510(k) SUMMARY

K240124

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4. Device Names: BioSieve™ Fentanyl FIA Test Kit
BioSieve™ ToxiSmart FIA Reader

Classification: Class 2

Product Code	Classification	Regulation Section	Panel
DJG	II	21 CFR § 862.3650 Opiate Test System	Toxicology (91)
KHO	I	21 CFR § 862.2560 Fluorometer for clinical use	Clinical Chemistry

5. Predicate Devices:

Superbio Fentanyl Urine Detection Kit, K220046;
Superbio Immunofluorescence Analyzer EASY-11, K220046

6. Indications for Use

BioSieve™ Fentanyl FIA Test Kit is a fluorescence immunoassay (FIA) for the qualitative determination of fentanyl in human urine at a cutoff concentration of 1.0 ng/mL. The assay is intended for use with BioSieve™ ToxiSmart FIA Reader.

It is for *in vitro* diagnostic use only. It is intended for prescription use.

The tests provide only preliminary results. A more specific alternative chemical method must be used in order to obtain a confirmed 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.

BioSieve™ ToxiSmart FIA Reader is a portable fluorescence instrument for *in vitro* diagnostic use only. The Reader is designed to perform *in vitro* diagnostic tests on urine specimens. This Reader can be used in a laboratory or in a point-of-care setting.

7. Device Description

This test uses a lateral flow design with location-dependent lines and zones. BioSieve™ ToxiSmart FIA Reader scans the test strip and displays results. The sample is added to the sample well of the

test card, and the sample is drawn by capillary action into and through the fluorescent labeled pad, through the nitrocellulose strip and into the adsorption pad. Within the fluorescent labeled pad, the specimen comes into contact with antibodies conjugated with fluorescent microspheres. During this interaction, if the amount of fentanyl antigen in the sample is greater than or equal to the cutoff value, the antigen in the sample and the fluorescence-labeled antibody bind to the FTY antigen-antibody complex when the sample passes through a pad of fluorescence-microbead-labeled antibody conjugate. As the sample flows and reaches the FTY antigen coated by the T-line of nitrocellulose membrane, the FTY antigen coated by the T-line and the antigen in the sample competitively bind the FTY antibody labeled with fluorescence, then the T-line captures fluorescence signal is weaker than the cutoff fluorescence signal. When the samples do not contain fentanyl antigen or levels below the cutoff value, as the sample flow, fluorescent microsphere labeled antibody to nitrocellulose membrane T line captures fluorescent signal is stronger than the cutoff fluorescence signal. Whether or not FTY antigen was present in the sample, the rabbit IgG fluorescent microsphere conjugate not bound to the test line continued to flow with the rest of the sample and soon encountered a control line composed of goatanti-rabbit IgG. The position of C-line will accumulate fluorescence signal. The C-line control area was scanned to confirm that adequate sample flow had occurred. High resolution, narrow band SMD LED was used as light source in the Immunofluorescence Analyzer. The central wavelength of the excitation spectrum is 365nm. The central response wavelength is 610nm.

8. Substantial Equivalence Information

A summary comparison of features of the BioSieve™ Fentanyl FIA Test Kit and the predicate devices is provided in following table.

Table 1: Features Comparison of BioSieve™ Fentanyl FIA Test Kit and the Predicate Devices

Item	Device	Predicate - K220046
Indication(s) for Use	For the qualitative determination of fentanyl in human urine.	Same
Calibrator and Cut-Off Values	Fentanyl (FTY) 1 ng/ml	Same
Methodology	Competitive binding, lateral flow immunochromatographic assays based on the principle of antigen antibody immunochemistry.	Same
Type of Test	Qualitative	Same
Specimen Type	Human Urine	Same
Intended Use	For prescription use	Same
Configurations	Test Card (chip on the back)	Test Card (no back chip)
Platform Required	Immunofluorescence Analyzer	Same
Storage	2-30˚C	4-30˚C

Table 2: Instrument Similarities and Differences

Item	Device	Predicate - K220046
Intended Use/ Indication for Use	Immunofluorescence analyzer designed to perform in vitro diagnostic tests on clinical specimens including drug urine test	Same
Principles of Assay Operation	Competitive immunofluorescence immunoassay	Same
Calibration Check	A Quality control test device is supplied with the Reader and used for check the Reader optics and calculation systems.	A Quality control card is supplied with Easy-11 and used for check Easy-11 optics and calculation. systems.
Development Modes	Two basic assay development modes: • Standard test: In standard test, the user insert the Reader immediately after adding the sample, and the Reader will display the test result when the countdown is finished • Quick test: In the quick test, the user need insert the Reader after the reaction time is completed, and the Reader will display the test result in a few seconds.	Two basic assay development modes: • Standard test: In standard test, the user immediately inserts Test Cassette into Easy-11 and click "start test". Easy-11 automatically counts the time. • Quick test: Manually timing, then insert the test card into Easy-11, and click "Start Test". The instrument will read the results.
User interface	1.54 inch LCD Screen display	8 inch Color LCD touchscreen display
Barcode scanner (sample)	Not equipped with a barcode scanner	Same
Assay/instrument interface	Drawer	Same
Light Source	LED Light	Same
Power Supply	Powered by a 3.7V lithium-ion battery Two charging methods: 1.Type C & USB 2 in 1 cable (computer charging) 2.Type C & USB 2 in 1 cable with the AC adapter (wall charging) Input: 100-240V~, 50/60Hz, 0.2A Max; Output: 5.0V⎓, 1.0A	AC100-240V
Dimensions	12.45 cm x 7.25 cm x 4 cm	28 cm x 28 cm x 16 cm

Weight	~0.36 lbs	~4.5 lbs

9. Test Principle

BioSieve™ Fentanyl FIA Test Kit uses the principle of competitive and fluorescence immunochromatography assay. The nitrocellulose membrane test area (T) of the test strip is correspondingly coated with fentanyl-bovine serum albumin conjugate, and the quality control area (C) is coated with goat anti-rabbit lgG polyclonal antibody. Both Fentanyl monoclonal antibody and rabbit lgG polyclonal antibody labeled with fluorescent microspheres are embedded on the conjugate pad. The labeled antibody will flow forward with the sample, when the urine sample is applied to the sample well of the test device. When the concentration of fentanyl in the sample is higher than or equal to the cut-off of the product, it will compete with the corresponding conjugate coated on the test area (T) to bind to the fluorescently labeled monoclonal antibody, the fluorescence signal rendering of the test line is inhibited and the result is positive; while when the sample does not contain fentanyl or its concentration is lower than the cut-off of the product, the corresponding conjugate on the test line reacts with sufficient fluorescently-labeled monoclonal antibodies, the test line will have fluorescence signal and the result is negative. The quality control area (C) will develop fluorescence signal, which is the criteria for judging whether the test process is normal or not. Signal intensity of fluorescence is detected by BioSieve™ ToxiSmart FIA Reader.

10. Performance Characteristics

1. Analytical Performance

a. Precision

Precision studies were carried out for samples with concentrations of -100% cut off, -75% cut off, -50% cut off, -25% cut off, cut off, +25% cut off, +50% cut off, +75% cut off and +100% cut off. These samples were prepared by spiking fentanyl in negative samples. Each fentanyl concentration was confirmed by LC/MS-MS. All sample aliquots were blindly labeled by the person who prepared the samples and didn't take part in the sample testing. For each concentration, tests were performed six runs per day for 10 days per device lot in a randomized order. Each device was read on one BioSieve™ ToxiSmart FIA Reader. The results obtained are summarized in the following tables.

Lot Number	-100% cut off	-75% cut off	-50% cut off	-25% cutoff	cut off	+25% cut off	+50% cut off	+75% cut off	+100% cut off
Lot 1	60-/0+	60-/0+	60-/0+	58-/2+	28-/32+	60+/0-	60+/0-	60+/0-	60+/0-
Lot 2	60-/0+	60-/0+	60-/0+	60-/0+	28-/32+	60+/0-	60+/0-	60+/0-	60+/0-
Lot 3	60-/0+	60-/0+	60-/0+	59-/1+	29-/31+	60+/0-	60+/0-	60+/0-	60+/0-

c. Stability

The devices are stable at 2-30°C for 24 months based on the accelerated stability study at 45°C. The real time stability study is ongoing.

d. Interference

Potential interfering substances found in human urine of physiological or pathological conditions were added to drug-free urine and target drug fentanyl urine with concentrations at 50% below and 50% above Cut-Off levels. These urine samples were tested using three batches of each device. Compounds that showed no interference at a

concentration of 100μg/mL or specified concentrations are summarized in the following tables.

Acetaminophen	Doxepin (50 μg/mL)	Nortriptyline (25 μg/mL)
Acetone (1000 mg/dL)	Ecgonine methyl ester	Noscapine
Acetophenetidin	Ephedrine	O-Hydroxyhippuric acid
Acetylsalicylic acid	Erythromycin	Octopamine
Albumin (100 mg/dL)	Ethanol (1%)	Oxalic acid (100 mg/dL)
Albuterol	Fenoprofen	Oxazepam
Aminopyrine	Fluphenazine	Oxolinic acid
Amitriptyline (35 μg/mL)	Furosemide	Oxymetazoline
Amobarbital	Galactose (10 mg/dL)	Papaverine
Amoxicillin	Gamma Globulin (500 mg/dL)	Penicillin G
Ampicillin	Gentisic acid	Perphenazine
Apomorphine	Glucose (3000 mg/dL)	Phencyclidine
Ascorbic acid	Hemoglobin	Phenelzine
Aspartame	Hydralazine	Phenobarbital
Atropine	Hydrochlorothiazide	Prednisone
Benzilic acid	Hydrocortisone	Propoxyphene (50 μg/mL)
Benzoic acid	Hydroxytyramine	Propranolol
Benzoylecgonine	Ibuprofen	Pseudoephedrine
Bilirubin	Imipramine (30 μg/mL)	Quinine
Boric Acid (1%)	Isoproterenol	Ranitidine
Bupropion (50 μg/mL)	Isoxsuprine	Riboflavin (7.5 mg/dL)
Caffeine	Ketamine	Salicylic acid
Carbamazepine	Ketoprofen	Secobarbital
Chloral hydrate	Labetalol	Serotonin (5-Hydroxytyramine)
Chloramphenicol	Lidocaine (50 μg/mL)	Sulfamethazine
Chlorothiazide	Loperamide	Sulindac
Chlorpromazine	Maprotiline (50 μg/mL)	Tetrahydrocortisone 3-(β-Dglucuronide)
Cholesterol	Meperidine	Tetrahydrocortisone 3-acetate
Clomipramine (50 μg/mL)	Meprobamate	Tetrahydrozoline
Clonidine	Methapyrilene (10 μg/mL)	Thiamine
Cortisone	Methaqualone (50 μg/mL)	Thioridazine
Cotinine	Methoxyphenamine	Triamterene
Creatinine	Metronidazole (300 μg/mL)	Trifluoperazine
Cyclobenzaprine (10 μg/mL)	N-Acetylprocainamide	Trimethoprim
Deoxycorticosterone	NaCl (4000 mg/dL)	Tyramine
Desipramine (50 μg/mL)	Nalidixic acid	Urea (2000 mg/dL)
Dextromethorphan	Naloxone	Uric acid
Diclofenac	Naltrexone	Valproic acid (250 μg/mL)
Diflunisal	Naproxen	Venlafaxine
Digoxin	Niacinamide	Verapamil
Diphenhydramine	Nicotine (10 μg/mL)	Zomepirac
DL-Tryptophan	Nifedipine	β-Estradiol
DL-Tyrosine	Norethindrone	

e. Specificity

To test specificity, drug metabolites and other components that are likely to interfere in urine samples were tested using three batches of device. The lowest concentration that caused a positive result for each compound are listed below.

Drug	Concentration (ng/mL)	% Cross-Reactivity
Acetyl fentanyl	1.2	83.33
Acrylfentanyl	1.2	83.33

Drug	Concentration (ng/mL)	% Cross-Reactivity
ω-1-Hydroxyfentanyl	20000	0.01
Isobutyryl fentanyl	1.5	66.67
Ocfentanil	1.5	66.67
Butyryl fentanyl	1.6	62.50
Furanyl fentanyl	1.75	57.14
Valeryl fentanyl	2.5	40.00
(±) β-hydroxythiofentanyl	2.8	35.71
4-Fluoro-isobutyrylfentanyl	3	33.33
Para-fluorobutyryl fentanyl	3	33.33
Para-fluoro fentanyl	3	33.33
(±)-3-cis-methyl fentanyl	5	20.00
Carfentanil	500	0.20
Sufentanil	625	0.16
Alfentanil	100000	0.00
Despropionyl fentanyl (4-ANPP)	50000	0.00

The following other Metabolites and opioids compounds were tested at a concentration of 100 µg/mL. Negative results were obtained for all these compounds. There is no cross-reactivity for these compounds using the BioSieve™ Fentanyl FIA Test Kit.

Remifentanil	Norfentanyl	Acetyl norfentanyl
Norcarfentanil	6-Acetyl morphine	Amphetamine
Buprenorphine	Buprenorphineglucuronide	Codeine
Dextromethorphan	Dihydrocodeine	EDDP
EMDP	Fluoxetine	Heroin
Hydrocodone	Hydromorphone	Ketamine
Levorphanol	Meperidine	Methadone
Morphine	Morphine-3-glucuronide	Naloxone
Naltrexone	Norbuprenorphine	Norcodeine
Norketamine	Normeperidine	Normorphine
Noroxycodone	Oxycodone	Oxymorphone
Pentazocine (Talwin)	Pipamperone	Risperidone
Tapentadol	Thioridazine	Tilidine
Tramadol	Tramadol-O- Desmethyl	Tramadol-N-Desmethyl

Trazodone		

f. Effect of Urine Specific Gravity and Urine pH

To investigate the effect of urine specific gravity and urine pH, urine samples, with 1.000 to 1.035 specific gravity or urine samples with pH 4 to 9 were spiked with target fentanyl at 50% below and 50% above Cut-Off levels. by three different operators per lot of device, with a total of three lots. Results were all positive for samples at and above +50% Cut-Off and all negative for samples at and below -50% Cut-Off.

2. Comparison Studies

Method comparison studies for the BioSieve™ Fentanyl FIA Test Kit. were performed at three different testing sites. Operators ran 80 (40 negative and 40 positive) unaltered clinical samples. The samples were blind labeled and compared to LC-MS/MS results. The results are presented in the tables below.

		Negative	Low Negative by LC-MS/MS (less than -50%)	Near Cutoff Negative by LC-MS/MS (Between -50% and cutoff)	Near Cutoff Positive by LC-MS/MS (Between the cutoff and +50%)	High Positive by LC-MS/MS (greater than +50%)
Site 1	Positive	0	0	4	19	20
	Negative	10	18	8	1	0
Site 2	Positive	0	0	3	18	20
	Negative	10	18	9	2	0
Site 3	Positive	0	0	2	19	20
	Negative	10	18	10	1	0

Discordant Results

Operator	**Sample Number**	**LC-MS/MS Result**	BioSieve **Results**
Site 1	VCFC021	0.849	Positive
Site 1	VCFC075	0.875	Positive
Site 1	VCFC059	0.985	Positive
Site 1	VCFC048	0.946	Positive
Site 1	VCFC057	1.063	Negative
Site 2	VCFC030	0.892	Positive
Site 2	VCFC010	0.934	Positive
Site 2	VCFC059	0.985	Positive
Site 2	VCFC057	1.063	Negative
Site 2	VCFC036	1.104	Negative
Site 3	VCFC010	0.934	Positive
Site 3	VCFC048	0.946	Positive
Site 3	VCFC070	1.129	Negative

3. Clinical Studies

Not applicable.

11. Conclusion

Based on the test principle and acceptable performance characteristics including precision, cut-off, interference, specificity, and method comparison studies of the devices, it's concluded a substantial equivalence decision.