

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

A. 510(k) Number:

K040274

B. Analyte:

Opiates

C. Type of Test:

Qualitative immunoassay

D. Applicant:

ACON Laboratories, Inc.

E. Proprietary and Established Names:

ACON OPI II One Step Opiate Test Strip
ACON OPI II One Step Opiate Test Device

F. Regulatory Information:

1. Regulation section:
§ 862.3650 Opiate Test System
2. Classification:
Class II
3. Product Code:
DJG
4. Panel:
Toxicology (91)

G. Intended Use:

1. Intended use(s):
Refer to Indications for use.

2. Indication(s) for use:

The ACON OPI II One Step Opiate Test Strip and ACON OPI II One Step Opiate Test Device are chromatographic immunoassay for the qualitative detection of opiate levels in urine at a designated cut-off concentration of 2,000 ng/mL. These assays provide only a preliminary analytical test result. A more specific alternate chemical method must be used in order to obtain a confirmed analytical result. Gas chromatography/mass spectrometry (GC/MS) is the preferred confirmatory method. Clinical consideration and professional judgment should be applied to any drug of abuse test result, particularly when preliminary positive results are used.

For in vitro diagnostic use only.

3. Special condition for use statement(s):

These assays provide only the preliminary analytical test results. A more specific alternate chemical method must be used in order to obtain a confirmed analytical result. Gas chromatography/mass spectrometry (GC/MS) is the preferred confirmatory method. Clinical consideration and professional judgment should be applied to any drug of abuse test result, particularly when preliminary positive results are used.

The assays are intended for use in point-of-care settings. The assays were evaluated in point-of-care settings.

4. Special instrument Requirements:

Not applicable. The devices are visually read single-use devices.

H. Device Description:

The ACON OPI II One Step Opiate Test Strip and ACON OPI II One Step Opiate Test Device are immunoassays based on the principle of competitive binding. Drugs which may be present in the urine specimen compete against the drug conjugate for binding sites on the antibody.

During testing, a urine specimen migrates upward by capillary action. Morphine, if present in the urine specimen below 2,000 ng/mL, will not saturate the binding sites of antibody-coated particles in the test strip. The morphine conjugate will be captured by antibody and visible color line will show up in the test line region. The colored line will not form in the test line region if the morphine level exceeds 2,000 ng/mL because it will saturate all the binding sites of anti-benzoyllecgonine antibodies.

A drug-positive urine specimen will not generate a colored line in the test line region because of drug competition, while a drug-negative urine specimen or a specimen containing the target drug in a concentration less than the cut-off level of the assay will generate a line in the test line region.

To serve as a procedural control, a colored line will always appear at the control line region, indicating that proper volume of specimen has been added and membrane wicking has occurred.

I. Substantial Equivalence Information:

1. Predicate device name(s):
ACON OPI One Step Opiate
2. Predicate K number(s):
K011353
3. Comparison with predicate:

Both devices are for the qualitative determination of the same analyte(s) in the same matrix, and utilize the same cutoff concentration. Both are visually-read single use devices.

The difference between the new tests and the predicate is in the components of the mobile phase and capture reagents used in the new devices. The new devices employ a particle membrane immunoassay using the mouse anti-drug monoclonal antibody-colored particle complex embedded in the conjugate pad as part of the mobile phase and drug-protein conjugate strip on the membrane as the capture reagent; while the predicate device employs a particle membrane immunoassay using a drug-protein-colored particle complex embedded in the conjugated pad as part of the mobile phase and mouse anti-drug monoclonal antibody strip on the membrane as the capture reagent.

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

The sponsor did not reference any standards in their submission.

K. Test Principle:

The tests employ lateral flow immunochromatographic technology.

Drug in the sample and drug-labeled conjugate (containing a chromagen) compete for antibody binding sites in the test area of the test strip. Binding of drug in the sample causes the absence of a line at the test area, i.e., a positive result. When drug is not present in the sample, the drug-labeled conjugate binds at the test line, resulting in formation of a line, i.e., a negative result. The absence or presence of the line is determined visually by the operator.

The devices also have an internal process controls which indicate that adequate volume of sample has been added and that the immunochromatographic strip is intact.

The test strip and device contain monoclonal anti-morphine antibody-coupled particles and morphine-protein conjugates. A gold anti-rabbit antibody is employed in the control line system.

L. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

For ACON OPI II One Step Opiate Test Strip, A study was conducted at 3 physician's offices by untrained operators using 3 different lots of product to demonstrate the within run, between run and between operator precision. An identical panel of coded specimens were blind labeled and tested at each site. The results are given below:

Morphine conc (ng/mL)	n per site	Site A			Site B			Site C		
		-	+	Invalid	-	+	Invalid	-	+	Invalid
0	15	15	0	0	15	0	0	15	0	0
1,000	15	15	0	0	14	1	0	15	0	0
1,500	15	14	1	0	11	4	0	6	9	0
2,500	15	0	15	0	1	14	0	0	15	0
3,000	15	0	15	0	0	15	0	0	15	0
Invalid	15	0	0	15	0	0	15	0	0	15

For ACON OPI II One Step Opiate Test Device, a study was conducted at 3 physician's offices by untrained operators using 3 different lots of product to demonstrate the within run, between run and between operator precision. An identical panel of coded specimens were blind labeled and tested at each site. The results are given below:

Morphine conc (ng/mL)	n per site	Site A			Site B			Site C		
		-	+	Invalid	-	+	Invalid	-	+	Invalid
0	15	15	0	0	15	0	0	15	0	0
1,000	15	15	0	0	14	1	0	15	0	0
1,500	15	14	1	0	10	5	0	6	9	0
2,500	15	0	15	0	1	14	0	0	15	0
3,000	15	0	15	0	0	15	0	0	15	0
Invalid	15	0	0	15	0	0	15	0	0	15

b. Linearity/assay reportable range:

Not applicable. The assay is intended for qualitative use.

c. Traceability (controls, calibrators, or method):

Procedural controls are included in the test strip and device. A red line appearing in the control region (C) is considered as an internal procedural control. It confirms sufficient specimen volume, adequate membrane wicking and correct procedural technique.

Control standards are not supplied with these kits; however, it is recommended that positive and negative controls be tested as a good laboratory practice to confirm the test procedure and to verify proper test performance. Users should follow local, state, and federal guidelines for testing QC materials.

d. Cutoff Studies:

For ACON OPI II One Step Opiate Test Strip, a drug-free urine pool was spiked with Morphine at the following concentrations: 0 ng/mL, 1,000 ng/mL, 1,500 ng/mL, 2,000 ng/mL, 2,500 ng/mL, 3,000 ng/mL and 4,000 ng/mL. The result demonstrates >99% analytical accuracy at 50% above and 50% below the cut-off concentration. The data are summarized below:

Morphine Concentration (ng/mL)	Percent of Cutoff	n	Visual Result	
			Negative	Positive
0	0%	30	30	0
1,000	-50%	30	30	0
1,500	-25%	30	24	6
2,000	Cutoff	30	14	16
2,500	+25%	30	7	23
3,000	+50%	30	0	30
4,000	+100%	30	0	30

For ACON OPI II One Step Opiate Test Device, a drug-free urine pool was spiked with Morphine at the following concentrations: 0 ng/ml, 1,000 ng/ml, 1,500 ng/ml, 2,000 ng/ml, 2,500 ng/ml, 3,000 ng/ml and 4,000 ng/ml. The result demonstrates >99% analytical accuracy at 50% above and 50% below the cut-off concentration. The data are summarized below:

Morphine Concentration (ng/mL)	Percent of Cutoff	n	Visual Result	
			Negative	Positive
0	0%	30	30	0
1,000	-50%	30	30	0
1,500	-25%	30	26	4
2,000	Cutoff	30	13	17
2,500	+25%	30	5	25
3,000	+50%	30	0	30
4,000	+100%	30	0	30

e. Analytical specificity:

Opiate and its related compounds listed in the following table were spiked to 100 ug/mL concentration in drug free urine, then serial diluted and tested with the ACON OPI II One Step Opiate Test Strip and Test Device until the concentrations at which initial negative results were obtained. The following table lists compounds that are positively detected in urine by the ACON OPI II One Step Opiate Test Strip at 5 minutes.

Compound	Concentration (ng/mL)	% Cross Reactivity
Morphine	2,000	100%
Codeine	2,000	100%
Hydrocodone	100,000	2%
Levorphanol	100,000	2%
Morphine-3- β -Glucuronide	12,500	16%
Norcodeine	50,000	4%
Thebaine	100,000	2%
Nalorphine	100,000	2%
Hydromorphone	100,000	2%
6-Monoacetylmorphine	1,500	133%
Ethylmorphine	6,250	32%
Heroin (Diacetylmorphine)	20,000	10%

Effect of Urinary Specific Gravity

Fifteen (15) urine samples of normal, high, and low specific gravity ranges were spiked with 1,000 ng/ml and 3,000 ng/ml of Morphine respectively. The ACON OPI II One Step Opiate Test Strip was tested in duplicate using the fifteen neat and spiked urine samples. The results demonstrate that specific gravity ranges from 1.004 to 1.034 did not affect the expected results or accuracy of the test.

Effect of Urinary pH

The pH of an aliquoted negative urine pool was adjusted to a pH range of 5 to 9 in 1 pH unit increments; four of the five aliquots were spiked with Morphine. Final morphine concentrations in the aliquots were 0, 1,000, 3,000 and 4,000 ng/ml. The spiked, pH-adjusted urine was tested with the ACON OPI II One Step Opiate Test Strip in duplicate and interpreted according to the package insert. The results demonstrate that varying ranges of pH does not interfere with the performance of the test.

Cross-Reactivity

A study was conducted to determine the cross-reactivity of the test with compounds in either drug-free urine or morphine positive urine. The following compounds show no cross-reactivity when tested with the ACON OPI II One Step Opiate Test Strip at a concentration of 100 μ g/mL.

Non Cross-Reacting Compounds

4-Acetaminophenol	Fenoprofen	Trans-2-Phenyl-cyclopropylamine
Acetophenetidin	Furosemide	L-Phenylephrine
6-Acetylcodeine	Gentisic acid	β -Phenylethylamine
N-Acetylprocainamide	Hemoglobin	Phenylpropanolamine
Acetylsalicylic acid	Hydralazine	Prednisolone
Aminopyrine	Hydrochlorothiazide	

Amitriptyline	O-Hydroxyhippuric acid	Prednisone
Amobarbital	p-OH-Amphetamine	Procaine
Amoxicillin	p-OH-Methamphetamine	Promazine
Ampicillin	3-Hydroxytyramine	Promethazine
L-Ascorbic acid	Ibuprofen	DL-Propranolol
D-Amphetamine	Imipramine	D-Propoxyphene
DL-Amphetamine	Iproniazid	D-Pseudoephedrine
L-Amphetamine	(+/-)-Isoproterenol	Quinacrine
Apomorphine	Isoxsuprine	Quinidine
Aspartame	Ketamine	Quinine
Atropine	Ketoprofen	Ranitidine
Benzilic acid	Labetalol	Salicylic acid
Benzoic acid	Loperamide	Secobarbital
Benzphetamine	Maprotiline	Serotonin
Bilirubin	Meperidine	Sulfamethazine
(±)-Brompheniramine	Mephentermine	Sulindac
Buspirone	Meprobamate	Sustiva (efavirenz)
Caffeine	D-Methamphetamine	Temazepam
Cannabidiol	Methadone	Tetracycline
Cannabinol	Methoxyphenamine	Tetrahydrocortisone, 3-acetate
Chloralhydrate	Methylphenidate	Tetrahydrocortisone, 3-β-Glucuronide
Chloramphenicol	MDA*	Tetrahydrozoline
Chlordiazepoxide	MDMA**	Theophylline
Chlorothiazide	Nalidixic acid	Thiamine
(±)-Chlorpheniramine	Naloxone	Thioridazine
Chlorpromazine	Naltrexone	Tolbutamide
Chloroquine	Naproxen	Trazodone
Cholesterol	Niacinamide	DL-Tyrosine
Clomipramine	Nifedipine	Triamterene
Clonidine	Nimesulide	Trifluoperazine
Cortisone	Norethindrone	Trimethoprim
(-)-Cotinine	Normorphone	Trimipramine
Creatinine	D-Norpropoxyphene	Tryptamine
Deoxycorticosterone	Noscapine	DL-Tryptophan
Dextromethorphan	D,L-Octopamine	Tyramine
Diazepam	Oxalic acid	Uric acid
Diclofenac	Oxazepam	Verapamil
Dicyclomine	Oxolinic acid	Zomepirac
Diflunisal	Oxymetazoline	
Digoxin	Oxycodone	
Diphenhydramine	Oxymorphone	
5,5-Diphenylhydantoin	Papaverine	
Doxylamine	Penicillin-G	
(-)-Ψ-Ephedrine	Pentazocine HCl	
[1R, 2S]-(-)-Ephedrine	Pentobarbital	
L-Epinephrine	Perphenazine	
Erythromycin	Phencyclidine	
β-Estradiol	Phenelzine	
Estrone-3-sulfate	Phenobarbital	
Ethyl-p-aminobenzoate	Phentermine	
		*(+/-)3,4- Methylenedioxyamphetamine
		**(+/-)3,4- Methylenedioxymethamphetamine

f. Assay cut-off:

The ACON OPI II One Step Opiate Test Strip and Device yield a positive result when the opiates in urine exceed 2,000 ng/mL. At present, the recommended screening cutoff for opiates positive

specimens as set by the Substance Abuse and Mental Health Services Administration (SAMHSA) is 2,000 ng/mL. Characterization of how the device performs analytically around the claimed cutoff concentration appears in the detection limit section, above.

2. Comparison studies:

a. *Method comparison with predicate device:*

A side-by-side comparison was conducted using the ACON OPI II One Step Opiate Test Strip/Device and a commercially available OPI rapid test. Testing was performed on specimens previously collected from subjects presenting for Drug Screen Testing. Presumptive positive results were confirmed by GC/MS, and on samples diluted with negative urine to challenge the cutoff. A total of 116 pre-screened positive samples, 18 diluted positive samples near the cutoff, and 168 pre-screened negative samples were used. The following results were tabulated:

Method		Other OPI Rapid Test		Total Results
ACON OPI II One Step Test Strip	Results	Positive	Negative	
	Positive	131	0	131
	Negative	1	168	169
Total Results		132	168	300
% Agreement with this commercial kit		99%	>99%	>99%

When compared to GC/MS at the cut-off of 2,000 ng/mL, the following results were tabulated:

Method	Specimen Cutoff Range by GC/MS Data				
	Result	<-25% Cutoff	-25% to Cutoff	Cutoff to +25%	>+25% Cutoff
ACON OPI II Test Strip	Positive	0	2	20	109
	Negative	0	14	3	2

A side-by-side comparison was conducted using the ACON OPI II One Step Opiate Test Device and a leading commercially available OPI rapid test. Testing was performed on specimens previously collected from subjects presenting for Drug Screen Testing. Presumptive positive results were confirmed by GC/MS. A total of 116 pre-screened positive samples, 18 diluted positive samples near the cutoff, and 168 pre-screened negative samples were used. The following results were tabulated:

Method		Other OPI Rapid Test		Total Results
Results		Positive	Negative	
ACON OPI II One Step Test Device	Positive	131	0	131
	Negative	1	168	169
Total Results		132	168	300
% Agreement with this commercial kit		99%	>99%	>99%

When compared to GC/MS at the cut-off of 2,000 ng/mL, the following results were tabulated:

Method	Specimen Cutoff Range by GC/MS Data				
	Result	<-25% Cutoff	-25% to Cutoff	Cutoff to +25%	>+25% Cutoff
ACON OPI II Test Device	Positive	0	2	20	109
	Negative	0	14	3	2

b. Matrix comparison:

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

3. Clinical studies:

a. Clinical sensitivity:

Not applicable. Clinical studies are not typically submitted for this device type.

b. Clinical specificity:

Not applicable. Clinical studies are not typically submitted for this device type.

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.

M. Conclusion:

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