

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

A. 510(k) Number:

K142609

B. Purpose for Submission:

New Device

C. Measurand:

Nortriptyline and Buprenorphine

D. Type of Test:

Qualitative chromatographic immunoassay

E. Applicant:

Guangzhou Wondfo Biotech Co., Ltd.

F. Proprietary and Established Names:

CR3 Keyless Split Sample Cup Nortriptyline–Buprenorphine

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
DJG	Class II	21 CFR part 862.3650 Opiate test system	Toxicology (91)
LFG	Class II	21 CFR part 862.3910 Tricyclic antidepressant drugs test system	Toxicology (91)

H. Intended Use:

1. Intended use(s):

Please see Indications for Use below.

2. Indication(s) for use:

CR3 Keyless Split Sample Cup Nortriptyline–Buprenorphine is a rapid test for the qualitative detection of Nortriptyline (a major metabolite of Tricyclic Antidepressants) and Buprenorphine in human urine at a cutoff concentration of 1000ng/mL and 10ng/mL, respectively. The test is the first step in a two-step process. The second step is to send the sample for laboratory testing if preliminary positive results are obtained. The test is intended for over-the-counter and for prescription use.

The test may yield preliminary positive results even when prescription drugs including Tricyclic Antidepressants and Buprenorphine are ingested, at prescribed doses; it is not intended to distinguish between prescription use or abuse of these drugs. There are no uniformly recognized cutoff concentration levels for Nortriptyline and Buprenorphine in urine. The test provides only preliminary test results. A more specific alternative chemical method must be used in order to obtain a confirmed analytical result. GC/MS is the preferred confirmatory method. 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.

3. Special conditions for use statement(s):

For Prescription and Over-the-counter Use

4. Special instrument requirements:

Not applicable; this is a visually read single use device.

I. Device Description:

The CR3 Keyless Split Sample Cup Nortriptyline–Buprenorphine test uses immunochromatographic assays for nortriptyline and buprenorphine. The test is a lateral flow system for the qualitative detection of nortriptyline and buprenorphine in human urine.

J. Substantial Equivalence Information:

1. Predicate device name(s):

UCP Multi-Drug Test Key Cups

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

k132812

3. Comparison with predicate:

Item	Device	Predicate
Indication(s) for use	For the qualitative determination of drugs of abuse in human urine	Same
Methodology	Competitive binding, lateral flow immunochromatographic assays based on the principle of antigen antibody immunochemistry.	Same
Results	Qualitative	Same
Specimen Type	Human urine	Same
Cut Off Values	Nortriptyline: 1000ng/ml Buprenorphine: 10ng/ml	Same for Tricyclic Antidepressant (Nortriptyline) and Buprenorphine
Configurations	Cup	Same
Conditions for Use	Over-the-Counter & Prescription Use	Over-the-counter

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

None were referenced.

L. Test Principle:

The CR3 Keyless Split Sample Cup Nortriptyline - Buprenorphine test is a rapid flow chromatographic immunoassay for the qualitative detection of Nortriptyline and Buprenorphine in urine samples. Each assay uses a mouse monoclonal anti-drug antibody-dye conjugate, fixed drug-protein conjugates, and anti-mouse IgG polyclonal antibodies coated on the test membranes. When the absorbent end of the test is immersed into a urine sample, the urine is absorbed into the device by capillary action and mixes with the antibody-dye conjugate, flowing across the pre-coated membrane. At analyte concentrations below the target cut-off, antibody-dye conjugates bind to the drug-protein conjugate immobilized in the

Test Region (T) of the device. This produces a colored test line that indicates a negative result. When analyte concentration is above the cut-off, analyte molecules bind to the antibody-dye conjugate, preventing the antibody-dye conjugate from binding to the drug-protein conjugate immobilized in the Test Region (T) of the device. No colored band shows in the Test Region, indicating a potentially positive result. A band should form in the Control Region (C) of the device regardless of the presence of drug or metabolite in the sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Precision studies were carried out for samples with concentrations of -100% cut-off, -75% cut-off, -50% cut-off, -25% cut-off, at the cut-off, +25% cut-off, +50% cut-off, +75% cut-off and +100% cut-off. For each concentration, tests were performed two runs per day for 25 days. All sample aliquots were masked and randomized. The results obtained are summarized in the following tables:

For Nortriptyline testing

Lot	-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
1	50-/0+	50-/0+	50-/0+	50-/0+	44+/6-	50+/0-	50+/0-	50+/0-	50+/0-
2	50-/0+	50-/0+	50-/0+	50-/0+	43+/7-	50+/0-	50+/0-	50+/0-	50+/0-
3	50-/0+	50-/0+	50-/0+	50-/0+	43+/7-	50+/0-	50+/0-	50+/0-	50+/0-

For Buprenorphine testing

Lot	-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
1	50-/0+	50-/0+	50-/0+	50-/0+	42+/8-	50+/0-	50+/0-	50+/0-	50+/0-
2	50-/0+	50-/0+	50-/0+	50-/0+	43+/7-	50+/0-	50+/0-	50+/0-	50+/0-
3	50-/0+	50-/0+	50-/0+	50-/0+	43+/7-	50+/0-	50+/0-	50+/0-	50+/0-

b. *Linearity/assay reportable range:*

Not applicable.

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

Shelf stability for the CR3 Keyless Split Sample Cup Nortriptyline - Buprenorphine was performed using accelerated and real-time stability testing. Protocols and acceptance criteria were reviewed and found to be acceptable. The sponsor claims that the device is stable at 4-30°C for 18 months.

Control materials are not provided with the device. The labeling provides information on how to obtain control materials.

d. *Detection limit:*

Not applicable.

e. *Analytical specificity:*

Potential interfering substances found in human urine of physiological or pathological conditions were added at a concentration of 100µg/mL to drug-free urine and to urine containing target drugs (nortriptyline or buprenorphine) at 25% below and 25% above the cut-off. The samples were tested using three lots of the CR3 Keyless Split Sample Cup Nortriptyline - Buprenorphine by three different operators. The compounds below showed no interference:

Nortriptyline

4-Acetamidophenol	Erythromycin	Oxycodone
Acetophenetidin	β-Estradiol	Oxymetazoline
N-Acetylprocainamide	Estrone-3-sulfate	Papaverine
Acetylsalicylic acid	Ethyl-p-aminobenzoate	Penicillin-G
Aminopyrine	Fenopropfen	Pentazocine hydrochloride
Amobarbital	Furosemide	Pentobarbital
Amoxicillin	Gentisic acid	Perphenazine
Ampicillin	Hemoglobin	Phencyclidine
L-ascorbic acid	Hydralazine	Phenelzine
DL-Amphetamine sulfate	Hydrochlorothiazide	Phenobarbital
Apomorphine	Hydrocodone	Phentermine
Aspartame	Hydrocortisone	β-Phenylethylamine
Atropine	O-Hydroxyhippuric acid	Trans-2-phenylcyclopropylamine hydrochloride
Benzilic acid	p-Hydroxyamphetamine	L-Phenylephrine
Benzoic acid	p-Hydroxy-methamphetamine	Phenylpropanolamine

Benzoyllecgonine	3-Hydroxytyramine	Prednisolone
Benzphetamine	Ibuprofen	Prednisone
Bilirubin	Iproniazid	Procaine
(±) - Brompheniramine	(±) – Isoproterenol	DL-Propranolol
Caffeine	Isoxsuprine	D-Propoxyphene
Cannabidiol	Ketamine	D-Pseudoephedrine
Cannabinol	Ketoprofen	Quinacrine
Chloralhydrate	Labetalol	Quinidine
Chloramphenicol	Loperamide	Quinine
Chlorothiazide	MDE	Ranitidine
(±) Chlorpheniramine	Meperidine	Salicylic acid
Chlorpromazine	Meprobamate	Secobarbital
Chlorquine	Methadone	Serotonin
Cholesterol	(L)Methamphetamine	Sulfamethazine
Clonidine	Methoxyphenamine	Sulindac
Cocaethylene	(±)-3,4- Methylenedioxyamphetami ne hydrochloride	Tetracycline
Cocaine hydrochloride	(+)3,4- Methylenedioxymethamph etamine hydrochloride	Tetrahydrocortisone, 3-acetate
Codeine	Morphine-3-β-Dglucuronide	Tetrahydrocortisone 3-(β-D- glucuronide)
Cortisone	Morphine sulfate	Tetrahydrozoline
(-) Cotinine	Nalidixic acid	Thiamine
Creatinine	Naloxone	Thioridazine
Deoxycorticosterone	Naltrexone	DL-Tyrosine
Dextromethorphan	Naproxen	Tolbutamide
Diclofenac	Niacinamide	Triamterene
Diflunisal	Nifedipine	Trifluoperazine
Digoxin	Norcodeine	Trimethoprim
Diphenhydramine	Norethindrone	Tryptamine
Doxylamine	D-Norpropoxyphene	DL-Tryptophan
hetamine hydrochloride		
Codeine	3-acetate Morphine-3-β- Dglucuronide	Tetrahydrocortisone 3- (β-D-glucuronide)
Cortisone	Morphine sulfate	Tetrahydrozoline
(-) Cotinine	Nalidixic acid	Thiamine
Creatinine	Naloxone	Thioridazine
Deoxycorticosterone	Naltrexone	DL-Tyrosine
Dextromethorphan	Naproxen	Tolbutamide
Diclofenac	Niacinamide	Triamterene
Diflunisal	Nifedipine	Trifluoperazine
Digoxin	Norcodeine	Trimethoprim
Diphenhydramine	Norethindrone	Tryptamine
Doxylamine	D-Norpropoxyphene	DL-Tryptophan

Ecgonine hydrochloride
Ecgonine methylester
Ephedrine
(L) - Epinephrine

Noscapine
Oxalic acid
Oxazepam
Oxolinic acid

Tyramine
Uric acid
Verapamil
Zomepirac

Buprenorphine

4-Acetamidophenol
Acetophenetidin
N-Acetylprocainamide
Acetylsalicylic acid
Aminopyrine
Amobarbital
Amoxicillin
Ampicillin
L-ascorbic acid
DL-Amphetamine sulfate
Apomorphine
Aspartame
Atropine

Erythromycin
 β -Estradiol
Estrone-3-sulfate
Ethyl-p-aminobenzoate
Fenoprofen
Furosemide
Gentisic acid
Hemoglobin
Hydralazine
Hydrochlorothiazide
Hydrocodone
Hydrocortisone
O-Hydroxyhippuric acid

Oxycodone
Oxymetazoline
Papaverine
Penicillin-G
Pentazocine hydrochloride
Pentobarbital
Perphenazine
Phencyclidine
Phenelzine
Phenobarbital
Phentermine
 β -Phenylethylamine
Trans-2-phenylcyclopropylamine hydrochloride
L-Phenylephrine
Phenylpropanolamine

Benzilic acid
Benzoic acid

Benzoylecgonine
Benzphetamine
Bilirubin
(\pm) - Brompheniramine
Caffeine
Cannabidiol
Cannabinol
Chloralhydrate
Chloramphenicol
Chlorothiazide
(\pm) Chlorpheniramine
Chlorpromazine
Chlorquine
Cholesterol
Clonidine
Cocaethylene

p-Hydroxyamphetamine
p-Hydroxy-methamphetamine
3-Hydroxytyramine
Ibuprofen
Iproniazid
(\pm) - Isoproterenol
Isoxsuprine
Ketamine
Ketoprofen
Labetalol
Loperamide
MDE
Meperidine
Meprobamate
Methadone
(L)Methamphetamine
Methoxyphenamine
(\pm)-3,4-Methylenedioxyamphetamin
e hydrochloride
(+)-3,4-Methylenedioxyamphetamin

Prednisolone
Prednisone
Procaine
DL-Propranolol
D-Propoxyphene
D-Pseudoephedrine
Quinacrine
Quinidine
Quinine
Ranitidine
Salicylic acid
Secobarbital
Serotonin
Sulfamethazine
Sulindac
Tetracycline

Tetrahydrocortisone,

Cocaine hydrochloride

hetamine hydrochloride	3-acetate	
Codeine	Morphine-3-β-Dglucuronide	Tetrahydrocortisone 3-(β-D-glucuronide)
Cortisone	Morphine sulfate	Tetrahydrozoline
(-) Cotinine	Nalidixic acid	Thiamine
Creatinine	Naloxone	Thioridazine
Deoxycorticosterone	Naltrexone	DL-Tyrosine
Dextromethorphan	Naproxen	Tolbutamide
Diclofenac	Niacinamide	Triamterene
Diflunisal	Nifedipine	Trifluoperazine
Digoxin	Norcodeine	Trimethoprim
Diphenhydramine	Norethindrone	Tryptamine
Doxylamine	D-Norpropoxyphene	DL-Tryptophan
Ecgonine hydrochloride	Noscapine	Tyramine
Ecgonine methylester	Oxalic acid	Uric acid
Ephedrine	Oxazepam	Verapamil
(L) - Epinephrine	Oxolinic acid	Zomepirac

Cross-reactivity was tested by adding various drug metabolites and other components that are likely to be present in negative urine samples. The drug metabolites and other components were tested at different concentrations. These samples were tested using three lots of the CR3 Keyless Split Sample Cup Nortriptyline–Buprenorphine by three different operators. The obtained lowest detectable concentration was used to calculate the cross-reactivity. Results are shown below:

Nortriptyline

Compound	Result	% Cross-Reactivity
Nortriptyline	Positive at 1000 ng/mL	100%
Nordoxepine	Positive at 1,000 ng/mL	100%
Trimipramine	Positive at 3,000 ng/mL	33%
Amitriptyline	Positive at 1,500 ng/mL	67%
Promazine	Positive at 1,500 ng/mL	67%
Desipramine	Positive at 200 ng/mL	500%
Imipramine	Positive at 400 ng/mL	250%
Clomipramine	Positive at 12,500 ng/mL	8%
Doxepine	Positive at 2,000 ng/mL	50%
Maprotiline	Positive at 2,000 ng/mL	50%
Promethazine	Positive at 25,000 ng/mL	4%

Buprenorphine

BUP (Buprenorphine, Cut-off=10 ng/mL)	Result	% Cross- Reactivity
Buprenorphine	Positive at 10 ng/mL	100%
Buprenorphine -3-D-Glucuronide	Positive at 15 ng/mL	67%
Norbuprenorphine	Positive at 20 ng/mL	50%
Norbuprenorphine -3-D-Glucuronide	Positive at 200 ng/mL	5%
Morphine	>100,000	<0.1%
Oxymorphone	>100,000	<0.1%
Hydromorphone	>100,000	<0.1%

Effect of Specific Gravity and pH

Twelve urine samples of normal, high, and low specific gravity ranges (1.000 to 1.035) were collected and spiked with either Nortriptyline or Buprenorphine at 25% below and 25% above the corresponding cut-off levels. The samples were tested using three lots of the CR3Keyless Split Sample Cup Nortriptyline–Buprenorphine by three different operators.

The pH of an aliquot negative urine pool was adjusted to pH ranges of 4.00 to 9.00 in 1 pH unit increments and spiked with Nortriptyline or Buprenorphine at 25% below and 25% above the corresponding cut-off levels. The samples were tested using three lots of the CR3Keyless Split Sample Cup Nortriptyline–Buprenorphine by three different operators.

The device performance was found to not be affected by varying urine specific gravity and pH.

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:*

The method comparison for the CR3 Keyless Split Sample Cup Nortriptyline–Buprenorphine was performed by three operators. Eighty (40 negative and 40 positive) unaltered clinical samples were masked, randomized and tested. The obtained test results were compared to GC/MS results. The results are presented in the table below:

Nortriptyline

Operators	Results	Negative	Low Negative by GC/MS (less than -50%)	Near Cutoff Negative by GC/MS (Between -50% and cutoff)	Near Cutoff Positive by GC/MS (Between the cutoff and +50%)	High Positive by GC/MS (greater than +50%)
Viewer A	Positive	0	0	3	9	28
	Negative	10	19	8	3	0
Viewer B	Positive	0	0	4	9	28
	Negative	10	19	7	3	0
Viewer C	Positive	0	0	3	8	28
	Negative	10	19	8	4	0

Discordant table:

Viewer	Sample number	GC/MS result	Viewer result
Viewer A	TCAC1061	919	positive
Viewer A	TCAC1062	964	positive
Viewer A	TCAC1063	944	positive
Viewer A	TCAC1064	1082	negative
Viewer A	TCAC1065	1012	negative
Viewer A	TCA 1218	1245	negative
Viewer B	TCAC1034	754	positive
Viewer B	TCAC1061	919	positive
Viewer B	TCAC1062	964	positive
Viewer B	TCAC1063	944	positive
Viewer B	TCAC1064	1082	negative
Viewer B	TCAC1065	1012	negative
Viewer B	TCAC1093	1237	negative

Viewer C	TCAC1061	919	positive
Viewer C	TCAC1062	964	positive
Viewer C	TCAC1063	944	positive
Viewer C	TCAC1064	1082	negative
Viewer C	TCAC1065	1012	negative
Viewer C	TCAC1093	1237	negative
Viewer C	TCA 1218	1245	negative

Buprenorphine:

Group Operators	Results	Negative	Low Negative by GC/MS (less than -50%)	Near Cutoff Negative by GC/MS (Between -50% and cutoff)	Near Cutoff Positive by GC/MS (Between the cutoff and +50%)	High Positive by GC/MS (greater than +50%)
Viewer A	Positive	0	0	3	13	23
	Negative	10	11	16	4	0
Viewer B	Positive	0	0	4	13	23
	Negative	10	11	15	4	0
Viewer C	Positive	0	0	5	14	23
	Negative	10	11	14	3	0

Discordant table:

Viewer	Sample number	GC/MS result	viewer results
Viewer A	BUPC1063	9	positive
Viewer A	BUPC1064	9	positive
Viewer A	BUP1217	9	positive
Viewer A	BUPC1061	11	negative
Viewer A	BUPC1062	10	negative
Viewer A	BUPC1093	12	negative
Viewer A	BUP1224	11	negative
Viewer B	BUPC1063	9	positive
Viewer B	BUPC1064	9	positive
Viewer B	BUP1216	8	positive
Viewer B	BUP1217	9	positive
Viewer B	BUPC1061	11	negative
Viewer B	BUPC1062	10	negative

Viewer B	BUPC1091	12	negative
Viewer B	BUP1224	11	negative
Viewer C	BUPC1033	8	positive
Viewer C	BUPC1065	9	positive
Viewer C	BUP1213	9	positive
Viewer C	BUP1216	8	positive
Viewer C	BUP1217	9	positive
Viewer C	BUPC1061	11	negative
Viewer C	BUPC1091	12	negative
Viewer C	BUP1224	11	negative

b. *Matrix comparison:*

Not applicable.

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):

Lay-user study

A lay user study was performed at three sites with 260 participants (20 tested drug-free samples, 120 tested nortriptyline samples, and 120 tested buprenorphine samples). They had diverse educational and professional backgrounds and ranged in age from 21 to > 50 years. Urine samples were prepared at the following concentrations; -100%, +/-75%, +/-50%, +/-25% of the cut-off by spiking drug(s) into drug free-pooled urine specimens. The concentrations of the samples were confirmed by GC/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:

Drug	Concentration	# of Samples	Negative	Positive	% Agreement With GC/MS
Drug -free	-100%	20	20	0	100%
Nortriptyline	-75%	20	20	0	100%
	-50%	20	20	0	100%
	-25%	20	17	3	85%
	+25%	20	3	17	85%
	+50%	20	0	20	100%
	+75%	20	0	20	100%
Buprenorphine	-75%	20	20	0	100%
	-50%	20	20	0	100%
	-25%	20	18	2	90%
	+25%	20	3	17	85%
	+50%	20	0	20	100%
	+75%	20	0	20	100%

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.

Temperature Strip

The temperature test strip that is a part of the test cup was evaluated for accuracy. The temperature test strip provides a reading in the temperature range of 32 to 38°C. To test for accuracy, water samples were adjusted to different temperatures (32, 33, 34, 36, 37 and 38 °C) and added to device test cups. Technicians read the temperature on the strip on the cup and recorded the results. The temperature of the water samples were also measured with a separate thermometer. Results obtained from the temperature strip were consistent with the thermometer readings.

To validate the performance of the temperature test strip in the hands of the intended user, a user study was conducted. In this user study, 100 lay users filled the device test cups with urine according to the device labeling and used the temperature test strip to record the temperature of their samples. Results were compared to readings of the same samples by professionals. The study demonstrated that the lay users could accurately read the test strip. Urine samples in the study were within the temperature range of the test strip.

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.