



**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY**

I Background Information:

A 510(k) Number

K243064

B Applicant

Eterbio, Inc.

C Proprietary and Established Names

ETERBIO Fentanyl/Norfentanyl Rapid Test (Colloidal Gold); ETERBIO Fentanyl/Norfentanyl Home Test

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
NGL	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/Norfentanyl

C Type of Test:

Qualitative

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

The ETERBIO Fentanyl/Norfentanyl Rapid Test (Colloidal Gold) is an immunoassay intended for the qualitative detection of Fentanyl (FTY) /Norfentanyl (NFTY) in human urine:

Drug (Identifier)	Calibrator	Cut-off Level
Fentanyl (FYL)	Fentanyl	1ng/mL
Norfentanyl (NFYL)	Norfentanyl	5ng/mL

The test is available as a single panel for FYL or NFYL, or as a dual panel combining both FYL and NFYL. It provides a preliminary screening result only. For a confirmed analytical outcome, a more specific chemical method is required. GC/MS or LC/MS is the preferred confirmatory method.

The ETERBIO Fentanyl/Norfentanyl Home Test is an immunoassay intended for the qualitative detection of Fentanyl (FTY) /Norfentanyl (NFTY) in human urine:

Drug (Identifier)	Calibrator	Cut-off Level
Fentanyl (FYL)	Fentanyl	1ng/mL
Norfentanyl (NFYL)	Norfentanyl	5ng/mL

The test is available as a single panel for FYL or NFYL, or as a dual panel combining both FYL and NFYL. This test provides only preliminary results. For a confirmed analytical outcome, a more specific chemical method is required. GC/MS or LC/MS is the preferred confirmatory method.

C Special Conditions for Use Statement(s):

OTC - Over the Counter

D Special Instrument Requirements:

Not applicable.

IV Device/System Characteristics:**A Device Description:**

The ETERBIO Fentanyl/Norfentanyl Rapid Test (Colloidal Gold) is an immunoassay designed for the qualitative detection of Fentanyl (FTY) and Norfentanyl (NFTY) in human urine. The test is available as a single panel for FTY or NFTY, or as a dual panel that detects both analytes. Each ETERBIO fentanyl/norfentanyl urine test device consists of a Test Panel and a package insert. Each Test Panel is sealed with sachets of desiccant in an aluminum pouch.

B Principle of Operation:

The ETERBIO Fentanyl/Norfentanyl Rapid Test (Colloidal Gold) is an immunoassay based on the principle of competitive binding. During the testing process, the urine specimen migrates through the test strip via capillary action. If the concentration of the target drug in the specimen is below the specified cutoff level, the binding sites of the antibody-coated particles in the test device remain unsaturated. As a result, these antibody-coated particles are captured by the immobilized drug conjugate, leading to the appearance of a visible colored line in the test line region.

However, if the drug concentration exceeds the cutoff level, the drug will fully saturate the binding sites of the anti-drug antibodies, preventing the formation of a colored line in the test line region.

A procedural control is built into the test, indicated by the consistent appearance of a colored line in the control line region. This confirms that the appropriate volume of specimen has been added and that the membrane wicking process has occurred correctly.

V Substantial Equivalence Information:

A Predicate Device Name(s):

Hightop® Home Use Fentanyl/Norfentanyl Urine Rapid Test Panel; Hightop® Fentanyl/Norfentanyl Urine Rapid Test Panel

B Predicate 510(k) Number(s):

K241969

C Comparison with Predicate(s):

Device & Predicate Device(s):	<u>K243064</u>	<u>K241969</u>
Device Trade Name	ETERBIO Fentanyl/Norfentanyl Rapid Test (Colloidal Gold)	Hightop® Home Use Fentanyl/Norfentanyl Urine Rapid Test Panel; Hightop® Fentanyl/Norfentanyl Urine Rapid Test Panel
General Device Characteristic Similarities		
Intended Use/Indications For Use	For the qualitative determination of fentanyl in human urine.	Same
Methodology	Competitive binding, lateral flow immunochromatographic assays based on the	Same

	principle of antigen antibody immunochemistry.	
Specimen Type	Human Urine	Same
Calibrator and Cut-Off Values	Fentanyl (FTY) 1 ng/ml Norfentanyl (NFTY) 5 ng/ml	Same
Configuration	Panel	Same
General Device Characteristic Differences		
Dip Time	10-15 seconds	5-10 seconds

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% 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 for each target drug. These samples were prepared by spiking fentanyl or norfentanyl in negative urine samples. Each fentanyl or norfentanyl concentration was confirmed by LC/MS. All sample aliquots were blindly labeled by the person who prepared the samples and didn't take part in the sample testing. Three operators tested blinded urine samples over a 10-day period in randomized order with six tests per day per concentration per operator (2 replicates x 3 lots per day x 9 concentrations) for a total of 54 tests per day per operator.

Fentanyl

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+	60-/0+	27+/33-	60+/0-	60+/0-	60+/0-	60+/0-
Lot 2	60-/0+	60-/0+	60-/0+	59-/1+	26+/34-	60+/0-	60+/0-	60+/0-	60+/0-
Lot 3	60-/0+	60-/0+	60-/0+	60-/1+	26+/34-	60+/0-	60+/0-	60+/0-	60+/0-

Norfentanyl

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
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Lot 1	60-/0+	60-/0+	60-/0+	59-/2+	33+/27-	60+/0-	60+/0-	60+/0-	60+/0-
Lot 2	60-/0+	60-/0+	60-/0+	60-/0+	34+/26-	60+/0-	60+/0-	60+/0-	60+/0-
Lot 3	60-/0+	60-/0+	60-/0+	60-/0+	34+/26-	60+/0-	60+/0-	60+/0-	60+/0-

2. Linearity:

Not applicable. These devices are intended for qualitative use only.

3. Analytical Specificity/Interference:

Potential interfering substances found in human urine of physiological or pathological conditions were added to drug-free urine and target drug fentanyl /norfentanyl 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	Ecgonine methyl ester	Oxolinic acid
Acetone (1000 mg/dL)	Ephedrine	Oxymetazoline
Acetophenetidin	Erythromycin	Papaverine
Acetylsalicylic acid	Estradiol	Penicillin G
Albumin (100 mg/dL)	Estrone	Perphenazine
Albuterol	Ethanol (1%)	Phencyclidine
7-Aminonitrazepam	Fenfluramine	Phenelzine
Amitriptyline	Fenofibrate	Phenobarbital
Amlodipine besylate	Fenopropfen	Phentermine
Amobarbital	Fluphenazine	Phenylethylamine
Amoxicillin	Fotemustine	Prednisone
Ampicillin	Furosemide	Promazine
Apomorphine	Galactose	Promethazine
Ascorbic acid	γ-Globulin (500 mg/dL)	Propoxyphene
Aspartame	Gemfibrozil	Propranolol
Aspirin	Gentisic acid	Pseudoephedrine
Atropine	Glucose (3000 mg/dL)	Pyridoxine
Baclofen	Guaiacolglyceryl ether	Pyrilamine
Benzilic acid	Hemoglobin	Pyrogallol
Benzocaine	Hexobarbital	Quinidine
Benzoic acid	Hydralazine	Quinine
Benzoyllecgonine	Hydrochlorothiazide	Quinolinic Acid
Benzylpiperiazine	Hydrocortisone	Ranitidine
Bilirubin	Hydroxybutyric Acid	Riboflavin
Boric Acid (1%)	Ibuprofen	Salicylic acid
Bromo-2,5-Dimethoxyphenethylamine	Imipramine	Secobarbital
Bupropion	Isoproterenol	Serotonin
Caffeine	Isoxsuprine (10 µg/mL)	Sodium Azide
Carbamazepine	Ketoprofen	Sulfamethazine
Carisoprodol	Labetalol	Sulindac

Cetirizine	Lamotrigine	Tetracycline
Chloral hydrate	Lidocaine	Tetrahydrocortisone3-(β-glucuronide)
Chloramphenicol	Lisinopril	Tetrahydrocortisone 3-acetate
Chlordiazepoxide	Loperamide	Tetrahydrozoline
Chlorothiazide	Loratidine	Thiamine
Chlorpheniramine	Maprotiline	Triamterene
Chlorpromazine	Meperidine	Trifluoperazine
Cholesterol	Meprobamate	Trifluoromethylphenyl-piperazine
Clofibrate	Methapyrilene	Trimethoprim
Clomipramine	Methaqualone	Tryptamine
Clonidine	Methoxyphenamine	Tyramine
Cortisone	Methylphenidate	Urea (2000 mg/dL)
Cotinine	Metoprolol	Uric acid
Creatine Hydrate	Metronidazole	Valproic acid (250 µg/mL)
Creatinine	N-Acetylprocainamide	Venlafaxine
Cyclobenzaprine	N-desmethyl Tapentadol	Verapamil
γ-Cyclodextrin	Nacl (4000 mg/dL)	Zolpidem
Cyproheptadine	Nalidixic acid	Zomepirac
Demoxepam	Naproxen	7-Aminoflunitrazepam
Deoxycorticosterone	Niacinamide	Metformin
Desipramine	Nicotine	Norpseudoephedrine
Diclofenac	Nicotinic Acid	Oxazepam Glucuronide
Diflunisal	Nifedipine	Lorazepam Glucuronide
Digoxin	Norethindrone	LSD
Dimethyl-aminoantipyrine	Norpropoxyphene	THC
Diphenhydramine	Nortriptyline	L-thyroxine
Diphenylhydantoin	Noscapine	Dextromethorphan
DL-Tryptophan	O-Hydroxyhippuric acid	Ketamine
DL-Tyrosine	Octopamine	Thioridazine
Dopamine (Hydroxytyramine)	Oxalic acid (100mg/dL)	Naloxone
Doxepin	Oxazepam	Naltrexone
Aminopyrine		

Specificity

To test specificity, drug metabolites and other components that are likely to interfere in urine samples were tested in analyte free urine samples using three batches of the device. The lowest concentration that caused a positive result for each compound are listed below. If no cross reactivity was observed the highest concentration tested is shown.

Fentanyl (Cutoff=1ng/mL)	Minimum concentration required to obtain a positive result (ng/mL)	% Cross- Reactivity

(±) β-hydroxythiofentanyl	2.8	35.7%
(±)-3-cis-methyl fentanyl	5	20%
4-Fluoro-isobutyrylfentanyl	3	33.3%
9-Hydroxy Risperidone	10000	0.01%
Acetyl fentanyl	1.2	83.3%
Acetyl norfentanyl	10000	0.01%
Acrylfentanyl	1.2	83.3%
Alfentanil	100000	0.001%
Butyryl fentanyl	1.6	62.5%
Carfentanil	500	0.20%
Despropionyl fentanyl (4-ANPP)	50000	0.002%
Fentanyl	1	100%
Furanyl fentanyl	1.75	57.1%
Isobutyryl fentanyl	1.5	66.7%
Labetalol Hydrochloride	100000	0.001%
MT-45	10000	0.01%
Norcarfentanil	10000	0.01%
Norfentanyl	5000	0.02%
Ocfentanil	1.5	66.7%
Para-fluoro fentanyl	3	33.3%
Para-fluorobutyryl fentanyl	3	33.3%
Remifentanil	10000	0.01%
Risperidone	1000	0.1%
Sufentanil	625	0.16%
Thienyl Fentanyl	1000	0.1%
Trans-d, I 3-Methylfentanyl	1000	0.1%
Trazodone	1000	0.1%
U-47700	100000	0.001%
Valeryl fentanyl	2.5	40 %
ω- 1-Hydroxyfentanyl	20000	0.005%

Norfentanyl (Cutoff=5ng/mL)	Minimum concentration required to obtain a positive result (ng/mL)	% Cross-Reactivity
(±) β-hydroxythiofentanyl	7	71.4%
(±)-3-cis-methyl fentanyl	10	50%
4-Fluoro-isobutyrylfentanyl	25	20%
9-Hydroxy Risperidone	10000	0.05%
Acetyl fentanyl	10	50%

Acetyl norfentanyl	200	2.5%
Acrylfentanyl	10	50%
Alfentanil	>100000/mL	<0.001%
Butyryl fentanyl	10	50%
Carfentanil	>100000/mL	<0.001%
Despropionyl fentanyl (4-ANPP)	>100000/mL	<0.001%
Fentanyl	15	33.3%
Furanyl fentanyl	9	55.6%
Isobutyryl fentanyl	8	62.5%
Labetalol Hydrochloride	20	25%
MT-45	100000	0.01%
Norcarfentanil	5000	0.1%
Norfentanyl	5	100%
Ocfentanil	15	33.3%
Para-fluoro fentanyl	5	100%
Para-fluorobutyryl fentanyl	40	12.5%
Remifentanil	>100000/mL	<0.001%
Risperidone	1000	0.5%
Sufentanil	>100000/mL	<0.001%
Thienyl Fentanyl	50	10%
Trans-d, 1 3-Methylfentanyl	50	10 %
Trazodone	>100000/mL	<0.001%
U-47700	100000	0.01%
Valeryl fentanyl	100	5%
ω- 1-Hydroxyfentanyl	500	1%

The following opioids compounds were tested at a concentration of 100ug/mL. Negative results were obtained for all these compounds. There is no cross-reactivity for these compounds using the ETERBIO Device.

6-Acetyl morphine	Naloxone
Amphetamine	Naltrexone
Buprenorphine	Norbuprenorphine
Buprenorphineglucuronide	Norcodeine
Codeine	Norketamine
Dextromethorphan	Normeperidine
Dihydrocodeine	Normorphine
EDDP	Noroxycodone
EMDP	Oxycodone
Fluoxetine	Oxymorphone
Heroin	Pentazocine (Talwin)
Hydrocodone	Pipamperone
Hydromorphone	Tapentadol
Ketamine	Thioridazine

Levorphanol	Tilidine
Meperidine	Tramadol
Methadone	Tramadol-O-Desmethyl
Morphine	Tramadol-N-Desmethyl
Morphine-3-glucuronide	

Effect of Urine Specific Gravity and Urine pH

To investigate the effect of urine specific gravity and urine pH, urine samples, with 1.000, 1.003, 1.008, 1.014, 1.018, 1.02, 1.022, 1.025, 1.028, 1.030, 1.032, and 1.035 specific gravity or urine samples with pH 4, 5, 6, 7, 8, and 9 were spiked with targets fentanyl and norfentanyl at 50% below and 50% above Cut-Off levels. These samples were tested using three lots of device. Results were all positive for samples at and above +50% Cut- Offs and all negative for samples at and below -50% Cut-Offs.

Read Time Study:

Fentanyl and Norfentanyl Standards with concentrations of -50% cutoff, +50% cutoff, and drug free urine were tested using three lots of the device and read at 10 time points (i.e. 3rd, 4th, 5th, 10th, 15th, 20th, 25th, 30th, 35th, 40th minutes) by three different operators according to procedures in the product insert. All the results were consistent with the required reading time at 5 minutes and not more than 10 minutes.

4. Assay Reportable Range:

Characterization of how the device performs analytically around the claimed cutoff concentration appears in the precision section VII.A.1 above.

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

All drug calibrators of the device are traceable to available commercial reference materials.

6. Detection Limit:

Characterization of how the device performs at low concentrations appears in the precision section, VII.A.1, above.

7. Assay Cut-Off:

Characterization of how the device performs analytically around the claimed cutoff concentration appears in the precision section, VII.A.1, above.

B Comparison Studies:

1. Method Comparison with Predicate Device:

Method comparison studies for the ETERBIO Fentanyl/Norfentanyl Urine Rapid Test Panel were performed by three different operators. Operators ran 80 (40 negative and 40 positive)

unaltered clinical samples. The samples were blind labeled and compared to LC/MS results. The results are presented in the tables below.

Fentanyl

		Negative	Low Negative by LC/MS (less than -50%)	Near Cutoff Negative by LC/MS (Between -50% and cutoff)	Near Cutoff Positive by LC/MS (Between the cutoff and +50%)	High Positive by LC/MS (greater than +50%)
Operator 1	Positive	0	0	2	19	20
	Negative	8	16	14	1	0
Operator 2	Positive	0	0	1	18	20
	Negative	8	16	15	2	0
Operator 3	Positive	0	0	2	20	20
	Negative	8	16	14	0	0

Discordant Results

Operator	Sample ID	LC/MS Result (ng/mL)	Rapid Test Result
Operator 1	MF046	0.986	+
Operator 1 & Operator 3	MF079	0.937	+
Operator 2	MF062	0.925	+
Operator 3	MF058	0.914	+
Operator 2	MF016	1.02	-
Operator 1	MF060	1.01	-
Operator 2	MF063	1.09	-

Norfentanyl

		Negative	Low Negative by LC/MS (less than -50%)	Near Cutoff Negative by LC/MS (Between -50% and cutoff)	Near Cutoff Positive by LC/MS (Between the cutoff and +50%)	High Positive by LC/MS (greater than +50%)
Operator 1	Positive	0	0	1	19	20
	Negative	8	17	14	1	0
Operator 2	Positive	0	0	1	19	20
	Negative	8	17	14	1	0
	Positive	0	0	1	20	20

Operator 3	Negative	8	17	14	0	0
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Discordant Results

Operator	Sample ID	LC/MS Result (ng/mL)	Rapid Test Result
Operator 1	MC083	5.2	-
Operator 2	MC019	5.25	-
Operator 1 & Operator 2	MC048	4.85	+
Operator 3	MC009	4.68	+

2. Matrix Comparison:

Not applicable. These devices are for use 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):

A lay user study was performed at three testing sites representative of intended use sites with 140 lay users. The lay users had diverse educational and professional backgrounds and ranged in age from 18 to >50 years. Three lots of the device were used in the study. Urine samples were prepared at the following concentrations: -100%, +/-75%, +/-50%, +/-25% of the cut-offs by spiking drug(s) into drug free-pooled urine specimens. The concentrations of the samples were confirmed by LC/MS. Each sample was aliquoted into individual containers, blind-labeled and randomized. Each participant was provided with the package insert, 1 blind labeled sample and a device. The results are summarized below:

% of Cutoff	Number of samples	Fentanyl Concentration by LC/MS (ng/mL)	Lay person results		The percentage of correct results (%)
			No. of Positive	No. of Negative	
-100% Cutoff	20	0	0	20	100.0%
-75% Cutoff	20	0.25	0	20	100.0%
-50% Cutoff	20	0.52	0	20	100.0%
-25% Cutoff	20	0.75	1	19	95.0%
+25% Cutoff	20	1.30	20	0	100.0%

+50% Cutoff	20	1.55	20	0	100.0%
+75% Cutoff	20	1.65	20	0	100.0%

% of Cutoff	Number of samples	Norfentanyl Concentration by LC/MS (ng/mL)	Lay person results		The percentage of correct results (%)
			No. of Positive	No. of Negative	
-100% Cutoff	20	0	0	20	100.0%
-75% Cutoff	20	1.27	0	20	100.0%
-50% Cutoff	20	2.54	0	20	100.0%
-25% Cutoff	20	3.78	0	20	100.0%
+25% Cutoff	20	6.55	20	0	100.0%
+50% Cutoff	20	7.85	20	0	100.0%
+75% Cutoff	20	8.95	20	0	100.0%

Lay-users were also given surveys on the ease of understanding the package insert instructions. All lay users indicated that the device instructions can be easily followed. A Flesch-Kincaid reading analysis was performed on the package insert and the score revealed a reading grade level of less than 7.

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.