	101.7
Bilirubin - conjugated	70 mg/dL	97.3	96.5
Bilirubin - unconjugated	70 mg/dL	101.1	98.3
Cholesterol	620 mg/dL	95.8	100.1
Gamma-Globulin	12 g/dL	103.5	98.5

		Percentage Recovery (%)	
Interfering Substance	**Interferent Concentration**	**2.0 µg/mL Lacosamide**	**15.0 µg/mL Lacosamide**
Hemoglobin	1000 mg/dL	101.0	101.6
Rheumatoid Factor	1000 IU/mL	97.3	96.8
Triglycerides	1000 mg/dL	97.9	96.2
Uric Acid	30 mg/dL	102.5	96.6

Specificity

Lacosamide is eliminated primarily from the systemic circulation by renal excretion and biotransformation. After oral and intravenous administration, approximately 95% of lacosamide administered is recovered in the urine and less than 0.5% in the feces. The major compounds excreted are unchanged lacosamide (approximately 40% of the dose), its O-desmethyl metabolite (approximately 30%), and a structurally unknown polar fraction (~20%). The plasma circulating levels of the major human metabolite, O-desmethyl-lacosamide, is approximately 10% of that of lacosamide. This metabolite has no known pharmacological activity.

The crossreactivity of O-desmethyl lacosamide metabolite (5.0 µg/mL or 30.0 µg/mL) in the ARK Lacosamide Assay was not clinically significant (≤ 3.0% crossreactivity). Lacosamide (2.00 µg/mL or 15.00 µg/mL in human serum) was tested in the absence or presence of metabolite at higher than expected concentrations of metabolite.

O-Desmethyl Lacosamide (µg/mL)	**Measured Lacosamide in Absence/Presence of Metabolite (µg/mL)**			
	Lacosamide (2.00 µg/mL)		**Lacosamide (15.00 µg/mL)**	
	Metabolite Absent	**Metabolite Present**	**Metabolite Absent**	**Metabolite Present**
5.0	2.18	2.23	Not Tested	
30.0	Not Tested		15.51	16.40

Crossreactivity

The compounds listed below did not interfere with the ARK Lacosamide Assay when tested in the presence of lacosamide (2.00 µg/mL and 15.00 µg/mL). Levels tested were at or above maximum physiological or pharmacological concentrations. Lacosamide concentrations of samples containing interferent were compared to the lacosamide level in a normal serum control. No significant interference was observed with other anti-epileptic or co-administered drugs at the concentrations tested. Recoveries ranged from 90.9% to 109.5%, within 10% of the expected level.

#	Compound	Concentration Tested (µg/mL)	Percentage Recovery (%)	
			Lacosamide (2.0 µg/mL)	Lacosamide (15.0 µg/mL)
1	Acetaminophen	200	100.9	100.1
2	Acetazolamide	100	100.5	100.9
3	Acetylsalicylic acid	1000	102.4	102.1
4	Amikacin	100	96.5	99.7
5	Amitriptyline	20	96.9	95.6
6	Amoxapine	10	97.4	99.5
7	Amphotericin B	100	98.6	99.7
8	Ampicillin	100	97.7	100.1
9	Ascorbic acid	100	102.8	104.0
10	Baclofen	100	98.8	100.3
11	Buproprion	10	100.0	99.0
12	Caffeine	100	102.4	102.7
13	Carbamazepine	100	99.0	101.8
14	Chloramphenicol	250	102.1	98.6
15	Chlorpromazine	10	96.3	97.3
16	Citalopram	10	97.5	96.0
17	Clobazam	100	98.9	96.0
18	Clonazepam	10	94.9	99.2
19	Cyclosporin A	40	100.2	98.5
20	Diazepam	20	97.8	98.2
21	Digoxin	10	95.9	97.3
22	Doxepin	10	96.9	99.2
23	Erythromycin	200	99.6	100.6
24	Ethanol	4000 (0.4%)	98.6	98.6
25	Ethotoin	100	103.9	102.0
26	Ethosuximide	250	103.2	98.4
27	Felbamate	250	102.6	100.7
28	Fluoxetine	10	98.1	98.3
29	Furosemide	100	100.7	101.0
30	Gabapentin	200	97.5	102.3
31	Gentamicin	100	98.2	98.5
32	Haloperidol	10	98.8	102.4
33	Heparin	200 U/mL	98.6	98.9
34	Ibuprofen	500	95.2	100.9
35	Imipramine	10	97.8	99.7
36	Kanamycin A	200	96.6	99.1
37	Lamotrigine	400	97.8	100.0
38	Levetiracetam	400	98.1	98.5
39	Lidocaine	100	97.9	98.9
40	Lincomycin	1000	105.0	104.4
41	Mephenytoin	100	109.5	102.9

#	Compound	Concentration Tested (µg/mL)	Percentage Recovery (%)	
			Lacosamide (2.0 µg/mL)	Lacosamide (15.0 µg/mL)
42	Mesoridazine	10	100.9	98.7
43	Methicillin	250	102.1	100.1
44	Naproxen	600	104.2	99.9
45	Neomycin	1000	98.9	97.4
46	Niacin	100	102.4	99.2
47	Nitrazepam	20	98.2	96.3
48	Nortriptyline	20	99.2	95.9
49	Olanzapine	10	101.9	99.2
50	Oxcarbazepine	100	104.8	101.1
51	Paroxetine	10	99.0	99.9
52	2-phenyl-2-ethyl-malonamide (PEMA)	1000	104.5	105.4
53	Penicillin V	100	100.1	95.9
54	Perphenazine	100	108.2	102.7
55	Phenobarbital	200	97.6	90.9
56	Phenytoin	200	108.3	91.8
57	Pregabalin	200	96.8	92.6
58	Primidone	100	103.0	95.2
59	Procainamide	100	103.2	98.7
60	Prochloroperazine	10	100.4	97.3
61	Ranitidine	100	102.6	106.4
62	Rifampin	100	103.2	99.1
63	Risperidone	10	100.2	103.1
64	Sertraline	100	102.9	103.7
65	Spectinomycin	100	96.4	99.8
66	Stiripentol	100	103.4	101.8
67	Sulfamethoxazole	400	103.1	105.2
68	Theophylline	200	100.6	106.6
69	Thioridazine	10	101.5	103.0
70	Tobramycin	100	100.5	101.9
71	Tiagabine	200	103.2	103.4
72	Topiramate	250	101.0	100.2
73	Trimethoprim	40	101.6	102.1
74	Valproic Acid	600	103.8	103.9
75	Vancomycin	250	99.1	101.2
76	Vigabatrin	150	100.4	100.4
77	Zonisamide	400	99.9	96.6

Sample Stability

Serum specimens were shown to be stable for at least forty-eight (48) hours at room temperature (22 °C), twenty-eight (28) days when refrigerated (2-8 °C), frozen (-20 ºC) for at least 34 months, and after three (3) successive freeze/thaw cycles based on supporting data.

Stability

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

On-Board Stability

Reagents were stable up to 60 days when stored on-board the instrument based on supporting data.

Calibration Curve Stability

A stored calibration curve was effective up to at least 14 days based on supporting data. Calibration curve stability may depend on individual laboratory performance.

Traceability

ARK Lacosamide Calibrators are prepared by volumetric dilution of high purity lacosamide (certified solution traceable to HPLC) into a synthetic proteinaceous matrix free of lacosamide.

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

As summarized above, the ARK Lacosamide Assay is substantially equivalent to the legally marketed predicate device K083799.