510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT

I Background Information:

A 510(k) Number

K240124

B Applicant

VivaChek Biotech (Hangzhou) Co., Ltd

C Proprietary and Established Names

BioSieve™ Fentanyl FIA Test Kit; BioSieve™ ToxiSmart FIA Reader

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
DJG	Class II	21 CFR 862.3650 - Opiate Test System	TX - Clinical Toxicology
KHO	Class I	21 CFR 862.2560 - Fluorometer for clinical use	CH - Clinical Chemistry

II Submission/Device Overview:

A Purpose for Submission:

New device

B Measurand:

Fentanyl

C Type of Test:

Qualitative, fluorescence immunoassay (FIA)

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) 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.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

Strips are not for visual read.

D Special Instrument Requirements:

BioSieve™ ToxiSmart FIA Reader

IV Device/System Characteristics:

A Device Description:

The assay consists of a test strip enclosed in a plastic cassette, a dropper, the BioSieve ToxiSmart FIA Reader, and associated labeling. External quality control materials are recommended but not included.

B Principle of Operation:

The BioSieve™ Fentanyl FIA Test Kit uses the principle of competitive and fluorescence immunochromatography. The nitrocellulose membrane test area (T) of the test strip is 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. Thus, fluorescence signal rendering of the test line is inhibited and the result is positive. If 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. Thus, the test line will develop a fluorescence signal and the result is negative. The quality control area (C) will also develop a fluorescence signal, indicating that the testing has been performed correctly.

C Instrument Description Information:

1. Instrument Name:

   BioSieve ToxiSmart FIA Reader

2. Specimen Identification:

   Sample identification numbers must be entered manually by the user.

3. Specimen Sampling and Handling:

   Specimen collection, preparation, and handling conditions are described in the package insert of the assay.

4. Calibration:

   The analyzer is factory calibrated and does not need to be recalibrated by the operator.

5. Quality Control:

   Quality control materials are recommended but not provided.

6. Operation Instruction:

   BioSieve ToxiSmart FIA Reader provides two test modes: Standard and Quick.

   Before the start of each mode, the reagent ID chip is inserted and the operator selects the sample type and test item. The test card is then removed from the protective pouch and placed on a horizontal flat surface.

   - Under the standard test mode, the sample is dropped into a sample well using the provided dropper. The test card with the sample is then placed into the instrument and the operator starts the test by pressing the “Start test” button on the instrument which

automatically starts a timer. At the end of the incubation period, the instrument will record the test results and the result will be available for reading and printing to the operator.

- Under the quick test mode, the sample is dropped into a sample well using the provided dropper. The test card with the sample is kept on a flat surface outside of the instrument and manually incubated using a timer. At the end of the incubation period, the test card with the patient sample is inserted into the instrument and the operator starts the test by pressing the "Start test" button on the instrument. The instrument will record the test results and the result will be available for reading and printing to the operator.

V Substantial Equivalence Information:

A Predicate Device Name(s):

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

B Predicate 510(k) Number(s):

K220046

C Comparison with Predicate(s):

Device & Predicate Device(s):	K240124	K220046
Device Trade Name	BioSieve™ Fentanyl FIA Test Kit, BioSieve™ ToxiSmart FIA Reader	Superbio Fentanyl Urine Detection Kit, Superbio Immunofluorescence Analyzer EASY-11
General Device Characteristic Similarities		
Intended Use/Indications For Use	For the qualitative determination of fentanyl in human urine	Same
Calibrator and Cut-Off Values	1 mg/mL	Same
Methodology	Competitive binding, lateral flow immunochromatographic assays based on the principle of antigen antibody immunochemistry	Same
Specimen Type	Urine	Same
Analyzer	Immunofluorescence Analyzer	Same

General Device Characteristic Differences		
Power Supply	3.7V lithium-ion battery	Mains (AC) powered
User interface	1.54 inch LCD display	8 inch color LCD touchscreen display
Dimensions	4.90 inches (12.45 cm) x 2.85 inches (7.25 cm) x 1.57 inches (4 cm)	11.0 in (28 cm) x 11.0 in (28 cm) x 6.3 in (16 cm)

VI Standards/Guidance Documents Referenced:

None referenced.

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

Precision studies were carried out for samples with concentrations of -100% cutoff, -75% cutoff, -50% cutoff, -25% cutoff, cutoff, +25% cutoff, +50% cutoff, +75% cutoff and +100% cutoff for fentanyl cut off concentration of 1 ng/mL. Samples with concentration of -100% cutoff were drug-free urines samples. Other samples were prepared by spiking target drug fentanyl in drug-free urine samples. Each drug concentration was confirmed by LC-MS/MS. All sample aliquots were blindly labeled by the person who prepared the samples but didn't take part in the sample testing. A sequential randomization algorithm was applied to assign the prepared samples to an arbitrary number.

The precision data was collected using three lots of reagent, three analyzers, and three sites, with one replicate per run per lot, with two runs per day collected over 10 days.

Each study site has at least one test operator to perform the test. There are six tests per day per concentration at each site (2 runs per day × 3 lots × 9 concentrations) for a total 54 tests per day per site. Results are summarized in the table below:

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

2. Linearity:

Not applicable, this device is intended for qualitative use only

3. Analytical Specificity/Interference:

Specificity Using Drug Free Samples:

The sponsor performed a specificity study to demonstrate negative results on drug-free samples using the BioSieve™ Fentanyl FIA Test Kit. In the study, 30 drug-free urine samples were collected. The concentration of these samples were tested and confirmed by LC-MS. The test was performed using three (3) analyzers, three (3) lots and three (3) operators. All tested samples had the expected negative result.

Cross Reactivity:
The sponsor performed a study to verify potential cross-reactants using the target drug, drug metabolites and other related compounds.

Target drugs, drug metabolites and other components that are likely to interfere in urine samples were added to drug-free urine at different concentrations of compounds and tested using three (3) different instruments, three (3) different lots, and three (3) operators. The lowest concentration that caused a positive result for each compound are listed below.

Percent cross reactivity of a compound is calculated by dividing the cutoff concentration by the minimum concentration required to obtain a positive result and then multiplying by 100%. The results are listed in the table below:

Fentanyl (Cutoff = 1 ng/mL)	Minimum Concentration Required to Obtain a Positive Result (ng/mL)	% Cross-Reactivity
Acetyl fentanyl	1.2	83.33
Acrylfentanyl	1.2	83.33
ω-1-Hydroxyfentanyl	20000	0.005
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

Fentanyl (Cutoff = 1 ng/mL)	Minimum Concentration Required to Obtain a Positive Result (ng/mL)	% Cross-Reactivity
Carfentanil	500	0.20
Sufentanil	625	0.16
Alfentanil	100000	0.001
Despropionyl fentanyl (4-ANPP)	50000	0.002
Remifentanil	>100000	Not detected
Norfentanyl	>100000	Not detected
Acetyl norfentanyl	>100000	Not detected
Norcarfentanil	>100000	Not detected

The following opioid compounds were tested and produced a negative result at a concentration of 100 µg/ml:

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

Interference:

1. Interference Study on the Effect of Specific Gravity and pH:

   To investigate the effect of urine specific gravity and urine pH, urine samples with specific gravity of 1.000 to 1.035 and urine samples with a pH of 4 to 9, in 1 pH unit increments, were spiked with target fentanyl at 50% below and 50% above cutoff levels. These samples were tested using three (3) lots of device, three (3) instruments and three (3) different operators. Results were all positive for samples at +50% cutoff and all negative for samples at and below -50% cutoff. The results demonstrate that varying ranges of specific gravity and pH do not interfere with the BioSieve™ Fentanyl Test Kit (FIA).

2. Interfering Substances

   Potential interfering substances found in human urine of physiological or pathological conditions were added at a concentration of 100 µg/mL or as specified in the table below.

   The potential interferents were added to drug-free urine spiked with fentanyl to concentrations at 50% below and 50% above cutoff levels. These urine samples were

tested using three (3) lots of the device and three (3) instruments by three (3) operators. The following compounds all produced the expected negative or positive result with the BioSieve™ Fentanyl Test Kit (FIA):

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- D-glucuronide)
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	

4. Assay Reportable Range:

   Not applicable, this device is intended for qualitative use only.

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

   The assay is traceable to a commercial standard from Cerilliant Corp.

6. Detection Limit:

   Not applicable

7. Assay Cut-Off:

   Analytical performance of the device around the claimed cutoff is described in the precision section VII.A1. above.

8. Accuracy (Instrument):

   See accuracy study in Section VII.B.1.

9. Carry-Over:

   To assess the possibility of carryover, the sponsor performed a study in which samples with concentrations at -50% of the cutoff (0.5 ng/mL) and at -100% of the cutoff (0 ng/mL) were analyzed immediately after a sample with a concentration of 100 ng/mL (100 times the cutoff). The data was collected by three operators using three lots and three instruments (one lot per instrument). In all instances the samples at 0.5 and 0 ng/mL produced a negative result when run immediately after a sample with a concentration of 100 ng/mL

B Comparison Studies:

1. Method Comparison with Predicate Device:

A comparison study between BioSieve™ Fentanyl Test Kit (FIA) and LC-MS/MS method was conducted in three different testing sites including two POC sites (physician's offices).

This study was a randomized and blinded accuracy study.

Clinical samples included a total of 80 urine samples (40 Negative and 40 positive). The clinical samples were labeled using randomized numbers by the person who prepares samples and did not perform the actual testing. Sample concentrations of fentanyl were confirmed by LC-MS/MS prior to testing on the candidate device.

The study was performed using three reagent lots and three analyzers, and by three operators. Results are summarized in the tables below:

Site	Positive/ Negative	Negative	Low Negative by LC/MS (< -50%) < 0.5 ng/mL	Near Cutoff Negative by LC/MS (between -50% and cutoff) 0.5 - 0.9	Near Cutoff Positive by LC/MS (between cutoff and +50%) 1.0 – 1.5	High Positive by LC/MS (> +50%) > 1.5 ng/mL
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

2. Matrix Comparison:

Not applicable. The assay is intended to be used with urine samples only.

C Clinical Studies:

1. Clinical Sensitivity:

Not applicable.

2. Clinical Specificity:

Not applicable.

3. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

Not applicable.

D Clinical Cut-Off:

Not applicable.

E Expected Values/Reference Range:

Not applicable.

F Other Supportive Instrument Performance Characteristics Data:

Not applicable.

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.