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

A. 510(k) Number:

k182103

B. Purpose for Submission:

New device

C. Measurand:

Fentanyl

D. Type of Test:

Qualitative screening test: enzyme immunoassay (EIA)
Quantitative confirmatory test: LC/MS/MS

E. Applicant:

Psychemedics Corporation

F. Proprietary and Established Names:

Psychemedics Microplate EIA for Fentanyl in Hair

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
DJG	Class II	21 CFR 862.3650	Toxicology (91)

H. Intended Use:

1. Intended use(s):

   Refer to Indications for Use below.

2. Indication(s) for use:

   The Psychemedics Microplate EIA For Fentanyl in Hair is an in vitro diagnostic device for the qualitative detection of fentanyl in hair. The assay is intended for use in workplace settings for the qualitative analysis of human head and body hair. The assay uses a cutoff

calibrator of 0.2 ng fentanyl/10 mg hair.

Psychemedics plans to perform this test at one site. Psychemedics has not performed an evaluation of reproducibility at different laboratories.

The Psychemedics Microplate EIA For Fentanyl in Hair provides only a preliminary analytical test result. A more specific alternate chemical method must be used to obtain a confirmed analytical result. Liquid Chromatography/Mass spectrometry/Mass spectrometry (LC/MS/MS) using deuterated internal standards in multiple reaction monitoring (MRM) mode is the confirmatory method used by Psychemedics Corporation. This confirmatory method uses a cutoff of 0.2 ng of fentanyl/10 mg hair.

3. Special conditions for use statement(s):

This assay is for over the counter use.

The Psychemedics Microplate EIA for Fentanyl in Hair combines a screening method (immunoassay) with a confirmation method (LC/MS/MS) in one test system.

The assay is to be performed only at Psychemedics Corporation.

4. Special instrument requirements:

The assay is designed only for human body and head hair.

The confirmation assay consists of an AB Sciex 6500+MSMS (SN CG21891608) with Binary Shimadzu LC-30AD Pump (SNs L20555452360, L20555452361), Shimadzu Communications Bus Module Controller (SN L20235356454) and PAL HTC-xt Autosampler (SN381406).

I. Device Description:

The screening assay consists of:

- BSA-fentanyl coated Microplate
- Cutoff calibrator and the controls around the cutoff, 8 mg of hair is spiked with fentanyl at 0.2 ng (cutoff), 0.1 ng (-50% control), or 0.4 ng/10 mg hair (+100% control)
- Controls (minus 50% of cutoff, and plus 100% of cutoff)
- Primary antibody against fentanyl
- HRP-labeled secondary antibody directed against the primary antibody species
- Substrate TMB (tetramethylbenzidine)
- Acidic stop solution (2 N HCl)
- Hair sample collection kit

The confirmation assay consists of an AB Sciex 6500+MSMS (SN CG21891608) with

Binary Shimadzu LC-30AD Pump (SNs L20555452360, L20555452361), Shimadzu Communications Bus Module Controller (SN L20235356454) and PAL HTC-xt Autosampler (SN381406).

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Psychemedics Opiates EIA

2. Predicate 510(k) number(s):

   k111926

3. Comparison with predicate:

Similarities and differences		
Item	Candidate Device:	Predicate (k111926):
Intended Use	Same	The Psychemedics Microplate EIA for Opiates in Hair is a qualitative kit for detection of opioids in hair. This assay provides only a preliminary analytical test result. A more specific alternative chemical method must be used in order to obtain a confirmed analytical result. Liquid Chromatography with MS/MS is the preferred confirmatory method.
Measurand	Fentanyl (an opioid)	Opioids
Test System	Psychemedics Microplate EIA for Fentanyl in Head and Body Hair	Psychemedics EIA for opiates in Hair
Sample Matrix	Same	Human hair
Method of Measurement	Same	Microplate reader, read at 450 nm
Cutoff	0.2 ng fentanyl/10 mg hair	2 ng morphine/10 mg hair
Type of Test	Enzyme Immunoassay and confirmatory LC-MS/MS system	Enzyme Immunoassay

Similarities and differences		
Item	Candidate Device:	Predicate (k111926):
Extraction Method	Same	Patented Digestion method
Screening Assay	Same	Enzyme Immunoassay
Confirmation Method	Same	LC/MS/MS

K. Standard/Guidance Document Referenced (if applicable):

None referenced

L. Test Principle:

The Psychemedics Microplate EIA For Fentanyl in Hair consists of (1) a screening immunoassay and (2) a confirmation test by LC-MS/MS.

The screening immunoassay consists of two parts; a pre-analytical hair treatment procedure (to remove fentanyl from solid hair matrix to a measurable liquid matrix), and the qualitative assay. The qualitative assay is an Enzyme-Linked ImmunoSorbent Assay (ELISA) based upon the competitive binding of fentanyl in the sample and solid-phase fentanyl in the microplate wells to the assay detection antibody. Sample is added to the microplate well, followed by primary antibody (monoclonal mouse anti-fentanyl), and then (after washing the plate) goat anti-mouse-horseradish peroxidase conjugate is added. Enzyme substrate is then added and the plate is read on a microplate reader at 450 nm.

Confirmatory testing:

Confirmation testing for fentanyl and norfentanyl in samples is performed on a 6-12 mg aliquot of the original hair specimen. The hair is washed with isopropanol, followed by phosphate buffer. After washing, samples are then spiked with deuterated fentanyl to a concentration of 1.0 ng/10 mg hair, processed by solid phase extraction and analyzed using the AB Sciex 6500+MSMS (SN CG21891608) operating in the Positive Multiple Reaction Mode. To account for variability in drug recovery during solid phase extraction the recovered concentration of the deuterated internal standards in each sample is used to normalize the data for that sample.

M. Performance Characteristics:

1. Analytical performance:

a. Precision/Reproducibility:

Precision of the immunoassay screening method

Hair samples previously tested and shown to be negative for fentanyl were

spiked with fentanyl at the following concentrations: 0, 0.25, 0.5, 0.75, 1.0, 1.25, 1.5, 1.75, and 2 ng/10 mg hair (negative, ±75%, ±50%, ±25%, cutoff, and +100% of the cutoff). Intra-Assay Precision was demonstrated by measuring these nine concentrations of fentanyl in hair samples in replicates of 10 within a single run. Results are summarized below.

Summary -Intra-Assay		
LEVEL	NEG	POS
Negative	10	0
-75%	10	0
-50%	10	0
-25%	10	0
Cutoff	5	5
+ 25%	0	10
+ 50%	0	10
+ 75%	0	10
+ 100%	0	10

Hair samples previously tested and shown to be negative for fentanyl were spiked at the following concentrations: 0, 0.25, 0.5, 0.75, 1.0, 1.25, 1.5, 1.75, and 2 ng/10 mg hair (negative, ±75%, ±50%, ±25%, cutoff, and +100% of the cutoff). Inter-Assay Precision of the assay was evaluated by measuring these nine concentrations of fentanyl in hair samples over the course of five days, in replicates of 10 per day. Results are summarized below.

Summary-Inter-Assay		
LEVEL	NEG	POS
Negative	50	0
-75%	50	0
-50%	50	0
-25%	50	0
Cutoff	25	25
+ 25%	0	50
+ 50%	0	50
+ 75%	0	50
+ 100%	0	50

Precision of the LC-MS/MS method

Within-run precision around the LC/MS/MS cutoff was conducted using drug

negative hair samples spiked with 0, 0.1, 0.15, 0.2, 0.25, 0.3 ng/10 mg hair of fentanyl or norfentanyl. Samples were prepared in replicates of 5, per each concentration for fentanyl and norfentanyl, and run over 5 days . Results for the fentanyl and norfentanyl, measured by the LC-MS/MS assay, are summarized below.

Fentanyl	**0**	**0.100**	**0.15**	**0.200**	**0.250**	**0.300**
	0.00	0.098	0.158	0.203	0.257	0.300
	0.00	0.105	0.158	0.204	0.264	0.308
	0.00	0.102	0.144	0.210	0.261	0.310
	0.00	0.101	0.146	0.207	0.258	0.315
	0.00	0.097	0.152	0.210	0.247	0.310
Average	0	0.10056	0.1516	0.2068	0.2574	0.3086
S.D.	0.000	0.0033	0.0065	0.0033	0.0064	0.0055
% CV	NA	3.24	4.32	1.58	2.50	1.77
95% CI	NA	0.101 - 0.109	0.138 - 0.154	0.193 - 0.201	0.243 - 0.2592	0.302 - 0.315
% of Target	NA	100.6	101.1	103.4	103.0	102.9
Norfentanyl	0.00	0.107	0.150	0.203	0.240	0.304
	0.00	0.111	0.140	0.194	0.258	0.322
	0.00	0.095	0.141	0.196	0.249	0.285
	0.00	0.106	0.150	0.199	0.251	0.302
	0.00	0.108	0.148	0.194	0.258	0.330
Average	0	0.10544	0.1458	0.1972	0.2512	0.3086
S.D.	0.0000	0.0060	0.0049	0.0038	0.0075	0.0177
% CV	NA	5.71	3.37	1.94	2.97	5.75
95% CI	NA	0.098 - 0.113	0.140 - 0.152	0.192 - 0.202	0.242 - 0.2605	0.287 - 0.331
% of Target	NA	105.4	97.2	98.6	100.5	102.9

Intermediate precision around the LC/MS/MS cutoff was conducted using drug negative hair samples spiked with 0.1, 0.2, and 0.3 ng/10 mg hair of fentanyl and norfentanyl. Samples were prepared in replicates of 5 per each concentration for fentanyl and norfentanyl, and run over 5 days. Results for fentanyl measured by the LC-MS/MS assay are summarized below.

	Fentanyl (ng/10 mg hair)		
Concentration	**0.10**	**0.20**	**0.30**
Average	0.0981	0.2011	0.3040
S.D.	0.0041	0.0068	0.0111
% CV	4.1710	3.3574	3.6668
95% CI	0.096 - 0.100	0.198 - 0.204	0.299 - 0.309
Percent of Target	98.1	100.5	101.3

	Norfentanyl (ng/10 mg hair)		
Concentratio	**0.10**	**0.20**	**0.30**
Average	0.0996	0.1948	0.2846
S.D.	0.0061	0.0071	0.0163
% CV	6.0982	3.6540	5.7325
95% CI	0.097 - 0.102	0.163 - 0.227	0.278 - 0.291
Percent of Target	99.6	97.4	94.9

b. Linearity/assay reportable range:

The screening immunoassay is a qualitative test only; therefore, a linearity evaluation is not applicable.

Linearity of the LC-MS/MS confirmation method

The linearity of the confirmation method was evaluated by spiking fentanyl and norfentanyl into negative hair over the range of 0.01 to 7.5 ng/10 mg hair. Thirteen concentrations within this range were evaluated (0.01, 0.02, 0.04, 0.06, 0.08, 0.1, 0.15, 0.2, 0.25, 1.5, 4.5, 6.0, 7.5 ng/10mg). All levels for fentanyl and norfentanyl demonstrated percent recoveries within +/- 15% of the expected value.

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

Controls and calibrators are prepared as a methanolic solution containing fentanyl / norfentanyl and are traceable to a commercial fentanyl / norfentanyl source.

Shipping stability: Five hair samples containing fentanyl and norfentanyl were shipped overnight to another location and returned to the original location by overnight shipping. Samples were tested by the routine LC-MS/MS procedure both before being shipped and after returning to Psychemedics. Both analytes were evaluated. Recovery of both was acceptable after shipping.

Sample storage stability: Five hair samples were stored in the same collection foil and card-envelope provided with the hair collection kit, following the instructions provided in the package insert. Samples were tested by LC-MS/MS on day 0 and 28 days later following storage conditions at 68 – 75 °F (20 – 24 °C). Both fentanyl and norfentanyl were evaluated and recoveries after storage were found to be acceptable.

d. Detection limit:

The screening immunoassay is a qualitative test only; therefore, a detection limit evaluation is not applicable. See section M.1.a. above for sensitivity around the immunoassay device

cutoff.

Detection Limit of the LC-MS/MS method

The sponsor performed a study to determine the Lower limit of Quantitation (LLOQ) of the LC-MS/MS assay for fentanyl and norfentanyl.

The LLOQ is the lowest concentration that meets chromatographic and retention time criteria, and that can be quantitated within 20% of the expected value. The method LLOQ is 0.01 ng/10 mg for fentanyl. The LLOQ is 0.01 ng/10 mg for norfentanyl.

e. Analytical specificity:

Specificity of the immunoassay screening method

Immunoassay: cross-reactivity with structurally related compounds
The cross-reactivity characteristics of the screening immunoassay was evaluated by spiking various concentrations of fentanyl into drug-free hair samples and comparing the result to the cutoff calibrator. The table below lists the percent cross-reactivity and the approximate concentration of each compound required to produce a response approximately equivalent to the cutoff concentration of the assay.

Compound	Percent Cross- reactivity	Concentration Equivalent to 0.2 ng Fentanyl/10 mg hair
Fentanyl	100	0.20
Butyryl fentanyl	200	0.10
Valeryl fentanyl	100	0.20
Furanyl fentanyl	100	0.20
Acetyl fentanyl	125	0.16
o-Fluorofentanyl	100	0.20
Acryl Fentanyl	100	0.20
Cyclopropyl fentanyl	100	0.20
Isobutyryl fentanyl	100	0.20
Ocfentanil	100	0.20
4-Fluoro-isobutyryl fentanyl	100	0.20
Acetyl fentanyl	125	0.16
(+/-)-cis-3-methylfentanyl	9.1	2.2
Methyl fentanyl	2	10.0
Despropionyl fentanyl	0.7	29.0

Sufentanil citrate	< 0.2	>100
Remifentanil	< 0.2	>100
Alfentanil	< 0.2	>100
Norfentanil	< 0.2	>100
Benzylfentanil	< 0.2	>100
Acetylnorfentanil oxalate	< 0.2	>100
Carfentanil Oxalate	< 0.2	>100

Immunoassay: Interference from structurally unrelated compounds

The following potentially interfering compounds were tested using the screening immunoassay on samples spiked with fentanyl at the cutoff and at ± 50% of the cutoff to assess possible positive or negative interference. All potential interferents listed below were tested at a concentration of 100 ng/10 mg hair. No positive or negative interference was observed in this study.

10,11-Dihydrocarbamazepine	Ecgonine	Nordoxepin
11-nor-9-Carboxy-delta-9-THC Delta8TH	Erythromycin	Normetanephrine
1S, 2R Ephedrine	Ethosuximide	Nortriptyline
4-Methylprimidone	Ethotoin	O-Desmethylvenlafaxine
5,5-Diphenylhydantoin	Ethylmorphine	Oxycodone
5-Hydroxyindole-3-acetic acid	Glutethimide	Oxymorphone
8(-)-11-nor-9-Carboxy-delta-9-THC	Haloperidol	PEMA
Acetaminophen	Homovanillic acid	Penicillin G
a-methyl-a-propylsuccimide	Hydrocodone	Pentazocine
Amitriptyline	Hydromorphone	Phendimetrazine
Amoxicillin	Imipramine	Phenmetrazine
Anhydroecgonine methyl ester	Lidocaine	Phenobarbital
Atropine	LSD	phensuximide
Barbital	Meperidine	Phenylephrine
Benzocaine	Mephenytoin	Primidone
Buprenorphine	Mephobarbital	Procaine
Buprofen	Mepivacaine	Promethazine
Bupropion	Meprobamate	Propanolol
C Streptomycin solution	Metanephrine	Propoxyphene
Caffeine	Methadone	R,R Pseudoephedrine
Cannabinol	Methamphetamine	Spice AM2201
Carbamazepine	Methaqualone	Spice C8 homologue
Chlorpheniramine maleate	metharbital	Spice CP 47

Chlorpromazine	Methocarbamol	Spice CP 497
Cis-Tramadol	methsuximide	Spice HU-211
Cocaethylene	Methyl PEMA	Spice JWH-019
Cocaine	Methyl phenidate	Spice JWH-081
Codeine	Methyprylon	Spice JWH-122
Cotinine	Morphine	Spice JWH-200
Desipramine	Nalorphine	Spice JWH-250
Despropionyl	Naloxone	Theophylline
Dextromethorphan	Naltrexone	Thioridazine
Diazepam	Naproxen	Triamterene
Doxylamine succinate	Nicotine	Vanilmandelic acid
Dyphylline	N-Normethsuximide	Venlafaxine hydrochloride

Immunoassay: Effect of cosmetic treatments

Hair samples negative for fentanyl and samples positive for fentanyl were treated with the following cosmetic treatments: permanent wave, relaxer, bleach, dye, and shampoo. After the treatments, these samples and an aliquot of the same hair samples untreated were digested for fentanyl analysis and then assayed by the Psychemedics Microplate EIA for Fentanyl in Hair. The EIA results with and without treatment are compared to detect interference in the assay or loss of drug due to the treatments. The study included 10 negative samples and 6 fentanyl-positive samples with one brand of each of the particular product types, and another set of 10 negative samples and 6 positive samples with a second brand of each of the product types for a total of 32 different combinations of hair and products. All negative results remained negative and all positive results remained positive after the treatments.

All of the positive samples were also analyzed by the confirmation procedure for fentanyl and norfentanyl using the LC-MS/MS method. Each of the samples was measured before and after the treatment. The percent change of fentanyl as well as the average across the 6 samples for each of the treatments is reported in the tables below.

Effect of Perm Product #1 on Fentanyl in Hair by LCMSMS					% Change of Fentanyl
Sample #	Before Treatment		After Treatment		
	Fentanyl	Norfentanyl	Fentanyl	Norfentanyl	
	ng/10 mg hair				
1	3.36	0.144	3.466	0.034	3.15
2	7.415	0.262	7.491	0.143	1.02
3	2.33	0.057	1.882	0.032	-19.23
4	19.194	1.707	18.714	0.851	-2.50
5	4.728	0.227	4.439	0.118	-6.11
6	6.127	0.127	5.359	0.075	-12.53
Average Percent Change of Fentanyl Concentration					**-6.03**

Effect of Perm Product #2 on Fentanyl in Hair by LCMSMS					% Change of Fentanyl
Sample #	Before Treatment		After Treatment		
	Fentanyl	Norfentanyl	Fentanyl	Norfentanyl	
	ng/10 mg hair				
7	4.519	0.059	4.939	0.068	9.3
8	7.52	0.261	8.016	0.254	6.6
9	1.809	0.044	1.647	0.035	-9.0
10	18.813	0.709	16.772	0.888	-10.8
11	5.322	0.229	5.651	0.196	6.2
12	4.246	0.066	5.177	0.091	-21.9
Average Percent Change of Fentanyl Concentration					**4.0**

Effect of Shampoo Product #1 on Fentanyl in Hair by LCMSMS					% Change of Fentanyl
Sample #	Before Treatment		After Treatment		
	Fentanyl	Norfentanyl	Fentanyl	Norfentanyl	
	ng/10 mg hair				
13	4.519	0.059	4.472	0.059	-1.0
14	7.52	0.261	7.415	0.262	-1.4
15	3.16	0.105	2.33	0.058	-26.3
16	18.813	0.25	17.742	0.243	-5.7
17	4.728	0.227	5.322	0.229	12.6
18	6.127	0.127	6.541	0.168	6.8
Average Percent Change of Fentanyl Concentration					**-2.51**

Effect of Shampoo Product #2 on Fentanyl in Hair by LCMSMS					% Change of Fentanyl
Sample #	Before Treatment		After Treatment		
	Fentanyl	Norfentanyl	Fentanyl	Norfentanyl	
	ng/10 mg hair				
19	4.519	0.059	4.572	0.074	1.2
20	7.52	0.261	7.667	0.303	2.0
21	3.16	0.105	4.099	0.129	29.7
22	18.813	0.709	19.195	1.707	2.0
23	4.728	0.227	5.601	0.291	18.5
24	10.9	0.537	10.168	0.285	-6.7
Average Percent Change of Fentanyl Concentration					**7.8**

Effect of Dye Product #1 on Fentanyl in Hair by LCMSMS					% Change of Fentanyl
Sample #	Before Treatment		After Treatment		
	Fentanyl	Norfentanyl	Fentanyl	Norfentanyl	
	ng/10 mg hair				
25	1.089	0.164	1.062	0.024	-2.48
26	15.668	1.08	13.19	1.247	-15.82
27	4.738	0.227	4.394	0.239	-7.26
28	6.788	0.251	6.251	0.148	-7.91
29	0.739	0.011	0.78	0.006	5.55
30	1.124	0.019	1.13	0.018	0.53
Average Percent Change of Fentanyl Concentration					**-4.56**

Effect of Dye Product #2 on Fentanyl in Hair by LCMSMS					% Change of Fentanyl
Sample #	Before Treatment		After Treatment		
	Fentanyl	Norfentanyl	Fentanyl	Norfentanyl	
	ng/10 mg hair				
31	7.415	0.262	7.52	0.0026	1.4
32	13.332	0.445	15.666	1.08	17.5
33	3.788	0.251	6.369	0.263	68.1
34	6.157	0.525	6.127	0.127	-0.5
35	0.739	0.011	0.884	0.066	19.6
36	1.54	0.022	1.508	0.002	-2.1
Average Percent Change of Fentanyl Concentration					**17.4**

Effect of Relaxer Product #1 on Fentanyl in Hair by LCMSMS					% Change of Fentanyl
Sample #	Before Treatment		After Treatment		
	Fentanyl	Norfentanyl	Fentanyl	Norfentanyl	
	ng/10 mg hair				
37	7.415	0.262	6.281	0.137	-15.3
38	1.809	0.044	1.471	0.026	-18.7
39	7.735	0.25	6.535	0.168	-15.5
40	3.859	0.37	4.313	0.173	11.8
41	19.33	0.969	14.793	0.46	-23.5
42	1.039	0.068	0.852	0.024	-18.0
Average Percent Change of Fentanyl Concentration					**-13.2**

Effect of Relaxer Product #2 on Fentanyl in Hair by LCMSMS					% Change of Fentanyl
Sample #	Before Treatment		After Treatment		
	Fentanyl	Norfentanyl	Fentanyl	Norfentanyl	
	ng/10 mg hair				
43	7.52	0.261	8.546	0.17	13.64
44	1.809	0.017	1.964	0.017	8.57
45	7.735	0.76	6.358	0.076	-17.80
46	3.859	0.168	4.584	0.168	18.79
47	19.33	0.427	16.937	0.427	-12.38
48	1.54	0.239	1.3829	0.0239	-10.20
Average Percent Change of Fentanyl Concentration					**0.10**

Specificity of the LC-MS/MS method

LC-MS/MS: Cross-reactivity with structurally related compounds

The cross-reactivity characteristics of the LC-MS/MS confirmation assay were evaluated by measuring hair samples spiked with fentanyl and norfentanyl at the cutoff of 0.20 ng/10 mg/hair, and also containing the following structurally related compounds at a concentration of 0.20 ng/10 mg/hair: butyryl fentanyl, valeryl fentanyl, acetyl fentanyl, para-fluorobutyryl fentanyl, cis-3-methylfentanyl, furanyl fentanyl, carfentanil, butyryl norfentanyl, acetyl norfentanyl, furanyl norfentanyl, norcarfentanil. All of the samples spiked with the potential cross-reactant and one of the target drugs at the cutoff produced a concentration within ± 15% of the spiked value of 0.20 ng/10 mg hair. The sponsor concluded that these compounds did not cross-react or cause interference with the LC-MS/MS assay.

LC-MS/MS: Interference from structurally unrelated compounds

The specificity of the LC-MS/MS confirmation assay with structurally unrelated compounds was evaluated by measuring samples spiked with fentanyl and norfentanyl at the cutoff of 0.20 ng/10 mg/hair, containing the following compounds at the concentrations listed: Cotinine (500 ng/10 mg hair), Nicotine (500 ng/10 mg hair), Caffeine (500 ng/10 mg hair), Ibuprofen (50 ng/10 mg hair), Naproxen (50 ng/10 mg hair), Phentermine (20 ng/10 mg hair), Pseudoephedrine (20 ng/10 mg hair), Morphine (200 ng/10 mg hair), Hydrocodone (200 ng/10 mg hair), Oxycodone (200 ng/10 mg hair), Codeine (200 ng/10 mg hair), Cocaine (200 ng/10 mg hair), Phencyclidine (200 ng/10 mg hair), Methamphetamine (200 ng/10 mg hair), Amphetamine ((200 ng/10 mg hair), Methadone (200 ng/10 mg hair), Phenobarbital (200 ng/10 mg hair), Phenytoin (200 ng/10 mg hair), Phenylephrine(200 ng/10 mg hair) , Carbamazepine (200 ng/10 mg hair), Gabapentin (500 ng/10 mg hair), Salicylic Acid (200 ng/10 mg hair), Valproic Acid (200 ng/10 mg hair), Oxcarbazepine (200 ng/10 mg hair), Propoxyphene (200 ng/10 mg hair), Acetaminophen (200 ng/10 mg hair), Norfloxacin (0.2 ng/10 mg hair), Psilocybin (200 ng/10 mg hair), Nimesulide (200 ng/10 mg hair), Etifoxine (200 ng/10 mg hair) , Chlorcyclizine (200 ng/10 mg hair), and Teriflunomide (200 ng/10 mg hair).

All of the samples spiked with the potential interfering compounds and each of the target drugs at the cutoff produced a concentration within ± 15% of the spiked value of 0.20 ng/10 mg/hair. The sponsor concluded that the potentially interfering compounds listed above did not cross-react or cause interference with the LC-MS/MS assay.

LC-MS/MS: Studies to evaluate environmental contamination

Studies were performed to evaluate environmental contamination. Two different aliquots of 10 different hair specimens, previously shown to be negative for fentanyl, were soaked in either a water-based solution containing 5 ng fentanyl/mL or a saline-based solution containing 5 ng fentanyl/mL, resulting in a range of fentanyl on the hair from below the Limit of Quantitation (LOQ) to 0.0527 ng of fentanyl /10 mg hair, prior to washing. After washing hair samples according to the instructions in the product insert, no samples contained an amount of drug above the LOQ of the confirmatory method.

f. Assay cut-off:

Analytical performance of the device around the claimed cutoff is described in precision section M.1.a. above.

2. Comparison studies:

a. Method comparison with predicate device:

Accuracy of the immunoassay screening method

A total of 197 hair specimens were used to compare the results of the Psychemedics Microplate EIA for Fentanyl in Hair with the LC-MS/MS method. The studies were comprised of the following hair samples: 138 samples from males, 59 samples from females; 98 black hair samples, 94 brown hair samples (from light brown to dark brown), 1 blond hair sample, and 2 grey hair samples, 134 head hair samples, and 63 body hair samples. 97 samples tested positive by the Psychemedics Microplate EIA for Fentanyl in Hair for fentanyl, and 100 tested negative.

There were no false negative results reported by the Microplate EIA for Fentanyl test. There were 10 false positives (confirmed by LC-MS/MS to have less than 0.2ng/10 mg cutoff of the EIA). The false positives were caused by the presence of structurally similar molecules that cross react in the EIA causing a falsely high result. In section M.1.e. above, the fentanyl immunoassay cross-reacts with butyryl fentanyl, valeryl fentanyl, furanyl fentanyl, acetyl fentanyl, acryl fentanyl, cyclopropyl fentanyl, isobutyryl fentanyl, ocfentanil, 4-fluoro-isobutyryl fentanyl. There were an additional 9 samples that were positive for fentanyl but not positive for norfentanyl, these are interpreted as negative / discordant results. These results are interpreted by the test as environmental contamination and were falsely positive due to inadequate washing procedures.

Recovery study for the LC-MS/MS:

The sponsor conducted a study to evaluate recovery for fentanyl at concentrations of 0.2, 3, and 7.5 ng/10 mg hair. For each combination of drug and concentration level, ten individual hair samples were prepared and analyzed. The recovery for fentanyl ranged from 87% to 100% and the recovery for norfentanyl ranged from 92 – 100%.

b. Matrix comparison:

Not applicable. The assay is intended for only one sample matrix.

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable.

b. Clinical specificity:

Not applicable.

c. Other clinical supportive data (when a. and b. are not applicable):

Not applicable.

4. Clinical cut-off:

The sponsor provided scientific literature to support the clinical validity for the fentanyl and norfentanyl cut-offs for the device.

5. Expected values/Reference range:

Not applicable.

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

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