

T-Cube®

One Step
Multi-Drug Oral Fluid Test Cube

For Forensic Use Only.

T-Cube® One Step Multi-Drug Oral Fluid Test Cube offers qualitative detection of the following drugs of abuse and their principal metabolites in human oral fluid at specified cut-off levels: Amphetamine (AMP),Barbiturates (BAR), Benzodiazepines (BZO), Buprenorphine (BUP), Cocaine (COC), Marijuana (THC), Methadone (MTD), Methamphetamine (MET), Methylenedioxymetham-phetamine (MDMA), Fentanyl (FTY),Opiate (OPI), Oxycodone (OXY), Phencyclidine (PCP), and Alcohol (ACL).

INTENDED USE

T-Cube® One Step Multi-Drug Oral Fluid Test Cube is a rapid oral fluid screening test. The test is a lateral flow, one-step immunoassay for the qualitative detection of specific drugs and their metabolites in human oral fluid at the following cut off concentrations:

Test	Calibrator	Cut off (ng/mL)
Amphetamine (AMP)	D-Amphetamine	50
Barbiturates (BAR)	Secobarbital	60
Benzodiazepines(BZO)	Oxazepam	30
Buprenorphine (BUP)	Buprenorphine	5
Cocaine (COC)	cocaine	20
Marijuana (THC)	11-nor-Δ ⁹ -THC-9-COOH Δ9-THC	12 75
Methadone (MTD)	Methadone	30
Methamphetamine (MET)	D-Methamphetamine	50
Methylenedioxymethampheta mine (MDMA)	3,4-Methylenedioxymethampheta mine(MDMA)	100
Fentanyl (FTY)	Norfentanyl	30
Opiate (OPI)	Morphine	40
Oxycodone (OXY)	Oxycodone	20
Phencyclidine (PCP)	Phencyclidine	10
Alcohol (ACL)	Alcohol	> 0.02% B.A.C

This test will detect other related compounds, please refer to the Analytical Specificity table in this package insert.

Amphetamine (AMP): Amphetamine is a sympathomimetic amine with therapeutic indications. The drug is often self-administered by nasal inhalation or oral ingestion.

Barbiturates (BAR): Barbiturates are a class of central nervous system depressants. Abuse of barbiturates can lead not only to impaired motor coordination and mental disorder, but also to respiratory collapse, coma and even death. Barbiturates are taken orally, rectally, or by intravenous and intramuscular injections.

Benzodiazepines (BZO): Benzodiazepines are medications that are frequently prescribed for the symptomatic treatment of anxiety and sleep disorders.

Buprenorphine (BUP): Buprenorphine is a potent analgesic often used in the treatment of opioid addiction. The drug is sold under the trade names Subutex™, Buprenex™, Temgesic™ and Suboxone™, which contain Buprenorphine HCl alone or in combination with Naloxone HCl. Therapeutically, Buprenorphine is used as a substitution treatment for opioid addicts. Substitution treatment is a form of medical care offered to opiate addicts (primarily heroin addicts) based on a similar or identical substance to the drug normally used. In substitution therapy, Buprenorphine is as effective as Methadone but demonstrates a lower level of physical dependence.

Cocaine (COC): Cocaine derived from leaves of coca plant, is a potent central nervous system stimulant and a local anesthetic. Among the psychological effects induced by using. cocaine are euphoria, confidence and a sense of increased energy, accompanied by increased heart rate, dilation of the pupils, fever, tremors and sweating.

Tetrahydrocannabinol (THC): Tetrahydrocannabinol, the active ingredient in the marijuana plant (cannabis sativa), 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.

Methadone (MTD): Methadone is a synthetic analgesic drug that is originally used in the treatment of narcotic addict. The drug is often administered orally or intravenously and is metabolized in the liver and excreted in urine.

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.

Methylenedioxymethamphetamine(MDMA): Methylenedioxymethamphetamine(ecstasy) is a designer drug first synthesized in 1914 by a German drug company for the treatment of obesity. Those who take the drug frequently report adverse effects, such as increased muscle tension and sweating. MDMA is not clearly a stimulant, although it has, in common with amphetamine drugs, a capacity to increase blood pressure and heart rate. MDMA does produce some perceptual changes in the form of increased sensitivity to light, difficulty in focusing, and blurred vision in some users.

Fentanyl (FTY): Fentanyl is a potent, synthetic narcotic analgesic with a rapid onset and short duration of action. It was first synthesized by Janssen Pharmaceutical (Belgium) in the late 1950s, and it is approximately 100 times more potent than morphine. Fentanyl is a strong agonist at the μ-opioid receptors. Historically it has been used to treat breakthrough pain and is commonly used in pre-procedures as a pain reliever as well as an anesthetic in combination with a benzodiazepine. Fentanyl is frequently given intrathecally as part of spinal anesthesia or epidurally for epidural anesthesia and analgesia.

Opiates (OPI): The opiates such as heroin, morphine, and codeine are derived from the resin of opium poppy. The principal metabolites of opiates are morphine, morphine-3-glucuronide, normorphine and codeine with a half-life of about 3 hours. Heroin is quickly metabolized to morphine. Thus, morphine and morphine glucuronide might both be found in the saliva of a person who has taken only heroin. The body also changes codeine to morphine. Thus, the presence of morphine (or the metabolite, morphine glucuronide) in the saliva indicates heroin, morphine and/or codeine use. The window of detection varies for different opiates. Codeine can be detected within one hour and up to 7-21 hours after a single oral dose. Morphine is detectable for several days after a dose.

Oxycodone (OXY): Oxycodone is known as Oxycontin, Roxicodone and is an ingredient of Percodan, Percocet, Roxicet and Tylox. Oxycodone is a semi-synthetic opiates derived from opium. Like other opiates, oxycodone is characterized by its analgesic properties, and the tendency for users to form a physical dependency and develop tolerance with extended use. Oxycodone is usually administered in combination with non-opiate analgesics such as acetaminophen and salicylates for the relief of moderate to severe pain. Oxycodone is a central nervous systemde pressant that may cause drowsiness, dizziness, lethargy, weakness and confusion. Toxicity in an overdose of oxycodone can lead to stupor, coma, muscle flaccidity, severe respiratory depression, hypotension, and cardiac arrest.

Phencyclidine (PCP): Phencyclidine is an arylcyclohexylamine that was originally used as an anesthetic agent and a veterinary tranquilizer. Phencyclidine can produce hallucinations, lethargy, disorientation, loss of coordination, trance-like ecstatic states, a sense of euphoria and visual distortions. It has many street names, such as “angel dust” and “crystal cyclone,” etc. phencyclidine can be administered orally, by nasal ingestion, smoking, or by intravenous injection.

Alcohol (ACL): Alcohol intoxication can lead to loss of alertness, coma, death and as well as birth defects. The blood alcohol concentration (BAC) at which a person becomes impaired is variable. The United States Department of Transportation (DOT) has established a BAC of 0.02% (0.02g/dL) as the cut off level at which an individual is considered positive for the presence of alcohol.

The assay provides a qualitative, preliminary test result. A more specific analytical method must be used in order to obtain a confirmed result. Gas Chromatography/Mass Spectrometry (GC/MS) or Liquid Chromatography/Tandem Mass Spectrometry (LC/MS-MS) are preferred confirmatory methods. Professional judgment should be applied to any drug test result, particularly when preliminary results are positive.

PRINCIPLE

(1) Drug test:

T-Cube® One Step Multi-Drug Oral Fluid Test Cube is a competitive immunoassay that is used to screen for the presence of drugs in oral fluid. It is a chromatographic absorbent device in which drugs or drug metabolites in a sample competitively combine to a limited

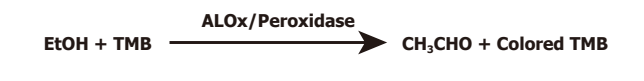
number of antibody-dye conjugate binding sites.

When the sponge end of the collector is immersed into the oral fluid sample, the sample is absorbed into the device by capillary action, mixes with the antibody-dye conjugate, and flows across the pre-coated membrane. When sample drug levels are zero or below the target cutoff (the detection sensitivity of the test), antibody-dye conjugate binds to the drug/protein conjugate immobilized in the Test Region (T) of the device. This produces a colored test line that, regardless of its intensity, indicates a negative result. When sample drug levels are at or above the target cutoff, the free drug in the sample binds to the antibody-dye conjugate preventing the antibody-dye conjugate from binding to the drug-protein conjugate immobilized in the Test Region (T) of the device. This prevents the development of a distinct colored band in the test region, indicating a potentially positive result.

To serve as a procedure control, a colored line will appear at the Control Region (C), if the test has been performed properly.

(2) Alcohol test:

It is based on the high specificity of alcohol oxidase (ALOX) for ethyl alcohol in the presence of peroxidase and enzyme substrate such as tetramethylbenzidine (TMB) as shown in the following:



The distinct color on reactive pad could be observed in less than 20 seconds after the absorbent end was contacted with oral fluid samples with the ethyl alcohol concentration greater than 0.02%. It should be pointed out that other alcohols such as methyl, propany and allyl alcohol would develop the similar color on the reactive pad. However, these alcohols are not normally present in oral fluid.

PRECAUTIONS

1. Do not swallow.
2. Discard after first use. The test cannot be used more than once.
3. Do not use the test kit beyond expiration date.
4. Do not use the test if the pouch is punctured or not sealed.
5. Keep out of the reach of children.
6. Do not read results after 5 minutes.
7. The used collector and cube should be discarded according to local regulations.

MATERIAL

Materials Provided

- Test Cube
- Sponge Collector
- Package Insert

Material Required but Not Provided

- Timer

STORAGE AND STABILITY

1. Store at 4°C - 30°C (40°F - 86°F) in the sealed pouch up to the expiration date
2. Keep away from direct sunlight, moisture and heat.
3. DO NOT FREEZE.
4. Preferably open the pouch only shortly before collection and testing.

SPECIMEN COLLECTION AND PREPARATION

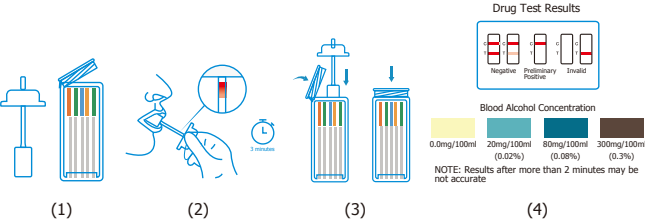
Collect the oral fluid sample using the sponge collector provided. Instruct the donor to not place anything in the mouth including food, drink, gum, or tobacco products for at least 10 minutes prior to collection. No other collection devices should be used with this assay. Oral fluid collected at any time of the day may be used.

TEST PROCEDURE

Allow the kit and specimen to come to room temperature (65°F-86°F/18°C-30°C) prior to testing. AVOID PLACING ANYTHING IN THE MOUTH 10 MINUTES PRIOR TO TESTING.

1. Remove the test cube and the sponge collector from the foil pouch by tearing at the notch. Place the test cube upright on a level surface.
2. Put the sponge end of the collector on your tongue or near cheek to collect oral fluid for about 3 minutes until color on saturation indicator strip appears RED in the indicator window. If color on saturation indicator has not turned red at 7 minutes, repeat the collection using a new device, beginning with Step 1.
3. Open the test cube and place the saturated oral fluid collector inside the test cube. Press the sponge collector down firmly until it reaches the bottom of the test cube then tightly close the cube lid. Keep test cube upright on flat surface and follow Step4.

- 4-1. Interpreting Alcohol Test Result:
Read result at 2 minutes. Do not read after 2 minutes.
NEGATIVE: No color changes on reaction pad.
POSITIVE: Compare the color of reaction pad with provided color chart to estimate the approximate blood alcohol level.
- 4-2. Interpreting Drug Test Results:
Read results at 5 minutes. Do not read after 5 minutes.



INTERPRETATION OF RESULTS

(1) Drug test results:

Negative (-)

A colored band is visible in the Control Region (C) and the appropriate Test Region (T). It indicates that the concentration of the corresponding drug of that specific test zone is zero or below the detection limit of the test.

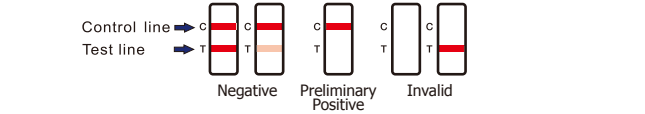
Preliminary Positive (+)

A colored band is visible in the Control Region (C). No color band appears in the appropriate test region. It indicates a positive result for the corresponding drug of that specific Test Region (T).

Invalid

If a colored band is not visible in the Control Region (C) the test is invalid. Another test should be run to re-evaluate the specimen. If test still fails, please contact the distributor with the lot number.

Note: There is no meaning attributed to line color intensity or width.



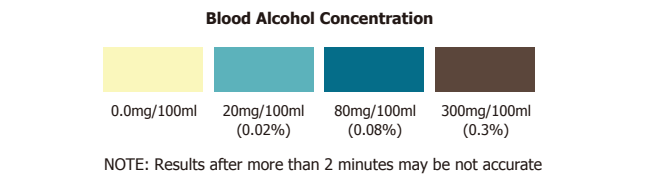
(2) Alcohol test results

Negative (-):

Almost no color change by comparing with the background. The negative result indicates that the BAC is less than 0.02%.

Positive (+):

A distinct color developed all over the pad. The positive result indicates that the BAC is 0.02% or higher. The alcohol concentrations are related to the colored chart below.



Invalid:
The test should be considered invalid if color only develops on the edge of the pad. The subject should be re-tested.

QUALITY CONTROL

Though there is an internal procedural control line in the test device of Control region, the use of external controls is strongly recommended as good laboratory testing practice to confirm the test procedure and to verify proper test performance. Positive and negative control should give the expected results. When testing the positive and negative control, the same assay procedure should be adopted.

LIMITATIONS OF PROCEDURE

1. The test provides only a qualitative, preliminary result. A secondary analytical method must be used to obtain a confirmed result. Gas Chromatography/Mass Spectrometry (GC/MS) or Liquid Chromatography/Tandem Mass Spectrometry (LC/MS-MS) are preferred confirmatory methods.
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

A. Analytical Sensitivity

Standard drugs were spiked into negative PBS pool to the concentration of -50% cut-off,-25% cut-off, cut-off, +25% cut-off and +50% cut-off. The results were summarized below.

Drug Conc. (Cut-off range)	n	AMP		BZO		MTD		THC		MET		PCP		BAR		COC	
		-	+	-	+	-	+	-	+	-	+	-	+	-	+	-	+
0% Cut-off	30	30	0	30	0	30	0	30	0	30	0	30	0	30	0	30	0
-50% Cut-off	30	30	0	30	0	30	0	30	0	30	0	30	0	30	0	30	0
-25% Cut-off	30	28	2	26	4	25	5	14	16	28	2	26	4	25	5	25	5
Cut-off	30	12	18	10	20	12	18	14	16	10	20	14	16	10	20	10	20
+25% Cut-off	30	8	22	5	25	6	24	5	25	8	22	5	25	6	24	6	24
+50% Cut-off	30	0	30	0	30	0	30	0	30	0	30	0	30	0	30	0	30

Drug Conc. (Cut-off range)	n	OPI		MDMA		FTY		BUP		OXY	
		-	+	-	+	-	+	-	+	-	+
0% Cut-off	30	30	0	30	0	30	0	30	0	30	0
-50% Cut-off	30	30	0	30	0	30	0	30	0	30	0
-25% Cut-off	30	14	16	25	5	25	5	26	4	14	16
Cut-off	30	10	20	10	20	11	19	14	16	14	16
+25% Cut-off	30	5	25	6	24	5	25	5	25	5	25
+50% Cut-off	30	0	30	0	30	0	30	0	30	0	30

For the alcohol test:

Oral fluid was obtained by rinsing with positive ethanol control solutions at various B.A.C (0.02%, 0.08%, 0.30%). Negative oral fluid was used to test at 0.00% concentration. For each concentration, a total of 30 tests were performed to validate the test performance.

Test	n	B.A.C							
		0.00%		0.02%		0.08%		0.30%	
		-	+	-	+	-	+	-	+
Alcohol	30	30	0	0	30	0	30	0	30

B. Analytical Specificity

The following table lists the concentration of compounds (ng/mL) above which the One Step Multi-Drug Oral Fluid Test Cube identified positive results at a read time of 5 minutes.

Amphetamine (AMP)		Methadone (MTD)	
D-Amphetamine	50	Methadone	30
D,L-Amphetamine	125	Doxylamine	5,000
β-Phenylethylamine	4,000		
Tryptamine	1,500	Methamphetamine (MET)	
p-Hydroxyamphetamine	800	D-Methamphetamine	50
(+),3,4-Methylenedioxyamph etamine (MDA)	250,000	Fenfluramine	10,000
Methamphetamine	11,000	p-Hydroxymethamphetamine	400
3,4-Methylenedioxy metham phetamine	100,000	Methoxyphenamine	25,000
Dopamine hydrochloride	8,000	3,4-Methylenedioxy metham phetamine (MDMA)	500
		L-Phenylephrine	4,000
Barbiturates(BAR)		Procaine	2,000
Secobarbital	60	(1R,2S) - (-) Ephedrine	400
Amobarbital	500		
Alphenol	15	Methylenedioxy methamp hetamine(MDMA)	
Aprobarbital	20	3,4-Methylenedioxy metham phetamine (MDMA)	100
Butabarbital	10	3,4-Methylenedioxy amphe tamine	300
Butathal	10	3,4-Methylenedioxyethylam phetamine	60
Butalbital	250		
Cyclopentobarbital	60	Fentanyl (FTY)	
Pentobarbital	500	Norfentanyl	30
Phenobarbital	2,500	Fentanyl	100
		Buspirone	13,000
Benzodiazepines (BZO)			
Oxazepam	30	Opiate (OPI)	
Alprazolam	50	Morphine	40
α-Hydroxylprazolam	300	Codeine	100
Bromazepam	50	Ethyl morphine	100
Chlordiazepoxide	10	Hydromorphone	1,000
Clobazam	45	Hydrocodone	2,000
Clonazepam	1,000	Levorphanol	400
Clorazepate dipotassium	50	Morphine 3- β -D- Glucuronide	50
Delorazepam	1,000	Norcodeine	1,500
Desalkylflurazepam	150	Normorphine	12,500
Diazepam	500	Nalorphine	10,000
Estazolam	25	Oxycodone	>300,000
Flunitrazepam	1,000	Oxymorphone	25,000
D,L-Lorazepam	100	Thebaine	10,000
Midazolam	1,000		
		Oxycodone(OXY)	
Buprenorphine(BUP)		Oxycodone	20
Buprenorphine	5	Dihydrocodeine	4,000
Buprenorphine-3-D- Glucuronide	10	Codeine	10,000

Norbuprenorphine	10	Hydromorphone	300,000
Norbuprenorphine-3-D- Glucuronide	10	Morphine	11,000
		Acetylmorphine	>100,000
Cocaine (COC)		Buprenorphine	>100,000
Cocaine	20	Ethyl morphine	>100,000
Benzoylcegonine	100		
Cocaeethylene	25	Phencyclidine (PCP)	
Ecgonine	40,000	Phencyclidine	10
Ecgonine methylester	12,500	4-Hydroxyphencyclidine	12,500
Marijuana (THC)			
11-nor- Δ ⁹ -THC-9-COOH	12		
11-nor- Δ ⁸ -THC-9-COOH	60		
11-hydroxy- Δ ⁹ -THC	2,500		
Δ ⁸ - THC	500		
Δ ⁹ - THC	75		
Cannabinol	500		
Cannabidiol	250,000		

C. Cross-Reactivity

A study was conducted to determine the cross-reactivity of the test with compounds spiked into drug-free PBS stock. The following components show no cross-reactivity when tested with **T-Cube®** One Step Multi-Drug Oral Fluid Test Cube at a concentration up to 100 µg/mL.

Acetaminophen	Loperamide
Acetophenetidin	Maprotiline
N-Acetylprocainamide	Meprobamate
Acetylsalicylic Acid	Labetalol
Aminopyrine	Meperidine
Amoxicillin	Meprobamate
Ampicillin	Methylphenidate
Ascorbic Acid	Nalidixic Acid
Apomorphine	Naloxone
Aspartame	Naltrexone
Atropine	Naproxen
Benzilic Acid	Niacinamide
Benzoic Acid	Nifedipine
Benzphetamine	Norethindrone
D,L -Brompheniramine	D-Norpropoxyphene
Caffeine	Noscapine
Chloralhydrate	D,L-Octopamine
Chloramphenicol	Oxalic Acid
Chlorothiazide	Oxolinic Acid
(±) Chlorpheniramine	Oxymetazoline
Chlorpromazine	Papaverine
Chloroquine	Penicillin-G
Cholesterol	Pentazocine
Clonidine	Perphenazine
Cortisone	Phenelzine
(-) Cotinine	D,L-Propranolol
Creatinine	D-Propoxyphene
Deoxycorticosterone	D-Pseudoephedrine
Dextromethorphan	Quinidine
Diclofenac	Quinine
Diffunisal	Ranitidine
Digoxin	Salicylic acid
Diphenhydramine	Serotonin (5- Hydroxytyramine)
(-) -ψ- Ephedrine	Sulfamethazine
β-Estradiol	Sulindac
Ethyl-p-aminobenzoate	Tetracycline
Fenoprofen	Tetrahydrocortisone, 3 Acetate
Furosemide	Thiamine
Gentisic Acid	Thioridazine
Hemoglobin	D, L-Tyrosine
Hydralazine	Tolbutamide

Hydrochlorothiazide	Triamterene
Hydrocortisone	Trifluoperazine
O-Hydroxyhippuric Acid	Trimethoprim
p-Hydroxytyramine	D, L-Tryptophan
Ibuprofen	Tyramine
Iproniazid	Uric Acid
Isoproterenol	Verapamil
Isosuprine	Zomepirac
Ketamine	Ketoprofen

BIBLIOGRAPHY OF SUGGESTED READING

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2. Kim, I, et al, "Plasma and oral fluid pharmacokinetics and pharmacodynamics after oral codeine administration", Clin Chem, 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. McCarron, MM, et al, "Detection of Phencyclidine Usage by Radioimmunoassay of Saliva," J Anal Tox. 1984 Sep-Oct.; 8 (5), pp 197-201.

INDEX OF SYMBOLS

	Keep away from sunlight
	Store between 4°C - 30°C (40°F - 86°F)
	Keep dry
	Do not re-use