DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

W.H.P.M., INC.
JOHN WAN
5358 IRWINDALE AVENUE
IRWINDALE CA 91706

February 26, 2015

Re: K150162
Trade/Device Name: First Sign® Drug Of Abuse Cup Test
First Sign® Drug Of Abuse Dip Card Test
Regulation Number: 21 CFR 862.3610
Regulation Name: Methamphetamine test system
Regulatory Class: II
Product Code: LAF, JXM, DJG
Dated: January 19, 2015
Received: January 26, 2015

Dear Mr. John Wan:

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 -A

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

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
k150162

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 Oxazepam , Methamphetamine , and Morphine in human urine at cut-off concentrations of 300 ng/mL, 1000 ng/mL, and 2000 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 drug Oxazepam is ingested, at prescribed doses; it is not intended to distinguish between prescription use or abuse of this drug. There is no uniformly recognized cutoff concentration level for oxazepam 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
k150162

1. Date: February 24, 2015

2. Submitter W.H.P.M., Inc.
5358 Irwindale Ave.
Irwindale, CA 91706

3. Contact person: John Wan
W.H.P.M., Inc.
5358 Irwindale Ave.
Irwindale, CA 91706
Telephone: 626-443-8480
Fax: 626-443-8065
Email: johnwan@whpm.com

4. Device Name: First Sign® Drug of Abuse Cup Test
First Sign® Drug of Abuse Dip Card Test

Classification: Class II

Product Code	**CFR #**	**Panel**
LAF	21 CFR, 862.3610 Methamphetamine Test System	Toxicology
JXM	21 CFR, 862.3170 Benzodiazepine Test System	Toxicology
DJG	21 CFR, 862.3650 Opiate Test System	Toxicology

5. Predicate Devices:
K052115
First Check Multi Drug Cup 12

6. Intended Use

First Sign™ Drug of Abuse Tests are immunochromatographic assays for the qualitative determination of Oxazepam , Methamphetamine , and Morphine in human urine at cut-off concentrations of 300 ng/mL, 1000 ng/mL, and 2000 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 drug Oxazepam is ingested, at prescribed doses; it is not intended to distinguish between prescription use or abuse of this drug. There is no uniformly recognized cutoff concentration level for oxazepam 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 Oxazepam , Methamphetamine , and Morphine 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™ Oxazepam Test and the Predicate Device

Item	Device	Predicate - K052115
Indication(s) for Use	For the qualitative determination of Oxazepam in human urine.	Same
Calibrator	Oxazepam	Same
Methodology	Competitive binding, lateral flow immunochromatographic assays based on the principle of antigen antibody immunochemistry.	Same
Specimen Type	Human Urine	Same
Cut-Off Values	300 ng/mL	Same

Item	Device	Predicate - K052115
Intended Population	For over-the-counter and prescription uses.	For over-the-counter use.
Configurations	Cup, Dip Card	Cup

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

Item	Device	Predicate - K052115
Indication(s) for Use	For the qualitative determination of methamphetamine in human urine.	Same
Calibrator	D-methamphetamine	Same
Methodology	Competitive binding, lateral flow immunochromatographic assays based on the principle of antigen antibody immunochemistry.	Same
Specimen Type	Human Urine	Same
Cut-Off Values	1000 ng/mL	Same
Intended Population	For over-the-counter and prescription uses.	For over-the-counter use.
Configurations	Cup, Dip Card	Cup

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

Item	Device	Predicate - K052115
Indication(s) for Use	For the qualitative determination of morphine in human urine.	For the qualitative determination of opiates in human urine, including morphine.
Calibrator	Morphine	Same
Methodology	Competitive binding, lateral flow immunochromatographic assays based on the principle of antigen antibody	Same

Item	Device	Predicate - K052115
	immunochemistry.	
Specimen Type	Human Urine	Same
Cut-Off Values	2000 ng/mL	Same
Intended Population	For over-the-counter and prescription uses.	For over-the-counter use.
Configurations	Cup, Dip Card	Cup

9. Test Principle

First Sign™ Drug of Abuse Tests are rapid tests for the qualitative detection of Oxazepam , Methamphetamine , and Morphine 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:

Oxazepam 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: D4010558	50-/0+	50-/0+	50-/0+	50-/0+	3-/47+	50+/0-	50+/0-	50+/0-	50+/0-
Lot: D4010560	50-/0+	50-/0+	50-/0+	50-/0+	4-/46+	50+/0-	50+/0-	50+/0-	50+/0-
Lot: D4010562	50-/0+	50-/0+	50-/0+	50-/0+	3-/47+	50+/0-	50+/0-	50+/0-	50+/0-

Oxazepam 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: D4010559	50-/0+	50-/0+	50-/0+	50-/0+	3-/47+	50+/0-	50+/0-	50+/0-	50+/0-
Lot: D4010561	50-/0+	50-/0+	50-/0+	50-/0+	3-/47+	50+/0-	50+/0-	50+/0-	50+/0-
Lot: D4010563	50-/0+	50-/0+	50-/0+	50-/0+	4-/46+	50+/0-	50+/0-	50+/0-	50+/0-

Methamphetamine (mAMP) 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: D4010558	50-/0+	50-/0+	50-/0+	50-/0+	4-/46+	50+/0-	50+/0-	50+/0-	50+/0-
Lot: D4010560	50-/0+	50-/0+	50-/0+	50-/0+	3-/47+	50+/0-	50+/0-	50+/0-	50+/0-
Lot: D4010562	50-/0+	50-/0+	50-/0+	50-/0+	3-/47+	50+/0-	50+/0-	50+/0-	50+/0-

(mAMP) 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: D4010559	50-/0+	50-/0+	50-/0+	50-/0+	3-/47+	50+/0-	50+/0-	50+/0-	50+/0-
Lot: D4010561	50-/0+	50-/0+	50-/0+	50-/0+	2-/48+	50+/0-	50+/0-	50+/0-	50+/0-
Lot: D4010563	50-/0+	50-/0+	50-/0+	50-/0+	3-/47+	50+/0-	50+/0-	50+/0-	50+/0-

Morphine 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: D4010558	50-/0+	50-/0+	50-/0+	50-/0+	3-/47+	50+/0-	50+/0-	50+/0-	50+/0-
Lot: D4010560	50-/0+	50-/0+	50-/0+	50-/0+	3-/47+	50+/0-	50+/0-	50+/0-	50+/0-
Lot: D4010562	50-/0+	50-/0+	50-/0+	50-/0+	4-/46+	50+/0-	50+/0-	50+/0-	50+/0-

Morphine 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: D4010559	**50-/0+**	**50-/0+**	**50-/0+**	**50-/0+**	**2-/48+**	**50+/0-**	**50+/0-**	**50+/0-**	**50+/0-**
Lot: D4010561	**50-/0+**	**50-/0+**	**50-/0+**	**50-/0+**	**3-/47+**	**50+/0-**	**50+/0-**	**50+/0-**	**50+/0-**
Lot: D4010563	**50-/0+**	**50-/0+**	**50-/0+**	**50-/0+**	**3-/47+**	**50+/0-**	**50+/0-**	**50+/0-**	**50+/0-**

b. Linearity

Not applicable.

c. Stability

The devices are stable at 4-30℃ (39-86^{o}F) for 24 months based on the accelerated stability study at 50℃. 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 Oxazepam, Methamphetamine and Morphine. The following cut-off values for the test devices have been verified.

Test	Calibrator	Cut-off (ng/mL)
One Step Oxazepam Test	Oxazepam	300
One Step Methamphetamine Test	D-methamphetamine	1000
One Step Morphine Test	Morphine	2000

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.

Oxazepam

4-Acetamidophenol	Diphenhydramine	D.L-Octopamine
Acetophenetidin	Doxylamine	Oxalic acid
N-Acetvprocainamide	Ecaonine dydrochloride	Oxolinic acid
Acetvsalicvlic acid	Ecqonine methylester	Pentobarbital
Aminopvrine	(-)-Y-Ephedrine	Perphenazine
Amityptvline	Fenoprofen	Phencyclidine
Amorbarbital	Furosemide	Phenelzine
Amoxicillin	Gentisic acid	Phenobarbital
Ampicillin	Hemoglobin	Phentermine
l-Ascorbic Acid	Hydrocortisone	L-Phenylephrine
D.L-Amphetamine	O-Hydroxyhippuric acid	B-Phenylethylamine
Apormorphine	p-Hydroxy-methamphetamine	Phenylpropanotamine
Aspartame	3-Hydroxytyramine	Prednisone
Atropine	Ibuprofen	D.L-Propanolol
Benzillic acid	Imipramine	D-Pseudoephedrine
Benzoic acid	Iproniazid	Quinine
Benzoylecaonine	(±)Isoproterenol	Ranitidine
Benzphetamine	Isoxsuprine	Salicylic acid
Bilirubin	Ketamine	Secobarbital
(±) Chlorpheniramine	Ketoprofen	Serotonin (5-Hydroxytyramine)
Caffeine	Labetalol	Sertraline
Cannabidiol	Loperamide	Sulfamethazine
Chloralhvdrate	Maprotiline	Sulindac
Chloramphenicol	Meperidine	Tetrahydrocortisone,(b-D glucuronide)
Chlorothiazide	Meprobamate	Tetrahydrozoline
(±)Chlorpheniramine	Methadone	Thiamine
Chlorpromazine	Methoxyphenamine	Thioridazine
Chlorquine	(+) 3,4-Methylenedioxy-amphetamine	D.L-Tyrosine
Cholesterol	(+)3,4-Methylenedioxy-methamphetamine	Tolbutamide
Clomipramine	Nalidixic acid	Triamterene
Clonidine	Nalorphine	Trifluoperazine
Cocaine hydrochloride	Naloxone	Trimethoprim
Cortisone	Naltrexone	Triyptamine
(-)cotinine	Naproxen	D.L-Tryptophan

Creatinine	Niacinamide	Tyramine
Dextromethlorphan	Nifedipine	Uric acid
Diclolrfenac	Norethindrone	Verapamil
Diflunisal	D-Norpropoxyphene	Zomepirac
Diaoxin	Noscapine	

Methamphetamine

Acetamidophen	Gentisic acid	Oxycodone
Acetophenetidin	Glucuronide	Oxymetazoline
N-Acetylprocainamide	Glutethimide	Papaverine
Acetylsalicylate	Guaifenesin	Penicillin-G
Aminopyrine	Hippuric acid	Pentazocine
Amitryptyline	Hydralazine	Pentobarbital
Amobarbital	Hydrochlorothiazide	Perphenazine
Amoxicillin	Hydrocodone	Phencyclidine
Ampicillin	Hydrocortisone	Phenelzine
Apomorphine	O-Hydroxyhippuric acid	Phenobarbital
Aspartame	3-Hydroxytyramine	Prednisolone
Atropine	Ibuprofen	Phenylpropanolamine
Benzilic acid	Imipramine	Prednisone
Benzoic acid	(-) Isoproterenol	Procaine
Benzoylecgonine	Isoxsuprine	Promazine
Butabartital	Ketamine	Promethazine
Cannabidiol	Ketoprofen	D,L-Propanolol
Chloralhydrate	Labetalol	D-Propoxyphene
Chloramphenicol	Levorphanol	D-Pseudoephedrine
Chlordiazepoxide	Loperamide	Quinidine
Chlorothiazide	Loxapine succinate	Quinine
Chlorpromazine	Maprotiline	Ranitidine
Cholesterol	Meperidine	Salicylic acid
Clomipramine	Meprobamate	Secobarbital
Clonidine	Methadone	Serotonin (5-Hydroxytyramine)
Cocaine hydrochloride	Methaqualone	Sulfamethazine
Codeine	Methylphenidal	Sulindac
Cortisone	Methyprylon	Temazepam
(-) Cotinine	Morphine-3-β-Dglucuronide	Tetracycline
Creatinine	Nalidixic acid	Tetrahydrocortisone 3 (β-D glucuronide)
Deoxycorticosterone	Nalorphine	Tetrahydrozoline

Dextromethorphan	Naloxone	Thebaine
Diazepam	Naltrexone	Thiamine
Diclofenac	Naproxen	Thioridazine
Diflunisal	Niacinamide	Tolbutamine
Digoxin	Nifedipine	Triamterene
Diphenhydramine	Norcodein	Trifluoperazine
Doxylamine	Norethindrone	Trimethoprim
Ecgonine hydrochloride	Noroxymorphone	Trimipramine
Ecgonine methyl ester	D-Norpropoxyphene	D, L-Tryptophan
Erythromycin	Noscapine	Tyramine
β-Estradiol	Nylidrin	D, L-Tyrosine
Estrone-3-sulfate	D,L-Octopamine	Uric acid
Ethyl-p-aminobenzoate	Oxalic acid	Verapamil
Fenoprofen	Oxazepam	Zomepirac
Furosemide	Oxolinic acid	

Morphine

4-Acetamidophenol	Ecgonine methylester	Oxolinic acid
Acetophenetidin	(-) -Y -Ephedrine	Oxymetazoline
N-Acetylprocainamide	Erythromycin	Papaverine
Acetylsalicylic acid	β-Estradiol	Penicillin-G
Aminopyrine	Estrone-3-sulfate	Pentazocine
Amitryptyline	Ethyl-p-aminobenzoate	Pentobarbital
Amobarbital	Fenoprofen	Perphenazine
Amoxicillin	Furosemide	Phencyclidine
Ampicillin	Gentisic acid	Phenelzine
Ascorbic acid	Hemoglobin	Phenobarbital
D,L-Amphetamine	Hydralazine	Phentermine
Apomorphine	Hydrochlorothiazide	L-Phenylephrine
Aspartame	Hydrocortisone	β-Phenylethylamine
Atropine	O-Hydroxyhippuric acid	Phenylpropanolamine
Benzilic acid	p-Hydroxy methamphetamine	Prednisone
Benzoic acid	3-Hydroxytyramine	D,L-Propanolol
Benzoylecgonine	Ibuprofen	D-Propoxyphene
Benzphetamine	Imipramine	D-Pseudoephedrine
Bilirubin (±)	Iproniazid	Quinidine
Brompheniramine	Isoproterenol	Quinine
Caffeine	Isoxsuprine	Ranitidine
Cannabidiol	Ketamine	Salicylic acid
Chloralhydrate	Ketoprofen	Secobarbital

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

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.

Oxazepam **Cut-off=300 ng/mL**	**Result**	**%** **Cross-Reactivity**
Oxazepam	Positive at 300 ng/mL	100%
Alprazolam	Positive at 125 ng/mL	240%
a-Hydroxyalprazolam	Positive at 2500 ng/mL	12%
Bromazepam	Positive at 1565 ng/mL	19%
Chlordiazepoxide	Positive at 1560 ng/mL	19%
Clobazam	Positive at 65 ng/mL	462%
Clonazepam	Positive at 10000 ng/mL	3%
Clorazepate dipotassium	Positive at 195ng/mL	154%
Delorazepam	Positive at 1560 ng/mL	19%
Desalkylflurazepam	Positive at 1560 ng/mL	19%
Diazepam	Positive at 115 ng/mL	261%
Estazolam	Positive at 165 ng/mL	182%
Flunitrazepam	Positive at 166 ng/mL	181%
Midazolam	Positive at 6500 ng/mL	5%
Nitrazepam	Positive at 300 ng/mL	100%
Norchlordiazepoxide	Positive at 250 ng/mL	120%
Nordiazepam	Positive at 400 ng/mL	75%
Temazepam	Positive at 100 ng/mL	300%
Triazolam	Positive at 2500 ng/mL	12%
D,L-Lorazepam	Negative at $\leq 10^5$ ng/mL	Not Detected
Methamphetamine	Negative at $\leq 10^5$ ng/mL	Not Detected
Morphine	Negative at $\leq 10^5$ ng/mL	Not Detected

mAMP (Methamphetamine**, Cut-off=1000 ng/mL)**	**Result**	**% Cross-Reactivity**
D-Methamphetamine	Positive at 1000 ng/mL	100%
(+/-)3,4-Methylenedioxy-n-ethylamphetamine(MDEA)	Positive at 41600 ng/mL	2%
D/L-Methamphetamine	Positive at 1000 ng/mL	100%
p-Hydroxymethamphetamine	Positive at 27000 ng/mL	4%
(+/-)3,4-Methylenedioxy methamphetamine (MDMA)	Positive at 8000 ng/mL	13%
L-Methamphetamine	Positive at 10000 ng/mL	10%
Trimethobenzamide	Negative at $\leq 10^5$ ng/mL	Not Detected
Chloroquine	Negative at $\leq 10^5$ ng/mL	Not Detected
Ephedrine	Negative at $\leq 10^5$ ng/mL	Not Detected
Fenfluramine	Negative at $\leq 10^5$ ng/mL	Not Detected
Procaine (Novocaine)	Negative at $\leq 10^5$ ng/mL	Not Detected
Ranitidine (Zantac)	Negative at $\leq 10^5$ ng/mL	Not Detected
D-amphetamine	Negative at $\leq 10^5$ ng/mL	Not Detected
L-amphetamine	Negative at $\leq 10^5$ ng/mL	Not Detected
Morphine	Negative at $\leq 10^5$ ng/mL	Not Detected
Oxazepam	Negative at $\leq 10^5$ ng/mL	Not Detected

Morphine Cut-off=2000 ng/mL	**Result**	**% Cross-Reactivity**
Morphine	Positive at 2000 ng/mL	100%
Codeine	Positive at 1000 ng/mL	200%
Ethylmorphine	Positive at 560 ng/mL	357%
Hydrocodone	Positive at 5000 ng/mL	40%
Hydromorphone	Positive at 7315 ng/mL	27%
Levorphanol	Positive at 16000 ng/mL	13%
σ-Monoacetylmorphine	Positive at 1000 ng/mL	200%
Morphine 3-b-D-glucuronide	Positive at 1300 ng/mL	154%
Thebaine	Negative at $\leq 10^5$ ng/mL	Not Detected
Norcodeine	Negative at $\leq 10^5$ ng/mL	Not Detected
Normorphone	Negative at $\leq 10^5$ ng/mL	Not Detected
Oxycodone	Negative at $\leq 10^5$ ng/mL	Not Detected
Oxymorphine	Negative at $\leq 10^5$ ng/mL	Not Detected
Procaine	Negative at $\leq 10^5$ ng/mL	Not Detected
Oxazepam	Negative at $\leq 10^5$ ng/mL	Not Detected
Methamphetamine	Negative at $\leq 10^5$ ng/mL	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 Oxazepam , Methamphetamine , and Morphine 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:

Oxazepam

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	13	25
	Negative	10	10	20	2	0
Viewer B	Positive	0	0	0	14	25
	Negative	10	10	20	1	0
Viewer C	Positive	0	0	0	13	25
	Negative	10	10	20	2	0

Discordant Results of Oxazepam Dip Card

Viewer	Sample Number	GC/MS Result	Dipcard Format Viewer Results
Viewer A	94638975	324	Negative
Viewer A	83001567	325	Negative
Viewer B	94638975	324	Negative
Viewer C	83002215	326	Negative
Viewer C	94639027	328	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	0	14	25
	Negative	10	10	20	1	0
Viewer B	Positive	0	0	0	14	25
	Negative	10	10	20	1	0
Viewer C	Positive	0	0	0	13	25
	Negative	10	10	20	2	0

Discordant Results of Oxazepam Cup

Viewer	Sample Number	GC/MS Result	Cup Format Viewer Results
Viewer A	83002215	326	Negative
Viewer B	83001567	325	Negative
Viewer C	83001567	325	Negative
Viewer C	94639027	328	Negative

Methamphetamine

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	18	21
	Negative	10	10	20	1	0
Viewer B	Positive	0	0	0	18	21
	Negative	10	10	20	1	0
Viewer C	Positive	0	0	0	17	21
	Negative	10	10	20	2	0

Discordant Results of Methamphetamine DipCard

Viewer	Sample Number	GC/MS Result	DipCard Format Viewer Results
Viewer A	83000530	1156	Negative
Viewer B	83001807	1094	Negative
Viewer C	83001811	1065	Negative
Viewer C	83001807	1094	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	0	18	21
	Negative	10	10	20	1	0
Viewer B	Positive	0	0	0	18	21
	Negative	10	10	20	1	0
Viewer C	Positive	0	0	0	17	21
	Negative	10	10	20	2	0

Discordant Results of Methamphetamine Cup

Viewer	Sample Number	GC/MS Result	Cup Format Viewer Results
Viewer A	83001821	1079	Negative
Viewer B	83001807	1094	Negative
Viewer C	83001821	1079	Negative
Viewer C	83001807	1094	Negative

Morphine

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	0	15	24
	Negative	10	10	20	1	0
Viewer B	Positive	0	0	0	15	24
	Negative	10	10	20	1	0
Viewer C	Positive	0	0	0	15	24
	Negative	10	10	20	1	0

Discordant Results of Morphine DipCard

Viewer	Sample Number	GC/MS Result	DipCard Format Viewer Results
Viewer A	94639012	2119	Negative
Viewer B	94639012	2119	Negative
Viewer C	83000219	2325	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	0	15	24
	Negative	10	10	20	1	0
Viewer B	Positive	0	0	0	15	24
	Negative	10	10	20	1	0
Viewer C	Positive	0	0	0	15	24
	Negative	10	10	20	1	0

Discordant Results of Morphine Cup

Viewer	Sample Number	GC/MS Result	Cup Format Viewer Results
Viewer A	83000219	2325	Negative
Viewer B	83000572	2227	Negative
Viewer C	94639012	2119	Negative

Lay-user study

A lay user study was performed at three intended user sites with 280 lay persons testing the Oxazepam devices, 280 lay persons testing the Methamphetamine devices and 280 lay persons testing the Morphine devices. A total of 139 females and 141 males tested the Oxazepam samples, 138 females and 142 males tested Methamphetamine samples, and 137 females and 143 males tested the Morphine 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 (Oxazepam DipCard)

% of Cutoff	Number of samples	Oxazepam 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	76	0	20	100%
-50% Cutoff	20	145	0	20	100%
-25% Cutoff	20	222	0	20	100%
+25% Cutoff	20	384	18	2	90%
+50% Cutoff	20	468	20	0	100%
+75% Cutoff	20	542	20	0	100%

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

% of Cutoff	Number of samples	Oxazepam 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	76	0	20	100%
-50% Cutoff	20	145	0	20	100%
-25% Cutoff	20	222	2	18	90%
+25% Cutoff	20	384	20	0	100%
+50% Cutoff	20	468	20	0	100%
+75% Cutoff	20	542	20	0	100%

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

% of Cutoff	Number of samples	Methamphetamine 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	245	0	20	100%
-50% Cutoff	20	488	0	20	100%
-25% Cutoff	20	729	0	20	100%
+25% Cutoff	20	1212	19	1	95%
+50% Cutoff	20	1441	20	0	100%
+75% Cutoff	20	1666	20	0	100%

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

% of Cutoff	Number of samples	Methamphetamine 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	245	0	20	100%
-50% Cutoff	20	488	0	20	100%
-25% Cutoff	20	729	0	20	100%
+25% Cutoff	20	1212	19	1	95%
+50% Cutoff	20	1441	20	0	100%
+75% Cutoff	20	1666	20	0	100%

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

% of Cutoff	Number of samples	Morphine 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	527	0	20	100%
-50% Cutoff	20	1053	0	20	100%
-25% Cutoff	20	1573	1	19	95%
+25% Cutoff	20	2652	20	0	100%
+50% Cutoff	20	3254	20	0	100%
+75% Cutoff	20	3711	20	0	100%

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

% of Cutoff	Number of samples	Morphine 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	527	0	20	100%
-50% Cutoff	20	1053	0	20	100%
-25% Cutoff	20	1573	0	20	100%
+25% Cutoff	20	2652	19	1	95%
+50% Cutoff	20	3254	20	0	100%
+75% Cutoff	20	3711	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.