February 26, 2020

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

Re: k200197
Trade/Device Name: ARK™ Fentanyl II Assay
Regulation Number: 21 CFR 862.3650
Regulation Name: Opiate Test System
Regulatory Class: Class II
Product Code: DJG
Dated: January 24, 2020
Received: January 27, 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, M.T., Ph.D.
Acting 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: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
k200197

Device Name
ARK™ Fentanyl II Assay

Indications for Use *(Describe)*
The ARK Fentanyl II Assay is an immunoassay intended for the qualitative detection of fentanyl in human urine at a cutoff concentration of 1.0 ng/mL. The assay is intended for use in laboratories with automated clinical chemistry analyzers. This in vitro diagnostic device is for prescription use only.

The ARK Fentanyl II Assay provides only a preliminary analytical result. A more specific alternative chemical method must be used in order to obtain a confirmed positive analytical result. Gas Chromatography/Mass Spectrometry (GC/MS) or Liquid Chromatography/tandem Mass Spectrometry (LC-MS/MS) is the preferred confirmatory method. Clinical consideration and professional judgment should be exercised with any drug test result, particularly when the preliminary test result is positive.

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 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 K200197.

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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Contact: Thomas Houts, Ph.D. – (510) 270-6296
Director, Quality, Regulatory and Planning

Date Prepared: February 25, 2020

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

Trade Name: ARK™ Fentanyl II Assay

Common Name: Homogeneous Enzyme Immunoassay, Opiate Test System

Classification:

Product Code	Classification	Regulation Section	Panel
DJG	Class II	21 CFR 862.3650 Opiate Test System	Toxicology (91)

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

ARK™ Fentanyl Assay – k180427

807.92 (a)(4): Device Description

The ARK Fentanyl II Assay is a homogeneous enzyme immunoassay technique used for the analysis of a specific compound in human urine. The assay is based on competition between drug in the specimen and drug labeled with recombinant glucose-6-phosphate dehydrogenase (rG6PDH) for antibody binding sites. 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 nicotinamide adenine dinucleotide (NAD) to NADH in the presence of glucose-6-phosphate (G6P), resulting in an absorbance change that is measured spectrophotometrically. Endogenous serum G6PDH does not interfere because the coenzyme NAD functions only with the bacterial enzyme used in the assay.

The ARK Fentanyl II Assay consists of reagents R1 anti-fentanyl monoclonal antibodies with substrate and R2 fentanyl derivative labeled with bacterial recombinant G6PDH enzyme.

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

ARK Fentanyl II Assay

The ARK Fentanyl II Assay is an immunoassay intended for the qualitative detection of fentanyl in human urine at a cutoff concentration of 1.0 ng/mL. The assay is intended for use in laboratories with automated clinical chemistry analyzers. This *in vitro* diagnostic device is for prescription use only.

The ARK Fentanyl II Assay provides only preliminary analytical result. A more specific alternative chemical method must be used in order to obtain a confirmed positive analytical result. Gas Chromatography/Mass Spectrometry (GC/MS) or Liquid Chromatography/tandem Mass Spectrometry (LC-MS/MS) is the preferred confirmatory method. Clinical consideration and professional judgment should be exercised with any drug test result, particularly when the preliminary test result is positive.

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

SUBSTANTIAL EQUIVALENCE COMPARATIVE TABLE

Comparison between the ARK™ Fentanyl Assay and the ARK™ Fentanyl II Assay

Characteristic	**Predicate Device** ARK™ Fentanyl Assay (k180427)	**Candidate Device** ARK™ Fentanyl II Assay
Similarities		
Test System	Homogenous enzyme immunoassay (EIA)	Same
Intended Use	For the qualitative detection of fentanyl in human urine at a cutoff concentration of 1.0 ng/mL	Same
Sample Matrix	Human urine	Same
Detection	Absorbance change measured spectrophotometrically at 340 nm.	Same
User Environment	Clinical laboratories; Prescription use only	Same
Mass Spectrometry Confirmation	Required to confirm preliminary positive analytical results	Same
Platform Required	Automated clinical chemistry analyzer	Same
Reagents Form	Liquid – Ready to use	Same
Reagent Materials	Two (2) reagent system: Antibody/substrate reagent and enzyme labeled conjugate Sodium azide preservative	Same
Storage	2-8˚C until expiration date	Same
Measured Analyte	Fentanyl	Same
Cutoff Level	1.0 ng/mL	Same

Characteristic	**Predicate Device** ARK™ Fentanyl Assay (k180427)	**Candidate Device** ARK™ Fentanyl II Assay
Differences		
Antibody	Rabbit polyclonal antibodies to fentanyl	Rabbit monoclonal antibodies to fentanyl

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.

Precision

Precision studies were performed using CLSI EP05-A3 as a guideline. Drug-free, negative human urine was supplemented with fentanyl (0.00 to 2.00 ng/mL). Each level was assayed in quadruplicate twice a day for 20 days (N=160). Results are summarized in the table below.

Human Urine (ng/mL)	Relative % Cutoff	# of Results	Qualitative Precision Results
0.00	-100	160	160 Negative
0.25	-75	160	160 Negative
0.50	-50	160	160 Negative
0.75	-25	160	160 Negative
1.00	Cutoff	160	84 Negative; 76 Positive
1.25	+25	160	160 Positive
1.50	+50	160	160 Positive
1.75	+75	160	160 Positive
2.00	+100	160	160 Positive

Analytical Specificity

All compounds tested were added to drug-free, negative human urine.

The cross-reactivity of the following metabolites and structural analogs of fentanyl was evaluated by spiking these compounds into drug-free, negative human urine and evaluated by dose-response to determine the approximate equivalence to the 1.0 ng/mL fentanyl cutoff. These concentrations were used to determine the percent cross-reactivity according to the formula:

% Cross-reactivity = (Cutoff concentration / Concentration approximately equivalent to the 1.0 ng/mL cutoff) X 100

For the compounds Alfentanil and Remifentanil that did not produce a positive result, the highest concentration tested was used to calculate percent cross-reactivity.

Cross-reactivity

Norfentanyl (Major Metabolite)

Compound	Concentration Tested (ng/mL)	Percent Crossreactivity (%)
Norfentanyl (Major Metabolite)	15	7

Other Metabolites and Structural Analogs of Fentanyl

Compound	Concentration Approximately Equivalent to the Cutoff (ng/mL)	Percent Crossreactivity (%)
Acetyl fentanyl	1.1	90.91
Isobutyryl fentanyl	1.1	90.91
ω-1-Hydroxyfentanyl	1.2	83.33
Acrylfentanyl	1.3	76.90
Butyryl fentanyl	1.4	71.43
Furanyl fentanyl	1.5	66.67
Para-fluoro fentanyl	1.5	66.67
Ocfentanil	1.6	62.50
4-Fluoro-isobutyryl fentanyl	1.9	52.63
Para-fluorobutyryl fentanyl (p-FBF)	1.9	52.63
Valeryl fentanyl	2.3	43.48
β-hydroxyfentanyl	9.5	10.53
Acetyl norfentanyl	12.1	8.26
(±) β-hydroxythiofentanyl	32.7	3.06
(±)-3-cis-methyl fentanyl	144.1	0.69
Carfentanil	448.2	0.22
Despropionyl fentanyl (4-ANPP)	471.8	0.21
Sufentanil	2,362	0.04
Remifentanil	10,000	<0.01
Norcarfentanil	38,196	0.003
Alfentanil	100,000	<0.001

The following opioids, structurally similar compounds, and functional analogs were negative at the concentrations tested in the ARK Fentanyl II Assay.

Compound	Concentration Tested (µg/mL)	Compound	Concentration Tested (µg/mL)
6-Acetyl morphine	100	Naltrexone	100
Buprenorphine	100	Norbuprenorphine	100
Buprenorphine glucuronide	100	Norcodeine	100
Codeine	100	Normeperidine	100
Dextromethorphan	100	Normorphine	100
Dihydrocodeine	100	Noroxycodone	100
EDDP	100	Oxycodone	100
EMDP	100	Oxymorphone	100
Heroin	100	Pentazocine (Talwin)	100
Hydrocodone	100	Pipamperone	90
Hydromorphone	100	Quinine	100
9-Hydroxyrisperidone	100	Quinidine	100
Labetalol	100	Risperidone	100
Levorphanol	100	Tapentadol	100
M-Chlorophenylpiperazine (m-CPP)	100	Thioridazine	100
Meperidine	100	Tilidine	100
Methadone	100	Tramadol	100
Morphine	100	Tramadol-O-Desmethyl	100
Morphine-3-glucuronide	100	Tramadol-N-Desmethyl	100
Naloxone	100	Trazodone	100

Interference – Structurally Unrelated Compounds

High concentrations of the following structurally unrelated compounds were added into fentanyl-spiked urine (± 50% of the cutoff concentration). The substances listed below did not yield a false result relative to the cutoff.

Compound	Concentration Tested (µg/mL)	0.5 ng/mL (-50% Cutoff)	1.5 ng/mL (+50% Cutoff)
Acetaminophen	500	Negative	Positive
Acetylsalicylic acid	1000	Negative	Positive
Albuterol	100	Negative	Positive
Amitriptyline	100	Negative	Positive
Amobarbital	100	Negative	Positive
Amphetamine	100	Negative	Positive
Benzoylecgonine	100	Negative	Positive
Bupropion	100	Negative	Positive
Caffeine	100	Negative	Positive
Carbamazepine	100	Negative	Positive
Chlorpromazine	100	Negative	Positive
Clomipramine	100	Negative	Positive
Cyclobenzaprine	100	Negative	Positive
Desipramine	100	Negative	Positive
Doxepin	100	Negative	Positive
Ecgonine	100	Negative	Positive
Ephedrine	100	Negative	Positive
Fluoxetine	100	Negative	Positive
Fluphenazine	100	Negative	Positive
Ibuprofen	500	Negative	Positive
Imipramine	100	Negative	Positive
Ketamine	100	Negative	Positive
Lidocaine	100	Negative	Positive
Maprotiline	100	Negative	Positive
Methapyrilene	100	Negative	Positive
Methaqualone	100	Negative	Positive
Metronidazole	300	Negative	Positive
Nicotine	100	Negative	Positive
Norketamine	100	Negative	Positive
Nortriptyline	60	Negative	Positive
Oxazepam	100	Negative	Positive
Phencyclidine	100	Negative	Positive
Phenobarbital	100	Negative	Positive
Propoxyphene	100	Negative	Positive
Ranitidine	100	Negative	Positive

Compound	Concentration Tested (µg/mL)	0.5 ng/mL (-50% Cutoff)	1.5 ng/mL (+50% Cutoff)
Secobarbital	100	Negative	Positive
Valproic acid	250	Negative	Positive
Venlafaxine	100	Negative	Positive

Interference – Endogenous Substances

Interference studies were performed using CLSI EP07-A3 as a guideline. High concentrations of the following endogenous substances were added into fentanyl-spiked urine (± 50% of the cutoff concentration). No interference was observed when tested with the ARK Fentanyl II Assay.

Compound	Concentration Tested (mg/dL)	0.5 ng/mL (-50% Cutoff)	1.5 ng/mL (+50% Cutoff)
Acetone	1000	Negative	Positive
Ascorbic Acid	560	Negative	Positive
Bilirubin	2	Negative	Positive
Creatinine	500	Negative	Positive
Ethanol	1000	Negative	Positive
Galactose	10	Negative	Positive
Gamma Globulin	500	Negative	Positive
Glucose	3000	Negative	Positive
Hemoglobin	500	Negative	Positive
Human Albumin	500	Negative	Positive
Oxalic Acid	100	Negative	Positive
Riboflavin	7.5	Negative	Positive
NaCl	4000	Negative	Positive
Urea	2000	Negative	Positive

Interference – Specific Gravity and pH

Urine samples with specific gravity values from 1.002 to 1.030 g/mL and pH values ranging from 3.0 to 11.0 were tested in the presence of the two levels of fentanyl at ± 50% of the cutoff concentration. No interference was observed when tested with the ARK Fentanyl II Assay.

Interference – Boric Acid

One percent (1%) w/v of boric acid was tested into fentanyl-spiked urine (± 50% of the cutoff concentration). Results are provided in the table below.

Compound	Concentration Tested	0.5 ng/mL (-50% Cutoff)	1.5 ng/mL (+50% Cutoff)
Boric Acid	1% w/v	Negative	Negative

The device labeling includes the following limitation: "Do not use Boric Acid as a preservative."

Method Comparison

A total of one hundred forty seven (147) unaltered clinical urine specimens that are not individually identifiable were analyzed for fentanyl with the ARK Fentanyl II Assay and by LC-MS/MS. The LC-MS/MS confirmatory method was performed by a licensed reference laboratory and used a fentanyl cutoff of 0.2 ng/mL.

Specimens were tested with the ARK Fentanyl II Assay in single replicates on a Beckman Coulter AU680 analyzer and compared to results obtained by LC-MS/MS. Groups of up to 31 specimens were assayed per run. Each run was verified by assaying the bi-level ARK Fentanyl Controls (0.5 ng/mL and 1.5 ng/mL) as quality control samples.

Results are summarized as follows:

ARK Result	Low Negative Less than 50% below the Cutoff (< 0.5 ng/mL by LC-MS/MS)	Near Cutoff Negative Between 50% below the Cutoff and the Cutoff (0.5 – 0.9 ng/mL by LC-MS/MS)	Near Cutoff Positive Between the Cutoff and 50% above the Cutoff (1.0 – 1.5 ng/mL by LC-MS/MS)	High Positive Greater than 50% above the Cutoff (> 1.5 ng/mL by LC-MS/MS)
Positive	1*	21	11	62
Negative	50	2	0	0

Discordant Results

*Norfentanyl was detected in this discordant sample (Sample ID #052) and contributed to the positive result obtained with the ARK Fentanyl Assay for this sample.

Sample ID Number	ARK Immunoassay Result	Fentanyl (ng/mL by LC-MS/MS)	Norfentanyl (ng/mL by LC-MS/MS)
052*	Positive	0.4	7.6
065	Positive	0.5	5.2
058	Positive	0.5	7.9
069	Positive	0.5	31.2
060	Positive	0.5	425.4
056	Positive	0.6	3.7
072	Positive	0.6	13.8
062	Positive	0.6	14.5
074	Positive	0.6	14.6
055	Positive	0.6	16.9

Sample ID Number	ARK Immunoassay Result	Fentanyl (ng/mL by LC-MS/MS)	Norfentanyl (ng/mL by LC-MS/MS)
071	Positive	0.6	19.0
070	Positive	0.6	161.7
051	Positive	0.7	2.1
066	Positive	0.7	3.1
064	Positive	0.8	15.9
073	Positive	0.8	45.8
063	Positive	0.9	2.2
061	Positive	0.9	6.5
057	Positive	0.9	12.3
053	Positive	0.9	14.0
059	Positive	0.9	62.6
054	Positive	0.9	63.4

Traceability and Value Assignment

ARK Fentanyl Calibrators and Controls are prepared by volumetric dilution of high purity fentanyl (certified solution traceable to HPLC) into non-sterile, processed human urine free of fentanyl. Testing is performed with the ARK Fentanyl II Assay on the Beckman Coulter AU680 automated clinical chemistry analyzer, calibrated with the ARK Fentanyl Calibrator.

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

As summarized above, the ARK Fentanyl II Assay system was shown to be substantially equivalent to the legally marketed predicate device, ARK Fentanyl Assay system: k180427.