510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K231904

B Applicant

Co-Innovation Biotech Co.,Ltd.

C Proprietary and Established Names

Rapid Fentanyl (FYL) Test Strip, Rapid Fentanyl (FYL) Test Dipcard

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
DJG	Class II	21 CFR 862.3650 - Opiate Test System	TX - Clinical Toxicology

II Submission/Device Overview:

A Purpose for Submission:
New Device

B Measurand:
Fentanyl in human urine.

C Type of Test:
Qualitative competitive binding, lateral flow immunochromatographic assay.

III Intended Use/Indications for Use:

A Intended Use(s):
See Indications for Use below.

B Indication(s) for Use:

The Rapid Fentanyl (FYL) Test Strip is a rapid, screening test for the qualitative detection of Fentanyl (FYL) in human urine at the cut-off concentration of 1 ng/mL. The tests is intended for in vitro diagnostics use. It is intended for prescription use including point of care sites. This assay provides only a preliminary analytical test result. To obtain a confirmed analytical result, a more specific alternative chemical method must be used. Gas Chromatography/ Mass spectrometry (GC/MS) or Liquid chromatography/Mass spectrometry (LC/MS) is the preferred confirmatory method. Clinical consideration and professional judgment should be applied to any drug of abuse test result, particularly when preliminary positive results are indicated.

The Rapid Fentanyl (FYL) Test Dipcard is a rapid, screening test for the qualitative detection of Fentanyl (FYL) in human urine at the cut-off concentration of 1 ng/mL. The tests is intended for in vitro diagnostics use. It is intended for prescription use including point of care sites. This assay provides only a preliminary analytical test result. To obtain a confirmed analytical result, a more specific alternative chemical method must be used. Gas Chromatography/ Mass spectrometry (GC/MS) or Liquid chromatography/Mass spectrometry (LC/MS) is the preferred confirmatory method. Clinical consideration and professional judgment should be applied to any drug of abuse test result, particularly when preliminary positive results are indicated.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

For in-vitro diagnostic use only.

D Special Instrument Requirements:

N/A

IV Device/System Characteristics:

A Device Description:

Rapid Fentanyl (FYL) Test Strip and Rapid Fentanyl (FYL) Test Dipcard are competitive binding, lateral flow immunochromatographic assays for qualitatively the detection of fentanyl at or above the cut-off concentration of 1 ng/mL. Test Strip and Test Dipcard use identical test strips made with same chemical formulation and manufacturing procedures.
Content of the kit:
Test Strip, one test in one pouch or Test Dipcard, one test in one pouch.
Desiccant. The desiccant is only for storage purposes only and is not used in the test procedures.
Leaflet with instructions for use.

B Principle of Operation:

The Rapid Fentanyl (FYL) Test Strip is a competitive immunoassay that is used to screen for the presence of Fentanyl and metabolites in urine. It is chromatographic absorbent device in which, drugs within a urine sample, competitively combined to a limited number of drug monoclonal antibody (mouse) conjugate binding sites.

When the test is activated, the urine is absorbed into test strip by capillary action, mixes with the respective drug monoclonal antibody conjugate, and flows across a pre-coated membrane. When drug within the urine sample is below the detection level of the test, respective drug monoclonal

antibody conjugate binds to the respective drug-protein conjugate immobilized in the Test Region (T) of the test strip. This produces a colored Test line in the Test Region (T) of the strip, which, regardless of its intensity, indicates a negative test result.

When sample drug levels are at or above the detection level of the test, the free drug in the sample binds to the respective drug monoclonal antibody conjugate, preventing the respective drug monoclonal antibody conjugate from binding to the respective drug-protein conjugate immobilized in the Test Region (T) of the device. This prevents the development of a distinct colored band in the test region, indicating a preliminary positive result.

To serve as a procedure control, a colored line will appear at the Control Region (C), of each strip, if the test has been performed properly.

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):	K231904	K220046
Device Trade Name	Rapid Fentanyl (FYL) Test Strip, Rapid Fentanyl (FYL) Test Dipcard	Superbio Fentanyl Urine Detection Kit
General Device Characteristic Similarities		
Intended Use/Indications for Use	Qualitative detection of fentanyl in urine,	Same
Intended Users	Prescription use only.	Same
Calibrator and Cutoff Values	1 ng/ml	Same
Type of Test	Qualitative	Same
Specimen Type	Human urine	Same
Methodology	Competitive binding, lateral flow immunochromatographic assay based on the principle of antigen antibody immunochemistry	Same

General Device Characteristic Differences		
Configurations	Test Strip and Dipcard	Test Card
Platform required	None	Immunofluorescence Analyzer
Storage/Operating Temp	4-30°C	4-35°C

VI Standards/Guidance Documents Referenced:

None

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

Precision studies were performed using 3 lots of test Strip and test Dipcard. Drug free specimens were spiked with target drug fentanyl at 0, ±75% cutoff, ±50% cutoff, ±25% cutoff and +100% cutoff of drug. The concentrations of the target drugs were confirmed with LC/MS. Each concentration of the urine specimen was divided into aliquots. Each aliquot was blindly labeled by a nonparticipant. Separate sets of blinded coded samples were assigned and randomized prior to testing. The study was conducted by 6 operators/nurses at 3 Point-of-Care sites. Two operators per location tested 3 aliquots at each concentration for each lot per day (3 runs/day) for 10 non-consecutive days using one device lot per location. One operator tested the test strip format, and the second operator tested the test dipcard format. There were 1620 observations by 3 sites at 9 concentrations.

Rapid Fentanyl (FYL) Test Strip:

Approximate concentration of sample	% of cutoff	Number of determinations per lot	Test Strip Lot 1		Test Strip Lot 2		Test Strip Lot 3	
			Positive	Negative	Positive	Negative	Positive	Negative
0ng/ml	Negative	60	0	60	0	60	0	60
0.25ng/ml	-75% cutoff	60	0	60	0	60	0	60
0.5ng/ml	-50% cutoff	60	0	60	0	60	0	60
0.75ng/ml	-25% cutoff	60	4	56	2	58	6	54
1ng/ml	cutoff	60	36	24	34	26	32	28
1.25ng/ml	+25% cutoff	60	54	6	56	4	56	4
1.5ng/ml	+50% cutoff	60	60	0	60	0	60	0
1.75ng/ml	+75% cutoff	60	60	0	60	0	60	0
2ng/ml	+100% cutoff	60	60	0	60	0	60	0

Rapid Fentanyl (FYL) Test Dipcard:

Approximate concentration of sample	% of cutoff	Number of determinations per lot	Test Dipcard Lot 1		Test Dipcard Lot 2		Test Dipcard Lot 3	
			Positive	Negative	Positive	Negative	Positive	Negative
0ng/ml	Negative	60	0	60	0	60	0	60
0.25ng/ml	-75% cutoff	60	0	60	0	60	0	60
0.5ng/ml	-50% cutoff	60	0	60	0	60	0	60
0.75ng/ml	-25% cutoff	60	4	56	4	56	2	58
1ng/ml	cutoff	60	34	26	34	26	36	24
1.25ng/ml	+25% cutoff	60	56	4	58	2	56	4
1.5ng/ml	+50% cutoff	60	60	0	60	0	60	0
1.75ng/ml	+75% cutoff	60	60	0	60	0	60	0
2ng/ml	+100% cutoff	60	60	0	60	0	60	0

2. Linearity:

Not applicable, this device is intended for qualitative use only

3. Analytical Specificity/Interference:

Cross Reactivity:

The sponsor performed a study to verify potential cross-reactants using the target drug, drug metabolites, and other related compounds. The target drugs, drug metabolites and other components that are likely to interfere in urine samples were added to drug-free urine specimens at a concentration of 100µg/ml. The study was conducted by 8 laboratory professionals. Two Laboratory professionals spiked the compound controls and divided them into individual containers, the other 6 laboratory professionals conducted the testing using the instructions for use package insert. Each sample was tested in 3 replicates using 3 lots of Rapid Fentanyl (FYL) Test Strip and the same protocol for Rapid Fentanyl (FYL) Test Dipcard. One operator conducted each individual lot (and product type; strip and dipcard) separately.

The formula for calculating the percent of cross-reactivity was calculated by dividing the cutoff concentration by the minimum concentration required to obtain a positive result and then multiplying by 100%. The lowest concentration that caused a positive result for each compound are listed below for both the Rapid Fentanyl (FYL) Test Strip and the same protocol for Rapid Fentanyl (FYL) Dipcard:

Rapid Fentanyl (FYL) Test-Strip:

Compound	Quantity equivalent to cutoff(ng/mL) conducted on 3 lots	% Cross Reactivity
Norfentanyl	10,000	0.01

Acetyl fentanyl	1.2	83.3
Acetyl norfentanyl	10,000	0.01
Acrylfentanyl	1.5	66.7
Butyryl fentanyl	1.6	62.5
Carfentanil	500	0.2
(±)-3-cis-methylfentanyl	5	20
4-Fluoro-isobutyrylfentanyl	3	33.3
Furanyl fentanyl	1.8	55.6
ω-1-Hydroxyfentanyl	20,000	0.01
(±) β-hydroxythiofentanyl	2.8	35.7
Isobutyryl fentanyl	1.5	66.7
Ocfentanil	1.8	55.6
Para-fluorobutyrylfentanyl (p-FBF)	3	33.3
Para-fluoro fentanyl	3	33.3
Sufentanil	625	0.16
Valeryl fentanyl	2.5	40

Rapid Fentanyl (FYL) Dipcard:

Compound	Quantity equivalent to cutoff(ng/mL) conducted on 3 lots	% Cross Reactivity
Norfentanyl	10,000	0.01
Acetyl fentanyl	1.2	83.3
Acetyl norfentanyl	10,000	0.01
Acrylfentanyl	1.5	66.7
Butyryl fentanyl	1.6	62.5
Carfentanil	500	0.2
(±)-3-cis-methylfentanyl	5	20
4-Fluoro-isobutyrylfentanyl	3	33.3
Furanyl fentanyl	1.8	55.6
ω-1-Hydroxyfentanyl	20,000	0.01
(±) β-hydroxythiofentanyl	2.8	35.7
Isobutyryl fentanyl	1.5	66.7

Ocfentanil	1.8	55.6
Para-fluorobutyrylfentanyl (p-FBF)	3	33.3
Para-fluoro fentanyl	3	33.3
Sufentanil	625	0.16
Valeryl fentanyl	2.5	40

Interference Study on the Effect of Specific Gravity and pH:
The specific Gravity study was conducted using 5 increments of specific gravity levels: 1.000, 1.010, 1.020, 1.030, and 1.040 on 3 different lots of the Rapid Fentanyl (FYL) Test Strip, and 3 different lots of the Rapid Fentanyl (FYL) Test Dipcard with drug free urine spiked with Fentanyl at 0.5ng/ml (50% below cutoff) and 1.5ng/ml (50% above cutoff). All concentrations were confirmed with LC/MS. No discrepant results were observed.

The pH study was conducted on 3 different lots of the Rapid Fentanyl (FYL) Test Strip, and 3 different lots of the Rapid Fentanyl (FYL) Test Dipcard using seven increments of pH level ranging from 3 to 9 in aliquot negative urine spiked with Fentanyl at 0.5ng/ml (50% below cutoff) and 1.5ng/ml (50% above cutoff). All concentrations were confirmed with LC/MS. No discrepant results were observed.

Interference

The sponsor conducted two different studies for interference, using their Test Strip and Test Dipcard for each. The first interference study was conducted using opioid compounds (a separate study from their Cross-Reactivity study), and the second interference study was conducted using commonly ingested medications/substances. Both are described below:

A. Interfering Substances (Opioid compounds):
   To test the interference of opioid compounds. This study was conducted by 8 laboratory professionals. 2 laboratory professionals spiked the compound controls and divided them into individual containers. The other 6 laboratory professionals conducted the following testing using the English package insert as guide and read the results at 5 minutes.

   Potential interfering opioid compounds, each at a concentration of 100 µg/mL (except Despropionly fentanyl (4-ANPP) was tested at 50µg/ml, norcarfentanil was tested at 5ug/mL and remifentanil was tested at 10 µg/ mL), were added to drug-free urine specimens spiked with fentanyl to concentrations at 50% below and 50% above cutoff levels at 0.5ng/ml and 1.5ng/ml level and were tested in replicates of 3 on 3 different lots of the Rapid Fentanyl (FYL) Test Strip, and 3 different lots of the Rapid Fentanyl (FYL) Test Dipcard. The compounds showed no interference with the Rapid Fentanyl (FYL) Test Strip or the Rapid Fentanyl (FYL) Test Dipcard.

   The following opioid compounds showed no interference with the Rapid Fentanyl (FYL) Test Strip or the Rapid Fentanyl (FYL) Test Dipcard:

   6-Acetyl morphine, Alfentanil, Amphetamine, Buprenorphine, Buprenorphineglucuronide, Codeine, Despropionyl fentanyl (4-ANPP),

Dextromethorphan, Dihydrocodeine, EDDP, EMDP, Fluoxetine, Heroin, Hydrocodone, Hydromorphone, Ketamine, Levorphanol, Meperidine, Methadone, Morphine, Morphine-3-glucuronide, Naloxone, Naltrexone, Norbuprenorphine, Norcarfentanil, Norcodeine, Norketamine, Normeperidine, Normorphine, Noroxycodone, Oxycodone, Oxymorphone, Pentazocine (Talwin), Pipamperone, Remifentanil, Risperidone, Tapentadol, Thioridazine, Tilidine, Tramadol, Tramadol-O-Desmethyl, Tramadol-NDesmethyl, Trazodone, Dextromethorphan, Meperidine, and Pentazocine

B. Interfering Substances (Commonly ingested medications/substances):
This study was conducted by 8 laboratory professionals. 2 laboratory professionals spiked the compound controls and divided them into individual containers. The other 6 laboratory professionals conducted the following testing using the English package insert as guide and read the results at 5 minutes.

Potential interfering substances, each at a concentration of 100µg/mL (or specified concentrations noted in the tables below), were added to drug-free urine specimens spiked with fentanyl to concentrations at 50% below and 50% above cutoff levels at 0.5ng/ml and 1.5ng/ml level and were used to test 3 different lots of the Rapid Fentanyl (FYL) Test Strip, and 3 different lots of the Rapid Fentanyl (FYL) Test Dipcard. The following substances showed no interference with the Rapid Fentanyl (FYL) Test Strip or the Rapid Fentanyl (FYL) Test Dipcard:

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

4. Assay Reportable Range:
   Not applicable, this device is intended for qualitative use only.

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):
   The device is traceable to a commercially available standard that was verified by LC/MS-MS

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 (1ng/ml).

B Comparison Studies:

1. Method Comparison with Predicate Device:

Four hundred eighty clinical urine samples collected from several hospitals and drug relief reformatories. All samples were unaltered clinical specimens, and the concentrations were confirmed with LC/MS. The samples were divided among the 6 nurses. All aliquots were blindly labeled by a nonparticipant and were randomized prior to testing.

The study was conducted by 6 nurses at three Point-of-Care sites. Each of the three sites were responsible for conducting testing on one lot of 80 samples for both the Rapid Fentanyl (FYL) Test Strip, and the Rapid Fentanyl (FYL) Test Dipcard (160 samples at each of the 3 sites=480). Each nurse only tested one format of Rapid Fentanyl Test, one tested with strip format another tested with Dipcard.

Comparison data of Rapid Fentanyl (FYL) Test (Strip)

Format		LC/MS					Total
		Neg. (drug free)	Neg. (<-50% cutoff)	Near cutoff neg. (-50% cutoff to cutoff)	Near cutoff pos. (cutoff to +50% cutoff)	Pos. (> +50% cutoff)	
Lot 1	Positive	0	0	1	8	31	80
	Negative	27	5	7	1	0	
Lot 2	Positive	0	0	1	8	31	80
	Negative	27	5	7	1	0	
Lot 3	Positive	0	0	1	8	31	80
	Negative	27	5	7	1	0	

Comparison data of Rapid Fentanyl (FYL) Test (Dipcard)

Format		LC/MS					Total
		Neg. (drug free)	Neg. (<-50% cutoff)	Near cutoff neg. (-50% cutoff to cutoff)	Near cutoff pos. (cutoff to +50% cutoff)	Pos. (> +50% cutoff)	
Test Dipcard Lot 1	Positive	0	0	1	8	31	80
	Negative	27	5	7	1	0	
Test Dipcard Lot 2	Positive	0	0	1	8	31	80
	Negative	27	5	7	1	0	
Test Dipcard Lot 3	Positive	0	0	1	8	31	80
	Negative	27	5	7	1	0	

2. Matrix Comparison:

   Not applicable. This device 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.

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.