PRECISION

Multi-Saliva Drugs of Abuse

Rapid Test Device

This test should be performed with assistance of the Handheld DOA Reader MD-S46

INTENDED USE

The Multi-Saliva Drugs of Abuse Rapid Test Device is a rapid visual immunoassay for the qualitative, presumptive detection of drugs of abuse in human oral fluid specimens. The test system consists of three membrane strips mounted in a plastic cassette.
This test detects combinations of the following drugs at the concentrations listed below. Specific combinations will vary according to the test in question:

Test	Calibrator	Cut-off(ng/mL)
Amphetamine (AMP)	D-Amphetamine	50
Benzodiazepine (BZO)	Oxazepam	10
Cocaine (COC)	Cocaine	20
Marijuana (THC)	11-nor-Δ9-THC-9-COOH	25
Methamphetamine (MET)	D-Methamphetamine	50
Opiates (OPI)	Morphine	40

PRINCIPLE

The Multi-Saliva Drugs of Abuse Rapid Test Device 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.

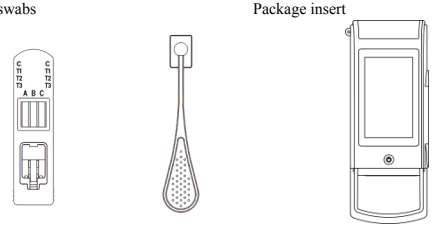
During testing, a portion of the oral fluid specimen migrates upward by capillary action. A drug, if present in the oral fluid specimen below its cut-off concentration, will not saturate the binding sites of its specific antibody. The antibody will then react with the drug-protein conjugate and a visible 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.

MATERIALS

Materials Provided

Individually packed test devices
Oral fluid swabs
Gloves
Package insert



Materials Required but Not provided

Timer
Precision Handheld DOA Reader(ATD 1100)
Positive and negative controls

INTRODUCTION

The Oral Fluid Drug Screen Device for AMP/BZO/COC/MET/OPI/THC is a rapid, oral fluid sc reening test that can be performed without the use of an instrument. The test utilizes monoclon al antibodies to selectively detect elevated levels of specific drugs in human oral fluid.

Amphetamine (AMP):
Amphetamine is a potent central nervous system stimulant currently prescribed to treat Attention-Deficit/Hyperactivity Disorder (ADHD) and narcolepsy. Acute higher doses induce euphoria, alertness and sense of increased energy and power. Although highly pH dependent, amphetamine is readily present and detectable in saliva; experiments indicate that the saliva/plasma ratio of amphetamine is 2,76. The cut-off level of amphetamine assay (50ng/mL) mirrors the saliva screening cut-off proposed by the Department of Health and Human Services (DHHS) for the Federal Drug Free Workplace Program.

Benzodiazepines (BZD):
Benzodiazepines are central nervous system (CNS) depressants commonly prescribed for the short-term treatment of anxiety and insomnia. In general, benzodiazepines act as hypnotics in high doses, as anxiolytics in moderate doses and as sedatives in low doses. The use of benzodiazepines can result in drowsiness and confusion. Psychological and physical dependence on benzodiazepines can develop if high doses of the drug are given over a prolonged period. Benzodiazepines are taken orally or by intramuscular or intravenous injection, and are extensively oxidized in the liver to metabolites. Benzodiazepines can be detected in oral fluid after use.

Benzoylecgonine/Cocaine(COC):
Cocaine is a potent central nervous system stimulant and a local anesthetic found in the leaves of the coca plant. The psychological effects induced by using cocaine are euphoria, confidence and sense of increased energy. These psychological effects are accompanied by increased heart rate, dilation of the pupils, fever, tremors and sweating. Cocaine and its metabolites, benzoylecgonine, and ecgonine methylester, can be detected in oral fluid after use[1,2].

Marijuana (THC-COOH 25):
Tetrahydrocannabinol is generally accepted to be the principle active component in marijuana. Once in the blood stream, Δ9 - THC (parent) is mainly quickly metabolized into THC metabolites in the liver. These psycho inactive THC metabolites are stored in the fatty tissue to some extent and are then discharged in urine over a period of between a few days to several weeks following consumption, where it is detected as THC-COOH (metabolite) in a positive test result. When ingested or smoked, it produces euphoric effects. Abusers exhibit central nervous system effects, altered mood and sensory perceptions, loss of coordination, impaired short term memory, anxiety, paranoia, depression, confusion, hallucinations and increased heart rate. The THC-COOH-Assay contained within the Oral Fluid Drug Screen Device yields a positive result when the THC-COOH concentration exceeds 25ng/mL.

Methamphetamine (MET):
Methamphetamine is a potent central nervous system stimulant. Acute higher doses induce euphoria, alertness, and sense of increased energy and power. More acute responses produce anxiety, paranoia, psychotic behaviour, and cardiac dysrhythmias. Depending on the route of administration, amphetamine or methamphetamine can be detected in oral fluid as early as 5-7 minutes after use and can be detected in oral fluid for up to 72 hours after use.

Opiates (OPI):
Opiates such as heroin, morphine, and codeine, are central nervous system (CNS) depressants. The use of opiates at high doses produces euphoria and release from anxiety. Physical dependence is apparent in users and leads to depressed coordination, disrupted decision making, decreased respiration, hypothermia and coma. After opiates are used, morphine and its metabolites are present in oral fluid[2,3].

PRECAUTIONS

- For professional *in vitro* diagnostic use only.
- Do not use after the expiration date indicated on the package. Do not use the test if the foil pouch is damaged. Do not reuse tests.
- Read the entire procedure carefully prior to testing.
- Do not eat, drink or smoke in the area where specimens and kits are handled. Handle all specimens as if they contain infectious agents. Observe established precautions again st microbiological hazards throughout the procedure and follow standard procedures for the proper disposal of specimens. Wear protective clothing such as laboratory coats, disposable gloves and eye protection when specimens are assayed.
- Humidity and temperature can adversely affect results.
- Used testing materials should be discarded in accordance with local regulations.

STORAGE AND STABILITY

- The kit should be stored at 2-30°C until the expiry date printed on the sealed pouch.
- The test must remain in the sealed pouch until use.
- Do not freeze.
- Kits should be kept out of direct sunlight.
- Care should be taken to protect the components of the kit from contamination. Do not use if there is evidence of microbial contamination or precipitation. Biological contamination of dispensing equipment, containers or reagents can lead to false results.

SPECIMEN COLLECTION AND STORAGE

- The Multi-Saliva Drugs of Abuse Rapid Test Device is intended for use with human oral fluid specimens only.
- Oral fluid specimens must be collected according to the directions in the Procedure section of this package insert.
- Perform testing immediately after specimen collection.

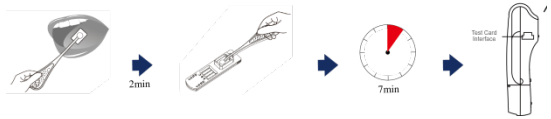
PROCEDURE

SPECIMEN COLLECTION AND TESTING PROCEDURE

1. The oral fluid specimen should be collected using the collector provided with the kit. No other collection devices should be used with this assay.
2. 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.
3. If test cassettes have been stored at refrigerated temperatures, allow them to warm to room temperature before testing.
4. Do not open sealed pouch until ready to perform the test.

TESTING

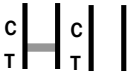
1. Remove the test cassette from the sealed pouch and place it on a clean and level surface.
2. Remove the collector from the sealed pouch and provide the collector to the donor.
3. Instruct the donor to place the sponge end of the collector into the mouth, actively swab the inside of the mouth and tongue to collect oral fluid until the sponge is fully saturated. This process may take up to 2 minutes. To be sure, that the collection is finished, wait till the colour appears on the saliva collector.
4. Remove the collector from mouth and insert into the collection area of the test cassette. Put the sponge in the application area and click down.
5. Test migration should be seen within 1 minute. Once migration is observed, the results can be read at 7 minutes.
6. Instrument detection(Selected)
   Please follow instruction for the Handheld DOA Reader: Put the test device into the Handheld DOA Reader at 7 minutes, click "Start Detection" to read the results.



INTERPRETATION OF RESULTS

(See previous illustration)
POSITIVE: Only one colored band appears, in the control region (C). No colored band appears in the test region (T) for the drug in question. A positive result indicates that the drug concentration exceeds the detectable level.

NEGATIVE: Two colored bands appear on the membrane. One band appears in the control region (C) and another band appears in the test region (T) for the drug in question. A negative result indicates that the drug concentration is below the detectable level.



INVALID: Control band fails to appear. Results from any test which has not produced a control band (C) at the specified read time must be discarded. Please review the procedure and repeat with a new test. If the problem persists, discontinue using the kit immediately and contact your local distributor.

NOTE:

1. The intensity of color in the test region (T) may vary depending on the concentration of analytes present in the specimen. Therefore, any shade of color in the test region (T) should be considered negative. Please note that this is a qualitative test only, and cannot determine the concentration of analytes in the specimen.
2. Insufficient specimen volume, incorrect operating procedure or expired tests are the most likely reasons for control band failure.

QUALITY CONTROL

- Internal procedural controls are included in the test. A colored band appearing in the control region (C) is considered an internal positive procedural control, confirming sufficient specimen volume and correct procedural technique.
- External controls are not supplied with this kit. It is recommended that positive and negative controls be tested as a good laboratory practice to confirm the test procedure and to verify proper test performance.

LIMITATIONS OF THE TEST

1. The Multi-Saliva Drugs of Abuse Rapid Test Device is for professional in vitro diagnostic use, and should be only used for the qualitative detection of drugs of abuse in oral fluid.
2. This assay provides a preliminary analytical test result only. A more specific alternative chemical method must be used in order to obtain a confirmed analytical result. Gas chromatography/mass spectrometry (GC/MS) has been established as the preferred confirmatory method by the National Institute on Drug Abuse (NIDA).
3. There is a possibility that technical or procedural errors as well as other substances and factors may interfere with the test and cause false results.
4. A positive result indicates the presence of a drug/metabolite only, and does not indicate or measure intoxication.
5. A negative result does not at any time rule out the presence of drugs/metabolites in saliva, as they may be present below the minimum detection level of the test.
6. This test does not distinguish between drugs of abuse and certain medications.

PERFORMANCE CHARACTERISTICS

A. Sensitivity

A phosphate-buffered saline (PBS) pool was spiked with drugs to target concentrations of ± 50% cut-off and ± 25% cut-off and tested with the Multi-Saliva Drugs of Abuse Rapid Test Device. The results are summarized below.

Drug Conc. (Cut-off range)	n	AMP		BZO		COC	
		-	+	-	+	-	+
0% Cut-off	30	30	0	30	0	30	0
-50% Cut-off	30	30	0	30	0	30	0
-25% Cut-off	30	30	0	28	2	29	1
Cut-off	30	18	12	11	19	13	17
+25% Cut-off	30	2	28	4	26	5	25
+50% Cut-off	30	0	30	0	30	0	30

Drug Conc. (Cut-off range)	n	MET		OPI25		THC25	
		-	+	-	+	-	+
0% Cut-off	30	30	0	30	0	30	0
-50% Cut-off	30	30	0	30	0	30	0
-25% Cut-off	30	30	0	27	3	28	2
Cut-off	30	13	17	9	21	13	17
+25% Cut-off	30	3	27	3	27	9	21
+50% Cut-off	30	0	30	0	30	0	30

B. Specificity

The following table lists the concentrations of compounds (ng/mL) above which the Multi-Saliva Drugs of Abuse Rapid Test Device identified positive results at 10 minutes.

Amphetamine-Related Compounds	Concentration (ng/mL)
D-Amphetamine	50
L-Amphetamine	4,000
(+)-3,4-Methylenedioxyamphetamine (MDA)	150
Phentermine	40,000
PMA	125
Tyramine	3,000

Benzodiazepine-Related Compounds	Concentration (ng/mL)
Oxacepam	10
Alprazolam	15
Bromazepam	8
Chlordiazepoxide	10
Clonazepam	40
Clorazepate	20
Clbazam	6
Diazepam	15
Estazolam	10
Desalkyflurazepam	8
Flunitrazepam	10
Flurazepam	10
Lorazepam	20
Medazepam	10
Nitrazepam	10
Nordiazepam	6
Prazepam	20
Temazepam	8
Triazola	15

Cocaine-Related Compounds	Concentration (ng/mL)
Cocaine	20
Benzoylecgonine	200
Ecgonine	100,000
Ecgonine methyl ester	10,000

Marijuana -Related Compounds	Concentration (ng/mL)
11-nor-Δ9 -THC-9 COOH	25
11-nor-Δ8-THC-9-COOH	25
Δ8-Tetrahydrocannabinol	7500
Δ9-Tetrahydrocannabinol	7500
Cannabinol	10,000

Methamphetamine-Related Compounds	Concentration (ng/mL)
D-Methamphetamine	50
Fenfluramine	3,000
L-Methamphetamine	500
L-Phenylephrine	2,500
MDEA	400
3,4-Methylenedioxymethamphetamine (MDMA)	75
Mephentermine	200
PMMA	50
Procaine	2,500
(-)-Ephedrine	250

Opiates -Related Compounds	Concentration (ng/mL)
Morphine	40
Codeine	10
Diacetylmorphine (Heroin)	50
Ethylmorphine	24
EDDP	20
Meperidine	20000
Hydrocodone	50
Hydromorphone	100
6-Monoacetylmorphine (6-MAM)	25
Morphine-3- β-d-glucuronide	50
Nalorphine	10000
Oxycodone	25000
Oxymorphone	25000
Thebaine	5000

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-Saliva Drugs of Abuse Rapid Test Device when tested at concentrations up to 100 µg/mL.

Acetaminophen	Digoxin	Metoclopramide
Acetone	Dihydrocodeine	(+)-Naproxen
Acetophenetidine	(+)-cis-Diltiazem	Nifedipine
Acetylcodeine	Dimenhydrinate	Nimesulide
Aspirin	4-Dimethylaminoantipyrine	Norchlordiazepoxide
Albumine	Diphenhydramine	Nordoxepinhydrochloride
α-hydroxyalprazolam	DL-Tryptophan	(±)-Norketamine
Alprazolam	DL-Tyrosine	Nortriptyline
Amantadine	Dopamine	Olanzapine
Amikacin	D-Propoxyphene	Opipramol
Aminopyrine	(+)-Ephedrine	Oxalic acid
Amitriptyline	(-)-Ephedrine	Oxymetazoline
Amoxicilline	(±)-Epinephrine	Pennicilline G
Ampicilline	Erythromycine	Perphenazine
Apomorphine	Estron 3 sulfate	Phenothiazine
Aspartame	Ethanol	(±)-Phenylpropanolamine
Atenolol	Etodolac	β-Phenylethylamine
Atropine	Flupentixol	Phenytoin
Baclofen	Fluoxetine	Prednisolone
Benzocaine	Furosemide	Prednisone
Bilirubin	Gastrozepin	Protriptyline
Caffeine	Gentamicin	Quetiapine
Carbamazepine	Gentisic acid	Quinidine
Cephalexin	Guaiacol Glyceryl Ether	Ranitidine
Chloramphenicol	Haloperidol	Rifampicine
Chloroquine	Hemoglobin	Risperidone
Chlorpheniramine	Hexobarbital	Salbutamol
Chlorprothixene	Hydralazine	Salicylic acid
Cholesterol	Hydrochlorothiazide	Sertraline
Chorptothixene	Hydrocortisone	Sodium chloride
Cimetidine	Ibuprofen	Spironolactone
Ciprofloxacin	Imipramine	Sulfamethoxazole
Citalopram	Indomethacin	Sulindac
Clindamycin	Insulin	Theophylline
Clobazam	(-)Isoproterenol	Thiamine
Clomipramine	Kanamycin	Thioridazine
Clonidine	Ketoprofen	Tobramycin
(-)-Cotinine	L-Thyroxine	Triazolam
Creatinine	Lincomycin	Triamterene
Creatine	Metoprolol	Trimethoprim
Cyclobenzaprine	Metronidazole	Trimipramine
Glucose	Midazolam	Valproic acid
Delorazepam	Mirtazapin	Vancomycin
Desipramine	Lidocaine	Venlafaxine
Dexamethasone	Lindane	Verapamil
Diclofenac	Loperamide	Zolpidem
Dicumarol	Lormetazepam	
Diflunisal	Maprotiline	
DL-Propanolol	N-Methylephedrine	

LITERATURE REFERENCES

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GLOSSARY OF SYMBOLS

REF	Catalog number		Temperature limitation
	Consult instructions for use	LOT	Batch code
	In vitro diagnostic medical device		Use by
	Manufacturer		Do not reuse

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