510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

ASSAY ONLY

I Background Information:

A 510(k) Number

K252684

B Applicant

MEDTOX Diagnostics, Inc.

C Proprietary and Established Names

Labcorp Fentanyl Urine Visual Test

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:
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 Labcorp Fentanyl Urine Visual Test is a lateral flow competitive immunoassay for the rapid qualitative detection of norfentanyl (fentanyl metabolite) in human urine at a cutoff of 5 ng/mL. It is intended for prescription use. For in vitro diagnostic use only.

This test provides only a preliminary result. Clinical consideration and professional judgment must be applied to any drug test result, particularly in evaluating a preliminary positive result. To confirm preliminary positive results, a more specific analytical method must be used. Gas Chromatography-Mass Spectrometry (GC-MS), Liquid Chromatography Tandem Mass Spectrometry (LC-MS/MS), and High Performance Liquid Chromatography (HPLC) are the preferred confirmatory methods.

C Special Conditions for Use Statement(s):
Rx - For Prescription Use Only

D Special Instrument Requirements:
This 510(k) premarket submission for the Labcorp Fentanyl Urine Visual Test assay only.

IV Device/System Characteristics:

A Device Description:

The Labcorp Fentanyl Urine Visual Test is a lateral flow competitive immunoassay for the rapid qualitative detection of Norfentanyl (nFEN), the primary urinary metabolite of Fentanyl, in human urine at concentrations above 5 ng/mL. It is intended for prescription use.

The single-use, in vitro diagnostic device is available in a cassette format with a disposable dropper provided for sample transfer.

The Labcorp Fentanyl Urine Visual Test contains a test strip that gives a qualitative result for presence of Norfentanyl in human urine. The test is read visually and has labeling with instructions for interpreting test results.

B Principle of Operation:

The Labcorp Fentanyl Urine Visual Test uses lateral flow immunoassay technology in which a modified drug (drug-protein conjugate) completes with drug that may be present in the urine. The colorless drug-protein conjugate is applied to the membrane of the test strip at the test line position. The colored drug-specific antibody-colloidal gold is applied to the sample pad of the test strip. When urine is transferred onto the sample pad it dissolves and migrates the colored antibody-colloidal gold across the strip membrane. If drug is not present or is below the cutoff, the drug-specific antibodies will bind to the conjugate line on the membrane and the colloidal gold will form a visible line, which indicates a negative result. If drug is present in the urine, the drug-specific antibodies will bind to the drug in solution and bypass the conjugate on the membrane and no line will form, which indicates a preliminary positive result.

A visible control line should form in the control line position regardless of whether drug is present to indicate that the test has been performed properly.

V Substantial Equivalence Information:

A Predicate Device Name(s):

Chemtrue® Drug Screen Fentanyl/Tramadol Cup Test, Chemtrue® Drug Screen Fentanyl/Tramadol Dip Card Test, Chemtrue® Multi-Panel Drug Screen Cup Test, Chemtrue® Multi-Panel Drug Screen Dip Card Test

B Predicate 510(k) Number(s):

K232736

C Comparison with Predicate(s):

Device & Predicate Device(s):	K252684	K232736
Device Trade Name	Labcorp Fentanyl Urine Visual Test	Chemtrue® Drug Screen Fentanyl Cup/Dip Card Tests
General Device Characteristic Similarities		
Indications For Use	Qualitative detection of norfentanyl in human urine at a cut-off of 5 ng/mL	Same
General Device Characteristic Differences		
Test Device Format	Cassette	Cup/Dip Card

VI Standards/Guidance Documents Referenced:

CLSI EP07 3rd Edition - Interference Testing in Clinical Chemistry

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:
   These studies were carried out using urine samples containing norfentanyl (nFEN) spiked into a drug-free urine pool with LC-MS/MS confirmed concentrations of 0%, 25%, 50%, 75%, 100%, 125%, 150%, and 200% of the test cutoff. These samples were prepared in a blind randomized panel in triplicate and evaluated by 3 in-house operators over 5 days using 3 different lots. Each result was visually interpreted at 10 minutes. Results are summarized below:

Test	Concentration Tested	Lot 1 Neg/Pos	Lot 2 Neg/Pos	Lot 3 Neg/Pos	Total Neg/Pos
nFEN	Negative	45/0	45/0	45/0	135/0

Test	Concentration Tested	Lot 1 Neg/Pos	Lot 2 Neg/Pos	Lot 3 Neg/Pos	Total Neg/Pos
	25% of Cutoff	45/0	45/0	45/0	135/0
	50% of Cutoff	45/0	45/0	45/0	135/0
	75% of Cutoff	40/5	35/10	31/14	106/29
	Cutoff	20/25	22/23	18/27	60/75
	125% of Cutoff	3/24	8/37	3/42	14/121
	150% of Cutoff	0/45	0/45	0/45	0/135
	200% of Cutoff	0/45	0/45	0/45	0/135

2. Linearity:
   Not applicable because this device is intended for qualitative use only for detection of norfentanyl in human urine at concentrations above 5 ng/mL.

3. Analytical Specificity/Interference:

   Interference and cross-reactivity studies were conducted based upon recommendations in the Clinical and Laboratory Standards Institute (CLSI) Guideline EP05-A3: Evaluation of Precision of Quantitative Measurement Methods. Test concentrations were determined using medically relevant calculations based on maximum daily doses, urinary excretion percentages, and minimum urine volumes. At least 9 professional laboratory operators performed visual readings.

   For each drug and cutoff, specificity was evaluated by spiking various concentrations of similarly structured drug compounds into drug-free urine. Results are expressed as a minimum concentration of metabolite or compound required to produce a response approximately equivalent to the cutoff concentration of the assay. The percent cross reactivity of those compounds is listed below (if no cross reactivity was observed, the highest concentration tested is shown as <1%):

Compound	Concentration	% Cross-Reactivity
Norfentanyl (nFEN) ***(Norfentanyl, 5 ng/mL)***		
Parent drug: Fentanyl	7.5 ng/mL	67%
Fentanyl/Norfentanyl analog cross-reactants		
3-Methylfentanyl	150 ng/mL	3%
4-Fluoro-Isobutyryl Fentanyl	15 ng/mL	33%
4'-Methylacetyl Fentanyl (para-Methacetyl Fentanyl)	750 ng/mL	1%
Acetyl Fentanyl	5 ng/mL	100%
Acetyl Norfentanyl	50 ng/mL	10%
Acryl Fentanyl	10 ng/mL	50%
Alfentanil	2,500 ng/mL	< 1%
Butyryl Fentanyl	10 ng/mL	50%
Cis-DL-3-Methylfentanyl	100 ng/mL	5%
Cyclopropyl Fentanyl	10 ng/mL	50%

Cyclopropyl Norfentanyl	7.5 ng/mL	67%
Fluorocyclopropyl Fentanyl (para-Fluorocyclopropyl Fentanyl)	15 ng/mL	33%
Furanyl Fentanyl	25 ng/mL	20%
Furanyl Norfentanyl	7.5 ng/mL	67%
(±) β-Hydroxythiofentanyl	10 ng/mL	50%
Isobutyryl Fentanyl	7.5 ng/mL	67%
Isobutyryl Norfentanyl	5 ng/mL	100%
Methoxyacetylfentanyl (MAF)	15 ng/mL	33%
N-Benzylfuranyl Norfentanyl	50 ng/mL	10%
N-Benzyl-Para-Fluoro Norfentanyl	25 ng/mL	20%
Octfentanil	500 ng/mL	1%
Para-Fluoro-Butyryl Fentanyl (p-FBF)	75 ng/mL	7%
Para-Fluorofentanyl	10 ng/mL	50%
Phenylacetyl Fentanyl	7.5 ng/mL	67%
Remifentanil	100 ng/mL	5%
THF Fentanyl (THFF)	35 ng/mL	14%
Thienyl Fentanyl	15 ng/mL	33%
Trans-DL-3-Methylfentanyl	10 ng/mL	50%
Valeryl Fentanyl	50 ng/mL	10%

Interference from endogenous compounds and non-structurally related exogenous compounds using samples containing drugs at 50% of cutoff and 150% of cutoff urine samples. Each compound and urine sample were tested by running at least 5 replicates and 3 lots. The following endogenous compounds showed no interference at the concentrations listed:

Endogenous Compound	**Concentration (ng/mL)**	**Endogenous Compound**	**Concentration (ng/mL)**
Acetone	10,000,000	Glucose	30,000,000
Albumin, Human	5,000,000	Hemoglobin, Human	3,000,000
Ascorbic Acid	5,000,000	Niacinamide	100,000
Atropine	100,000	Nicotinic Acid	100,000
Beta-Hydroxybutyric Acid	100,000	Octopamine	150,000
Bilirubin	20,000	Oxalic Acid	100,000
Biotin	100,000	Potassium Chloride	10,000,000
Calcium Chloride	3,000,000	Pyridoxine	90,000
Cholesterol	100,000	Quinolinic Acid	100,000
Creatine Hydrate	100,000	Riboflavin	75,000
Creatinine	5,000,000	Sodium Chloride	10,000,000
Deoxycorticosterone	100,000	Thiamine	100,000
Dopamine (3-Hydroxytyramine)	100,000	Tryptamine	100,000
Ethanol	10,000,000	Tyramine	100,000
Galactose	100,000	Urea	60,000,000
Gamma Globulin	5,000,000	Uric Acid	100,000

The following non-structurally related compounds showed no interference at the concentrations listed:

Common Drug	Concentration (ng/mL)	Common Drug	Concentration (ng/mL)
1-(3-Trifluoromethylphenyl)-piperazine	100,000	Isotonitazene	10,000
11-Hydroxy- 9-THC	10,000	Ketamine	100,000
11-Nor-9-carboxy- 9-THC	10,000	Labetalol	1,800,000
4-Bromo-2,5, Dimethoxyphenethylamine	100,000	Lamotrigine	100,000
6-Acetylmorphine (6-MAM)	100,000	Lansoprazole	100,000
7-Aminoclonazepam	100,000	L-Cotinine	100,000
7-Aminoflunitrazepam	100,000	L-Erythromycin	100,000
7-Aminonitrazepam	10,000	Levonorgestrel	100,000
Acetaminophen	2,900,000	Levorphanol	100,000
Acetylsalicylic Acid	100,000	Levothyroxine (L-Thyroxine)	100,000
AH-7921 (Doxylam)	10,000	Lisinopril	100,000
AH-8529	100,000	L-Methamphetamine	100,000
AH-8533	100,000	Loperamide	100,000
Albuterol	100,000	Loratadine	100,000
Allopurinol	100,000	Lorazepam	100,000
Alprazolam	100,000	Losartan	100,000
Aminopyrine (4-Dimethylaminoantipyrine)	100,000	Lurasidone	10,000
Amlodipine Besylate	100,000	Lysergic Acid Diethylamide (LSD)	10,000
Amoxicillin	2,600,000	Maprotiline	100,000
Ampicillin	100,000	Meperidine	100,000
Apixaban	100,000	Meprobamate	100,000
Apomorphine	100,000	Metformin	2,900,000
Aspartame	100,000	Methadone	100,000
Atenolol	200,000	Methapyrilene	100,000
Atorvastatin	100,000	Methylphenidate	100,000
Baclofen	100,000	Metonitazene	10,000
Benzocaine	100,000	Metoprolol	550,000
Benzoic Acid	100,000	Mitragynine	100,000
Benzoylecgonine	100,000	Morphine	300,000
Benzylpiperiazine	10,000	Morphine-3-glucuronide	10,000
Brompheniramine	100,000	Nalidixic Acid	100,000
Buprenorphine	100,000	Naloxegol	100,000

Common Drug	Concentration (ng/mL)	Common Drug	Concentration (ng/mL)
Bupropion	100,000	Naloxone	100,000
Caffeine	1,200,000	Naltrexone	100,000
Cannabidiol	100,000	Naproxen	1,800,000
Carbamazepine	100,000	N-Desmethyltapentadol	10,000
Carisoprodol	100,000	Nifedipine	100,000
Carvedilol	100,000	Norbuprenorphine	100,000
Cetirizine	100,000	Norcodeine	100,000
Chloramphenicol	100,000	Nordiazepam	100,000
Chlorcyclizine	100,000	Norethindrone	100,000
Chlordiazepoxide	100,000	Norketamine	100,000
Chlorpheniramine	100,000	Normeperidine	100,000
Chlorpromazine	15,000	Normorphine	10,000
Cimetidine	1,800,000	Noroxycodone	100,000
Citalopram	100,000	Norpropoxyphene	100,000
Clofibrate	100,000	Norpseudoephedrine (Cathine)	100,000
Clomipramine	100,000	Noscapine	100,000
Clonazepam	100,000	Omeprazole	100,000
Clonidine	100,000	Oxazepam	100,000
Clopidogrel	200,000	Oxazepam Glucuronide	1,000
Codeine	120,000	Oxycodone	100,000
Cortisone	100,000	Oxymetazoline	100,000
Cyclobenzaprine	100,000	Oxymorphone	100,000
Cyclodextrin-r	100,000	Pantoprazole	100,000
Cyproheptadine	100,000	Papaverine	100,000
DL-Isoproterenol	100,000	Penicillin-G (Benzylpenicillin)	100,000
D-Amphetamine	350,000	Pentazocine	35,000
Demoxepam	100,000	Perospirone	10,000
Dextromethorphan	100,000	Phenelzine	100,000
Diclofenac	200,000	Pheniramine	100,000
Difunisal	100,000	Phentermine	100,000
Dihydrocodeine	100,000	Phenylephrine	100,000
Diphenhydramine	100,000	Phenylethylamine	100,000
Diphenylhydantoin (Phenytoin)	100,000	Pravastatin	100,000
D-Methamphetamine	100,000	Prednisone	100,000
Doxylamine	100,000	Promazine	100,000
D-Pseudoephedrine	250,000	Promethazine	100,000
Duloxetine	150,000	Propoxyphene	10,000

Common Drug	Concentration (ng/mL)	Common Drug	Concentration (ng/mL)
EDDP (Methadone metabolite)	100,000	Propranolol	700,000
Ephedrine	100,000	Propylhexedrine	50,000
Ergocalciferol	100,000	Pyrilamine	150,000
Escitalopram	100,000	Pyrogallol	100,000
Esomeprazole Mg hydrate	250,000	Ranitidine	150,000
Estrone	100,000	Rosuvastatin	100,000
Ethinyl Estradiol	100,000	Salicylic Acid	1,000,000
Famotidine	1,000,000	Sertindole	10,000
Fenfluramine	100,000	Sertraline	30,000
Fenofibrate	100,000	Simvastatin	100,000
Fexofenadine	75,000	Sodium Azide	100,000
Fluoxetine	100,000	Sulfamethazine	100,000
Fluticasone	100,000	Sulindac	100,000
Furosemide	500,000	Tamsulosin	100,000
Gabapentin	4,500,000	Temazepam	100,000
Gemfibrozil	100,000	Tetracycline	100,000
Gentisic Acid	100,000	Tetrahydrozoline	100,000
Glipizide	100,000	Thioridazine	100,000
Guaifenesin	100,000	Tianeptine	100,000
Heroin (Diacetylmorphine)	100,000	Tramadol	450,000
Hexobarbital	10,000	Trazodone	10,000
Hydralazine	100,000	Trifluoperazine	100,000
Hydrochlorothiazide	150,000	Venlafaxine	100,000
Hydrocodone	100,000	Xylazine	100,000
Hydrocortisone	100,000	Ziprasidone	100,000
Hydromorphone	100,000	Zolpidem	100,000
Ibuprofen	2,700,000	Zolpidem Tartrate	100,000
Insulin	100,000		

Positive interference was observed for the following compounds when tested at concentrations above those listed in the table above: Pentazocine and Fexofenadine.

Negative interference was observed for the following compounds when tested at concentrations above those listed in the table above: Baclofen, Chlorpromazine, Fexofenadine Propranolol, Sertraline, Potassium Chloride, Pyridoxine. The following Norfentanyl analogs were also observed to cause negative interference above those listed in the table below: Carfentanil, MT-45, 4-Methoxybutyryl Fentanyl, and U-4770.

The following non-structurally related compounds showed interference and/or cross reactivity at the concentrations listed:

Non-Fentanyl Cross Reactive Compounds		
Compound	**Concentration**	**% Cross Reactivity**
Fluphenazine	Positive at 50,000 ng/mL	< 1%
Perphenazine	Positive at 75,000 ng/mL	< 1%
Quinidine	Positive at 25,000 ng/mL	< 1%
Quinine	Positive at 50,000 ng/mL	< 1%
Risperidone	Positive at 2,500 ng/mL	< 1%
Risperidone Metabolite: 9-Hydroxyrisperidone	Positive at 2,500 ng/mL	< 1%

Non-reactive Fentanyl/Norfentanyl analogs		
Compound	**Concentration**	**% Cross Reactivity**
Carfentanil	Negative at 500 ng/mL	N/A
Despropionylfentanyl (4-ANPP)	Negative at 1,000 ng/mL	N/A
MT-45	Negative at 3,500 ng/mL	N/A
4-Methoxybutyryl Fentanyl	Negative at 5,000 ng/mL	N/A
Norcarfentanil	Negative at 1,000 ng/mL	N/A
Sufentanil	Negative at 1,000 ng/mL	N/A
U-47700	Negative at 5,000 ng/mL	N/A

pH study: To evaluate the effect of pH value on the test results, urine controls at 50% and 150% of the cutoff value was used. Each control level was adjusted by either 6N NaOH solution or 6N HCl to pH levels of 4.0, 4.5, 5.0, 5.5, 6.0, 6.5, 7.0, 7.5, 8.0 and 9.0. A total of 5 replicates per sample were tested.

Specific gravity study: To evaluate the effect of specific gravity, urine controls at 50% and 150% of the cutoff values were mixed and pooled as needed to obtain specific gravities of 1.001, 1.004, 1.010, 1.014, 1.020, 1.025, and 1.030. A total of 5 replicates per sample were tested.

The results demonstrated that pH and specific gravity do not affect the results from the device at the conditions tested.

4. Assay Reportable Range:
   Not applicable because this device is intended for qualitative use only for detection of norfentanyl in human urine at concentrations above 5 ng/mL.

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:

The sponsor performed a method comparison study comparing the performance of the test strips to the LC/MS reference method. A total of 40 samples that did not contain norfentanyl (or fentanyl) and 47 samples containing varying concentrations of norfentanyl (and fentanyl), including 7 below the test cutoff, were assayed on 3 lots using a different operator for each lot and run in a random order over 3 days. The results are summarized below:

Fentanyl Test (nFEN) (5 ng/mL Cutoff)		Concentration by LC-MS/MS (ng/mL)				
		No Drug Present	Low Negative (<50% of cutoff)	Near Cutoff Negative (50% - 100% of cutoff)	Near Cutoff Positive (100% - 150% of cutoff)	True Positive (>150% of cutoff)
Lot 1	Positive	0	0	3	4	36
	Negative	40	3	1	0	0
Lot 2	Positive	0	0	3	4	36
	Negative	40	3	1	0	0
Lot 3	Positive	0	0	3	4	36
	Negative	40	3	1	0	0

Three near cutoff negative clinical samples produced positive discordant results with all three strip lots. Discordant results are summarized below:

Fentanyl Test (nFEN) Result	LC-MS/MS Norfentanyl (ng/mL)
Positive (+)	4.76
Positive (+)	3.86
Positive (+)	3.34

2. Matrix Comparison:
Not applicable. This device is 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):
   Not applicable.

D Clinical Cut-Off:
Not applicable.

E Expected Values/Reference Range:
Not applicable.

VIII Proposed Labeling:

The labeling does support the finding of substantial equivalence for this device.

IX Conclusion:

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