Rapid Response™

Multi-Drug Test Panel
(Urine)

REF D3.38-1P29-25 Product Insert

For forensic use only.

Intended Use

The Rapid Response™ Multi-Drug Test Panel is a rapid chromatographic immunoassay for the detection of multiple drugs in human urine at the following cut-off concentrations listed below:

Test	Calibrator	Cut-off (ng/mL)
Xylazine (XYL)	4-Hydroxy Xylazine	10
Fentanyl (FYL)	Norfentanyl	10
Nitazenes (NTZ)	Isotonitazene	500

This test will detect other related compounds, please refer to the Analytical Specificity table in this product insert.
This assay provides only a qualitative, preliminary analytical test result only. A more specific alternate chemical method must be used in order to obtain a confirmed analytical result. Gas chromatography mass spectrometry (GC/MS) or Liquid Chromatography mass spectrometry (LC/MS) is the preferred confirmatory method.

Summary

Xylazine (XYL)

Xylazine was created in 1962 and found to be a potent central alpha2 adrenergic blocking agent. The drug causes sedation and anesthesia, respiratory depression, slow heart rate, muscle relaxation and potentiates pain relief. However, in humans, it also causes significant slowing of the heart rate and low blood pressure. Because of this, it was never FDA approved for human use. However, it is a potent veterinary agent, used as an animal "takedown" agent and anesthetic and is known by the trade name Rompun™. In the early 2000s, xylazine became a drug of abuse in Puerto Rico and was added to heroin or included in "speedballs" as an addition to or as a substitute for heroin. Appropriately so, it was called anesthesia de caballo (horse anesthesia) on the street. Since it has many of the same effects as opioids, it could be substituted for the opioid or the two together have additive effects. Since then, the drug has shown up intermittently with the National Forensic Lab Information System and between 2006-2018; the Philadelphia Medical Examiners Office recorded increasing incidence of cases. [1,2]

Fentanyl (FYL)

Fentanyl, belongs to powerful narcotics analgesics, and is a μ special opiates receptor stimulant. Fentanyl is one of the varieties that been listed in management of United Nations "Single Convention of narcotic drug in 1961". Among the opiates agents that under international control, fentanyl is one of the most commonly used to cure moderate to severe pain[3]. After continuous injection of fentanyl, the sufferer will have the performance of protracted opioid abstinence syndrome, such as ataxia and irritability etc[4,5], which presents the addiction after taking fentanyl in a long time. Compared with drug addicts of amphetamine, drug addicts who take fentanyl mainly have got the possibility of higher infection rate of HIV, more dangerous injection behavior and more lifelong medication overdose[6].

Nitazene (NTZ)

Nitazene is a group of compounds developed in the 1950s as opioid analgesics, but they were never approved to market. As such, they are not well known outside of academic research laboratories. A characteristic of nitazene is their high potency (e.g., hundreds to thousands fold more potent than morphine and other opioids and tenfold more potent than fentanyl). In the past few years, several nitazene, including "designer analogs," have been detected in the illicit drug supply and have been implicated in overdose mortality, primarily due to their exceptionally high potency. In the street drug supply, nitazene is often found mixed with fentanyl or other agents but their presence is not always disclosed to drug buyers, who may not even be familiar with nitazene. These drugs pose a particular challenge since there is little experience in how to reverse a nitazene overdose or potential drug-drug or drug-alcohol interactions.[7,8,9]

Principle

The Rapid Response™ Multi-Drug Test Panel is an immunoassay based on the principle of competitive binding. Drugs that may be present in the sample compete against their respective drug conjugate for binding sites on their specific antibody.
During testing, a portion of the sample migrates upward by capillary action. A drug, if present in the sample below its cut-off concentration, will not saturate the binding sites of its specific antibody. The antibody will then react with the drug-protein conjugate and a visible colored line will show up in the test line region of the specific drug strip. The presence of drug above the cut-off concentration in the sample will saturate all the binding sites of the antibody. Therefore, the colored line will not form in the test line region.
A drug-positive sample will not generate a colored line in the specific test line region of the strip because of drug competition, while a drug-negative sample will generate a line in the test line region because of the absence of drug competition.
To serve as a procedural control, a colored line will always appear at the control line region, indicating that proper volume of specimen has been added and membrane wicking has occurred.

Reagents

Each test line contains anti-drug antibody and corresponding drug-protein conjugates. The control line contains goat anti-rabbit IgG polyclonal antibodies and rabbit IgG.

Precautions

- For forensic use only. Do not use after the expiration date.
- For individually packed test, the test should remain in the sealed pouch until use.
- The used test should be discarded according to local regulations.
- If any serious incident that has occurred in relation to this test shall be reported to us and the competent authority of the Member State in which the user and/or the patient is established.
- Please read all the information in this product insert before performing the test.

Materials

Materials provided

- Test panels
- Product insert

Materials required but not provided

- Timer
- Specimen collection container
- External positive and negative controls

Storage and Stability

Store as packaged in the sealed pouch at 35.6-86°F (2-30°C). The test is stable through the expiration date printed on the sealed pouch. The test cassettes must remain in the sealed pouch until use. **DO NOT FREEZE.** Do not use beyond the expiration date.

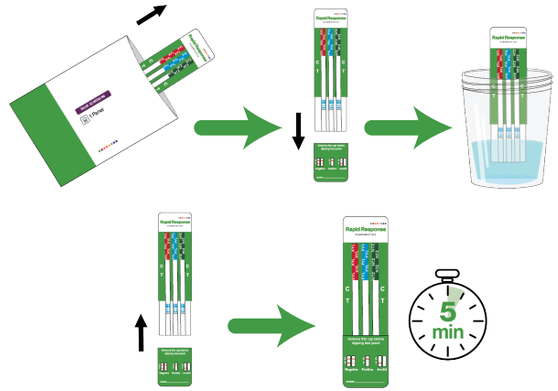
Sample Collection and Preparation

The specimen should be collected using a clean and dry container. Follow the detailed Test Procedure below.

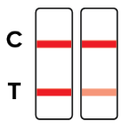
Test Procedure

Allow the test, urine, and/or controls to equilibrate to room temperature (59-86°F; 15-30°C) prior to testing.

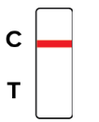
1. Bring the pouch to room temperature before opening it. Remove the test panel from the sealed pouch and use it within one hour.
2. Write the donor name or ID on the panel in the provided space, then remove the cap.
3. With the arrows pointing toward the urine specimen, immerse the sample tips vertically in the urine specimen for at least 20 seconds. Replace the cap back onto the panel and place the panel on a flat surface.
4. Read test results at 5 minutes. Do not interpret result(s) after 10 minutes.



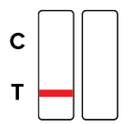
Results Interpretation



NEGATIVE*: Two lines appear. One colored line should be in the control region (C), and another apparent colored line adjacent should be in the test region (T). This negative result indicates that the drug concentration is below the detectable level.
***NOTE:** The shade of color in the test line region (T) will vary, but it should be considered negative whenever there is even a faint line.



POSITIVE: One colored line appears in the control region (C). No line appears in the test region (T). This positive result indicates that the drug concentration is above the detectable level.



INVALID: Control line fails to appear. Insufficient specimen volume or incorrect procedural techniques are the most likely reasons for control line failure. Review the procedure and repeat the test using a new test. If the problem persists, discontinue using the lot immediately and contact the manufacturer.

Quality Control

A procedural control is included in the test. A colored line appearing in the control region (C) is considered an internal procedural control. It confirms sufficient specimen volume, adequate membrane wicking and correct procedural technique.

Limitations

1. The Rapid Response™ Multi-Drug Test Panel provides only a qualitative, preliminary analytical result. A secondary analytical method must be used to obtain a confirmed result. Gas chromatography/mass spectrometry (GC/MS), gas chromatography/tandem mass spectrometry (GC/MS/MS), liquid chromatography/mass spectrometry (LC/MS) or liquid chromatography/tandem mass spectrometry (LC/MS/MS) are the preferred confirmatory methods.
2. A positive result indicates the presence of drugs only and does not indicate quantity.
3. A negative result does not at any time rule out the presence of drugs, as they may be present below the minimum detection level of the test.
4. Not for testing Cocaine, methamphetamine, ketamine or any other nonopioid substances.
5. This test panel does not distinguish between illicit drugs and certain medications.
6. Do not use after the expiration date. Do not use if test panel pouch has been punctured or damaged. Do not reuse test panel.
7. It is possible that technical or procedural errors, as well as other interfering substances in the sample may cause erroneous results.

Performance Characteristics

Accuracy

The accuracy of the Rapid Response™ Multi-Drug Test Panel was evaluated in comparison to GC/MS and LC/MS. Drug-free urine samples collected from presumed non-user volunteers were tested with the Rapid Response™ Multi-Drug Test Panel. Of these negative samples, all were correctly identified as negative. 10% of the negative samples were confirmed with GC/MS as drug negative. At least 30 drug positive urine specimens for each drug test were obtained from reference labs. Drug concentrations were confirmed with GC/MS and LC/MS. A summary of the accuracy results on the Rapid Response™ Multi-Drug Test Panel are shown in the following table.

Summary of Accuracy Results

Drug Test/ Cutoff (ng/ml)	Result	Range of GC/MS Data						
		Drug-free	-50% - <-25% C/O	-25% C/O - C/O	C/O - +25% C/O	>+25% - +50% C/O	>+50/% C/O	% Agreement
XYL/10	Neg	40	4	1	0	0	0	100%
	Pos	0	0	0	1	4	35	100%
FYL/10	Neg	40	3	0	0	0	0	97.7%
	Pos	0	0	1	2	2	45	100%
NTZ/500	Neg	40	2	0	0	0	0	97.7%
	Pos	0	0	1	3	2	42	100%

Analytical specificity

The following compounds are detected positive in urine by the Rapid Response™ Multi-Drug Test Panel. Concentrations are given in ng/ml; percent cross-reactivity is shown in parentheses.

XYL10

Compound	Concentration (ng/mL)	Compound	Concentration (ng/mL)
4-Hydroxy Xylazine	10 (100%)	Xylazine	100 (10%)
3-Hydroxy Xylazine	10 (100%)	Cimetidine	100,000 (0.01%)
(1R, 2S) - (-)-Ephedrine	100,000 (0.01%)	Clonidine	100,000 (0.01%)
Benztropine	100,000 (0.01%)	Nimesulide	100,000 (0.01%)
Tetrahydrozoline	100,000 (0.01%)	Codeine	100,000 (0.01%)
Levorphanol	100,000 (0.01%)	(-) Epinephrine	100,000 (0.01%)
Heroin	100,000 (0.01%)	D, L-Homatropine Hydrobromide	100,000 (0.01%)
Gatifloxacin	100,000 (0.01%)	S-(-)-Nicotine	100,000 (0.01%)

FYL10

Compound	Concentration (ng/mL)	Compound	Concentration (ng/mL)
Norfentanyl	10 (100%)	Fentanyl	>100,000 (<0.01%)

NTZ500

Compound	Concentration (ng/mL)	Compound	Concentration (ng/mL)
Isotonitazene	500 (100%)	Protonitazene	3,000 (16.67)
N-Pyrrolidinoetonitazene	500 (100%)	Metodesinitazene	>100,000 (0.5%)
Etonitazene	500 (100%)	N-PyrrolidinoMetonitazene	500 (100%)
Etodesnitazene	>100,000 (<0.5%)	N-desethyl Isotonitazene	2,000 (25%)
N-desethylMetonitazene	100 (500%)	N-desethyl Etonitazene	1,000 (50%)
N-PiperidinylMetonitazene	1,000(50%)	N-Piperidinyl Etonitazene	1,000 (50%)

Interference

The following compounds were evaluated for potential positive or negative interference with the Rapid Response™ Multi-Drug Test Panel. All compounds were dissolved in drug control solutions 50% below and 50% above their respective cutoff concentrations and tested with the Rapid Response™ Multi-Drug Test Panel. An unaltered sample was used as control. No interference was found for following compounds at a concentration of 100 µg/mL.

Acetaminophen	Dextromethorphan
Niacinamide	Acetone
4-Dimethylaminoantipyrine	(+/-)-Norephedrine
Albumin	Diphenhydramine
Oxalic acid	Ampicillin
Dopamine	Penicillin-G
Ascorbic acid	(+/-)-Isoproterenol
Pheniramine	Aspartame
(+)-Naproxen	Phenothiazine
Aspirin	Erythromycin
L-Phenylephrine	Atropine
Ethanol	B-Phenylethylamine
Benzocaine	Furosemide
Procaine	Bilirubin
Glucose	Quinidine
Caffeine	Guaiacol glyceryl ether
Ranitidine	Chloroquine
Hemoglobin	Riboflavin
(+)-Chlorpheniramine	Ibuprofen
Sodium chloride	(+/-)-Chlorpheniramine
(+/-)-Isoproterenol	Sulindac
Creatine	Lidocaine
Theophylline	Dexbrompheniramine
(1R,2S)-(-)-n-Methylephedrine	Tyramine

Bibliography

1. M Colić, V Cupić, L Pavicić, et al. Xylazine, an alpha 2-adrenergic agonist, modulates proliferation of rat thymocytes in vivo and in vitro[J]. Methods Find Exp Clin Pharmacol, 2000, 22(7):557-562.
2. K Ruiz-Colón, Chavez-Arias C , JE Díaz-Alcalá, et al. Xylazine intoxication in humans and its importance as an emerging adulterant in abused drugs: A comprehensive review of the literature[J]. Forensic Science International, 2014, 240(240C):1-8.
3. International Narcotics Control Board.Report of the International Narcotics Control Board for 2009[R].New York: UN，2010
4. Lane JC, Tennison MB, Lawless ST, et al.Movement disorder after withdrawal of fentanyl infusion.J Pediatr，1991，119（4）：649-651
5. Dominguez KD, Lomako DM， Katz RW， et al. Opioid withdraw in critically ill neonates.Ann Pharmacotherm，2003，37（4）：473-477
6. European Monitoring Centre for Drugs and Drug Addiction.Annual Report 2009[R].Lisbon：EMCDDA，2010
7. Vandeputte MM, Van Uytfanghe K, Layle NK, St Germaine DM, Iula DM, Stove CP. Synthesis, Chemical Characterization, and µ-Opioid Receptor Activity Assessment of the Emerging Group of "Nitazene" 2-Benzylbenzimidazole Synthetic Opioids. ACS Chem Neurosci. 2021 Apr 7;12(7):1241-1251.
8. Kanamori T, Okada Y, Segawa H, Yamamuro T, Kuwayama K, Tsujikawa K, Iwata YT. Analysis of highly potent synthetic opioid nitazene analogs and their positional isomers. Drug Test Anal. 2023 Apr;15(4):449-457.
9. Krotulski AJ, Papsun DM, Kacinko SL, Logan BK. Isotonitazene Quantitation and Metabolite Discovery in Authentic Forensic Casework. J Anal Toxicol. 2020 Jul 31;44(6):521-530.

Glossary of Symbols

Consult instructions for use

Test per Kit

Do Not Reuse

Store between 35.6˚F to 86˚F

Use by

REF Catalogue #

LOT Lot Number

Do not use if package is damaged

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