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

A. 510(k) Number:

k181305

B. Purpose for Submission:

Modification of a previously cleared device to include new test analytes, methadone and oxycodone.

C. Measurands:

Amphetamine, cocaine, cannabinoids, methamphetamine, morphine, phencyclidine, oxycodone and methadone.

D. Type of Test:

Qualitative, lateral flow immunochromatographic

E. Applicant:

Premier Biotech, Inc.

F. Proprietary and Established Names:

OralTox® Oral Fluid Drug Test

G. Regulatory Information:

Product Code	Classification	Relation Section	Panel
DKZ	Class II	21CFR 862.3100, Amphetamine Test System	Toxicology (91)
DIO	Class II	21 CFR 862.3250, Cocaine and metabolites TEST System	Toxicology (91)
LDJ	Class II	21 CFR 862.3870, Cannabinoids Test System	Toxicology (91)
DJC	Class II	21 CFR 862.3610, Methamphetamine Test System	Toxicology (91)
LCM	Class II	Unclassified, Enzyme immunoassay Phencyclidine	Toxicology (91)
DJG	Class II	21 CFR 862.3650, Opiate Test System	Toxicology (91)

DJR	Class II	21 CFR, 862.3610 Methadone Test System	Toxicology (91)

H. Intended Use:

1. Intended use(s):

   Refer to Indications for Use below.

2. Indication(s) for use:

   The OralTox® Oral Fluid Drug Test is a competitive binding, lateral flow immunochromatographic assay for the qualitative and simultaneous detection of amphetamine, cocaine, marijuana (THC), methamphetamine, opiates, phencyclidine, oxycodone and methadone in human oral fluid at the cut-off concentrations listed below and their metabolites:

Drug (Identifier)	Calibrator	Cut-off level
Amphetamine (AMP)	D-Amphetamine	50 ng/mL
Cocaine (COC)	Benzoylecgonine	20 ng/mL
Cannabinoids (THC)	Delta-8-Tetrahydrocannabinol	40 ng/mL
Methamphetamine (MET)	D-Methamphetamine	50 ng/mL
Opiates (OPI)	Morphine	40 ng/mL
Phencyclidine (PCP)	Phencyclidine	10 ng/mL
Oxycodone (OXY)	Oxycodone	20 ng/mL
Methadone (MTD)	Methadone	30 ng/mL

   The test provides only preliminary test results. A more specific alternative chemical method must be used in order to obtain a confirmed analytical result. Liquid Chromatography/Mass Spectrometry/Mass Spectrometry (LC-MS/MS) is the preferred confirmatory method. It is not intended to detect intermittent dosing of oxycodone. Clinical consideration and professional judgment should be exercised with any drug of abuse test result, particularly when the preliminary result is positive.

   For in vitro diagnostic use only. The tests are intended for prescription use.

3. Special conditions for use statement(s):

   For prescription point-of-care use.

4. Special instrument requirements:

   Not applicable; the device is a visually-read single use device.

I. Device Description:

The OralTox® Oral Fluid Drug Test is an immunochromatographic assay that uses a lateral flow system for the qualitative detection of amphetamine, cocaine, cannabinoids, methamphetamine, morphine, phencyclidine, oxycodone and methadone (target analytes) in human oral fluid.

The products are single-use in vitro diagnostic devices. Each test kit contains a test cup, a package insert and a sample collection sponge. Each test device is sealed with a desiccant in an aluminum pouch.

The device has a built-in sample collection tool, including collection swab and sponge, as well as a saturation indicator strip. The saturation indicator strip turns red when a volume of oral fluid has been collected that is adequate to both run the OralTox® test and to conduct confirmation testing at a laboratory if the result is a presumptive positive. OralTox® Oral Fluid Drug Tests are the first step in a two-step process. The second step is to send the sample for confirmatory laboratory testing using a more specific method (e.g., LC-MS/MS) if preliminary positive results are obtained.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   OralTox® Oral Fluid Drug Test

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

   k171403

3. Comparison with predicate:

Similarities		
Item	Proposed device	Predicate device
Intended Use	Same	Preliminary Drug screening test for the qualitative detection of drug analytes in oral fluid (human saliva) For *In Vitro* Diagnostic Use
Drug analytes detected	D-Amphetamine Cocaine Delta-9-Tetrahydrocannabinol D-Methamphetamine Morphine Phencyclidine Methadone	D-Amphetamine Cocaine Delta-9-Tetrahydrocannabinol D-Methamphetamine Morphine Phencyclidine

Similarities		
Item	Proposed device	Predicate device
	Oxycodone	
Methodology	Same	Competitive binding, lateral flow immunochromatographic assays based on the principle of antigen antibody immunochemistry
Type of Test	Same	Qualitative
Specimen Type	Same	Human Oral fluid
Cut-offs	AMP 50 ng/mL COC 20 ng/mL THC 40 ng/mL MET 50 ng/mL OPI 40 ng/mL PCP 10 ng/mL OXY 20 ng/mL MTD 30 ng/mL	AMP 50 ng/mL COC 20 ng/mL THC 40 ng/mL MET 50 ng/mL MOP 40 ng/ML PCP 10 ng/mL
Differences		
Item	Device	Predicate
Drug analytes detected	D-Amphetamine Cocaine Delta-9-Tetrahydrocannabinol D-Methamphetamine Morphine Phencyclidine Methadone Oxycodone	D-Amphetamine Cocaine Delta-9-Tetrahydrocannabinol D-Methamphetamine Morphine Phencyclidine
Number of analytes detected	8	6

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

None Referenced.

L. Test Principle:

The OralTox® Oral Fluid Drug Test is an immunochromatographic assay that uses a lateral flow system for the qualitative detection of amphetamine, cocaine, cannabinoids, methamphetamine, morphine, and phencyclidine, methadone, and oxycodone, (target analytes) in human oral fluid. The tests are lateral flow chromatographic immunoassays. During testing, an oral fluid specimen migrates upward by capillary action. If target drugs present in the oral fluid specimen are below the cut-off concentration, it will not saturate the

binding sites of its specific monoclonal mouse antibody coated on the particles. The antibody-coated particles will then be captured by immobilized drug-conjugate and a visible colored line will show up in the test line region. The colored line will not form in the test line region if the target drug level exceeds its cut-off-concentration because it will saturate all the binding sites of the antibody coated on the particles. A band should form in the control region of the devices regardless of the presence of drug or metabolite in the sample to indicate that the tests have been performed properly.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

The analytical performance of the device for the measurement of d-amphetamine (AMP), cocaine (COC), delta-8-tetrahydrocannibinol (THC), d-methamphetamine (MET), morphine (OPI), and phencyclidine (PCP), was reviewed in k171403. Please see the decision summary for k171403 for information regarding performance of these analytes.

a. Precision/Reproducibility:

Precision-reproducibility-cut-off 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. Testing was repeated across three sites. These samples were prepared by spiking drug in negative oral fluid samples. The sponsor has stated that each drug concentration was confirmed by LC-MS/MS. All sample aliquots were blindly labeled by the person who prepared the samples and didn't take part in the sample testing. For each concentration, tests were performed two runs per day for 10 days per device lot in a randomized order. The sponsor provided the following summaries:

Methadone	-100% cut-off	-75% cut-off	-50% cut-off	-25% cut-off	cut-off	+25% cut-off	+50% cut-off	+75% cut-off	+100% cut-off
Lot 1	60-/0+	60-/0+	60-/0+	54-/6+	49+/11-	55+/5-	60+/0-	60+/0-	60+/0-
Lot 2	60-/0+	60-/0+	60-/0+	55-/5+	48+/12-	56+/4-	60+/0-	60+/0-	60+/0-
Lot 3	60-/0+	60-/0+	60-/0+	55-/5+	50+/10-	55+/5-	60+/0-	60+/0-	60+/0-

Oxycodone	-100% cut-off	-75% cut-off	-50% cut-off	-25% cut-off	cut-off	+25% cut-off	+50% cut-off	+75% cut-off	+100% cut-off
Lot 1	60-/0+	60-/0+	60-/0+	55-/5+	50+/10-	55+/5-	60+/0-	60+/0-	60+/0-
Lot 2	60-/0+	60-/0+	60-/0+	54-/6+	49+/11-	56+/4-	60+/0-	60+/0-	60+/0-
Lot 3	60-/0+	60-/0+	60-/0+	56-/4+	49+/11-	57+/3-	60+/0-	60+/0-	60+/0-

The device has been developed with the following cut-offs:

Calibrator	**Cut-off (ng/mL)**
D-methamphetamine	50
Cocaine	20
Morphine	40
D-amphetamine	50
Phencyclidine	10
Delta-9-tetrahydrocannabinol	40
Methadone	30
Oxycodone	20

Sample Volume:

A sample volume study was conducted in k171403 to confirm the reproducibility of adequate sample volume collection by the device and found to be acceptable.

b. *Linearity/assay reportable range:*

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

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):* Accelerated stability and real time studies have been conducted for the device. Protocols and acceptance criteria were described and found to be acceptable. The manufacturer claims that when stored un-opened at 4-30 º C, the device is stable for 24 months.

Sample Recovery

Volume recovery**:**

A sample volume recovery study was provided in k171403 and found to be acceptable.

Analyte recovery:

In order to confirm that preliminary positive results can be adequately measured via confirmation testing after being subject to the temperature conditions required for shipping and storage, negative oral fluid samples in glass bottles were spiked with a single analyte/bottle to concentrations approximately -50% and +50% of the cut-off. Samples were spiked using known standards. Each drug concentration was confirmed by LC-MS/MS. The samples were transferred to OralTox® devices using the collection sponges. For each of 3 storage conditions (-20°C, 20-25°C, and 40°C), 12 devices were used (4 devices from each of 3 lots. For each device, drug was measured by LC-MS/MS at time zero and the devices containing the specimens were

stored under the specified condition. Drug in the devices stored at 20-25°C and 40°C was measured by LC-MS/MS at two (2) days, and drug in the devices stored at -20°C was measured by LC-MS/MS at 90 days.

The minimum and maximum recovery from 12 devices per lot per storage condition is shown below. Analyte recovery for d-amphetamine (AMP), cocaine (COC), delta-8-tetrahydrocannibinol (THC), d-methamphetamine (MET), morphine (OPI), and phencyclidine (PCP) was provided in k171403.

Room Temperature 20-25°C (two day storage)

	OXY +50	OXY -50	MTD +50	MTD -50
Max	99	99	100	99
Min	91	91	92	92

40 °C (two day storage)

	OXY +50	OXY -50	MTD +50	MTD -50
Max	98	99	100	93
Min	92	93	92	97

-20 °C (90 day storage)

	OXY +50	OXY -50	MTD +50	MTD -50
Max	100	98	101	105
Min	93	93	93	91

Results indicate that samples may be stored at room temperature for up to two days, elevated temperature for up to do days (40 °C), and for up to 90 days at – 20 °C, prior to confirmatory testing.

d. Detection limit:

See Precision/Reproducibility section in M.1.a above.

e. Analytical specificity:

To test cross reactivity, drug metabolites and other components that may be present in oral fluid samples were tested using three lots of the OralTox® device. The following is a summary of the cross-reactivity study. A cross-reactivity study for d-amphetamine (AMP), cocaine (COC), delta-8-tetrahydrocannibinol (THC), d-methamphetamine (MET), morphine (OPI), and phencyclidine (PCP) was provided in k171403.

Oxycodone (Cut-off=20 ng/mL)	Result Positive at (ng/mL)	% Cross-Reactivity
Oxycodone	20	100%
Hydrocodone	1000	2%
Hydromorphone	6250	0.3%
Naloxone	6250	0.3%
Oxymorphone	1000	2%
Dihydrocodeine	Negative at 10000	<0.2%
Buprenorphine	Negative at 10000	<0.2%
6-AM	Negative at 10000	<0.2%
Codeine	Negative at 10000	<0.2%
Heroin	Negative at 10000	<0.2%
Morphine	Negative at 10000	<0.2%
Morphine -3-β-d-	Negative at 10000	<0.2%
Ethylmorphine	Negative at 10000	<0.2%

Methadone (Cut-off=30 ng/mL)	Result Positive at(ng/ml)	% Cross-Reactivity
Alpha-methadol	125	24%
Doxylamine	12500	0.24%
2-Ethylidene-1,5-dimethyl-3,3-diphenyl pyrrolidine (EDDP)	10000	0.3%
Phencyclidine	12500	0.24%
2-Ethyl-5-methyl-3,3-diphenylpyrroline (EMDP)	100000	0.03%
LAAM	10000	0.3%

Exogenous Interference: Potential interference from structurally unrelated compounds were tested by spiking the potentially interfering compound at a concentration of 10 ug/mL into drug free oral fluid or fluid containing the target drug with concentrations of 50% below and 50% above cut-off level. The following compounds were found not to interfere with test results at a concentration of 10ug/mL for all samples tested. An exogenous interference study for D-Amphetamine (AMP), Cocaine (COC), Delta-8-Tetrahydrocannibinol (THC), D-Methamphetamine (MET), Morphine (OPI), and Phencyclidine (PCP) was provided in k171403.

Acetaminophen	Digoxin	Nicotinamide
Acetylcodeine	Dihydrocodeine	Nicotine
Allobarbital	diltiazem HCl	Noscapine
Alprazolam	Diphenhydramine HCl	Omeprazole
Amobarbital	DL-Propranolol	Papaverine

Apomorphine	Doxylamine	Pentazocine
Atenolol	Ecgonine methylester	Phentermine
Atropine	Estradiol	Phenylpropanolamine
Baclofen	Estrone	Phenytoin
Benzocaine	Fluconazole	Pioglitazone HCl
Butabarbital	Furosemide	Prednisolone
Caffeine	Hexobarbital	Prednisone
Cannabidiol	Hydrochlorothiazide	Procainamide HCl
Carbamazepine	Ibuprofen	Procaine HCL
Chlordiazepoxide	Imipramine	Promethazine
Chlorpromazine	Lamotrigine	Quinine HCl
Cimetidine	Levetiracetam	R,r(-)-pseudoephedrine
Citalopram HBr	Lidocaine	Salicylic Acid
Clobazam	Lormetazepam	Sertraline HCL
Clomipramine	L-thyroxine	Simvastin
Clonazepam	Metformin HCl	Theophylline
Clonidine	Methylphenidate HCl	Thiamine
Clopidogrel bisulfate	Metoprolol	Topiramate
Cortisol	Metronidazole	Valproic acid
Cotinine	Montelukast sodium salt	Verapamil
D,l-Salbutamol	Naloxone	Zonisamide
Deoxycorticosterone	Naltrexone	
Dextromethorphan	Naproxen	

The following potential interference from substances commonly present in oral fluid were evaluated by spiking into drug free oral fluid or oral fluid containing the target drug with concentrations of 50% below and 50% above cut-off level to a concentration of 5%: alcohol, baking soda, chewing gum, coffee, cola, cough syrup, cranberry juice, food coloring (blue, green, and red), methanol cough drops, milk, mouthwash, MSG, orange juice, salt, sugar, tea, toothpaste, and tomatoes. None of these substances showed any interference with the detection of any analyte (OXY, MTD) using the device. A study testing these substances for interference to detection of d-amphetamine (AMP), cocaine (COC), delta-8-tetrahydrocannibinol (THC), d-methamphetamine (MET), morphine (OPI), and phencyclidine (PCP) was provided in k171403.

Potential interference from cigarette smoking, was evaluated by asking a participant to smoke a cigarette. After 15 minutes of smoking, an oral fluid sample was collected and spiked with each drug at concentrations of cut-off +/- 50%. No interference with the detection of any analyte (OXY, MTD) using the device was observed. A study testing potential interference from cigarette smoking to detection of d-amphetamine (AMP), cocaine (COC), delta-8-tetrahydrocannibinol (THC), d-methamphetamine

(MET), morphine (OPI), and phencyclidine (PCP) was provided in k171403.

Potential interference from hemoglobin was evaluated by adding it to drug free oral fluid or oral fluid containing the target drug with concentrations of 50% above and 50% below cut-off level to a concentration of 100ug/mL. No interference with the detection of any analyte (OXY, MTD) using the device was observed. A study testing for potential interference from hemoglobin to detection of d-amphetamine (AMP), cocaine (COC), delta-8-tetrahydrocannibinol (THC), d-methamphetamine (MET), morphine (OPI), and phencyclidine (PCP) was provided in k171403.

Effect of oral fluid pH: To investigate the effect of oral fluid pH, oral fluid samples with pH 4 to 9 were spiked with target drugs at 50% below and 50% above cut-off levels. These samples were tested using three lots of the device. Results were all positive for samples (OXY, MTD) at and above +50% cut-off and all negative for samples at and below -50% Cut-Off. A study to test the potential interference due to pH for d-amphetamine (AMP), cocaine (COC), delta-8-tetrahydrocannibinol (THC), d-methamphetamine (MET), morphine (OPI), and phencyclidine (PCP) was provided in k171403.

There is the possibility that other substances and/or factors not listed above may interfere with the test and cause false results, e.g., technical or procedural errors.

f. Assay cut-off:

Characterization of how the device performs analytically around the claimed cut-off concentration appears in the precision section, M.1.a., above.

2. Comparison studies:

a. Method comparison:

Method comparison studies for the OralTox® Oral fluid Drug Test were performed, testing a total of 932 samples. 434 samples were evaluated for oxycodone at four sites, and 498 samples were evaluated for methadone at four sites. Each site utilized three operators. Device results were compared to LC-MS/MS results. The results are presented in the tables below. A method comparison study for d-amphetamine (AMP), cocaine (COC), delta-8-tetrahydrocannibinol (THC), d-methamphetamine (MET), morphine (OPI), and phencyclidine (PCP) was provided in k171403.

Oxycodone

Concentration (% of Cut-off) by LC/MS	Number of samples	OralTox Results		The percentage of correct results (%)
		No. of Positive	No. of Negative	
Drug free (0%)	152	0	152	100
<50% of cut-off	47	0	47	100
50% of cut-off to cut-off	32	5	27	84.4
Cut-off to 150% of cut-off	29	25	4	86.2
>150% of cut-off	174	174	0	100

Discordant results (oxycodone)

Sample	LC/MS Result	Device Result
1	18.0	Positive
2	17.2	Positive
3	19.05	Positive
4	18.23	Positive
5	18.52	Positive
6	23.29	Negative
7	22.04	Negative
8	22.4	Negative
9	22.34	Negative

Methadone

% of Cut-off	Number of samples	OralTox Results		The percentage of correct results (%)
		No. of Positive	No. of Negative	
Drug free (0%)	277	0	277	100
<50% of cut-off	13	0	13	100
50% of cut-off to cut-off	20	4	16	80
cut-off to 150% of cut-off	15	13	2	87
>150% of cut-off	173	173	0	100

Discordant results (methadone)

Sample Number	LC/MS Result	Device Result
1	26.9	Positive
2	27.85	Positive
3	28.26	Positive
4	28.82	Positive
5	31.07	Negative
6	31.29	Negative

b. Matrix comparison:

Not applicable. These devices are for use with oral fluid samples only.

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:

Not applicable.

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.