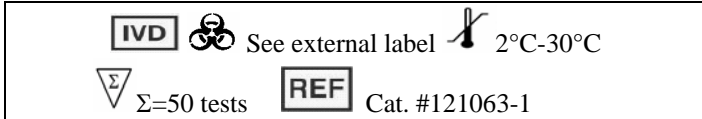




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## OneStep Benzodiazepine RapiDip InstaTest

### INTENDED USE

The Cortez Diagnostic, Inc. OneStep Benzodiazepine InstaStrip is a rapid qualitative, competitive binding immunoassay for determination of benzodiazepines in urine at or above the cut-off level of 300 ng/ml. OneStep Benzodiazepine InstaStrip is not intended to monitor drug levels, but only to screen urine for the presence of benzodiazepine and its major metabolites.

*Note: The test provides only preliminary data, which should be confirmed by other methods, such as gas chromatography/mass spectrometry (GC/MS). Clinical considerations and professional judgement should be applied to any drugs of abuse result, particularly when preliminary positive results are indicated.*

### SUMMARY AND EXPLANATION OF THE TEST

The OneStep Benzodiazepine InstaStrip is an easy, fast, and visually read competitive binding immunoassay method for screening without the need for instrumentation to arrive at determination. The test system employs a unique mixture of monoclonal and polyclonal antibodies to selectively identify Benzodiazepine in test samples with a high degree of sensitivity.

Benzodiazepines (BZD) as a class of drugs exert their primary effects on the central nervous system and are used therapeutically as anxiolytics, anticonvulsants, and sedative hypnotics. Benzodiazepines manifest their presence by analgesia, drowsiness, confusion, diminished reflexes, lowering of body temperature, respiratory depression, blockade of adrenocortical response and a decrease in peripheral resistance without an impact on the cardiac index.

The major pathways of elimination are the kidneys (urine) and the liver, where it is conjugated to glucuronic acid. Large doses of Benzodiazepine could develop tolerances and physiological dependency and lead to its abuse.

### PRINCIPLE OF THE TEST

The OneStep Benzodiazepine InstaStrip consists of a chromatographic absorbent device in which the drug or drug metabolites in the sample compete with a drug conjugate immobilized on a porous membrane for limited antibody sites. As the test sample flows up through the absorbent device, the free drug in the specimen competes with immobilized antigen conjugate in the test zone by binding to the antibody-dye conjugate forming an antibody-antigen complex and

preventing the formation of a rose-pink color band when the drug is at or above the detection level of 300 ng/ml.

In the case where free drug in the sample is below the detection level of 300 ng/ml, antibody-dye conjugate is free to bind to the immobilized antigen in the test zone, producing a rose-pink color band. Furthermore, unbound dye conjugate binds to the reagent in the control zone, producing a rose-pink color band, demonstrating that the reagents and device are functioning correctly.

A **NEGATIVE** specimen produces two distinct color bands in both the test zone and the control zone. A **POSITIVE** specimen produces only one color band in the control zone.

### REAGENTS AND MATERIALS PROVIDED

1. Test Dipstick. The test strip contains membrane-immobilized reagents in a protein matrix containing sodium azide.
2. Urine Cups (optional)
3. Test Instructions

### MATERIALS REQUIRED BUT NOT PROVIDED

1. Clock or timer.
2. Sample collection containers.

### WARNINGS AND PRECAUTIONS

1. For *in vitro* diagnostic and *professional* use only.
2. Do not use the test strip beyond the expiration date.
3. Urine specimens may be infectious; properly handle and dispose of all used reaction devices in a biohazard container.
4. Visually inspect the foil package to insure it is intact. If the package is not intact, discard the device.

### STORAGE AND STABILITY

Store test kit below  $28^{\circ}\text{C}$ ; do not freeze. Refer to the expiration date for stability.

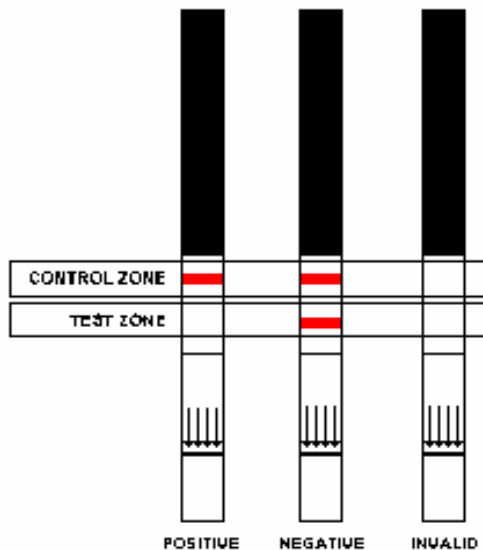
### SAMPLE COLLECTION AND PREPARATION

The sample must be collected in a clean, dry container, either plastic or glass, without any preservatives. Urine specimens may be refrigerated ( $2^{\circ}-8^{\circ}\text{C}$ ) and stored up to forty-eight hours or frozen ( $-20^{\circ}\text{C}$  or below) prior to assaying. If samples are refrigerated or frozen, they should be allowed to come to room temperature before testing. Urine samples exhibiting visible precipitates should be filtered, centrifuged or allowed to settle, so that clear aliquots can be obtained for testing.

### TEST PROCEDURE

1. Bring test components and urine sample specimen to room temperature ( $15^{\circ}-28^{\circ}\text{C}$ ).
2. Do not break the seal of the pouch until ready to begin testing.
3. Open the foil pouch at the notch and remove the test dipstick. Place the dipstick into the urine sample. Do not allow the urine level to go above the maximum-level line indicated by the arrows.
4. Read the test result at five minutes.  
*IMPORTANT: Do not interpret a test result after more than five minutes. Waiting longer than five minutes may cause inaccurate interpretation. To avoid confusion, discard the test device after reading the result at five minutes.*

## INTERPRETATION OF RESULTS



- Positive.** One rose-pink band appears in the Control Zone, with no apparent band in the Test Zone. A positive result indicates that benzodiazepine levels are at or above 300 ng/ml.
- Negative.** Two rose-pink bands appear-- one in the Control Zone and one in the Test Zone. A negative result indicates that benzodiazepine levels are below 300 ng/ml.
- Invalid.** No rose-pink bands appear, or a band appears in the Test Zone but not in the Control Zone. An invalid result may be due to improper testing procedures or deterioration of the kit components. Repeat the assay sequence using a new device.

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

## QUALITY CONTROL

An internal procedure control has been incorporated into the test to ensure proper kit performance and reliability.

The use of an external control is recommended to verify proper kit performance. Quality control samples should be tested according to quality control requirements established by the testing laboratory.

## LIMITATIONS OF THE TEST

- This product is designed for use with human urine only.
- Although the test is very accurate in detecting Benzodiazepine in urine, there is a possibility that false results will occur due to the presence of interfering substances in the urine and/or factors beyond the control of the manufacturer, e.g technical or procedural errors associated with the testing.
- The test is a qualitative screening assay and is not for determining quantitative concentration levels or the level of intoxication.
- Adulterants such as bleach or other strong oxidizing agents, when added to urine specimens, may produce erroneous test results regardless of the analysis method used. If adulteration is suspected, obtain another urine specimen and retest.

## PERFORMANCE CHARACTERISTICS

- Sensitivity.** The OneStep Benzodiazepine InstaStrip detects benzodiazepine and the major metabolites of benzodiazepine in urine at concentrations equal to or greater than 300 ng/ml.
- Specificity.** A study was conducted with the OneStep Benzodiazepine InstaStrip to determine the cross-reactivity of non-benzodiazepine related compounds with the test at concentrations much higher than normally found in the urine of people using or abusing them. No cross-reactivity was detected with the substances listed in **Table I**.

A separate study was conducted to determine the cross-reactivity of benzodiazepine-related compounds with the test. Substances listed in **Table II** produced results approximately equivalent to the cut-off level for benzodiazepine.

**Table I: Compounds tested and found not to cross-react with the test at a 10 mg/ml concentration in urine:**

Acetaminophen	Doxylamine	Penicillin G
Acetylsalicylic Acid	Ecgonine HCl	Pentobarbital
Amikacin	Ecgonine Methyl Ester	d-Propoxyphene
Amitriptyline	Glucose	Hydrochlorothiazide
Ampicillin	Histamine	Propranolol
Arterenol	Hydrocodone	Phencyclidine
Aspartame	Hydromorphone	Phenobarbital
Atropine Sulfate	Indomethacin	Phentermine
Benzoic Acid	Ketoprofen	Phenylpropranolamine
Benzoylcegonine HCl	Levorphanol	L-Phenylephrine
Caffeine	$\Delta$ -9-THC	Quinine
Chlorpheniramine	11-nor- $\Delta$ -9-carboxy-THC-	Ranitidine
Chlorpromazine HCl	9-COOH	Sodium Salicylate
Cimetidine	Meperidine	Tryptophan
Codeine	Methylphenidate	Tetracycline
Deoxyephedrine	Methadone	Tetrahydrozoline
Dextromethorphan	Methaqualone	Theophylline
Diazepam	Morp. Glucuronide	Thioridazine
Diethylpropion	Morphine Sulfate	Trifluoperazine
Diphenylhydantoin	Oxycodone	
	Pendimetrazine	

**Table II: Concentration of Benzodiazepine-related compounds showing a positive response approximately equivalent to the benzodiazepine cut-off for the test:**

Compound / Concentration in ng/ml	
Alpha hydroxyaltriazolam	200
Alprazolam	62.5
Bromazepam	250
Clobazam	2500
Chlrazepate	50
Clonazepam	500
Diazepam	50
Desmethyldiazepam	50
Flunitrazepam	250
Flurazepam	100

- Accuracy.** The accuracy of the OneStep Benzodiazepine InstaStrip was first tested through an in-house study by Cortez and subsequently in a clinical trial submitted to a NIDA certified laboratory. Each urine specimen was tested with the OneStep Benzodiazepine InstaStrip and a commercially available test (Syva EMIT II). Positive results were confirmed by GC/MS. The results are summarized as follows:

	<u>Syva EMIT II Positive</u>	<u>Syva</u>	<u>EMIT II</u>
<b>Negative</b>			
<b>OneStep Positive</b>	<b>210</b>		<b>0</b>
<b>OneStep Negative</b>	<b>9</b>		<b>221</b>

When compared to EMIT II the relative sensitivity between positive samples was 95.9% . The relative specificity between negative samples was 100%. The concordance of the combined data with respect to EMIT II was 97.95%.

4. **Precision.** The precision was determined by replicate assays of three different patient urine samples with kits from three different production lots. The resultant data indicated 100% precision for the duplicates within each lot and no appreciable interlot variation when testing both positive and negative spiked samples across three (3) different lots of devices.

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