



Food and Drug Administration
10903 New Hampshire Avenue
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Silver Spring, MD 20993-0002

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

August 17, 2016

Re: k160793

Trade/Device Name: First Sign Drug of Abuse MDMA Cup Test; First Sign Drug of Abuse MDMA Dip Card Test; First Sign Drug of Abuse EDDP Cup Test; First Sign Drug of Abuse EDDP Dip Card Test; First Sign Drug of Abuse Nortriptyline Cup Test; First Sign Drug of Abuse Nortriptyline Dip Card Test
Regulation Number: 21 CFR 862.3620
Regulation Name: Methadone test system
Regulatory Class: II
Product Code: DJR, LAF, LFG
Dated: June 29, 2016
Received: July 7, 2016

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)
k160793

Device Name

First Sign Drug of Abuse MDMA Cup Test; First Sign Drug of Abuse MDMA Dip Card Test
First Sign Drug of Abuse EDDP Cup Test; First Sign Drug of Abuse EDDP Dip Card Test
First Sign Drug of Abuse Nortriptyline Cup Test; First Sign Drug of Abuse Nortriptyline Dip Card Test

Indications for Use (Describe)

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

First Sign Drug of Abuse MDMA Tests are immunoassay tests. The test can detect MDMA in human urine. The cut-off value is 500 ng/mL. The tests are available in a Cup format and a Dip Card format.

The tests provide only preliminary test results. If you want to get a confirmed result, you must use a more specific chemical method. Gas Chromatography/Mass Spectrometry is the preferred confirmatory method. Clinical consideration and professional judgment should be used when you get any drug of abuse test result. It should be used 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.

First Sign Drug of Abuse EDDP Cup Test

First Sign Drug of Abuse EDDP Dip Card Test

First Sign Drug of Abuse EDDP Tests are immunoassay tests. The test can detect EDDP in human urine. The cut-off value is 300 ng/mL. The tests are available in a Cup format and a Dip Card format.

The tests provide only preliminary test results. If you want to get a confirmed result, you must use a more specific chemical method. Gas Chromatography/Mass Spectrometry is the preferred confirmatory method. Clinical consideration and professional judgment should be used when you get any drug of abuse test result. It should be used 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.

First Sign Drug of Abuse Nortriptyline Cup Test

First Sign Drug of Abuse Nortriptyline Dip Card Test

First Sign Drug of Abuse Nortriptyline Tests are immunoassay tests. The test can detect Nortriptyline in human urine. The cut-off value is 1,000 ng/mL. The tests are available in a Cup format and a Dip Card format.

The tests provide only preliminary test results. If you want to get a confirmed result, you must use a more specific chemical method. Gas Chromatography/Mass Spectrometry is the preferred confirmatory method. Clinical consideration and professional judgment should be used when you get any drug of abuse test result. It should be used 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

1. Date: March 15, 2016
2. Submitter: W.H.P.M., Inc.
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4. Device Name: First Sign® Drug of Abuse MDMA Cup Test
First Sign® Drug of Abuse MDMA Dip Card Test
First Sign® Drug of Abuse EDDP Cup Test
First Sign® Drug of Abuse EDDP Dip Card Test
First Sign® Drug of Abuse Nortriptyline Cup Test
First Sign® Drug of Abuse Nortriptyline Dip Card Test

Common Name: MDMA Urine Test
EDDP Urine Test
Nortriptyline Urine Test

Product Code	Class	CFR #	Panel
LAF	Class II	21 CFR, 862.3610 Methamphetamine Test System	Toxicology
DJR	Class II	21 CFR, 862.3620 Methadone Test System	Toxicology
LFG	Class II	21 CFR, 862.3910 Tricyclic Antidepressant Drugs Test System	Toxicology

5. Predicate Devices:
K142800, Co-Innovation Rapid Single/Multi Drug Test
K140748, Co-Innovation One Step Single/Multi Drug Test
6. Intended Use
First Sign® Drug of Abuse MDMA Cup Test
First Sign® Drug of Abuse MDMA Dip Card Test

First Sign® Drug of Abuse MDMA Tests are immunoassay tests. The test can detect MDMA in human urine. The cut-off value is 500 ng/mL. The tests are available in a Cup format and a Dip Card format.

The tests provide only preliminary test results. If you want to get a confirmed result, you must use a more specific chemical method. Gas Chromatography/Mass Spectrometry is the preferred confirmatory method. Clinical consideration and professional judgment should be used when you get any drug of abuse test result. It should be used 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.

First Sign® Drug of Abuse EDDP Cup Test

First Sign® Drug of Abuse EDDP Dip Card Test

First Sign® Drug of Abuse EDDP Tests are immunoassay tests. The test can detect EDDP in human urine. The cut-off value is 300 ng/mL. The tests are available in a Cup format and a Dip Card format.

The tests provide only preliminary test results. If you want to get a confirmed result, you must use a more specific chemical method. Gas Chromatography/Mass Spectrometry is the preferred confirmatory method. Clinical consideration and professional judgment should be used when you get any drug of abuse test result. It should be used 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.

First Sign® Drug of Abuse Nortriptyline Cup Test

First Sign® Drug of Abuse Nortriptyline Dip Card Test

First Sign® Drug of Abuse Nortriptyline Tests are immunoassay tests. The test can detect Nortriptyline in human urine. The cut-off value is 1,000 ng/mL. The tests are available in a Cup format and a Dip Card format.

The tests provide only preliminary test results. If you want to get a confirmed result, you must use a more specific chemical method. Gas Chromatography/Mass Spectrometry is the preferred confirmatory method. Clinical consideration and professional judgment should be used when you get any drug of abuse test result. It should be used 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 MDMA Test, First Sign™ Drug of Abuse EDDP Test and First Sign™ Drug of Abuse Nortriptyline Test are immunochromatographic assays. Each assay test is a lateral flow system for the qualitative detection of MDMA, or EDDP or Nortriptyline in human urine. The products are single-use in vitro diagnostic devices, which come in the formats of Dip Cards 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 candidate device and the predicate device is provided in Table 1, Table 2 & Table 3.

Table 1: Features Comparison of First Sign® Drug of Abuse MDMA Test and the Predicate Device

Item	Candidate Device First Sign® Drug of Abuse MDMA Test	Predicate Device (k142800) Co-Innovation Multi Drug Test
Indication(s) for Use	For the qualitative determination of MDMA in human urine.	Same
Calibrator	MDMA	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	500 ng/mL	Same
Intended Population	For over-the-counter and prescription uses.	Same
Configurations	Cup, Dip Card	Same

Table 2: Features Comparison of First Sign® Drug of Abuse EDDP Test and the Predicate Device

Item	Candidate Device First Sign® Drug of Abuse EDDP Test	Predicate Device (k140748) Co-Innovation Multi Drug Test
Indication(s) for Use	For the qualitative determination of EDDP in human urine.	Same
Calibrator	EDDP	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
Intended Population	For over-the-counter and prescription uses.	Same
Configurations	Cup, Dip Card	Same

Table 3: Features Comparison of First Sign® Drug of Abuse Nortriptyline Test and the Predicate Device

Item	Candidate Device First Sign® Drug of Abuse Nortriptyline Test	Predicate Device (k140748) Co-Innovation Multi Drug Test
Indication(s) for Use	For the qualitative determination of Nortriptyline in human urine.	Same
Calibrator	Nortriptyline	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.	Same
Configurations	Cup, Dip Card	Same

9. Test Principle

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

First Sign® Drug of Abuse MDMA Test

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 urine 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:

MDMA 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+	2-/48+	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-

MDMA 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+	2-/48+	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 39-86°F (4-30°C) 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 MDMA. The following cut-off value for the test devices have been verified.

Test	Calibrator	Cut-off (ng/mL)
First Sign® Drug of Abuse MDMA Test	MDMA	500

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 lots 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.

4-Acetamidophenol	(L) - Epinephrine	Pentobarbital
Acetophenetidin	Erythromycin	Perphenazine
N-Acetylprocainamide	β-Estradiol	Phencyclidine
Acetylsalicylic acid	Estrone-3-sulfate	Phenelzine
Aminopyrine	Ethyl-p-aminobenzoate	Phenobarbital
Amitriptyline	Fenoprofen	Phentermine
Amobarbital	Furosemide	Trans-2-phenylcyclopropylamine hydrochloride
Amoxicillin	Gentisic acid	L-Phenylephrine
Ampicillin	Hemoglobin	β-Phenylethylamine
L-Ascorbic acid	Hydralazine	Phenylpropanolamine
Apomorphine	Hydrochlorothiazide	Prednisolone
Aspartame	Hydrocodone	Prednisone
Atropine	Hydrocortisone	Procaine
Benzilic acid	O-Hydroxyhippuric acid	Promazine
Benzoic acid	3-Hydroxytyramine	Promethazine
Benzoylcegonine	Ibuprofen	DL-Propranolol
Bilirubin	Imipramine	D-Propoxyphene
(±) - Brompheniramine	Iproniazid	D-Pseudoephedrine
Buspiron	(±) - Isoproterenol	Quinacrine
Caffeine	Isoxsuprine	Quinidine
Cannabidiol	Ketamine	Quinine
Cannabinol	Ketoprofen	Ranitidine
Chloralhydrate	Labetalol	Salicylic acid
Chloramphenicol	Levorphanol	Secobarbital
Chlordiazepoxide	Loperamide	Serotonin (5- Hydroxytyramine)
Chlorothiazide	Maprotiline	Sulfamethazine
(±) - Chlorpheniramine	Meperidine	Sulindac
Chlorpromazine	Meprobamate	Sustiva
Chloroquine	Methadone	Temazepam
Cholesterol	Morphine-3-β-Dglucuronide	Tetracycline
Clomipramine	Morphine sulfate	Tetrahydrocortisone 3-(β-Dglucuronide)
Clonidine	Nalidixic acid	Tetrahydrozoline
Cocaehtylene	Naloxone	Thebaine
Cocaine hydrochloride	Naltrexone	Theophyinine
Codeine	Naproxen	Thiamine

Cortisone	Niacinamide	Thioridazine
(-) Cotinine	Nifedipine	Tolbutamide
Creatinine	Nimesulidate	Trazodone
Deoxycorticosterone	Norcodein	Triamterene
Dextromethorphan	Norethindrone	DL-Tyrosine
Diclofenac	D-Norpropoxyphene	Trifluoperazine
Diazepam	Noscapine	Trimethoprim
Diffunisal	D,L-Octopamine	Trimipramine
Digoxin	Oxalic acid	Tryptamine
Dicylomine	Oxazepam	D L-Tryptophan
Diphenhydramine	Oxolinic acid	Tyramine
5,5 - Diphenylhydantoin	Oxycodone	Uric acid
Doxylamine	Oxymetazoline	Verapamil
Ecgonine hydrochloride	Papaverine	Zomepirac
Ecgonine methylester	Penicillin-G	
[1R,2S](-) Ephedrine	Pentazocinehydrochloride	

f. Specificity

To test the specificity, drug metabolites and other components that are likely to interfere in urine samples were tested using three lots 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.

Drug	Concentration (ng/ml)	% Cross-Reactivity
Methylenedioxyamphetamine (MDMA)	500	100%
3,4-Methylenedioxyamphetamine (MDA)	8000	6.3%
3,4-Methylenedioxyethylamphetamine (MDEA)	1000	50%
Ephedrine	40000	1.3%
d-methamphetamine	Negative at 100000	Not Detected
d-amphetamine	Negative at 100000	Not Detected
l-amphetamine	Negative at 100000	Not Detected
l-methamphetamine	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 lots 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.

h. Comparison Studies

The method comparison studies for the First Sign® Drug of Abuse MDMA Test was 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. The samples were blind labeled and compared to GC/MS results. The results are presented in the tables below:

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	26
	Negative	10	10	20	1	0
Viewer B	Positive	0	0	1	14	26
	Negative	10	10	19	0	0
Viewer C	Positive	0	0	1	13	26
	Negative	10	10	19	1	0

Discordant Results

Viewer	Sample Number	GC/MS (ng/mL) Result	Dipcard Format Viewer Results
Viewer A	2014111947	561	Negative
Viewer B	2014102405	468	Positive
Viewer C	2014111901	474	Positive
Viewer C	2014102302	544	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	14	26
	Negative	10	10	19	0	0
Viewer B	Positive	0	0	0	13	26
	Negative	10	10	20	1	0

Viewer C	Positive	0	0	1	14	26
	Negative	10	10	19	0	0

Discordant Results

Viewer	Sample Number	GC/MS (ng/mL) Result	Cup Format Viewer Results
Viewer A	2014102306	477	Positive
Viewer B	2014111950	517	Negative
Viewer C	2014102315	470	Positive

i. Lay-user study

A lay user study was performed at three intended user sites with 280 lay persons testing the MDMA devices. 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 (MDMA DipCard)

% of Cutoff	Number of samples	MDMA 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	115	0	20	100%
-50% Cutoff	20	237	0	20	100%
-25% Cutoff	20	358	0	20	100%
+25% Cutoff	20	598	19	1	95%
+50% Cutoff	20	755	20	0	100%
+75% Cutoff	20	912	20	0	100%

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

% of Cutoff	Number of samples	MDMA 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	115	0	20	100%
-50% Cutoff	20	237	0	20	100%
-25% Cutoff	20	358	1	19	95%
+25% Cutoff	20	598	20	0	100%
+50% Cutoff	20	755	20	0	100%
+75% Cutoff	20	912	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.

j. Clinical Studies

Not applicable.

First Sign® Drug of Abuse EDDP Test

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 urine 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:

EDDP Dip Card Format

Drug \ Result	-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-

EDDP Cup Format

Drug \ Result	-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+	2-/48+	50+/0-	50+/0-	50+/0-	50+/0-
Lot 5	50-/0+	50-/0+	50-/0+	50-/0+	2-/48+	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-

b. Linearity

Not applicable.

c. Stability

The devices are stable at 39-86°F (4-30°C) 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 EDDP. The following cut-off value for the test devices have been verified.

Test	Calibrator	Cut-off (ng/mL)
First Sign® Drug of Abuse EDDP Test	EDDP	300

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 lots 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.

Acetaminophen	Ecgonine hydrochloride	O-Hydroxyhippuric acid
Acetophenetidin	Ecgonine methylester	Oxalic acid
Acetylsalicylic acid	(1R,2S)(-)-Ephedrine	Oxazepam
Amobarbital	Erythromycin	Oxolinic acid
Aminopyrine	β-Estradiol	Oxycodone
Amitriptyline	Estrone-3-sulfate	Oxymetazoline
Amoxicillin	Ethyl-p-aminobenzoate	Papaverine
DL-Amphetamine sulfate	Fenoprofen	Penicillin-G
Ampicillin	Furosemide	Pentazocine
Apomorphine	Gentisic acid	Pentobarbital
Ascorbic acid	Hemoglobin	Perphenazine
Aspartame	Hydralazine	Phencyclidine
Atropine	Hydrochlorothiazide	Phenelzine
Benzilic acid	Hydrocodone	Phenobarbital
Benzoic acid	Hydrocortisone	Phentermine
Benzoylcegonine	p-Hydroxyamphetamine	β-Phenylethylamine
Bilirubin	p-Hydroxymethamphetamine	Phenylpropanolamine
Brompheniramine	3-Hydroxytyramine	Prednisolone

Caffeine	Ibuprofen	Prednisone
Cannabidiol	Imipramine	Procaine
Cannabinol	(-) Isoproterenol	Promazine
Chloralhydrate	Isoxsuprine	Promethazine
Chloramphenicol	Ketamine	Quinidine
Chlorothiazide	Ketoprofen	Quinine
(±) - Chlorpheniramine	Labetalol	Ranitidine
Chlorpromazine	Levorphanol	Salicylic acid
Chloroquine	Loperamide	Secobarbital
Cholesterol	L-Phenylephrine	Serotonin
Clomipramine	Maprotiline	Sulfamethazine
Clonidine	Meperidine	Sulindac
Cocaine hydrochloride	Meprobamate	Temazepam
Codeine	Methamphetamine	Tetracycline
(-) Cotinine	Methoxyphenamine	Tetrahydrocortisone 3- (β-D-glucuronide)
Cortisone	(±) - 3,4-Methylenedioxy-amphetamine hydrochloride	Tetrahydrozoline
Creatinine	(±)-3,4-Methylenedioxy-methamphetamine hydrochloride	Thebaine
Deoxycorticosterone	Morphine Sulfate	Thiamine
Dextromethorphan	Morphine-3-β-D glucuronide	Thioridazine
Diazepam	N-Acetylprocainamide	Triamterene
Diclofenac	Nalidixic acid	Trifluoperazine
Diflunisal	Naloxone	Trimethoprim
Digoxin	Naltrexone	Trimipramine
Diphenhydramine	Naproxen	Tryptamine
D-Norpropoxyphene	Niacinamide	DL-Tryptophan
D-Propoxyphene	Nifedipine	Tyramine
D,L-Tyrosine	Norcodein	Uric acid
DL-Octopamine	Norethindrone	Verapamil
DL-Propranolol	Noscapine	Zomepirac

f. Specificity

To test the specificity, drug metabolites and other components that are likely to interfere in urine samples were tested using three lots 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.

Drug	Concentration (ng/ml)	% Cross-Reactivity
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EDDP (2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine)	300	100%
EMDP (2-Ethyl-5-methyl-3,3-diphenylpyrroline)	Negative at 100000	Not Detected
Disopyramide	Negative at 100000	Not Detected
Methadone	Negative at 100000	Not Detected
LAAM (Levo-alpha-acetylmethadol)	Negative at 100000	Not Detected
Alpha Methadol	Negative at 100000	Not Detected
Doxylamine	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 lots 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.

h. Comparison Studies

The method comparison studies for the First Sign® Drug of Abuse EDDP Test was 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. The samples were blind labeled and compared to GC/MS results. The results are presented in the tables below:

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	14	26
	Negative	10	10	19	0	0
Viewer C	Positive	0	0	1	13	26
	Negative	10	10	19	1	0

Discordant Results

Viewer	Sample Number	GC/MS (ng/mL) Result	DipCard Format Viewer Results
Viewer A	94911951	340	Negative
Viewer A	94910121	276	Positive
Viewer B	94911312	269	Positive
Viewer C	94911296	344	Negative
Viewer C	94911562	260	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	0	13	26
	Negative	10	10	20	1	0
Viewer C	Positive	0	0	1	13	26
	Negative	10	10	19	1	0

Discordant Results

Viewer	Sample Number	GC/MS (ng/mL) Result	Cup Format Viewer Results
Viewer A	94911296	344	Negative
Viewer A	94910742	269	Positive
Viewer B	94911951	340	Negative
Viewer C	94911928	342	Negative
Viewer C	94910755	266	Positive

i. Lay-user study

A lay user study was performed at three intended user sites with 280 lay persons testing the EDDP devices. 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 (EDDP DipCard)

% of Cutoff	Number of samples	EDDP 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	81	0	20	100%
-50% Cutoff	20	157	0	20	100%
-25% Cutoff	20	235	2	18	90%
+25% Cutoff	20	410	20	0	100%
+50% Cutoff	20	485	20	0	100%
+75% Cutoff	20	566	20	0	100%

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

% of Cutoff	Number of samples	EDDP 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	81	0	20	100%
-50% Cutoff	20	157	0	20	100%
-25% Cutoff	20	235	1	19	95%
+25% Cutoff	20	410	20	0	100%
+50% Cutoff	20	485	20	0	100%
+75% Cutoff	20	566	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.

j. Clinical Studies

Not applicable.

First Sign® Drug of Abuse Nortriptyline Test

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 urine 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:

Nortriptyline 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-

Nortriptyline 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+	2-/48+	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-

b. Linearity

Not applicable.

c. Stability

The devices are stable at 39-86°F (4-30°C) 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 Nortriptyline. The following cut-off value for the test devices have been verified.

Test	Calibrator	Cut-off (ng/mL)
First Sign® Drug of Abuse Nortriptyline Test	Nortriptyline	1000

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 lots 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.

4-Acetamidophenol	Erythromycin	Oxycodone
Acetophenetidin	β-Estradiol	Oxymetazoline
N-Acetylprocainamide	Estrone-3-sulfate	Papaverine
Acetylsalicylic acid	Ethyl-p-aminobenzoate	Penicillin-G
Aminopyrine	Fenoprofen	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
Benzoylcegonine	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
Chloroquine	Methadone	Serotonin
Cholesterol	(L)Methamphetamine	Sulfamethazine
Clonidine	Methoxyphenamine	Sulindac
Cocaethylene	(±)-3,4-Methylenedioxyamphetamine hydrochloride	Tetracycline
Cocaine hydrochloride	(+)-3,4-Methylenedioxymethamphetamine hydrochloride	Tetrahydrocortisone 3-(β-D-glucuronide)
Codeine	Morphine-3-β-Dglucuronide	Tetrahydrozoline

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

f. Specificity

To test the specificity, drug metabolites and other components that are likely to interfere in urine samples were tested using three lots 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.

Drug	Concentration (ng/ml)	% Cross-Reactivity
Nortriptyline	1000	100%
Amitriptyline	1500	67%
Clomipramine	15000	6.7%
Desipramine	1000	100%
Doxepine	2000	50%
Imipramine	600	167%
Nordoxepin	1000	100%
Promazine	24000	4%
Trimipramine	4000	25%
Cyclobenzaprine	1500	67%
Maprotiline	Negative at 100000	Not Detected
Promethazine	Negative at 100000	Not Detected
Norclomipramine	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 lots 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.

h. Comparison Studies

The method comparison studies for the First Sign® Drug of Abuse Nortriptyline Test was performed in-house with three different laboratory assistants for each format of the device. Operators ran 80 (40 negative and 40 positive) unaltered clinical. The samples were blind labeled and compared to GC/MS results. The results are presented in the tables below:

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	1	14	26
	Negative	10	10	19	0	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

Viewer	Sample Number	GC/MS (ng/mL) Result	DipCard Format Viewer Results
Viewer A	2014122464	863	Positive
Viewer B	2014122434	1069	Negative
Viewer B	2014122358	851	Positive
Viewer C	2014122445	1125	Negative
Viewer C	2014122607	879	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	14	26
	Negative	10	10	19	0	0

Viewer C	Positive	0	0	0	13	26
	Negative	10	10	20	1	0

Discordant Results

Viewer	Sample Number	GC/MS (ng/mL) Result	Cup Format Viewer Results
Viewer A	2014122358	851	Positive
Viewer A	2014122809	1084	Negative
Viewer B	2014122620	870	Positive
Viewer C	2014122390	1135	Negative

i. Lay-user study

A lay user study was performed at three intended user sites with 280 lay persons testing the Nortriptyline devices. 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 (Nortriptyline DipCard)

% of Cutoff	Number of samples	Nortriptyline 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	261	0	20	100%
-50% Cutoff	20	495	0	20	100%
-25% Cutoff	20	720	1	19	95%
+25% Cutoff	20	1180	20	0	100%
+50% Cutoff	20	1485	20	0	100%
+75% Cutoff	20	1687	20	0	100%

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

% of Cutoff	Number of samples	Nortriptyline 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	261	0	20	100%
-50% Cutoff	20	495	0	20	100%
-25% Cutoff	20	720	1	19	95%
+25% Cutoff	20	1180	19	1	95%
+50% Cutoff	20	1485	20	0	100%

+75% Cutoff	20	1687	20	0	100%
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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.

j. 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 MDMA Test and First Sign® Drug of Abuse EDDP Test and First Sign® Drug of Abuse Nortriptyline Test are substantially equivalent to the predicate.