*i*Screen®DX Multi-Drugs of Abuse Dip Test Quick Reference Guide

This is a CLIA-Waived Test. A CLIA Certificate of Waiver is needed to perform testing in waived settings. Read this entire Instruction Sheet carefully before use. If a laboratory modifies the following test instructions including QC, the test will be considered high complexity and no longer considered CLIA-Waived and subject to all CLIA regulations. The Alere *i*Screen®DX Multi-Drugs of Abuse Dip Test is for use with human urine only. This Instruction Sheet and the manufacturer's package insert that is provided with the product must be followed.

This is a preliminary screening test that detects drug-of-abuse in urine at specified detection levels. To confirm preliminary positive results, a more specific method such as Gas Chromatography/Mass Spectrometry (GC/MS) must be used.

Warnings and Precautions

- For *in vitro* diagnostic use only (not for internal use).
- Store the Alere *i*Screen®DX Multi-Drugs of Abuse Dip Test at room temperature 59˚F to 86˚F (15˚C to 30˚C).
- Keep the Alere *i*Screen®DX Multi-Drugs of Abuse Dip Test in its original sealed pouch until ready for use. Do not use the test if the pouch is ripped or torn.
- Do not use the Alere *i*Screen®DX Multi-Drugs of Abuse Dip Test after the expiration date printed on the pouch.
- Be careful when handling urine because it may contain infectious agents. Always wear gloves and wash hands with soap and water after handling urine.
- To ensure that the test will work properly the testing instructions must be followed. Failure to do so may result in inaccurate screening results.
- Do not use this test if you are color-blind.

Limitations of the Test

- Use the test with human urine only.
- The test is for one time use only; it is not reusable.
- This test is a screening device; it does not detect the actual concentration of a drug.
- Contaminated or tainted urine sample may give false results.
- Certain foods or medications may cause the test to give false results.
- Send preliminary positive or uncertain results to a laboratory to confirm results.
- The colors of human urine usually range from amber yellow to very light yellow. Dark urine or urine with a brown or abnormal color should not be tested using this test. Dark urines should be sent to a laboratory for testing.
- The Alere *i*Screen®DX Multi-Drugs of Abuse Dip Test should give negative results when testing the urine of a normal healthy person. The Alere *i*Screen®DX device will give a preliminary positive result when the drug or drug metabolite is present in the urine at or above the detection level. See the Expected Results section of the enclosed Package Insert.

Detection Levels

The Alere *i*Screen®DX Multi-Drugs of Abuse Dip Test may not detect drug amounts lower than the detection levels.

Test ID	Drug/Metabolite	Detection Level
COC	Benzoylecgonine	300 ng/mL
MOP	Morphine	300 ng/mL
MET	d-Methamphetamine	500 ng/mL
THC	11-nor-Δ9-Tetrahydrocannabinol-9-carboxylic acid	50 ng/mL
AMP	d-Amphetamine	1000 ng/mL
PCP	Phencyclidine	25 ng/mL
BZO	Oxazepam	300 ng/mL
BAR	Secobarbital	300 ng/mL
MTD	Methadone	300 ng/mL
TCA	Nortriptyline	1000 ng/mL
MDMA	3,4-Methylenedioxymethamphetamine	500 ng/mL
OXY	Oxycodone	100 ng/mL
BUP	Buprenorphine	10 ng/mL

Quality Control

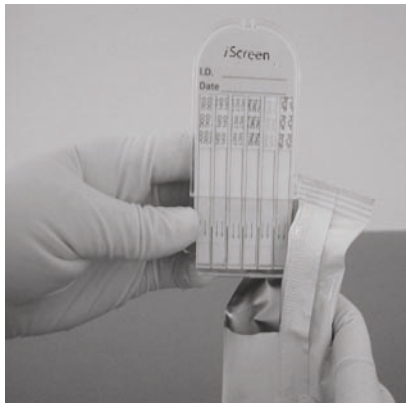
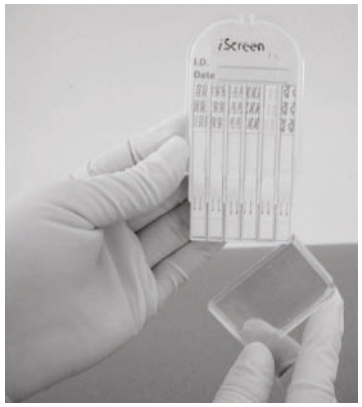
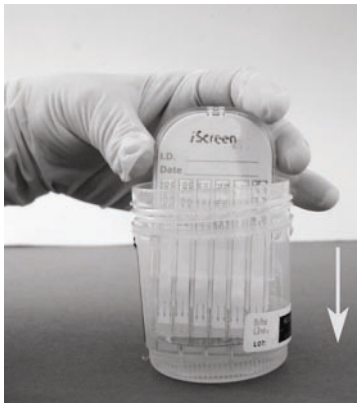
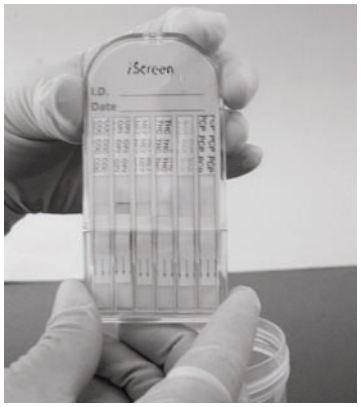
An internal procedural control has been built into the test to ensure that the test performs properly. The appearance of a line in the control region (C) serves as the internal procedural control to verify that the reagents in the test are still working, and that the test is valid.

The use of external controls is recommended to verify proper test kit performance. Quality Control samples should be tested with each new lot according to the quality control requirements of the testing facility. It is also recommended to test the products in storage monthly. When testing quality control samples, follow the same testing procedure as for testing urine samples. CLIA waived laboratories should follow the manufacturer's quality control recommendations.

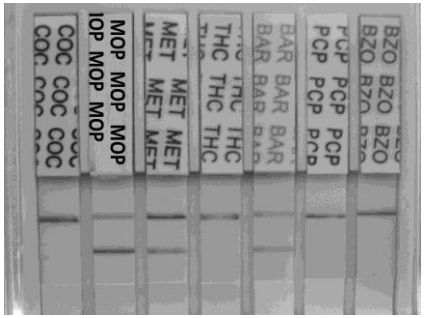
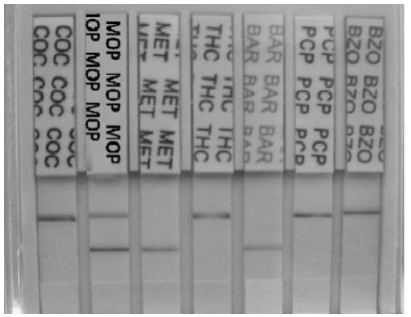
To obtain the appropriate external controls, contact the Customer Service Department at Alere Toxicology at 1-800-340-4029 or email to inquiries@tryi.com. Do not use commercially available urine controls since these products may not be compatible with the Alere *i*Screen®DX Multi-Drugs of Abuse Dip Test.

Refer to Quality Control section in the package insert for troubleshooting instructions.

Step-by-Step Testing Instructions

			
1. Remove the Alere *i*Screen®DX Multi-Drugs of Abuse Dip Test from the pouch by tearing at the notch.	2. Detach the bottom cover by pulling gently.	3. Dip the Alere *i*Screen®DX Multi-Drugs of Abuse Dip Test straight into the urine for a minimum of 10 seconds. **DO NOT dip beyond the tip of the arrows.**	4. Remove the Alere *i*Screen®DX Multi-Drugs of Abuse Dip Test from the urine. Re-attach the bottom cover and lay the device on a flat surface.

Interpretation of Results

			
Interpretation of Result. Look at each test strip separately. Read the test results on one side, then turn the device over and read results on the other side. Read test results at 5 minutes.	**Negative (–)** *Look at each test strip separately* The result is negative when there are two red lines, one in the control region (C) and one in the test region (T). This means that the urine sample does not contain that particular drug, or that the drug level is lower than the detection level. In the above example, MOP, MET, and BAR tests are negatives. **Note: Any visible test line (T), even a very faint test line, is considered a negative result.**	**Preliminary Positive (+)** *Look at each test strip separately* The result is preliminary positive when there is a red line in the control region (C) and no line in the test region (T). This means that the urine sample is preliminary positive for that particular drug. In the above example, COC, THC, PCP and BZO tests are preliminary positives. All urine samples with preliminary positive results should be sent to a laboratory for confirmation.	**Invalid** *Look at each test strip separately* The result is invalid when no line appears at the control region (C). When there is no line in the control region (C), the test is invalid even if there is a line in the test region (T). Do not use this result. In the above example, MET and BAR tests are invalid. If no line appears at the control region (C), the test may not have performed properly. Check testing procedure and repeat the test using a new Alere *i*Screen®DX Multi-Drugs of Abuse Dip Test.

Alere™ *i*Screen® DX

Alere *i*Screen®DX Multi-Drugs of Abuse Dip Test

COC/MOP/MET/THC/AMP/PCP/BZO/BAR/MTD/TCA/MDMA/OXY/BUP

This package insert covers combination test of cocaine, opiates, methamphetamine, THC, amphetamine, phencyclidine, benzodiazepines, barbiturates, methadone, tricyclic antidepressants, MDMA, oxycodone, or buprenorphine in the Alere *i*Screen®DX devices.

Intended Use

The Alere *i*Screen®DX Multi-Drugs of Abuse Dip Test Test is an *in vitro* screen test for the rapid detection of multiple drugs and drug metabolites in human urine at or above the following cutoff concentrations:

COC	Benzoylecgonine	300 ng/ml
MOP	Morphine	300 ng/mll
MET	Methamphetamine	500 ng/ml
THC	11-nor-Δ9-Tetrahydrocannabinol-9-carboxylic acid	50 ng/ml
AMP	Amphetamine	1000 ng/ml
PCP	Phencyclidine	25 ng/ml
BZO	Oxazepam	300 ng/ml
BAR	Secobarbital	300 ng/ml
MTD	Methadone	300 ng/ml
TCA	Nortriptyline	1000 ng/ml
MDMA	3,4-methylenedioxymethamphetamine	500 ng/ml
OXY	Oxycodone	100 ng/ml
BUP	Buprenorphine	10 ng/ml

The Alere *i*Screen®DX Multi-Drugs of Abuse Dip Test provides visual qualitative results and is intended for professional *in vitro* diagnostic use only. It is not intended for over-the-counter sale to non-professionals.

The Alere *i*Screen®DX Multi-Drugs of Abuse Dip Test provides only preliminary test results for drugs-of-abuse. For a quantitative result or to confirm positive results obtained by the Alere *i*Screen®DX Multi-Drugs of Abuse Dip Test, a more specific alternative method must be used. Gas Chromatography/Mass Spectrometry (GC/MS) is the preferred confirmatory method.

Summary and Explanation

COC: Cocaine derived from the leaves of the coca plant, is a potent central nervous system stimulant, and has been used as a local anesthetic. Cocaine use induces euphoria, confidence, and a sense of increased energy; these psychological effects are accompanied by increased heart rate, pupil dilation, fever, tremors, and sweating. Cocaine is generally smoked or administered intravenously or orally. Cocaine base can be smoked in the form commonly known as “crack”, which is likely to lead to dependence since the effect is more rapid and heightened. Cocaine is primarily excreted as benzoylecgonine and can generally be detected for 24–60 hours after cocaine use or exposure.[2]

MOP: Heroin, morphine and codeine are Opiates that are derived from the resin of the opium poppy. Heroin is quickly metabolized to morphine. Thus, morphine and morphine glucuronide may both be found in the urine of a person who has taken only heroin. The body also converts codeine to morphine. Thus, the presence of morphine (or morphine metabolite) in the urine indicates heroin, morphine and/or codeine use. Generally, morphine and other Opiates can be detected in the urine within 2 to 6 hours after use and remains detectable up to 3 days.[2,3] However, the length of time following drug use for which a positive result may occur is dependent upon several factors including the frequency and amount of usage, metabolic rate, excretion rate, drug half-life, and the drug user’s age, weight, activity and diet.

MET: Methamphetamine is a potent sympathomimetic agent with therapeutic applications. Methamphetamine use in acute higher doses lead to enhanced stimulation of the central nervous system and induce euphoria, alertness, and a sense of increased energy and power. Methamphetamine is excreted in the urine as amphetamine and oxidized as deaminated derivatives. However, 40% of methamphetamine is excreted unchanged. Thus the presence of the parent compound in the urine indicates methamphetamine use. Methamphetamine can be detected in the urine within 4-6 hours after use and for 3-5 days, depending on urine pH level.[2,3]

THC: THC use may impair short-term memory and inhibit learning capacity. It may also alter mood and sensory perceptions, cause loss of coordination, induce anxiety, paranoia, hallucinations, depression, confusion, and increased heart rate. A tolerance to the cardiac and psychotropic effects can occur. Long-term THC use may be associated with behavioral disorders. Withdrawal from marijuana use may produce restlessness, insomnia, anorexia, and nausea.

AMP: Amphetamine is chemically related to the human body’s natural catecholamines, epinephrine, and norepinephrine. It has therapeutic applications and is a potent sympathomimetic agent. Amphetamine use in acute higher doses leads to enhanced stimulation of the central nervous system and induces euphoria, alertness, reduced appetite, and a sense of increased energy and power. Generally about 30% of amphetamine is excreted unchanged in 24-hour urine.

PCP: Phencyclidine is an arychlohexylamine that is used as a veterinary anesthetic. It is used illegally as a hallucinogen, and is commonly referred to as PCP, Angel Dust, Crystal Cyclone, Love Boat, Hog, or Killer Weed. PCP can produce lethargy, disorientation, and loss of coordination, visual distortion, euphoria, ataxia, and even coma. PCP can be taken orally, by nasal ingestion, smoking, or intravenous injection. It is metabolized in the liver and excreted through the kidneys. The half-life of phencyclidine is about three days.

BZO: Benzodiazepines are anxiolytic drugs that are most widely prescribed and used as anti-anxiety agents. They are also used as hypnotics, muscle relaxants and anti-convulsants. Some metabolites of benzodiazepines also exhibit pharmacological activities. Use of benzodiazepines can result in drowsiness and confusion; it also potentiates alcohol and other central nervous system depressants. Psychological and physical dependence on benzodiazepines can develop if higher doses of the drug are given over a prolonged period.[1,2] Benzodiazepines are taken orally or by injection. The drug is metabolized in the liver and excreted in the urine as the parent compound or as oxazepam (in the case of chlorodiazepoxide and diazepam). Oxazepam is detectable in the urine for up to 7 days. [2,3]

BAR: Barbiturates are a class of central nervous system depressants. Phenobarbital has been used as a daytime sedative and extensively as an anticonvulsant. Phenobarbital is an example of long acting barbiturate derivative while pentobarbital and secobarbital are examples of short acting barbiturate sedatives. Barbiturate abuse can lead not only to impaired motor coordination and mental disorder, but also to respiratory collapse, coma and even death. Short acting barbiturates will generally be excreted in urine as metabolites, while long acting barbiturates will primarily appear unchanged. Barbiturates normally remain detectable in urine for 4 to 6 days after use (up to 30 days for Phenobarbital).[2,3]

MTD: Methadone is a synthetic analgesic drug that is originally used for the treatment of narcotic addiction. Methadone use induced psychological effects such as analgesia, sedation and respiratory depression. Overdose of methadone may cause coma or even death. Methadone is taken orally or intravenously and is metabolized in the liver. The major route of methadone excretion is in the urine. The effects of methadone last up to 24 hours after use and can be detected in the urine up to 14 days.[2,3] The length of time following drug use for which a positive result may occur is dependent upon several factors including the frequency and amount of drug, metabolic rate, excretion rate, drug half-life, and the user’s age, weight, activity and diet.

TCA: Tricyclic antidepressants (TCAs) are a type of prescription drugs used for the treatment of depressive disorders. Tricyclic Antidepressants consist of two main chemical classes. The tertiary amines boost serotonin levels and are usually prescribed for insomnia, irritability and overstimulation; these include amitryptiline, imipramine, trimipramine and doxepin. The secondary amines, which include nortryptiline, desipramine and protryptiline, enhance norepinephrine levels and are prescribed for fatigue; withdrawal and inertness.[4-5] TCA abuse can result in respiratory depression, convulsions, blood pressure deviation, severe cardiac conditions, and coma. TCAs are taken orally or sometimes by injection. TCAs are excreted in the urine mostly in the form of metabolites for up to ten days.

MDMA: 3,4-methylenedioxymethamphetamine (MDMA) is a synthetic drug that is chemically related to the amphetamine family of compounds. MDMA has been available as a street drug since the 1980s, however, since the 1990s its use has increased, particularly among teenagers and young adults. The drug has street names that include "Ecstasy, XTC, Clarity, Essence and Adam". MDMA is typically available in tablet form containing appropriately 60-150 milligrams of MDMA. The common method of use is oral ingestion, although the powder form can be snorted and occasionally smoked. MDMA has properties of both stimulants and hallucinogens. The effects of the drug last up to 6 hours after oral ingestion. The adverse effects include elevated blood pressure, increased heart rate, hyperthermia, dehydration, anxiety, paranoia and insomnia. The detection period of MDMA in urine is 1-3 days for single use and up to 5 days for heavy use.[1]

OXY: Oxycodone is a synthetic analgesic drug administered orally for the relief of pain. The major route of oxycodone excretion is in the urine. The effects of oxycodone last up to 4 hours after use. The length of time following drug use for which a positive result may occur is dependent upon several factors including the frequency and amount of usage, metabolic rate, excretion rate, drug half-life, and the drug user’s age, weight, activity, and diet.[2,3]

BUP: Buprenorphine is a synthetic derivative of thebaine with partial agonist and antagonist actions[6]. It is 25 to 40 times more potent than morphine as an analgesic. It has been used for the treatment of opiate addiction as an alternative to methadone. Buprenorphine has a half-life of 2-4 hours in plasma and complete elimination of a single dose can take up to 6 days.

Test Principle

Urine based screening tests for drugs-of-abuse are available from simple immunoassay tests to complex analytical procedures. Due to speed and sensitivity, immunoassays have become the most widely accepted method for urine-based drugs-of-abuse screening tests. The Alere *i*Screen®$_{DX}$ family of urine drug screen tests is based on the principle of the highly specific immunochemical reactions between antigens and antibodies. The Alere *i*Screen®$_{DX}$ Multi-Drugs of Abuse Dip Test is based on a competitive immunoassay procedure in which immobilized drug conjugates compete with the drug(s) present in urine for limited antibody binding sites. The test device consists of individual test strips assembled into separate chambers of a plastic insert. On each membrane strip, a drug conjugate is pre-coated at a specific region known as the test region. A colored antibody-colloidal gold conjugate is coated onto a pad and placed at one end of the membrane strip. In the test procedure, the Alere *i*Screen®$_{DX}$ Multi-Drugs of Abuse Dip Test device is dipped into a urine sample. This allows the urine into contact with the sample pads of the Alere *i*Screen®$_{DX}$ Multi-Drugs of Abuse Dip Test device. The urine then migrates across the membrane by capillary action. If any drug is present in the urine, it competes with the drug conjugate, which is immobilized on the membrane for the limited binding sites on the colored antibody colloidal gold conjugate. When a sufficient amount of drug is present, the drug will saturate the antibody binding sites and the colored colloidal gold conjugate cannot bind to the drug conjugate on the membrane. The absence of a color band at a specific test region indicates a positive result for that particular test. If there is no drug or drug metabolite present to compete for the binding sites of the colored colloidal gold conjugate, it binds to the immobilized drug conjugate to form a visible band at the specific test region of the membrane. The presence of a color band at a specific test region indicates a negative result for that particular test.

A control band with a different antigen/antibody reaction is added to the immuno-chromatographic membrane strip at the control region (C) to indicate that the test performed properly. This control band should always appear regardless of the presence of drug or metabolite.

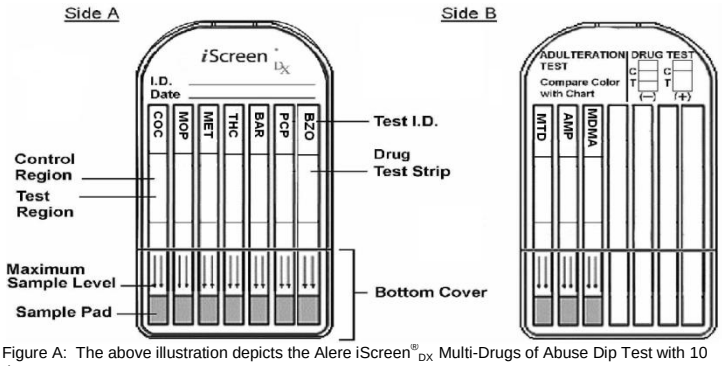


Figure A: The above illustration depicts the Alere iScreen®$_{DX}$ Multi-Drugs of Abuse Dip Test with 10 drug tests.

Reagents

Protein conjugate for benzoylecgonine, morphine, methamphetamine, THC, amphetamine, phencyclidine, benzodiazepine, barbiturate, methadone, nortriptyline, MDMA, oxycodone, or buprenorphine is coated onto the test region of the membrane.

The colored conjugate pad for each strip contains antibodies for benzoylecgonine, morphine, methamphetamine, THC, amphetamine, phencyclidine, benzodiazepine, barbiturate, methadone, tricyclic antidepressant, MDMA, oxycodone, or buprenorphine.

Materials Provided

Each Alere *i*Screen®$_{DX}$ Multi-Drugs of Abuse Dip Test Kit contains:

1. 1 Package Insert (directions for use).
2. 25 Alere *i*Screen®$_{DX}$ test devices. Each test device is packaged with a desiccant and sealed in a foil pouch.

Warnings and Precautions

- FOR *IN VITRO* DIAGNOSTIC USE ONLY
- For professional 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.
- Handle all urine specimens as if potentially infectious. Proper handling and disposal methods should be established.
- Avoid cross-contamination of urine samples by using a new specimen collection container for each urine sample.
- **Dip device up to, but not beyond the tip of the arrows.**
- Do not drop device into sample collection cup.

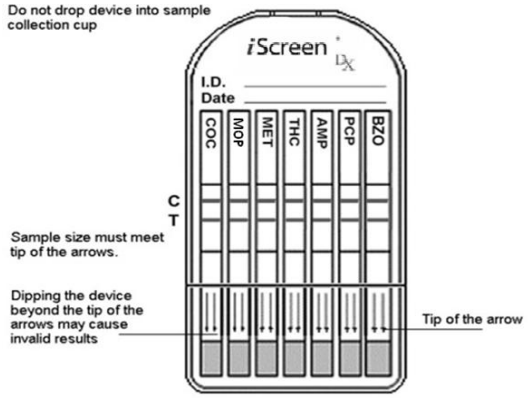


Figure B

Product Storage

The Alere *i*Screen®$_{DX}$ Multi-Drugs of Abuse Dip Test should be stored at room temperature (15°–30°C) until the expiration date on the label. Do not open pouch until ready to perform the assay.

Specimen Collection and Handling

The Alere *i*Screen®$_{DX}$ Multi-Drugs of Abuse Dip Tests are formulated for use with urine specimens. Use only freshly voided, untreated urine.[4] Do not centrifuge or add preservatives to urine. Urine samples should be collected so that testing may be performed as soon as possible, preferably during the same day. Specimens that have been refrigerated must be brought to room temperature prior to testing. Previously frozen specimens must be thawed, brought to room temperature, and mixed thoroughly prior to testing.

Note: *All materials coming in contact with urine specimens should be handled and disposed of as if potentially infectious. Avoid contact and follow good laboratory practice.*

Test Procedure

IMPORTANT: Donor sample (urine specimen) should be brought to room temperature (15°-30°C) prior to testing. Do not open pouch until ready to perform the assay.

1. Collect urine in a collection cup.
2. Remove the test device from the sealed pouch by tearing at the notch.
3. Detach the bottom cover and dip the sample pads of the Alere *i*Screen®DX Multi-Drugs of Abuse Dip Test device straight into the urine. Dip for a minimum of 10 seconds. **Dip up to, but not beyond the tip of the arrows. Please refer to Fig. B in Warnings and Precautions.**
4. Remove the Alere *i*Screen®$_{DX}$ Multi-Drugs of Abuse Dip Test device from the sample and re-attach the bottom cover.
5. Once the control band (C) appears (in 5 minutes or less) results are ready to interpret. Read results at 5 minutes.

Interpretation of Results

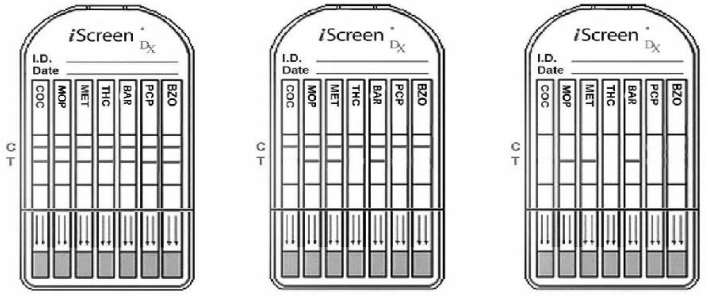


Figure C

**Note: The above results are for illustration purposes only; see the explanations below for interpretation of results.*

Negative: The presence of a colored band at the control region (C) and a colored band at a specific test region regardless of the intensity indicate that the result is negative for that particular test.

Positive: The presence of a colored band at the control region (C) and the absence of a colored band at the test region indicate a positive result for that particular test.

Invalid: No band appears at the control region (C). The test is inconclusive even if there is a band in the test region. If the test device does not produce a band at the control region, check testing procedures, samples, and/or control materials, and repeat the test using a new device.

Important: <u>Read each test independently. Do not compare color intensity of one test to another</u>. Samples with faint test bands at the test regions should be considered negative. The Alere *i*Screen®DX Multi-Drugs of Abuse Dip Test provides qualitative results for the presence of drug(s) at specified cut-off concentrations. It is recommended that samples with questionable test bands and positive results be confirmed with a more specific quantitative method (Gas Chromatography/Mass Spectrometry).

Quality Control

Non-CLIA Waived Laboratories:

An internal procedural control has been built into the test to ensure that the test performs properly. The appearance of a line in the control region (C) serves as the internal procedural control to verify that the reagents in the test are still working, and that the test is valid. The manufacturer's recommendation for daily quality control is to document the appearance of the control line for the first sample tested each day.

The use of external controls is recommended to verify proper kit performance. Quality Control samples should be tested with each new lot, each new shipment and according to the quality control requirements of the testing facility, and/or applicable federal, state or local guidelines. When testing quality control samples, follow the same testing procedure as for testing urine samples.

CLIA-Waived Laboratories:

An internal procedural control has been built into the test to ensure that the test performs properly. The appearance of a line in the control region (C) serves as the internal procedural control to verify that the reagents in the test are still working, and that the test is valid. The manufacturer's recommendation for daily quality control is to document the appearance of the control line for the first sample tested each day.

The use of external controls is recommended to verify proper kit performance. Quality Control samples should be tested with each new lot, each new shipment and according to the quality control requirements of the testing facility. It is also recommended to test the products in storage monthly. When testing quality control samples, follow the same testing procedure as for testing urine samples.

Contact the Customer Service Department at Alere Toxicology at 1-800-340-4029 or email to inquiries@tryi.com with any questions regarding quality control or to order the appropriate external controls. Do not use commercially available urine controls since these products may not be compatible with the Alere *i*Screen®DX Multi-Drugs of Abuse Dip Test.

Limitations of Procedure

- The assay is designed for use with human urine only.
- Positive results only indicate the presence of drug/metabolites and do not indicate or measure intoxication.
- There is a possibility that technical or procedural error, as well as other substances in certain food and medication, may interfere with the test and cause false results. See Specificity section for the list of substances that will produce either positive results, and Interference section for the list of components that do not interfere with test performance.
- If a drug/metabolite is found present in the urine specimen, the assay does not indicate frequency of drug use or distinguish between drugs of abuse and certain food and/or medication.
- If it is suspected that the sample may have been mislabeled a new specimen should be collected.
- If it is suspected that the sample may have been tampered, a new specimen should be collected.

Performance Characteristics

Precision

For each specific drug test, drug-free normal urine was spiked with drug standards to various concentrations (-50%, -25%, +25% and +50%). For each concentration, a minimum of 25 tests were performed to validate the test performance around the cut-off concentration. The results for each drug test in the Alere *i*Screen®DX Multi-Drugs of Abuse Dip Test are summarized below:

Drug Test	Total # of Test / Conc.	Concentration							
		-50%		-25%		+25%		+50%	
		-	+	-	+	-	+	-	+
COC300	30	30	0	26	4	2	28	0	30
MOP300	30	30	0	24	6	3	27	0	30
MET500	30	30	0	24	6	3	27	0	30
THC50	30	30	0	26	4	4	26	0	30
AMP1000	30	30	0	24	6	3	27	0	30
PCP25	30	30	0	26	4	4	26	0	30
BZO300	30	30	0	27	3	5	25	0	30
BAR300	30	30	0	26	4	4	26	0	30
MTD300	30	30	0	27	3	5	25	0	30
TCA1000	30	30	0	28	2	6	24	0	30
MDMA500	30	30	0	25	5	4	26	0	30
OXY100	30	30	0	25	5	4	26	0	30
BUP10	25	25	0	25	0	0	25	0	25

Accuracy

The accuracy of the Alere *i*Screen®DX Multi-Drugs of Abuse Dip Test device was evaluated in comparison to the results from GC/MS analysis or other commercially available confirmatory methods. A minimum of thirty-six (36) negative urine samples were collected from volunteer donors and tested with each drug strip. Of the negative urine samples tested, all were found negative by both methods (100% agreement).

Additionally, for each drug test a minimum of 40 clinical urine samples previously analyzed by GC/MS method with known concentration(s) of drug(s) values were blind labeled and evaluated. The results are summarized below:

Drug Test		GC/MS Neg.	GC/MS < -50%	GC/MS -50% to < C/O	GC/MS ≥ C/O to +50%	GC/MS > +50%	% Agreement w/ GC/MS	
							Neg (-)	Pos (+)
COC300	Pos. (+)	0	0	2	6	34	95.3%	100.0%
	Neg. (-)	36	0	5	0	0		
MOP300	Pos. (+)	0	0	2	5	36	95.0%	100.0%
	Neg. (-)	36	0	2	0	0		
MET500	Pos. (+)	0	0	2	5	34	95.0%	97.5%
	Neg. (-)	36	0	2	1	0		
THC50	Pos. (+)	0	0	1	5	33	97.6%	95.0%
	Neg. (-)	36	0	4	2	0		
AMP1000	Pos. (+)	0	0	2	5	34	95.6%	97.5%
	Neg. (-)	36	0	7	1	0		
PCP25	Pos. (+)	0	0	1	4	36	97.5%	100.0%
	Neg. (-)	36	0	3	0	0		
BZO300	Pos. (+)	0	0	1	4	34	97.5%	95.0%
	Neg. (-)	36	0	3	2	0		
BAR300	Pos. (+)	0	0	2	4	34	95.3%	95.0%
	Neg. (-)	36	0	5	2	0		
MTD300	Pos. (+)	0	0	2	4	34	95.2%	95.0%
	Neg. (-)	36	0	4	2	0		
TCA1000	Pos. (+)	0	0	1	29	11	97.6%	97.6%
	Neg. (-)	36	0	5	1	0		
MDMA500	Pos. (+)	0	0	0	2	36	100.0%	95.0%
	Neg. (-)	36	0	4	2	0		
OXY100	Pos. (+)	0	0	2	4	35	95.1%	97.5%
	Neg. (-)	36	0	3	1	0		
BUP10	Pos. (+)	0	0	3	6	33	94.1%	100%
	Neg. (-)	40	3	5	0	0		

CLIA Waiver Performance

Accuracy and Precision

To demonstrate that the Alere *i*Screen®DX Multi-Drugs of Abuse Dip Test device is a simple test and can be used by untrained users to obtain accurate test results, site studies were conducted at three (3) non-laboratory sites. The participants (untrained users) at these sites are non-laboratory professionals with no training or previous experience with drugs-of-abuse tests or the Alere *i*Screen®DX Multi-Drugs of Abuse Dip Test device. The participants are a demographically diverse population that includes a range of ages, educational and regional background and are representative of the users of a CLIA Waived test.

For each specific drug test contained in the Alere *i*Screen®DX Multi-Drugs of Abuse Dip Test device, drug-free normal urine was spiked with drug standards to various concentrations (-50%, -20%, +20% and +50%). Each of the concentration was divided into 20 aliquots and each aliquot was blind-labeled with a unique code. A total of 20 tests per concentration were performed at each of the three sites to validate the test performance around the cut-off concentration. The results are summarized below:

			Alere *i*Screen®DX Multi-Drugs of Abuse Dip Test							
Site	Conc.	# of sample per conc. Per test	COC		MOP		MET		THC	
			-	+	-	+	-	+	-	+
1	-50%	20	20	0	20	0	20	0	20	0
	-20%	20	19	1	18	2	18	2	20	0
	+20%	20	2	18	0	20	2	18	0	20
	+50%	20	0	20	0	20	0	20	0	20
2	-50%	20	20	0	20	0	20	0	20	0
	-20%	20	19	1	18	2	18	2	19	1
	+20%	20	1	19	1	19	1	19	1	19
	+50%	20	0	20	0	20	0	20	0	20
3	-50%	20	20	0	20	0	20	0	20	0
	-20%	20	19	1	19	1	18	2	20	0
	+20%	20	1	19	0	20	0	20	2	18
	+50%	20	0	20	0	20	0	20	0	20
	Total (-) per test		121	N/A	116	N/A	117	N/A	122	N/A
	Total (+) per test		N/A	119	N/A	124	N/A	123	N/A	118

Site	Conc.	# of sample per conc. Per test	Alere *i*Screen®DX Multi-Drugs of Abuse Dip Test							
			AMP		PCP		BZO		BAR	
			-	+	-	+	-	+	-	+
1	-50%	20	20	0	20	0	20	0	20	0
	-20%	20	19	1	19	1	19	1	18	2
	+20%	20	0	20	2	18	1	19	1	19
	+50%	20	0	20	0	20	0	20	0	20
2	-50%	20	20	0	20	0	20	0	20	0
	-20%	20	18	2	19	1	20	0	17	3
	+20%	20	0	20	2	18	1	19	0	20
	+50%	20	0	20	0	20	0	20	0	20
3	-50%	20	20	0	20	0	20	0	20	0
	-20%	20	19	1	20	0	19	1	19	1
	+20%	20	0	20	0	20	1	19	1	19
	+50%	20	0	20	0	20	0	20	0	20
	Total (-) per test		116	N/A	122	N/A	121	N/A	116	N/A
	Total (+) per test		N/A	124	N/A	118	N/A	119	N/A	124

Site	Conc.	# of sample per conc. Per test	Alere *i*Screen®DX Multi-Drugs of Abuse Dip Test									
			MTD		TCA		MDMA		OXY		BUP	
			-	+	-	+	-	+	-	+	-	+
1	-50%	20	20	0	20	0	20	0	20	0	20	0
	-20%	20	18	2	20	0	19	1	18	2	20	0
	+20%	20	1	19	1	19	0	20	1	19	0	20
	+50%	20	0	20	0	20	0	20	0	20	0	20
2	-50%	20	20	0	20	0	20	0	20	0	20	0
	-20%	20	18	2	18	2	19	1	18	2	20	0
	+20%	20	0	20	1	19	2	18	0	20	1	19
	+50%	20	0	20	0	20	0	20	0	20	0	20
3	-50%	20	20	0	20	0	20	0	20	0	20	0
	-20%	20	18	2	19	1	19	1	19	1	20	0
	+20%	20	0	20	0	20	2	18	1	19	1	19
	+50%	20	0	20	0	20	0	20	0	20	0	20
	Total (-) per test		115		119		121		117		122	
	Total (+) per test			125		121		119		123		118

The percent of correct results of all the drug tests for the strong negative (-50%) and strong positive (+50%) was 100% (95% CI: 93% to 100.0%). The percent correct results for the weak negative (-20%) was from 90% (95% CI: 80% to 96%) for the MET, BAR and MTD tests to 100% (95% CI: 93% to 100.0%) for the BUP test. The percent correct results for the weak positive (+20%) was from 93% (95% CI: 84% to 98%) for the COC, PCP and MDMA tests to 100% (95% CI: 94% to 100%) for the AMP test.

The data demonstrated that there was no statistically significant difference in the percent of correct results among the three sites for strong negative, weak negative, weak positive, and strong positive concentrations for all above-mentioned drug tests.

Specificity

The specificity study for each of the drug test of the Alere *i*Screen®DX Multi-Drugs of Abuse Dip Test device was evaluated separately by adding structurally related compounds to normal human urine. The results are expressed as the amount in ng/ml of the compound that was observed to produce a positive result.

COC 300 ng/ml

Compound	ng/ml	Compound	ng/ml
Benzoylecgonine	300	Ecgonine	100,000

MOP 300 ng/ml

Compound	ng/ml	Compound	ng/ml
6-Acetylmorphine	500	Hydrocodone	1,000
Codeine	300	Hydromorphone	400
Dihydrocodeine	500	Morphine	300
Ethyl morphine	300	Morphine-3-β-D-Glucuronide	500
Heroin	100	Nalorphine	5,000

MET 500 ng/ml

Compound	ng/ml	Compound	ng/ml
Ephedrine	10,000	l-Methamphetamine	25,000
p-Hydroxymethamphetamine	1,750	Procaine	50,000
d,l-3,4-MDMA	1000	Trimethobenzamide	75,000
d-Methamphetamine	500		

THC 50 ng/ml

Compound	ng/ml	Compound	ng/ml
Cannabidiol	100,000	11-Hydroxy-Δ9-THC	2,500
Cannabinol	50,000	Δ-8-Tetrahydrocannabinol	7,000
11-nor-Δ-8-THC-9-COOH	50	Δ-9-Tetrahydrocannabinol	10,500
11-nor-Δ-9-THC-9-COOH	50		

AMP 1000 ng/ml

Compound	ng/ml	Compound	ng/ml
d-Amphetamine	1,000	Phentermine	3,000
l-Amphetamine	25,000	β-Phenylethylamine	100,000
d,l-3,4-MDA	5,000		

PCP 25 ng/ml

Compound	ng/ml
Phencyclidine	25

BZO 300 ng/ml

Compound	ng/ml	Compound	ng/ml
Alprazolam	150	Lorazepam	1,500
Bromazepam	800	Lormetazepam	1,000
Chlordiazepoxide	2,000	Medazepam	2,000
Clobazam	200	Nitrazepam	1,000
Clonazepam	4,000	Nordiazepam	100
Delorazepam	6,000	Oxazepam	300
Diazepam	150	Prazepam	1,000
Estazolam	300	Temazepam	150
Flunitrazepam	1,000	Triazolam	1,500
Flurazepam	300		

BAR 300 ng/ml

Compound	ng/ml	Compound	ng/ml
Alphenal	400	Butalbital	300
Allobarbital	1,500	Butethal	400
Amobarbital	1,500	Pentobarbital	400
Aprobarbital	400	Phenobarbital	400
Barbital	400	Secobarbital	300
Butabarbital	400		

MTD 300 ng/ml

Compound	ng/ml	Compound	ng/ml
Doxylamine	50,000	Methadone	300
2-Ethylidene-1.5-Dimethyl-1,3-Diphenylpyrolidine	50,000	Pheniramine	75,000

TCA 1000 ng/ml

Compound	ng/ml	Compound	ng/ml
Amitryptiline	1,000	Nordoxepin	1,000
Clomipramine	7,500	Nortriptyline	1,000
Cyclobenzaprine	1,500	Perphenazine	50,000
Desipramine	750	Promazine	10,000
Doxepin	1,000	Protryptiline	350
Imipramine	750	Trimipramine	1,500

MDMA 500 ng/ml

Compound	ng/ml	Compound	ng/ml
d,l-3,4-MDA	2,000	d,l-3,4-MDMA	500
d,l-3,4-MDEA	250	d-Methamphetamine	50,000

OXY 100 ng/ml

Compound	ng/ml	Compound	ng/ml
Codeine	10,000	Oxycodone	100
Hydrocodone	600	Hydromorphone	25,000

BUP 10 ng/ml

Compound	ng/ml	Compound	ng/ml
Buprenorphine	10	Norbuprenorphine	50
Buprenorphine Glucuronide	5	Norbuprenorphine Glucuronide	50

The effects of pH and specific gravity of the specimen on the performance of the drugs-of-abuse tests at cutoff level were tested. Results obtained were acceptable and not affected by any urine samples with pH range of 4.5 to 8.5 and specific gravity range of 1.005 to 1.030.

Interferences

Various drugs, drug metabolites, and other constituents commonly found in urine were evaluated for interferences and cross-reactivity. The following compounds were found not to cross-react with the Alere *i*Screen®DX Multi-Drugs of Abuse Dip Test device when tested at concentrations of 100 µg/ml (100,000 ng/ml):

Acetaminophen (4-Acetamidophenol; APAP; N-Acetyl-p-aminophenol)
Acetone
6-Acetylmorphine *(except MOP assay)*
Acetylsalicylic acid (Aspirin)
Albumin
Allobarbital *(except BAR assay)*
Alphenal *(except BAR assay)*
Alprazolam *(except BZO assay)*
Amitriptyline *(except TCA assay)*
Amobarbital *(except BAR assay)*
Amoxapine
Amoxicillin
Aprobarbital *(except BAR assay)*
d-Amphetamine *(except AMP assay)*
l-Amphetamine *(except AMP assay)*
Ampicillin
Apomorphine
l-Ascorbic Acid (Vitamin C)
Aspartame
Atropine
Barbital *(except BAR assay)*
Benzilic acid
Benzocaine (Ethyl p-Aminobenzoate)
Ibuprofen
Imipramine *(except TCA assay)*
l-Isoproterenol
d,l-Isoproterenol
Ketaime HCl*)*
Lidocaine
Lorazepam *(except BZO assay)*
Lormetazepam *(except BZO assay)*
Medazepam *(except BZO assay)*
Meperidine
Methadone *(except MTD assay)*
Methamphetamine *(except MET& MDMA assays)*
l-Methamphetamine (*except MET assay)*
Methaqualone
Methoxyphenamine
(1R,2S) N-Methyl-Ephedrine
2-Methylamine-Propiophenone
d,l-3,4-Methylenedioxyamphetamine *(except AMP & MDMA assays)*
d,l-3-4-Methylenedioxyethylamphetamine (*except MDMA assay*)

Benzoic acid
Benzoylecgonine *(except COC assay)*
Benzphetamine
Bilirubin
Bromazepam *(except BZO assay)*
d-Brompheniramine
Buprenorphine *(except BUP assay)*
Buprenorphine Glucuronide *(except BUP assay)*
Butabarbital *(except BAR assay)*
Butalbital *(except BAR assay)*
Butethal *(except BAR assay)*
Caffeine
Cannabidiol *(except THC assay)*
Cannabinol *(except THC assay)*
Chlordiazepoxide *(except BZO assay)*
Chloroquine
d-Chlorpheniramine
d,l-Chlorpheniramine
Chlorpromazine
Cholesterol
Clobazam *(except BZO assay)*
Clomipramine *(except TCA assay)*
Clonazepam *(except BZO assay)*
Cocaine
Codeine *(except MOP & OXY assays)*
Cortisone
l-Cotinine
Creatine
Creatinine
Cyclobenzaprine *(except TCA assay)*
Delorazepam *(except BZO assay)*
Deoxycorticosterone
Desipramine *(except TCA assay)*
Dextromethorphan
Diazepam *(except BZO assay)*
Dihydrocodeine *(except MOP assay)*
4-Dimethylaminoantipyrine
Diphenhydramine
Dopamine (3-Hydroxytyramine)
Doxepin *(except TCA assay)*
Doxylamine *(except MTD assays)*
Ecgonine *(except COC assay)*
Ecgonine Methyl Ester
d,l-Ephedrine *(except MET assay)*
l-Epinephrine
Erythromycin
Estazolam *(except BZO assay)*
β-Estradiol
Estrone-3-Sulfate
Ethanol
Ethyl Morphine *(except MOP assay)*
Ethyl-p-aminobenzoate
2-Ethylidene-1.5-Dimethyl-1-3.3-Diphenylpyrolidone *(except MTD assay)*
Flunitrazepam *(except BZO assay)*
Flurazepam *(except BZO assay)*
Furosemide
Gentisic acid
Glucose
Glutethimide
Guaiacol Glyceryl Ether
Hemoglobin
Heroin *(except MOP assay)*
Hippuric acid
Hydrochlorothizide
Hydrocodone *(except MOP & OXY assays)*
Hydrocortisone
Hydromorphone *(except MOP & OXY assays)*
p-Hydroxymethamphetamine *(except MET assay)*
11-Hydroxy-Δ-9-THC *(except THC assay)*
d,l-3,4-Methylenedioxymethamphetamine *(except MET& MDMA assays)*
Methylphenidate
Morphine *(except MOP assay)*
Morphine-3-β-D-Glucuronide *(except MOP assay)*
Nalidixic acid
Nalorphine *(except for MOP assay)*
Naloxone
d-Naproxen
Niacinamide
Nicotine
Nitrazepam *(except BZO assay)*
Norbuprenorphine *(except BUP assay)*
Norbuprenorphine Glucuronide *(except BUP assay)*
Nordiazepam *(except BZO assay)*
Nordoxepin *(except TCA assay)*
d,l-Norephedrine
Norethindrone
Nortriptyline *(except TCA assay)*
Oxalic Acid
Oxazepam *(except BZO assay)*
Oxolinic acid
Oxycodone *(except OXY assay)*
Papaverine
Penicillin-G (Benzylpenicillin)
Pentazocaine
Pentobarbital *(except BAR assay)*
Perphenazine *(except TCA assay)*
Phencyclidine *(except PCP assay)*
Pheniramine *(except MTD assay)*
Phenobarbital *(except BAR assay)*
Phenothiazine (Thiodiphenylamine)
Phentermine *(except AMP assay)*
Phenylephrine
β-Phenylethylamine *(except AMP assay)*
d-Phenylpropanolamine
Prednisolone
Prazepam *(except BZO assay)*
Procaine (except MET assay)
Promazine *(except TCA assay)*
Promethazine
Protryptiline *(except TCA assay)*
d-Pseudoephedrine
Pyrolidine
Quinidine
Quinine
Ranitidine
RiboflavinSalicylic acid
Secobarbital *(except BAR assay)*
Serotonin
Sodium Chloride Sulfamethazine
Sulindac
Temazepam *(except BZO assay)*
Tetracycline
Δ8-THC *(except THC assay)*
Δ9-THC *(except THC assay)*
11-nor-Δ-8-THC-9-Carboxylic Acid *(except THC assay)*
11-nor-Δ-9-THC-9-Carboxylic Acid *(except THC assay)*
Thiamine
Thioridazine
Triazolam *(except BZO assay)*
Trifluoperazine
Trimethobenzamide *(except MET assay)*
Trimipramine Maleate *(except TCA assay)*
Tryptamine
d,l-Tryptophan
Tyramine
d,l-Tyrosine
Uric Acid
Verapamil
Zomepirac

Bibliography of Suggested Reading

1. Wong, R., The Current Status of Drug Testing in the US Workforce, Am. Clin. Lab., 2002; 21(1): 21-23
2. Baselt, R.C. Disposition of Toxic Drugs and Chemicals in Man, Biomedical Publications, Davis, CA, 1982.
3. Urine testing for Drugs of Abuse. National Institute on Drug Abuse (NIDA), Research Monograph 73, 1986.
4. Wong, R., The Effect of Adulterants on Urine Screen for Drugs of Abuse: Detection by an On-site Dipstick Device, Am. Clin. Lab., 2002; 21(3); 14-18
5. Fed. Register, Department of Health and Human Services, Mandatory Guidelines for Federal Workplace Drug Testing Programs, 53, 69, 11970-11979, 1988.
6. McBay, A.J. Clin. Chem. 33, 33B-40B, 1987.
7. Gilman, A.G., and Goodman, L.S. The Pharmacological Basis of Therapeutics, Eds. MacMillan Publishing, New York, NY, 1980.
8. Ringsrud, K.M and Linne, J.J., Urinalysis and Body Fluids, A color Text and Atlas, Mosby-Year Book, Inc., 1995.
9. U.S Department of Transportation, Drug Testing Procedures Handbook

Manufactured for:
Alere Toxicology Services – Products Division
Portsmouth, VA 23704 USA
Phone: 1-800.340.4029
Fax: 1-888.340.4029
Web: www.aleretoxicology.com

Part No.: PI-X11-MDT Rev: A, 03/2013