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PROFESSIONAL MEDICAL PRODUCTS

MULTI DRUG SALIVA MIDSTREAM TEST 6 DRUGS 8 PARAMETERS - FOR PROFESSIONAL USE

User manual

ATTENTION: *The operators must carefully read and completely understand the present manual before using the product.*

A rapid test for the simultaneous, qualitative detection of multiple drugs and drug metabolites in human oral fluid. For healthcare professionals including professionals at point of care sites. Immunoassay for in vitro diagnostic use only.

INTENDED USE

The Multi-Drug Rapid Test Midstream for OPI/ COC/ AMP/ OXY/ MET/ THC is a lateral flow chromatographic immunoassay for the qualitative detection of multiple drugs and drug metabolites in oral fluid at the following cut-off concentrations:

Test	Calibrator	Cut-off (ng/ml)
Opiates (OPI/MOP)	Morphine	40
	6-Monoacetylmorphine	4
Cocaine (COC)	Benzoylecgonine	30
Amphetamine (AMP)	d-Amphetamine	40
Oxycodone (OXY)	Oxycodone	40
Methamphetamine (MET)	d-Methamphetamine	40
	3,4-Methylenedioxymethamphetamine (MDMA)	50
Marijuana (THC)	11-nor-Δ9 -THC-9 COOH	10

This assay provides only a preliminary analytical test result. A more specific alternate chemical method must be used in order to obtain a confirmed analytical result. Gas chromatography/mass spectrometry (GC/MS) and gas chromatography/tandem mass spectrometry (GC/MS) are the preferred confirmatory methods. Professional judgment should be applied to any drug of abuse test result, particularly when preliminary positive results are indicated.

SUMMARY

The Multi-Drug Rapid Test Midstream for OPI/ COC/ AMP/ OXY/ MET/ THC and their metabolites is a rapid, oral fluid screening test that can be performed without the use of an instrument. The test utilizes monoclonal antibodies to selectively detect elevated levels of specific drugs in human oral fluid

Amphetamine (AMP)

Amphetamine is a sympathomimetic amine with therapeutic indications. The drug is often self-administered by nasal inhalation or oral ingestion. Depending on the route of administration, amphetamine can be detected in oral fluid as early as 5-10 minutes following use[1]. Amphetamine can be detected in oral fluid for up to 72 hours after use[1].

The amphetamine assay contained within the Multi-Drug Rapid Test Midstream yields a positive result when the amphetamine concentration in oral fluid exceeds 40ng/ml.

Methamphetamine (MET)

Methamphetamine is a potent stimulant chemically related to amphetamine but with greater CNS stimulation properties. The drug is often self-administered by nasal inhalation, smoking or oral ingestion. Depending on the route of administration, methamphetamine can be detected in oral fluid as early as 5-10 minutes following use[1]. Methamphetamine can be detected in oral fluid for up to 72 hours after use[1].

The Methamphetamine assay contained within the Multi-Drug Rapid Test Midstream yields a positive result when the methamphetamine concentration in oral fluid exceeds 40ng/ml,or the 3,4-Methylenedioxymethamphetamine concentration in oral fluid exceeds 50ng/ml.

Cocaine (COC)

Cocaine is a potent central nervous system (CNS) stimulant and a local anesthetic derived from the coca plant (erythroxylum coca). The drug is often self-administered by nasal inhalation, intravenous injection and free-base smoking. Depending on the route of administration, cocaine and metabolites benzoylecgonine and ecgonine methyl ester can be detected in oral fluid as early as 5-10 minutes following use[1]. Cocaine and benzoylecgonine can be detected in oral fluid for up to 24 hours after use[1].

The cocaine assay contained within the Multi-Drug Rapid Test Midstream for cocaine and opiates yields a positive result when the cocaine metabolite in oral fluid exceeds 30ng/ml.

Opiates (OPI)

The drug class opiates refers to any drug that is derived from the opium poppy, including naturally occurring compounds such as morphine and codeine and semi-synthetic drugs such as heroin. Opiates act to control pain by depressing the central nervous system. The drugs demonstrate addictive properties when used for sustained periods of time; symptoms of withdrawal may include sweating, shaking, nausea and irritability. Opiates can be taken orally or by injection routes including intravenous, intramuscular and subcutaneous; illegal users may also take the intravenously or by nasal inhalation. Using an immunoassay cutoff level of 40ng/ml, codeine can be detected in the oral fluid within 1 hour following a single oral dose and can remain detectable for 7-21 hours after the dose[1]. Heroin metabolite 6-monoacetylmorphine (6-MAM) is found more prevalently in excreted unmetabolized, and is also the major metabolic product of codeine and heroin[2].

The opiates assay contained within the Multi-Drug Rapid Test Midstream yields a positive result when the opiates concentration in oral fluid exceeds 40ng/ml,or the 6-Monoacetylmorphine concentration in oral fluid exceeds 4ng/ml.

Marijuana (THC)

11-nor-Δ9-tetrahydrocannabinol-9-carboxylic acid (Δ9-THC-COOH), the metabolite of THC (Δ9-tetrahydrocannabinol), is detectable in oral fluid shortly after use. The detection of the drug is thought to be primarily due to the direct exposure of the drug to the mouth (oral and smoking administrations) and the subsequent sequestering of the drug in the buccal cavity[3]. Historical studies have shown a window of detection for THC in oral fluid of up to 14 hours after drug use[3].

The THC assay contained within the Multi-Drug Rapid Test Midstream yields a positive result when the Δ9-THC-COOH concentration in oral fluid exceeds 10 ng/ml.

Oxycodone (OXY)

Oxycodone is a semi-synthetic opioid with a structural similarity to codeine. The drug is manufactured by modifying thebaine, an alkaloid found in the opium poppy.Oxycodone, like all opiate agonists, provides pain relief by acting on opioid receptors in the spinal cord, brain, and possibly directly in the affected tissues. Oxycodone is prescribed for the relief of moderate to high pain under the well-known pharmaceutical trade names of OxyContin®, Tylox®, Percodan® and Percocet®. While Tylox®, Percodan® and Percocet® contain only small doses of oxycodone hydrochloride combined with other analgesics such as acetaminophen or aspirin, OxyContin consists solely of oxycodone hydrochloride in a time-release form. Oxycodone is known to metabolize by demethylation into oxymorphone and noroxycodone. The OXY assay contained within the Multi-Drug Rapid Test Midstream yields a positive result when the OXY concentration in oral fluid exceeds 40ng/ml.

ASSAY PRINCIPLE

The Multi-Drug Rapid Test Midstream for OPI/ COC/ AMP/ OXY/ MET/ THC is an immunoassay based on the principle of competitive binding. Drugs that may be present in the oral fluid specimen compete against their respective drug conjugate for binding sites on their specific antibody.

During testing, a portion of the oral fluid specimen migrates upward by capillary action. A drug, if present in the oral fluid specimen below its cut-off concentration, will not saturate the binding sites of its specific antibody. The antibody will then react with the drug-protein conjugate and a visible colored line will show up in the test line region of the specific drug strip. The presence of drug above the cut-off concentration in the oral fluid specimen will saturate all the binding sites of the antibody. Therefore, the colored line will not form in the test line region.

A drug-positive oral fluid specimen will not generate a colored line in the specific test line region of the strip because of drug competition, while a drug-negative oral fluid specimen will generate a line in the test line region because of the absence of drug competition.

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

REAGENTS

The test contains membrane strips coated with drug-protein conjugates (purified bovine albumin) on the test line, a goat polyclonal antibody against gold-protein conjugate at the control line, and a dye pad which contains colloidal gold particles coated with mouse monoclonal antibody specific to Amphetamine, Methamphetamine, Cocaine, Opiates, Δ9-THC-COOH and Oxycodone,

PRECAUTIONS

- Do not use after the expiration date.
- The test should remain in the sealed pouch until use.
- Oral fluid is not classified as biological hazard unless derived from a dental procedure.
- The used collector and Midstream should be discarded according to local regulations.

STORAGE AND STABILITY

Store as packaged in the sealed pouch at 2-30°C. The test is stable through the expiration date printed on the sealed pouch. The test Midstream must remain in the sealed pouch until use. DO NOT FREEZE. Do not use beyond the expiration date.

SPECIMEN COLLECTION AND PREPARATION

The oral fluid specimen should be collected using the collector provided with the kit. Follow the detailed Directions for Use below. No other collection Midstream should be used with this assay. Oral fluid collected at any time of the day may be used.

MATERIALS

Materials Provided

- Test Midstream • Package insert

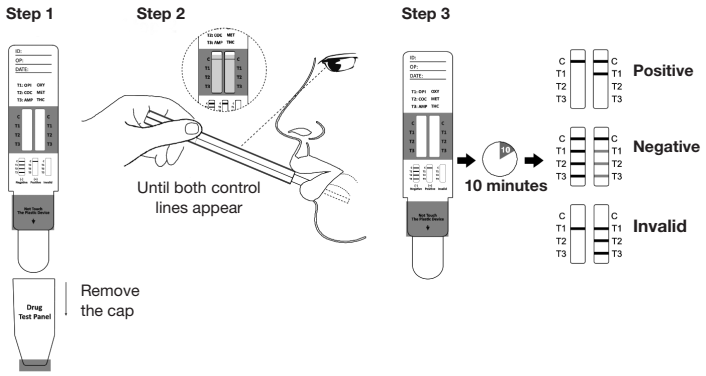
Materials Required but Not Provided

- Timer

DIRECTIONS FOR USE

Allow the test Midstream, specimen, and/or controls to reach room temperature (15-30°C) prior to testing. Instruct the donor to not place anything in the mouth including food, drink, gum or tobacco products for at least 10 minutes prior to collection.

1. Bring the pouch to room temperature before opening it. Remove the test from the sealed pouch and use it within one hour.
2. Take off the Midstream cap and insert the absorbent wick to the mouth .put it under the tongue to collect oral fluid until the control line appears and then take out the midstream.
3. Place the test Midstream on a clean and level surface. See illustration below.
4. Read drug strip results at 10 minutes. Do not read results after 15 minutes.



INTERPRETATION OF RESULTS

(Please refer to the previous illustration)

NEGATIVE:* A colored line appears in the Control region (C) and colored lines appear in the Test region (T). This negative result means that the concentrations in the oral fluid sample are below the designated cut-off levels for a particular drug tested.

***NOTE:** The shade of the colored lines(s) in the Test region (T) may vary. The result should be considered negative whenever there is even a faint line.

POSITIVE: A colored line appears in the Control region (C) and NO line appears in the Test region (T). The positive result means that the drug concentration in the oral fluid sample is greater than the designated cut-off for a specific drug.

INVALID: No line appears in the Control region (C). Insufficient specimen volume or incorrect procedural techniques are the most likely reasons for Control line failure. Read the directions again and repeat the test with a new test card. If the result is still invalid, contact your manufacturer.

QUALITY CONTROL

A procedural control is included in the test. A colored line appearing in the control region (C) is considered an internal procedural control. It confirms sufficient specimen volume, adequate membrane wicking and correct procedural technique.

LIMITATIONS

1. The Multi-Drug Rapid Test Midstream provides only a qualitative, preliminary analytical result. A secondary analytical method must be used to obtain a confirmed result. Gas chromatography/mass spectrometry (GC/MS) or gas chromatography/tandem mass spectrometry (GC/MS/MS) is preferred confirmatory methods.[4]
2. A positive test result does not indicate the concentration of drug in the specimen or the route of administration.
3. A negative result may not necessarily indicate a drug-free specimen. Drug may be present in the specimen below the cutoff level of the assay.

PERFORMANCE CHARACTERISTICS

Analytical Sensitivity

A Phosphate-buffered saline (PBS) pool was spiked with drugs to target concentrations of ± 50% cut-off, ± 25% cut-off and +300% cut-off and tested with the Multi-Drug Rapid Test Midstream. The results are summarized below.

Drug Concentration Cut-off Range	AMP		MET		THC		COC		OPI		OXY	
	-	+	-	+	-	+	-	+	-	+	-	+
0% Cut-off	30	0	30	0	30	0	30	0	30	0	30	0
-50% Cut-off	30	0	30	0	30	0	30	0	30	0	30	0
-25% Cut-off	27	3	28	2	27	3	27	3	27	3	27	3
Cut-off	15	15	16	14	12	18	15	15	13	17	20	10
+25% Cut-off	7	23	6	24	8	22	8	22	7	23	4	26
+50% Cut-off	0	30	0	30	0	30	0	30	0	30	0	30
+300% Cut-off	0	30	0	30	0	30	0	30	0	30	0	30

Analytical Specificity
The following table lists the concentration of compounds (ng/mL) above which the Multi-Drug Rapid Test Midstream for OPI/ COC/ AMP/ OXY/ MET/ THC identified positive results at a read time of 10 minutes.

Compound	ng/ml
AMPHETAMINE (AMP)	
d-Amphetamine	40
d/l-Amphetamine	100
ß-Phenylethylamine	25,000
Tryptamine	12,500
p-Hydroxyamphetamine	100
(+)3,4-Methylenedioxyamphetamine (MDA)	100
l-Amphetamine	25,000
Methoxyphenamine	12,500
METHAMPHETAMINE (MET)	
d-Methamphetamine	40
Fenfluramine	60,000
p-Hydroxymethamphetamine	400
Methoxyphenamine	25,000
Mephentermine	1,500
3,4-Methylenedioxymethamphetamine (MDMA)	50
l-Phenylephrine (R)-(-)-Phenylephrine	6,250
Procaine	2,000
(1R,2S) - (-)Ephedrine	400
Ephedrine	400
Benzphetamine	25,000
MARIJUANA (THC)	
11-nor-Δ9 -THC-9 COOH	10
Cannabinol	12,500
Δ8 -THC	6,000
Δ9 -THC	10,000
11-nor-Δ8-THC-9 COOH	10
COCAINE (COC)	
Benzoylecgonine	20
Cocaine	20
Cocaethylene	30
Ecgonine	1,500
Ecgonine methyl ester	12,500
OPIATES (OPI)	
Morphine	40
Codeine	25
Ethylmorphine	25
Hydromorphine	100
Hydrocodone	100
Levorphanol	400
Oxycodone	25,000
Morphine 3-β-D-Glucuronide	50
Norcodeine	6,250
Normorphine	25,000
Nalorphine	10,000
Oxymorphone	25,000
Thebaine	2,000
Diacetylmorphine (Heroin)	50
6-Monoacetylmorphine	4
OXYCODONE (OXY)	
Oxycodone	40
Oxymorphone	40
Levorphanol	10,000
Hydrocodone	1,500
Hydromorphone	10,000
Naloxone	5,000
Naltrexone	5,000

Cross-Reactivity
A study was conducted to determine the cross-reactivity of the test with compounds spiked into drug-free PBS stock. The following compounds demonstrated no false positive results on the Multi-Drug Rapid Test Midstream when tested with at concentrations up to 100 µg/mL.

N-Acetylprocainamide	Creatinine	Meprobamate	Quinidine
Acetylsalicylic acid	Diazepam	Methadone	Quinine
Aminopyrine	Diclofenac	Methylphenidate	Secobarbital
Amitryptyline	Diflunisal	Methyprylon	Serotonin (5-Hydroxytyramine)
Amobarbital	Digoxin	Nalidixic acid	Sulfamethazine
Amoxicillin	Diphenhydramine	Nifedipine	Sulindac
Ampicillin	Doxylamine	Norcodein	Temazepam
L-Ascorbic acid	β-Estradiol	Norethindrone	Tetracycline
Apomorphine	Estrone-3-sulfate	D-Norpropoxyphene	Tetrahydrocortisone,
Aspartame	Ethyl-p-aminobenzoate	Noscapine	3-Acetate
Atropine	Fenoprofen	D,L-Octopamine	Tetrahydrocortisone
Benzilic acid	Furosemide	Oxalic acid	3 (β-D-glucuronide)
Benzoic acid	Gentisic acid	Oxazepam	Tetrahydrozoline
Bilirubin	Hemoglobin	Oxolinic acid	Thiamine
(±) - Brompheniramine	Hydralazine	Oxymetazoline	Thioridazine
Caffeine	Hydrochlorothiazide	Papaverine	D, L-Thyroxine
Cannabidiol	Hydrocortisone	Penicillin-G	Tolbutamine
Chloralhydrate	O-Hydroxyhippuric acid	Pentazocine	Triamterene
Chloramphenicol	3-Hydroxytyramine	Pentobarbital	Trifluoperazine
Chlordiazepoxide	Ibuprofen	Perphenazine	Trimethoprim
Chlorothiazide	Imipramine	Phencyclidine	Trimipramine
(±) Chlorpheniramine	Iproniazid	Phenelzine	L-Phenylephrine
Chlorpromazine	(±) - Isoproterenol	Phenobarbital	D, L-Tryptophan
Chlorquine	Isoxsuprine	Phentermine	Tyramine
Cholesterol	Ketamine	Promazine	D, L-Tyrosine
Clomipramine	Ketoprofen	Promethazine	Uric acid
Clonidine	Labetalol	D,L-Propanolol	Verapamil
Cortisone	Loperamide	D-Propoxyphene	Zomepirac
(-) Cotinine	Maprotiline	D-Pseudoephedrine	

BIBLIOGRAPHY

1. Moolchan, E., et al, "Saliva and Plasma Testing for Drugs of Abuse: Comparison of the Disposition and Pharmacological Effects of Cocaine", Addiction Research Center, IRP, NIDA, NIH, Baltimore, MD. As presented at the SOFT-TIAFT meeting October 1998.
2. Kim, I, et al, "Plasma and oral fluid pharmacokinetics and pharmacodynamics after oral codeine administration", ClinChem, 2002 Sept.; 48 (9), pp 1486-96.
3. Schramm, W. et al, "Drugs of Abuse in Saliva: A Review," J Anal Tox, 1992 Jan-Feb; 16 (1), pp 1-9
4. Baselt RC. Disposition of Toxic Drugs and Chemicals in Man. 2nd Ed. Biomedical Publ., Davis, CA. 1982; 488.

Index of Symbols

	Keep away from sunlight	CE	Product complies with European Directive no. 98/79/EC on In Vitro diagnostic devices		Expiration date (see box / package)
	Keep in a cool, dry place	IVD	For in vitro diagnostic use only	REF	Product code
	Please read instructions carefully		Read instructions carefully	LOT	Lot number (see box / package)
Σ 20	Contains sufficient for "n" tests	2°C 30°C	Store between and °C		Manufacturer
	Do not use if package is damaged		Disposable device, do not re-use		

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