



Food and Drug Administration  
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Silver Spring, MD 20993-0002

W.H.P.M., INC.  
C/O JOE SHIA  
MANAGER  
504 E DIAMOND AVE., SUITE I  
GAITHERSBURG MD 20877

June 29, 2015

Re: K151441  
Trade/Device Name: First Sign® Drug Of Abuse Cup Test,  
First Sign® Drug Of Abuse Dip Card Test  
Regulation Number: 21 CFR 862.3620  
Regulation Name: Methadone test system  
Regulatory Class: II  
Product Code: DJR, LCM, DJG  
Dated: May 22, 2015  
Received: May 29, 2015

Dear Joe Shia:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address <http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm>. Also, please note the regulation entitled, “Misbranding by reference to premarket notification” (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to <http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm> for the CDRH’s Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address <http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm>.

Sincerely yours,

  
**Katherine Serrano -S**

For : Courtney H. Lias, Ph.D.  
Director  
Division of Chemistry and Toxicology Devices  
Office of In Vitro Diagnostics  
and Radiological Health  
Center for Devices and Radiological Health

Enclosure

## Indications for Use

510(k) Number (if known)  
k151441

Device Name

First Sign® Drug of Abuse Cup Test  
First Sign® Drug of Abuse Dip Card Test

Indications for Use (Describe)

First Sign™ Drug of Abuse Tests are immunochromatographic assays for the qualitative determination of Methadone, Phencyclidine, and Oxycodone in human urine at cut-off concentrations of 300 ng/mL, 25 ng/mL, and 100 ng/mL, respectively. The tests are available in a Cup format and a Dip Card format.

The tests may yield preliminary positive results even when prescription drugs Methadone and Oxycodone are ingested, at prescribed doses; it is not intended to distinguish between prescription use or abuse of this drug. There are no uniformly recognized cutoff concentration levels for Methadone and Oxycodone in urine. The tests provide only preliminary test results. A more specific alternative chemical method must be used in order to obtain a confirmed analytical result. Gas Chromatography/Mass Spectrometry 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. The tests are intended for over-the-counter and for prescription use.

Type of Use (Select one or both, as applicable)

Prescription Use (Part 21 CFR 801 Subpart D)

Over-The-Counter Use (21 CFR 801 Subpart C)

### CONTINUE ON A SEPARATE PAGE IF NEEDED.

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510(k) SUMMARY

k151441

1. Date: June 26, 2015
2. Submitter: W.H.P.M., Inc.  
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4. Device Name: First Sign<sup>®</sup> Drug of Abuse Cup Test  
First Sign<sup>®</sup> Drug of Abuse Dip Card Test

Product Code	Class	CFR #	Panel
DJR	Class II	21 CFR, 862.3620 Methadone Test System	Toxicology
LCM	Unclassified	Phencyclidine	Toxicology
DJG	Class II	21 CFR, 862.3650 Opiate Test System	Toxicology

5. Predicate Devices:

K052115

First Check Multi Drug Cup 12

6. Intended Use

First Sign<sup>™</sup> Drug of Abuse Tests are immunochromatographic assays for the qualitative determination of Methadone, Phencyclidine, and Oxycodone in human urine at cut-off concentrations of 300 ng/mL, 25 ng/mL, and 100 ng/mL, respectively. The tests are available in a Cup format and a Dip Card format.

The tests may yield preliminary positive results even when prescription drugs Methadone and Oxycodone are ingested, at prescribed doses; it is not intended to distinguish between prescription use or abuse of this drug. There are no uniformly recognized cutoff concentration levels for Methadone and Oxycodone in urine. The tests provide only preliminary test results. A more specific alternative chemical method must be used in order to obtain a confirmed analytical result. Gas Chromatography/Mass Spectrometry 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. The tests are intended for over-the-counter and for prescription use.

7. Device Description

First Sign™ Drug of Abuse Tests are immunochromatographic assays. Each assay test is a lateral flow system for the qualitative detection of Methadone, Phencyclidine, and Oxycodone in human urine. The products are single-use in vitro diagnostic devices, which come in the formats of DipCards or Cups. Each test kit contains a Test Device (in one of the two formats), a package insert and a urine cup for sample collection. Each test device is sealed with a desiccant in an aluminum pouch.

8. Substantial Equivalence Information

A summary comparison of features of the First Sign™ Drug of Abuse Test and the predicate device is provided in Table 1, Table 2 & Table 3.

**Table 1: Features Comparison of First Sign™ Methadone Test and the Predicate Device**

<b>Item</b>	<b>Device</b>	<b>Predicate - K052115</b>
<b>Indication(s) for Use</b>	For the qualitative determination of Methadone in human urine.	Same
<b>Calibrator</b>	Methadone	Same
<b>Methodology</b>	Competitive binding, lateral flow immunochromatographic assays based on the principle of antigen antibody immunochemistry.	Same
<b>Specimen Type</b>	Human Urine	Same
<b>Cut-Off Values</b>	300 ng/mL	Same
<b>Intended Population</b>	For over-the-counter and prescription uses.	For over-the-counter use.
<b>Configurations</b>	Cup, Dip Card	Cup

**Table 2: Features Comparison of First Sign™ Phencyclidine Test and the Predicate Device**

<b>Item</b>	<b>Device</b>	<b>Predicate - K052115</b>
<b>Indication(s) for Use</b>	For the qualitative determination of Phencyclidine in human urine.	Same
<b>Calibrator</b>	Phencyclidine	Same
<b>Methodology</b>	Competitive binding, lateral flow	Same

Item	Device	Predicate - K052115
	immunochemical assays based on the principle of antigen antibody immunochemistry.	
<b>Specimen Type</b>	Human Urine	Same
<b>Cut-Off Values</b>	25 ng/mL	Same
<b>Intended Population</b>	For over-the-counter and prescription uses.	For over-the-counter use.
<b>Configurations</b>	Cup, Dip Card	Cup

**Table 3: Features Comparison of First Sign™ Oxycodone Test and the Predicate Device**

Item	Device	Predicate - K052115
<b>Indication(s) for Use</b>	For the qualitative determination of Oxycodone in human urine.	Same
<b>Calibrator</b>	Oxycodone	Same
<b>Methodology</b>	Competitive binding, lateral flow immunochemical assays based on the principle of antigen antibody immunochemistry.	Same
<b>Specimen Type</b>	Human Urine	Same
<b>Cut-Off Values</b>	100 ng/mL	Same
<b>Intended Population</b>	For over-the-counter and prescription uses.	For over-the-counter use.
<b>Configurations</b>	Cup, Dip Card	Cup

#### 9. Test Principle

First Sign™ Drug of Abuse Tests are rapid tests for the qualitative detection of Methadone, Phencyclidine, and Oxycodone in urine samples. Each assay test is a lateral flow chromatographic immunoassay. During testing, a urine specimen migrates upward by capillary action. If target drugs are present in the urine specimen below its cut-off concentration, it will not saturate the binding sites of its specific antibody (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.

10. Performance Characteristics

1. Analytical Performance

a. Precision

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. These samples were prepared by spiking drug in negative samples. Each drug concentration was confirmed by GC/MS. All sample aliquots were blind-labeled and randomized by the person who prepared samples and did not take part in the sample testing. For each concentration, tests were performed two runs per day for 25 days by three different operators for each format of devices. Different set of operators tested each format. The results obtained are summarized in the following tables:

**Methadone Dip Card Format**

Result Drug	-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	50-/0+	50-/0+	50-/0+	50-/0+	3-/47+	50+/0-	50+/0-	50+/0-	50+/0-
Lot 2	50-/0+	50-/0+	50-/0+	50-/0+	3-/47+	50+/0-	50+/0-	50+/0-	50+/0-
Lot 3	50-/0+	50-/0+	50-/0+	50-/0+	1-/49+	50+/0-	50+/0-	50+/0-	50+/0-

**Methadone Cup Format**

Result Drug	-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 4	50-/0+	50-/0+	50-/0+	50-/0+	3-/47+	50+/0-	50+/0-	50+/0-	50+/0-
Lot 5	50-/0+	50-/0+	50-/0+	50-/0+	3-/47+	50+/0-	50+/0-	50+/0-	50+/0-
Lot 6	50-/0+	50-/0+	50-/0+	50-/0+	3-/47+	50+/0-	50+/0-	50+/0-	50+/0-

**Phencyclidine Dip Card Format**

Result Drug	-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	50-/0+	50-/0+	50-/0+	50-/0+	3-/47+	50+/0-	50+/0-	50+/0-	50+/0-
Lot 2	50-/0+	50-/0+	50-/0+	50-/0+	2-/48+	50+/0-	50+/0-	50+/0-	50+/0-
Lot 3	50-/0+	50-/0+	50-/0+	50-/0+	2-/48+	50+/0-	50+/0-	50+/0-	50+/0-

**Phencyclidine Cup Format**

Result Drug	-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 4	50-/0+	50-/0+	50-/0+	50-/0+	3-/47+	50+/0-	50+/0-	50+/0-	50+/0-
Lot 5	50-/0+	50-/0+	50-/0+	50-/0+	3-/47+	50+/0-	50+/0-	50+/0-	50+/0-
Lot 6	50-/0+	50-/0+	50-/0+	50-/0+	3-/47+	50+/0-	50+/0-	50+/0-	50+/0-

### Oxycodone Dip Card Format

Result Drug	-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	50-/0+	50-/0+	50-/0+	50-/0+	4-/46+	50+/0-	50+/0-	50+/0-	50+/0-
Lot 2	50-/0+	50-/0+	50-/0+	50-/0+	3-/47+	50+/0-	50+/0-	50+/0-	50+/0-
Lot 3	50-/0+	50-/0+	50-/0+	50-/0+	3-/47+	50+/0-	50+/0-	50+/0-	50+/0-

### Oxycodone Cup Format

Result Drug	-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 4	50-/0+	50-/0+	50-/0+	50-/0+	3-/47+	50+/0-	50+/0-	50+/0-	50+/0-
Lot 5	50-/0+	50-/0+	50-/0+	50-/0+	3-/47+	50+/0-	50+/0-	50+/0-	50+/0-
Lot 6	50-/0+	50-/0+	50-/0+	50-/0+	2-/48+	50+/0-	50+/0-	50+/0-	50+/0-

b. Linearity

Not applicable.

c. Stability

The devices are stable at 4-30°C (39-86°F) for 24 months based on the accelerated stability study at 50°C. Control materials are not provided with the device. The labeling provides information on how to obtain control materials.

d. Cut-off

A total of 150 samples equally distributed at concentrations of -50% cut-off; -25% cut-off; cut-off; +25% cut-off; +50% cut-off were tested using three different lots of each device by three different operators. Results were all positive at and above +25% cut-off and all negative at and below -25% cut-off for Methadone, Phencyclidine and Oxycodone. The following cut-off values for the test devices have been verified.

Test	Calibrator	Cut-off (ng/mL)
First Sign™ Methadone Test	Methadone	300
First Sign™ Phencyclidine Test	Phencyclidine	25
First Sign™ Oxycodone Test	Oxycodone	100

e. Interference

Potential interfering substances found in human urine of physiological or pathological conditions were added to drug-free urine and to urine containing target drugs at 25% below and 25% above cut-off levels. These urine samples were tested using three batches of each device for all formats.

Compounds that showed no interference at a concentration of 100µg/mL are summarized in the following tables. There were no differences observed for different formats.

### **Methadone**

Aminopyrine	Ethyl-p-aminobenzoate	Papaverine
Amitriptyline	Fenoprofen	Penicillin-G
Amobarbital	Furosemide	Pentazocine hydrochloride
Amoxicillin	Gentisic acid	Pentobarbital
Ampicillin	Hemoglobin	Perphenazine
L-Ascorbic acid	Hydralazine	Phencyclidine
DL-Amphetamine sulfate	Hydrochlorothiazide	Phenelzine
Apomorphine	Hydrocodone	Phenobarbital
Aspartame	Hydrocortisone	Phentermine
Atropine	O-Hydroxyhippuric acid	L-Phenylephrine
Benzilic acid	p-Hydroxyamphetamine	β-Phenylethylamine
Benzoic acid	p-Hydroxymethamphetamine	Phenylpropanolamine
Benzoyllecgonine	3-Hydroxytyramine	Prednisolone
Benzphetamine	Ibuprofen	Prednisone
Bilirubin	Imipramine	Procaine
Caffeine	Iproniazid	Promazine
Cannabidiol	(±) - Isoproterenol	Promethazine
Cannabinol	Isoxsuprine	DL-Propranolol
Chloralhydrate	Ketamine	D-Propoxyphene
Chloramphenicol	Ketoprofen	D-Pseudoephedrine
Chlorothiazide	Labetalol	Quinacrine
Chlorpromazine	Levorphanol	Quinidine
Chlorquine	Loperamide	Quinine
Cholesterol	Maprotiline	Ranitidine
Clomipramine	Meperidine	Salicylic acid
Clonidine	Meprobamate	Secobarbital
Cocaethylene	Methamphetamine	Serotonin
Temazepam	Methoxyphenamine	Sulfamethazine
Cocaine hydrochloride	(±)-3,4-Methylenedioxy-amphetamine hydrochloride	Sulindac
Codeine	(±)-3,4-Methylenedioxy-methamphetamine hydrochloride	Tetracycline
Cortisone	Morphine-3-β-D glucuronide	Tetrahydrocortisone 3- (β-D-glucuronide)
(-) Cotinine	Morphine Sulfate	Tetrahydrozoline
Creatinine	Nalidixic acid	Thebaine

Deoxycorticosterone	Naloxone	Thiamine
Dextromethorphan	Naltrexone	Thioridazine
Diazepam	Naproxen	DL-Tyrosine
Diclofenac	Niacinamide	Tolbutamide
Diflunisal	Nifedipine	Triamterene
Digoxin	Norcodein	Trifluoperazine
Diphenhydramine	Norethindrone	Trimethoprim
Ecgonine hydrochloride	D-Norpropoxyphene	Trimipramine
Ecgonine methyl ester	Noscapine	Tryptamine
(-) - $\Psi$ -Ephedrine	DL-Octopamine	DL-Tryptophan
[1R,2S] (-) Ephedrine	Oxalic acid	Tyramine
(L) - Epinephrine	Oxazepam	Uric acid
Erythromycin	Oxolinic acid	Verapamil
$\beta$ -Estradiol	Oxycodone	Zomepirac
Estrone-3-sulfate	Oxymetazoline	

### Phencyclidine

Acetaminophen	(-) Y Ephedrine	Oxycodone
Acetophenetidin	Erythromycin	Oxymetazoline
N-Acetylprocainamide	$\beta$ -Estradiol	Papaverine
Acetylsalicylic acid	Estrone-3-sulfate	Penicillin-G
Aminopyrine	Ethyl-p-aminobenzoate	Pentazocine hydrochloride
Amitriptyline	Fenoprofen	Pentobarbital
Amobarbital	Furosemide	Perphenazine
Amoxicillin	Gentisic acid	Phenelzine
Ampicillin	Hemoglobin	Phenobarbital
Ascorbic acid	Hydralazine	Phentermine
D,L-Amphetamine	Hydrochlorothiazide	L-Phenylephrine
Apomorphine acid	Hydrocodone	$\beta$ -Phenylethylamine
Aspartame	Hydrocortisone	Phenylpropanolamine
Atropine	O-Hydroxyhippuric	Prednisolone
Benzilic acid	p-Hydroxymethamphetamine	Prednisone
Benzoic acid	3-Hydroxytyramine	Procaine
Benzoylecgonine	Ibuprofen	Promazine
Benzphetamine	Imipramine	Promethazine
Bilirubin	Iproniazid	D,L-Propranolol
Brompheniramine	( $\pm$ ) - Isoproterenol	D-Propoxyphene
Caffeine	Isoxsuprine	D-Pseudoephedrine
Cannabidiol	Ketamine	Quinidine
Cannabinol	Ketoprofen	Quinine

Chloralhydrate	Labetalol	Ranitidine
Chloramphenicol	Loperamide	Salicylic acid
Chlordiazepoxide	Maprotiline	Secobarbital
Chlorothiazide	Meperidine	Serotonin (5-Hydroxytyramine)
(±) Chlorpheniramine	Meprobamate	Sulfamethazine
Chlorpromazine	Methadone	Sulindac
Chlorquine	Methoxyphenamine	Temazepam
Cholesterol	(+) 3,4-Methylenedioxy-amphetamine	Tetracycline
Clomipramine	(+)3,4-Methylenedioxy-methamphetamine	Tetrahydrocortisone3 (β-D glucuronide)
Clonidine	Morphine-3-β-D glucuronide	Tetrahydrozoline
Cocaine hydrochloride	Morphine Sulfate	Thiamine
Codeine	Nalidixic acid	Thioridazine
Cortisone	Naloxone	D, L-Tyrosine
(-) Cotinine	Naltrexone	Tolbutamide
Creatinine	Naproxen	Triamterene
Deoxycorticosterone	Niacinamide	Trifluoperazine
Dextromethorphan	Nifedipine	Trimethoprim
Diazepam	Norcodein	Trimipramine
Diclofenac	Norethindrone	Tryptamine
Diflunisal	D-Norpropoxyphene	D, L-Tryptophan
Digoxin	Noscapine	Tyramine
Diphenhydramine	D,L-Octopamine	Uric acid
Doxylamine	Oxalic acid	Verapamil
Ecgonine hydrochloride	Oxazepam	Zomepirac
Ecgonine methylester	Oxolinic acid	

### **Oxycodone**

Acetophenetidin	Ethyl-p-aminobenzoate	Papaverine
Acetylsalicylic acid	β-Estradiol	Penicillin-G
Aminopyrine	Estrone-3-sulfate	Perphenazine
Amoxicillin	Erythromycin	Phenelzine
Ampicillin	Fenopropfen	L-Phenylephrine
Apomorphine	Furosemide	β-Phenylethylamine
Aspartame	Gentisic acid	Phenylpropanolamine
Atropine	Hemoglobin	Prednisone
Benzilic acid	Hydralazine	Loperamide

Benzoic acid	Hydrochlorothiazide	Quinine
Benzphetamine	Hydrocortisone	Quinidine
Bilirubin	O-Hydroxyhippuric acid	Ranitidine
Deoxycorticosterone	3-Hydroxytyramine	Salicylic acid
Caffeine	Labetalol	Serotonin
Chloralhydrate	D, L-Isoproterenol	Sulfamethazine
Chloramphenicol	Meprobamate	Sulindac
Chlorothiazide	Methoxyphenamine	Tetracycline
D,L-Chlorpheniramine	Nalidixic acid	Tetrahydrocortisone
Chlorpromazine	Naloxone	Morphine-3-β-D-glucuronide
Chlorquine	Naltrexone	Tetrahydrozoline
Cholesterol	Naproxen	Thiamine
Clonidine	Niacinamide	Thioridazine
L-Cotinine	Nifedipine	D,L-Tyrosine
Cortisone	Isoxsuprine	Tolbutamide
Creatinine	D,L-Propranolol	Triamterene
D-Pseudoephedrine	Ketoprofen	Trifluoperazine
Dextromethorphan	Norethindrone	Trimethoprim
Diclofenac	D-Norpropoxyphene	Tyramine
Diflunisal	Noscapine	D,L-Tryptophan
Digoxin	D,L-Octopamine	Urine acid
Diphenhydramine	Oxalic acid	Verapamil
L-Ephedrine	Oxolinic acid	Zomepirac
Ecgonine methylester	Oxymetazoline	

f. Specificity

To test the specificity, drug metabolites and other components that are likely to interfere in urine samples were tested using three batches of each device for all formats. The obtained lowest detectable concentration was used to calculate the cross-reactivity. There were no differences observed for different formats.

<b>Methadone Cut-off=300 ng/mL</b>	<b>Result</b>	<b>% Cross-Reactivity</b>
Methadone	Positive at 300 ng/mL	100%
LAAM	Positive at 10000	3%
Alpha Methadol	Negative at 100000	Not Detected

Doxylamine	Negative at 100000	Not Detected
EMDP	Negative at 100000	Not Detected
EDDP	Negative at 100000	Not Detected

<b>Phencyclidine Cut-off=25 ng/mL)</b>	<b>Result</b>	<b>% Cross- Reactivity</b>
Phencyclidine	Positive at 25 ng/mL	100%
4-Hydroxyphencyclidine	Positive at 250 ng/mL	10%
Phencyclidine Morpholine	Positive at 625 ng/mL	4%

<b>Oxycodone Cut-off=100 ng/mL</b>	<b>Result</b>	<b>% Cross- Reactivity</b>
Oxycodone	Positive at 100 ng/mL	100%
Dihydrocodeine	Positive at 50000 ng/mL	0.2%
Hydrocodone	Positive at 10000 ng/mL	1%
Heroin	Negative at 100000	Not Detected
Morphine-3-b-glucuronide	Negative at 100000	Not Detected
Codeine	Negative at 100000	Not Detected
Hydromorphone	Negative at 100000	Not Detected
Morphine	Negative at 100000	Not Detected
Acetylmorphine	Negative at 100000	Not Detected
Buprenorphine	Negative at 100000	Not Detected
Ethylmorphine	Negative at 100000	Not Detected

g. Effect of Urine Specific Gravity and Urine pH

To investigate the effect of urine specific gravity and urine pH, urine samples with a range of 1.000 to 1.035 specific gravity or urine samples with a range of pH 4 to 9 were spiked with target drugs at 25% below and 25% above cut-off levels. These samples were tested using three batches of each device for all formats. Results were all positive for samples at and above +25% Cut-Off and all negative for samples at and below -25% Cut-Off. There were no differences observed for different formats.

2. Comparison Studies

The method comparison studies for the First Sign™ Drug Tests (Cup and Dip Card) for Methadone, Phencyclidine, and Oxycodone were performed in-house with three different laboratory assistants for each format of the device. Operators ran 80 (40 negative and 40 positive) unaltered clinical

samples for each drug. The samples were blind labeled and compared to GC/MS results. The results are presented in the tables below:

**Methadone**

Dip Card format		Negative	Low Negative by GC/MS (less than - 50%)	Near Cutoff Negative by GC/MS (Between - 50% and cut-off)	Near Cutoff Positive by GC/MS (Between the cut-off and +50%)	High Positive by GC/MS (greater than +50%)
Viewer A	Positive	0	0	0	12	26
	Negative	10	10	20	2	0
Viewer B	Positive	0	0	1	13	26
	Negative	10	10	19	1	0
Viewer C	Positive	0	0	1	13	26
	Negative	10	10	19	1	0

**Discordant Results of Methadone Dip Card**

Viewer	Sample Number	GC/MS Result	Dipcard Format Viewer Results
Viewer A	83001724	325	Negative
Viewer A	83001691	337	Negative
Viewer B	94639074	353	Negative
Viewer B	83001695	274	Positive
Viewer C	83002140	366	Negative
Viewer C	83002176	289	Positive

Cup format		Negative	Low Negative by GC/MS (less than - 50%)	Near Cutoff Negative by GC/MS (Between - 50% and cut-off)	Near Cutoff Positive by GC/MS (Between the cut-off and +50%)	High Positive by GC/MS (greater than +50%)
Viewer A	Positive	0	0	1	13	26
	Negative	10	10	19	1	0
Viewer B	Positive	0	0	1	13	26
	Negative	10	10	19	1	0
Viewer C	Positive	0	0	1	12	26
	Negative	10	10	19	2	0

**Discordant Results of Methadone Cup**

<b>Viewer</b>	<b>Sample Number</b>	<b>GC/MS Result</b>	<b>Cup Format Viewer Results</b>
<b>Viewer A</b>	83001695	274	Positive
<b>Viewer A</b>	83001691	337	Negative
<b>Viewer B</b>	83002176	289	Positive
<b>Viewer B</b>	83001707	331	Negative
<b>Viewer C</b>	83002164	242	Positive
<b>Viewer C</b>	83001724	325	Negative
<b>Viewer C</b>	94639074	353	Negative

### Phencyclidine

Dip Card format		Negative	Low Negative by GC/MS (less than - 50%)	Near Cutoff Negative by GC/MS (Between - 50% and cut-off)	Near Cutoff Positive by GC/MS (Between the cut-off and +50%)	High Positive by GC/MS (greater than +50%)
Viewer A	Positive	0	0	1	13	26
	Negative	10	10	19	1	0
Viewer B	Positive	0	0	1	13	26
	Negative	10	10	19	1	0
Viewer C	Positive	0	0	0	12	26
	Negative	10	10	20	2	0

### Discordant Results of Phencyclidine DipCard

<b>Viewer</b>	<b>Sample Number</b>	<b>GC/MS Result</b>	<b>DipCard Format Viewer Results</b>
<b>Viewer A</b>	83002015	20.6	Positive
<b>Viewer A</b>	83002085	27.9	Negative
<b>Viewer B</b>	83001968	21.4	Positive
<b>Viewer B</b>	83002029	28.3	Negative
<b>Viewer C</b>	83002085	27.9	Negative
<b>Viewer C</b>	83002062	28.7	Negative

Cup format		Negative	Low Negative by GC/MS (less than - 50%)	Near Cutoff Negative by GC/MS (Between - 50% and cut-off)	Near Cutoff Positive by GC/MS	High Positive by GC/MS (greater than +50%)
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					(Between the cut-off and +50%)	
Viewer A	Positive	0	0	2	13	26
	Negative	10	10	18	1	0
Viewer B	Positive	0	0	0	12	26
	Negative	10	10	20	2	0
Viewer C	Positive	0	0	0	13	26
	Negative	10	10	20	1	0

**Discordant Results of Phencyclidine Cup**

Viewer	Sample Number	GC/MS Result	Cup Format Viewer Results
<b>Viewer A</b>	83002015	20.6	Positive
<b>Viewer A</b>	83001780	21.3	Positive
<b>Viewer A</b>	83002077	29.3	Negative
<b>Viewer B</b>	83002085	27.9	Negative
<b>Viewer B</b>	83002029	28.3	Negative
<b>Viewer C</b>	83001978	27.7	Negative

**Oxycodone**

DipCard format		Negative	Low Negative by GC/MS (less than - 50%)	Near Cutoff Negative by GC/MS (Between - 50% and cut-off)	Near Cutoff Positive by GC/MS (Between the cut-off and +50%)	High Positive by GC/MS (greater than +50%)
Viewer A	Positive	0	0	2	13	26
	Negative	10	10	18	1	0
Viewer B	Positive	0	0	0	12	26
	Negative	10	10	20	2	0
Viewer C	Positive	0	0	1	13	26
	Negative	10	10	19	1	0

**Discordant Results of Oxycodone DipCard**

Viewer	Sample Number	GC/MS Result	DipCard Format Viewer Results
<b>Viewer A</b>	83002095	89	Positive
<b>Viewer A</b>	83002040	99	Positive

<b>Viewer A</b>	83001639	120	Negative
<b>Viewer B</b>	83001639	120	Negative
<b>Viewer B</b>	83002092	116	Negative
<b>Viewer C</b>	94639011	85	Positive
<b>Viewer C</b>	83002092	116	Negative

Cup format		Negative	Low Negative by GC/MS (less than - 50%)	Near Cutoff Negative by GC/MS (Between - 50% and cut-off)	Near Cutoff Positive by GC/MS (Between the cut-off and +50%)	High Positive by GC/MS (greater than +50%)
Viewer A	Positive	0	0	1	12	26
	Negative	10	10	19	2	0
Viewer B	Positive	0	0	2	13	26
	Negative	10	10	18	1	0
Viewer C	Positive	0	0	0	12	26
	Negative	10	10	20	2	0

#### Discordant Results of Oxycodone Cup

Viewer	Sample Number	GC/MS Result	Cup Format Viewer Results
<b>Viewer A</b>	83002095	89	Positive
<b>Viewer A</b>	83001639	120	Negative
<b>Viewer A</b>	83002092	116	Negative
<b>Viewer B</b>	83002096	85	Positive
<b>Viewer B</b>	83002040	99	Positive
<b>Viewer B</b>	83001638	117	Negative
<b>Viewer C</b>	83001639	120	Negative
<b>Viewer C</b>	83001638	117	Negative

#### Lay-user study

A lay user study was performed at three intended user sites with 280 lay persons testing the Methadone devices, 280 lay persons testing the Phencyclidine devices and 280 lay persons testing the Oxycodone devices. A total of 136 females and 144 males tested the Methadone samples, 141 females and 139 males tested Phencyclidine samples, and 141 females and 139 males tested the Oxycodone 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; negative, +/- 75%, +/-50%, +/-25% of the cutoff by spiking drugs into drug free-pooled urine specimens. The concentrations of the samples were confirmed by GC/MS. Each sample was aliquoted into

individual containers and blind-labeled. Each participant was provided with the package insert, 1 blind labeled sample and a device. The results are summarized below.

**Comparison between GC/MS and Lay Person Results (Methadone DipCard)**

% of Cutoff	Number of samples	Methadone Concentration by GC/MS (ng/mL)	Lay person results		The percentage of correct results (%)
			No. of Positive	No. of Negative	
-100% Cutoff	20	0	0	20	100%
-75% Cutoff	20	74	0	20	100%
-50% Cutoff	20	148	0	20	100%
-25% Cutoff	20	222	2	18	90%
+25% Cutoff	20	378	19	1	95%
+50% Cutoff	20	452	20	0	100%
+75% Cutoff	20	530	20	0	100%

**Comparison between GC/MS and Lay Person Results (Methadone Cup)**

% of Cutoff	Number of samples	Methadone Concentration by GC/MS (ng/mL)	Lay person results		The percentage of correct results (%)
			No. of Positive	No. of Negative	
-100% Cutoff	20	0	0	20	100%
-75% Cutoff	20	74	0	20	100%
-50% Cutoff	20	148	0	20	100%
-25% Cutoff	20	222	1	19	95%
+25% Cutoff	20	378	19	1	95%
+50% Cutoff	20	452	20	0	100%
+75% Cutoff	20	530	20	0	100%

**Comparison between GC/MS and Lay Person Results (Phencyclidine DipCard)**

% of Cutoff	Number of samples	Phencyclidine Concentration by GC/MS (ng/mL)	Lay person results		The percentage of correct results (%)
			No. of Positive	No. of Negative	
-100% Cutoff	20	0	0	20	100%
-75% Cutoff	20	6	0	20	100%
-50% Cutoff	20	12.2	0	20	100%
-25% Cutoff	20	19	0	20	100%
+25% Cutoff	20	31.3	19	1	95%
+50% Cutoff	20	37	20	0	100%
+75% Cutoff	20	44	20	0	100%

**Comparison between GC/MS and Lay Person Results (Phencyclidine Cup)**

% of Cutoff	Number of samples	Phencyclidine Concentration by GC/MS (ng/mL)	Lay person results		The percentage of correct results (%)
			No. of Positive	No. of Negative	
<b>-100% Cutoff</b>	20	0	0	20	100%
<b>-75% Cutoff</b>	20	6	0	20	100%
<b>-50% Cutoff</b>	20	12.2	0	20	100%
<b>-25% Cutoff</b>	20	19	0	20	100%
<b>+25% Cutoff</b>	20	31.3	18	2	90%
<b>+50% Cutoff</b>	20	37	20	0	100%
<b>+75% Cutoff</b>	20	44	20	0	100%

**Comparison between GC/MS and Lay Person Results (Oxycodone DipCard)**

% of Cutoff	Number of samples	Oxycodone Concentration by GC/MS (ng/mL)	Lay person results		The percentage of correct results (%)
			No. of Positive	No. of Negative	
<b>-100% Cutoff</b>	20	0	0	20	100%
<b>-75% Cutoff</b>	20	24	0	20	100%
<b>-50% Cutoff</b>	20	49	0	20	100%
<b>-25% Cutoff</b>	20	74	1	19	95%
<b>+25% Cutoff</b>	20	124	19	1	95%
<b>+50% Cutoff</b>	20	148	20	0	100%
<b>+75% Cutoff</b>	20	173	20	0	100%

**Comparison between GC/MS and Lay Person Results (Oxycodone Cup)**

% of Cutoff	Number of samples	Oxycodone Concentration by GC/MS (ng/mL)	Lay person results		The percentage of correct results (%)
			No. of Positive	No. of Negative	
<b>-100% Cutoff</b>	20	0	0	20	100%
<b>-75% Cutoff</b>	20	24	0	20	100%
<b>-50% Cutoff</b>	20	49	0	20	100%
<b>-25% Cutoff</b>	20	74	1	19	95%
<b>+25% Cutoff</b>	20	124	19	1	95%
<b>+50% Cutoff</b>	20	148	20	0	100%
<b>+75% Cutoff</b>	20	173	20	0	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 each package insert and the scores revealed a reading Grade Level of 7.

### 3. Clinical Studies

Not applicable.

### 11. Conclusion

Based on the test principle and acceptable performance characteristics including precision, cut-off, interference, specificity and method comparison of the devices, it's concluded that the First Sign™ Drug of Abuse Dip Card Test and First Sign™ Drug of Abuse Cup Test are substantially equivalent to the predicate.