Oratect® Oral Fluid Drug Screen Device

The Oratect® Oral Fluid Drug Screen Device is a one-step lateral flow immunoassay device for the qualitative detection of d-Methamphetamine (ME), Delta-9-Tetrahydrocannabinol (TH), Cocaine (CO), d-Amphetamine (AM), Morphine (OP), and Phencyclidine (PC) in human oral fluid. The Oratect® Test detects these drugs at the cut-off concentration listed below and their metabolites. The test is a prescription assay. This product is for *in vitro* diagnostic use and it can be used at the Point-of-Care site.

The Oratect® Test device detects these drugs at the following cut-off concentrations:

ME	d-Methamphetamine	50 ng/ml
TH	Delta-9-Tetrahydrocannabinol	40 ng/ml
CO	Cocaine	20 ng/ml
AM	d-Amphetamine	50 ng/ml
OP	Morphine	40 ng/ml
PC	Phencyclidine	10 ng/ml

The Oratect® Oral Fluid Drug Screen Device provides only preliminary drug test results. For a quantitative result or for a confirmation of a presumptive positive result obtained by the Oratect® Oral Fluid Drug Screen Device, a more specific alternative method must be used. GC/MS or LC/MS is the preferred confirmatory method. The samples for confirmatory testing should be collected with the oral fluid confirmation tube provided.

Summary and Explanation

Illegal drug consumption contributes to many accidents, injuries and medical conditions. Screening individuals for drugs of abuse is an important method in identifying those who may cause harm to themselves and to others.

Oratect® Oral Fluid Drug Screen Device is developed to detect active drugs-of-abuse present in saliva. Studies on methamphetamine, cannabinoid, cocaine, amphetamine, opiates, and phencyclidine show that all of these drugs are detectable in oral fluids[5]. Oratect® Oral Fluid Drug Screen Device is designed to integrate oral fluid collection and lateral flow immunoassay screen testing for drugs-of-abuse in one single device.

Test Principle

The Oratect® Oral Fluid Drug Screen Device is based on a competitive immunoassay procedure in which drug derivatives immobilized on the membrane compete with the drug(s) which may be present in oral fluid for limited antibody binding sites on the colored colloidal gold antibody conjugate. During testing, oral fluid is collected at the collection pad and migrates across the membrane. If no drug is present in the oral fluid, the colored colloidal gold antibody conjugate will bind to the drug derivatives on the membrane to form visible bands at specific test regions. Therefore, the **presence of a purple-red band** at a specific test region indicates a **negative result**. If any drug(s) is (are) present in the oral fluid, it competes with the immobilized drug conjugate for limited antibody binding sites of the colored colloidal gold conjugate. When a sufficient amount of drug is present, the drug will saturate the antibodies, and the colored colloidal gold conjugate cannot bind to the drug derivative on the membrane. **Therefore, the absence of a purple-red band at the test region indicates a presumptive positive result for that particular test.**

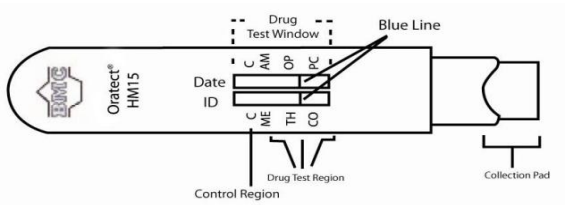

Fig. a Detail regions of Oratect® Oral Fluid Drug Screen Device. Note: This is a representative drawing detail for catalogue number HM15. Other catalogue numbers will have slightly different configurations.

The presence of a blue line in each window indicates that the device is unused. The movement of the blue lines indicates that a sufficient amount of oral fluid has been collected. A control band at the control region (C) indicates the test has performed properly. This control band should always appear regardless of the presence of drug or metabolite.

Reagents

The Oratect® Oral Fluid Drug Screen Device contains one or two membrane strips and a collection pad. Each strip consists of a membrane, a colloidal gold conjugate pad, a sample pad and an absorbent pad.
The number of drugs per strip may vary depending on the selected product catalogue number.

Membrane:
ME/TH/CO test strip: Methamphetamine, THC and Cocaine-protein conjugates are coated onto specific region on the membrane known as the "Test Region".

AM/OP/PC test strip: Amphetamine, Morphine, Phencyclidine protein conjugates are coated onto the test region of the membrane.

Colloidal Gold Conjugate Pad: The colloidal gold conjugate pad for the ME/TH/CO test strip contains mouse monoclonal anti-methamphetamine, anti-THC and anti-cocaine antibody colloidal gold conjugates coated onto a fibrous pad. The colloidal gold conjugate pad for the AM/OP/PC test strip contains mouse monoclonal anti-amphetamine, anti-morphine, anti-phencyclidine antibody colloidal gold conjugates.

Collection Pad: The collection pad consists of an absorbent material.

Materials Provided

Each Oratect® Oral Fluid Drug Screen Device kit contains:

1. 1 Package Insert
2. 25 test devices. Each device consists of a plastic holder and a detachable cap. The devices are packaged individually in a foil pouch with a desiccant.
3. 1 Oral Fluid Collection Tube (50 mL polypropylene tube) for confirmation shipping. The Oratect® Oral Fluid Collection Tube provided in this kit should only be used for the confirmation sample.

Warnings and Precautions

- For *in vitro* diagnostic use only
- The test device should remain in its original sealed pouch until ready for use.
- Discard the test device if package is ripped or torn.
- Do not use the test device beyond the expiration date indicated on the kit.
- Handle all oral specimens as potentially infectious. Proper handling and disposal methods should be established.

Product Storage

The Oratect® Oral Fluid Drug Screen Device pouch should be stored at room temperature (15°-30°C). Do not open pouch until ready to perform the assay.

Specimen Collection and Handling

IMPORTANT: At least 10 minutes prior to administering the test, instruct the donor not to eat, drink, smoke or chew tobacco products.

Presumptive positive samples are collected in the 50 ml collection tube supplied and mailed immediately to confirm the test.

Confirmation laboratory may keep samples for up to 2 weeks when stored at 2 – 8 °C or up to 24 months when stored below -15°C.

Test Procedure

1. Remove the test device from the sealed pouch.
2. Carefully remove the blue cap by holding the sides and pull gently. This will expose the collection pad.
3. Ensure that the blue line is present in each test window.
4. The oral fluid collection process must be observed. Instruct the donor to hold the top portion of the device (above the test windows).
5. When placing device into the mouth, **keep head level**.
   a. Open mouth and rub the collection pad inside mouth against one cheek gently in a circular motion several (approximately 15-20) times. **(Fig. b)**
   b. Still keeping head level, gently rub the collection pad against the opposite cheek in a circular motion (approximately 15-20) several times. **(Fig. b)**

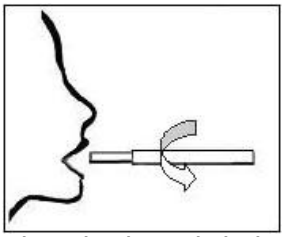

Fig. b Gently rub the collection pad against each cheek several (approximately 15-20) times.

c. Rub the collection pad on top of the tongue several times and then underneath the tongue several (approximately 15-20) times. **(Fig c. and Fig d.). Do not chew, suck, bite or bend the collection pad.**

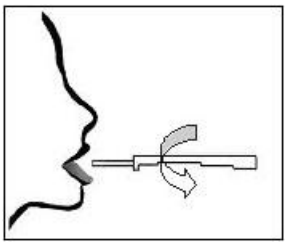

Fig. c Gently rub the collection pad on top of the tongue several (approximately 15-20) times.

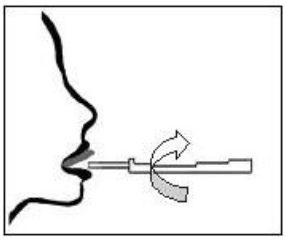

Fig. d Gently rub the collection pad underneath the tongue several (approximately 15-20) times.

6. Place the collection pad underneath the tongue for approximately 30 seconds to collect saliva. Instruct the donor to hold the device in place with their hand.
7. The movement of the blue lines indicates the collection of a sufficient amount of saliva has occurred. If blue lines are still stationary after placing the collection pad underneath the tongue for 30 seconds, repeat the procedure in steps 5 and 6 until the blue lines move.
8. Remove the device from mouth as soon as the blue lines start moving at both test windows.

   Note: The flow of the blue lines should appear in the test windows within 5 minutes. If no flow is observed after 5 minutes in the mouth, discard the device, review procedures 4-7 above with the donor and repeat the test using a new device.
9. Re-cap the device, lay it on a flat surface and **read results in approximately 5 minutes after removing device from mouth. Do not read results after 15 minutes.**

Interpreting Test Results

Negative Results

For each of the test windows, purple-red colored bands should be observed; one band at the control region (C) and one band at the specific drug abbreviation (e.g. AM, OP, CO) in the test region. See example Fig e.

The color of the test band may be slightly darker or lighter than the control band. Any band that can be seen visually, no matter how faint, is a **negative** result. Read each test independently. Do not compare color intensity of one test to another.

In the **Fig. e** below, the oral fluid sample is negative for Amphetamine, Opiate and Cocaine **<u>because bands are visible in the AM, OP, and CO test regions</u>**.

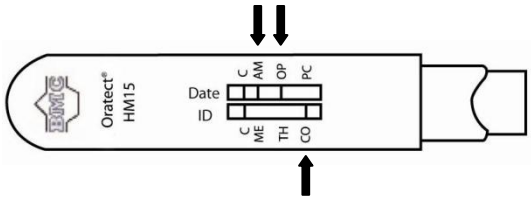

Fig e. Example of Negative Test Results

Presumptive Positive Results

When the control band is visible in the control region (C) and **no** band or shadow band appears at the specific test region, the result is a **presumptive positive** for that particular drug. In **Fig. f** below, the oral fluid sample is presumptive positive for Phencyclidine, Methamphetamine and THC **<u>because no bands are visible in the test regions of PC, ME, and TH.</u>**

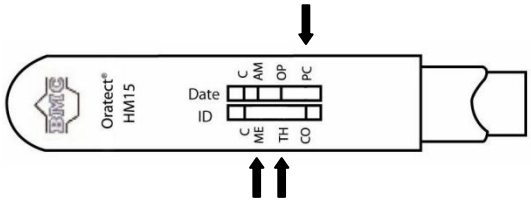

Fig. f Example of Presumptive Positive Test Results

Invalid Results

When **no** band appears in the control (C) region, **the test is invalid** regardless of the results in the test region. If the test is invalid, check testing procedures. **Repeat the test using a new device.** In **Fig. g** below, the test is invalid because there are **<u>no bands in the control regions.</u>**

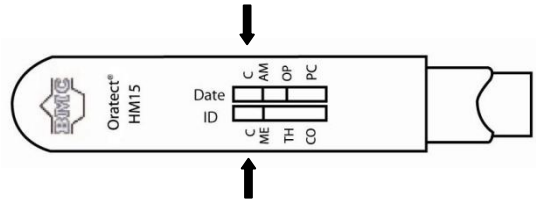

Fig. g Example of Invalid Test Results

Important: Read each test independently. Do not compare color intensity of one test band to another. When a faint purple-red band for a specific test is obtained in the test region along with the presence of the control line (C), the sample should be considered negative. The Oratect® Oral Fluid Drug Screen Device only provides qualitative results for the presence of drug(s) at specified cut-off concentration(s). For confirmation of a presumptive positive result, a more specific method (GC/MS or LC/MS/MS) must be used.

Instructions for collecting a confirmation oral fluid sample.

1. If a user of this product obtains a presumptive positive test result, the user should obtain confirmation testing using a more specific test method such as Gas Chromatography/Mass Spectrometry (GC/MS) or Liquid Chromatography/Mass Spectrometry (LC/MS/MS). The test sample for this confirmation testing should be collected immediately after obtaining the presumptive positive test result(s).
2. Use only the Oratect® Oral Fluid Collection Tube (50ml polypropylene tube) provided in this kit. Note: If additional sample collection tubes are needed, please contact Branan customer service at 1-866-468-3287 Remove cap from collection tube and carefully spit into tube several times until half of the bottom cone (~ 2.5 mLs) is collected.
3. Tightly re-cap sample collection tube.
4. Complete the tube label affixed to sample collection tube with the requested information.
5. Avoid high temperatures and sunlight pending shipment.
6. Mail the sample immediately to a license test laboratory for GC/MS or LC/MS confirmation testing. The sample should be shipped by an overnight courier service using a small shipping box or padded envelope.

Quality Control

Internal control: The Oratect® Oral Fluid Drug Screen Device provides a built-in control bands in each window at the control regions (C) to indicate that the test has performed properly. These control bands should always appear regardless of the presence of drugs. The flow of the blue lines indicates that a sufficient amount of oral fluid has been collected. The presence of the purple-red bands in the control regions verifies that proper flow was obtained. If the control bands do not appear, the test device should be discarded.

External control: It is recommended that negative and positive saliva controls be used to initially test each new lot of product to ensure proper kit performance. The use of the Branan Medical Corporation OratectCheck™ Oral Fluid Controls under catalogue number OC001 may be used as external quality control material. The pipette test procedure provided with the OratectCheck™ Oral Fluid Controls package insert should be followed. Each Laboratory should establish and run its own QC program as it is familiar with its own environment. When external controls do not produce the expected results, repeat with a new unopened bottle of controls..

Quality control testing at regular intervals is a good laboratory practice and laboratories should comply with all federal, state, and local laws, guidelines and regulations. Always check with the appropriate licensing or accrediting bodies to ensure that the quality program employed meets the established standards.

Limitations of Procedure

- The assay is designed for human oral fluid use only.
- Positive results only indicate the presumptive presence of drugs and do not indicate or measure intoxication.
- Technical or procedural errors as well as substances in certain foods and certain medications may interfere with the test and cause false results.
- Do not use the device past expiration date
- Read instructions before testing
- Subjects with dry mouth symptoms have difficulty with this test

Performance Characteristics Comparison and Accuracy

The accuracy of Oratect® was evaluated by testing Oratect product with clinical saliva samples which were subsequently analyzed by GC/MS or LC/MS/MS method. A minimum of forty negative samples and forty positive samples were tested. Of the forty positive samples, at least 4 samples were near negative (between 50% to 100%) and 4 samples were near positive (between 100% to 150%). The results are summarized below:

Drug Name		GC/MS Negative	GC/MS negative <50%	Near cutoff negative ≥50% to <100%	Near cutoff positive ≥100% to <150%	GC/MS positive ≥150%	% Agreement with GC/MS
ME	+	0	0	5	3	58	97.5%
	-	180	9	9	1	0	98.4%
TH	+	0	0	10	7	36	100%
	-	185	20	7	0	0	95.5%
CO	+	0	0	3	5	38	100%
	-	210	6	3	0	0	98.6%
AM	+	0	0	7	12	34	100%
	-	170	38	4	0	0	96.8%
OP	+	0	0	4	3	55	96.7%
	-	186	12	3	2	0	98.0%
PC	+	0	0	1	2	38	95.2%
	-	223	1	5	2	0	99.6%

Precision

For each specific drug test, pooled oral fluid solution was spiked with a drug standard at various concentrations (0%, 25%, 50%, 75%, 100%, 125%, 150%, 175% and 200%). Three lots of Oratect® were tested by at least 3 operators at 3 different sites to validate the test performance. The results for each drug of the Oratect® Oral Fluid Drug Screen Device Tests are summarized below:

Cut-off level	Drug Test											
	ME		TH		CO		AM		OP		PC	
	-	+	-	+	-	+	-	+	-	+	-	+
0%	360	0	360	0	360	0	360	0	360	0	360	0
-75%	45	0	45	0	45	0	45	0	45	0	45	0
-50%	45	0	45	0	45	0	45	0	45	0	45	0
-25%	43	2	42	3	43	2	41	4	43	2	41	4
100%	26	19	25	20	27	18	22	23	23	22	25	20
+125%	3	42	2	43	4	41	1	44	1	44	1	44
+150%	0	45	0	45	0	45	0	45	0	45	0	45
+175%	0	45	0	45	0	45	0	45	0	45	0	45
+200%	0	45	0	45	0	45	0	45	0	45	0	45

Specificity

The specificity study for each drug test was evaluated by adding structurally related compounds to pooled oral fluid sample. The results are expressed as the amount of the compound, in ng/ml, that produced a positive result.

Drug Test	Approximate Concentration(ng/ml)	Approximate % Cross Reactivity
ME		
d-Methamphetamine	50	100%
d,l-Ephedrine	10,000	0.5%
1R, 2S l-Ephedrine	6,000	0.8%
p-Hydroxymethamphetamine	1,500	3.3%
MDEA	1,500	3.3%
MDMA	150	33.3%
d,l-Methamphetamine	60	83.3%
l-Methamphetamine	3,000	1.7%
Methoxyphenamine	10,000	0.5%
TH		
Δ-9-Tetrahydrocannabinol	40	100%
Cannabinol	100	40%
Δ-8-Tetrahydrocannabinol	100	40%
11-nor-Δ-8-THC-9-COOH	20	200%
11-nor-Δ-9-THC-9-COOH	10	400%
11-Hydroxy-Δ9-THC	400	10%
CO		
Cocaine	20	100%
Benzoylecgonine	600	3.3%
AM		
d-Amphetamine	50	100%
l-Amphetamine	2,000	2.5%
d,l-p-Chloramphetamine	400	12.5%
MDA	400	12.5%
Phentermine	100	50%
β-Phenylethylamine	10,000	0.5%
Tyramine	10,000	0.5%
OP		
Morphine	40	100%
6-Acetylcodeine	40	100%
6-Acetylmorphine	50	80%
Codeine	40	100%
Dihydrocodeine	200	20%
Ethyl morphine	75	53.3%
Heroin	40	100%
Hydrocodone	200	20%
Hydromophone	300	13.3%
Nalorphine	1,000	4%
PC		
Phencyclidine	10	100%
Dextromethorphan	>10,000	<0.1%
Doxylamine	>10,000	<0.1%
4-Hydroxy-Phencyclidine	50	20%
Ketamine	>10,000	<0.1%
Metaphit	125	8%
Phencyclidine Morpholine	750	1.3%

Interference

The Oratect® Oral Fluid Drug Screen Test performance at ± 50% cut-off levels is not affected by any oral fluid samples with pH range of 2.0 to 8.5.

The following compounds were spiked into ± 50% oral fluid controls and found not to cross-react with the Oratect® Oral Fluid Drug Screen Device when tested at concentration of 10 µg/ml (10,000ng/ml)

Acetaminophen	Hemoglobin
α-Amylase	Human IgA
Albumin from human serum	Human IgG
l-Ascorbic Acid	Human IgM
Aspartame	Ibuprofen
Benzillic acid	Ketamine
Benzocaine	Lidocaine
Benzoic acid	Meperidine
Bilirubin	Naloxone
Butethal	Naltrexone hydrochloride
Caffeine	d-Naproxen
d-Chlorpheniramine	Papaverine
Cholesterol	Pentazocine
Dextromethorphan	Promazine
Diphenhydramine	Promethazine
Doxylamine	Ranitidine
1R, 2S l- Ephedrine *(except ME assay)*	Riboflavin
	Salicylic acid
1S, 2R d-Ephedrine	Serotonin
l-Epinephrine	Tetracycline
Erythromycin	Thiamine
Ethanol	Tryptamine
Glutethimide	d,l-Tryptophan

Food/Beverage/Hygiene Products Interference

Foods, drinks and hygiene products were spiked at 1% concentration in ±25% and ±50% oral fluid controls to evaluate the interference with Oratect® test results. For interference of cigarette, oral fluid samples were collected from 6 subjects within 15 minutes after consuming a cigarette and then spiked with drug standards (MET, THC, COC, AMP, OPI, and PCP). The following substances were found not to interfere with Oratect® Oral Fluid Drug Screen Test performance.

Mouth wash	Orange juice	Alcohol
MSG	Sugar	Cranberry juice
Salt	Food color: Red	Carbonated Cola
Toothpaste	Food color: Green	Baking Soda
Gum	Food color: Blue	Cigarette
Cough Syrup	Tea	

Bibliography of Suggested Reading

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4. Mandatory Guidelines for Federal Workplace Drug Testing Programs, April 13, 2004 (69 FR 19644).
5. Wong, R. On-site Oral Fluid Drug Testing by Oratect, in Drugs of Abuse: Body Fluid Testing, Wong, R and Tse, H ed., Humana Press, p146-158, 2005.

Part No.: PI-HM15 Rev: A, 04/2012

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