Interpretation of Drug Testing Results in Medication Assisted Treatment

By: Paul L. Cary
Independent Forensic
Toxicology Consultant

What Does This Result Mean?

Two-Step Testing Approach

- screening test – designed to separate negative samples from samples that are "presumptively" positive
- confirmation test – follow-up procedure designed to validate positive test results
- why can't you adjudicate based on the screening test results?
- FALSE POSITIVES

Drug tests & cross reactivity:

- screening tests can and do react to “non-target” compounds
  - amphetamines
  - benzodiazepines
- obtain list of interfering compounds from lab or on-site test vendor
- study results have demonstrated accuracy rates for initial screening tests as low as 70%
- confirm positive results

Typical Cutoff Levels

screening & confirmation

■ amphetamines *	500 ng/mL	250 ng/mL
■ benzodiazepines	300 ng/mL	variable
■ cannabinoids *	20 & 50 ng/mL	15 ng/mL
■ cocaine (crack)*	150 ng/mL	100 ng/mL
■ opiates (heroin) *	300/2000 ng/mL	variable
■ phencyclidine (PCP) *	25 ng/mL	25 ng/mL
■ alcohol	20 mg/dL	10 mg/dL

- * SAMHSA (formerly NIDA) drugs

What is a “cutoff” level ?

- cutoffs are not designed to frustrate CJ professionals
- a drug concentration, ***administratively*** established for a drug test that allows the test to distinguish between negative and positive sample - “threshold”
- cutoffs provide important safeguards:
  - scientific purposes (detection accuracy)
  - legal protections (evidentiary admissibility)
- measured in ng/mL = ppb

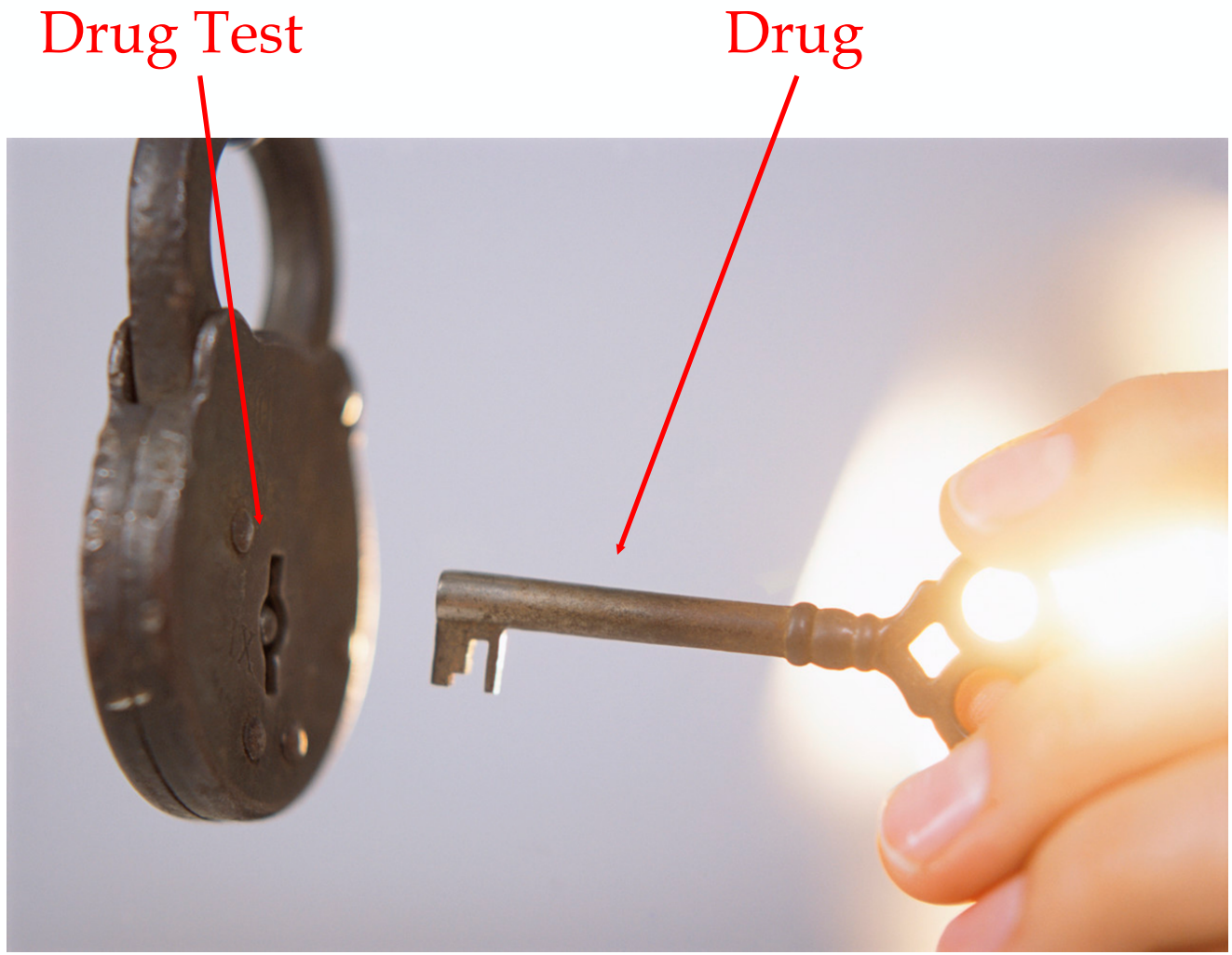
Cutoffs and False Positives

as you lower the cutoff level of a drug test

you increase the potential for false positive test results

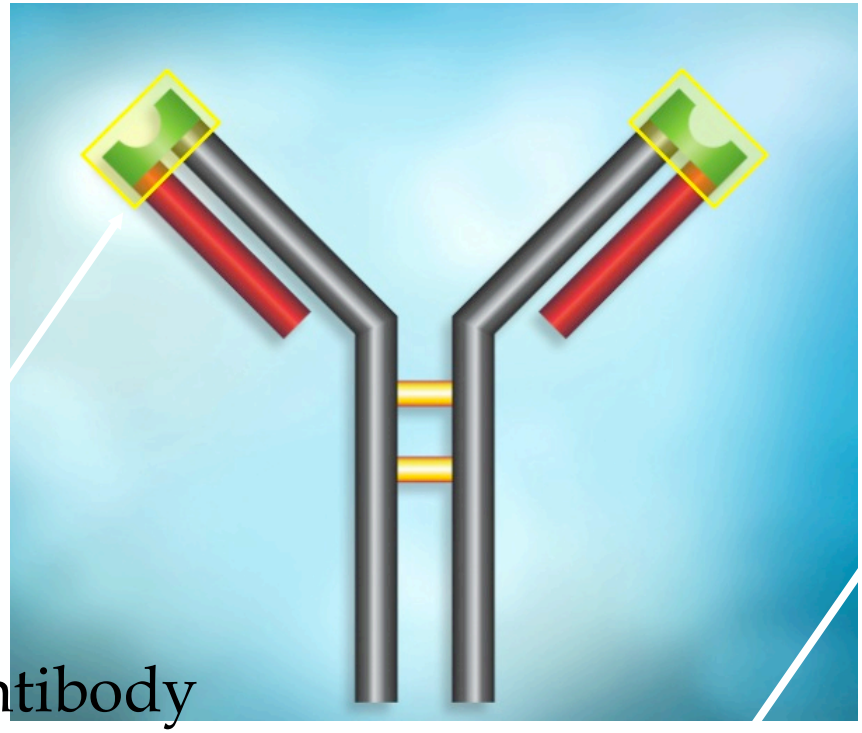
How Do Drug Tests Work?

Drug tests & cross reactivity:

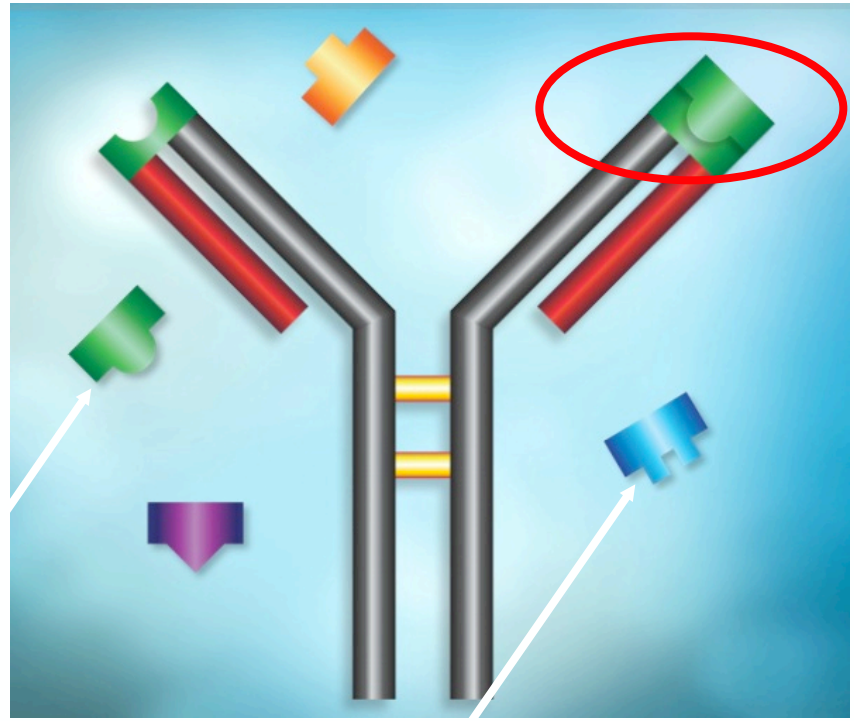


Drug tests & cross reactivity:

Immunoassay screening tests



opiates antibody



opiates fit = positive test

methadone doesn't fit = negative test

Drug tests & cross reactivity:

morphine	100%
codeine	200%
heroin	80%
hydrocodone	75%
hydromorphone	45%
oxycodone	20%

Drug tests & cross reactivity:

(300 ng/mL opiate cutoff test)

→ 150 ng/mL codeine

→ 1500 ng/mL oxycodone

If oxycodone is a major substance of abuse in your jurisdiction, you should consider a separate drug test for oxycodone as part of your initial screening analysis.

Result Interpretation for MAT Drugs

Medication-Assisted Treatment (MAT) is a form of pharmacotherapy and refers to any treatment for a substance use disorder that includes a pharmacologic intervention as part of a comprehensive substance abuse treatment plan with an ultimate goal of participant recovery with full social function.

Medication-Assisted Treatment in Drug Courts

Recommended Strategies

CENTER FOR COURT INNOVATION

State of New York
EXCELSIOR
Unified Court System

LEGAL ACTION CENTER

Conclusions

- Scientific evidence overwhelmingly shows that MAT is a critical tool in the treatment of opioid addiction and essential in fighting the opioid epidemic.
- Drug treatment courts can play a key role in ensuring that participants have access to this effective, evidence-based treatment.

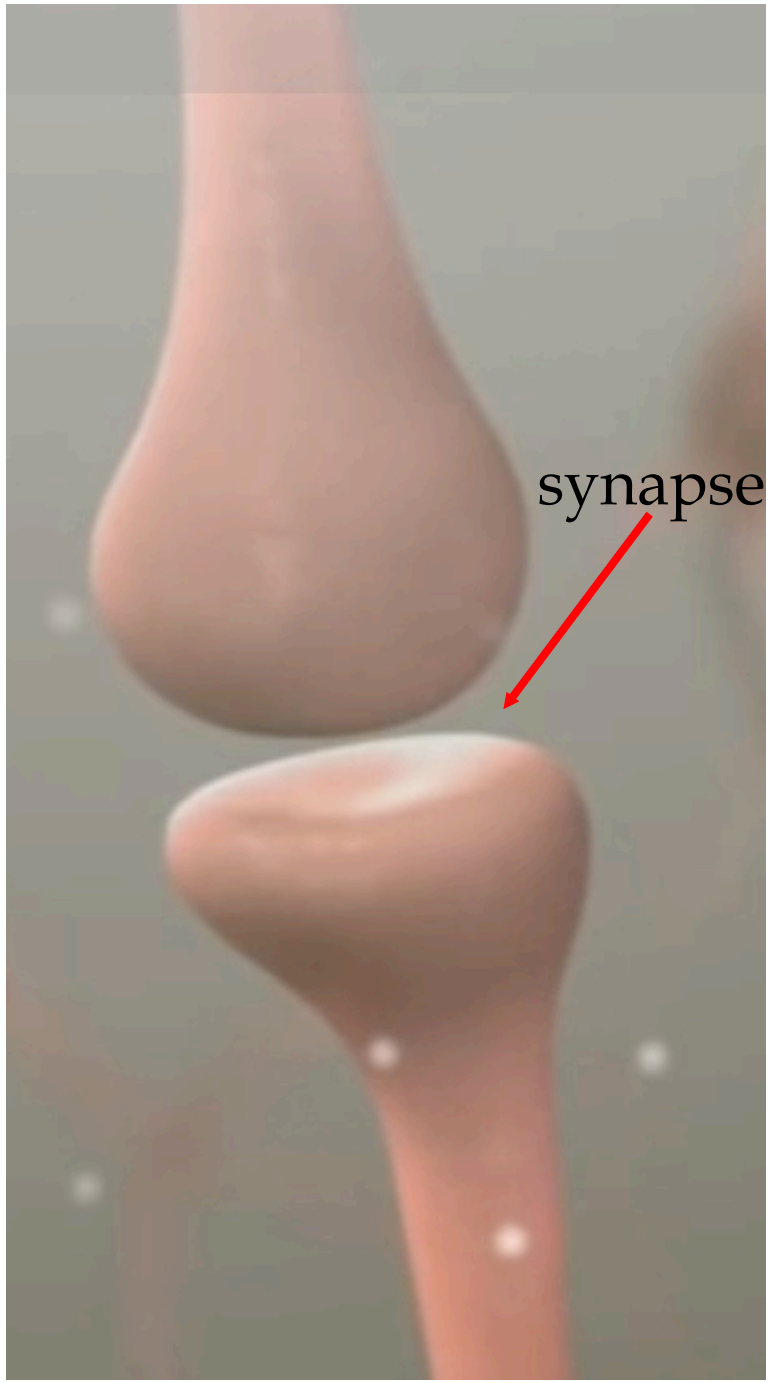
MAT Drugs

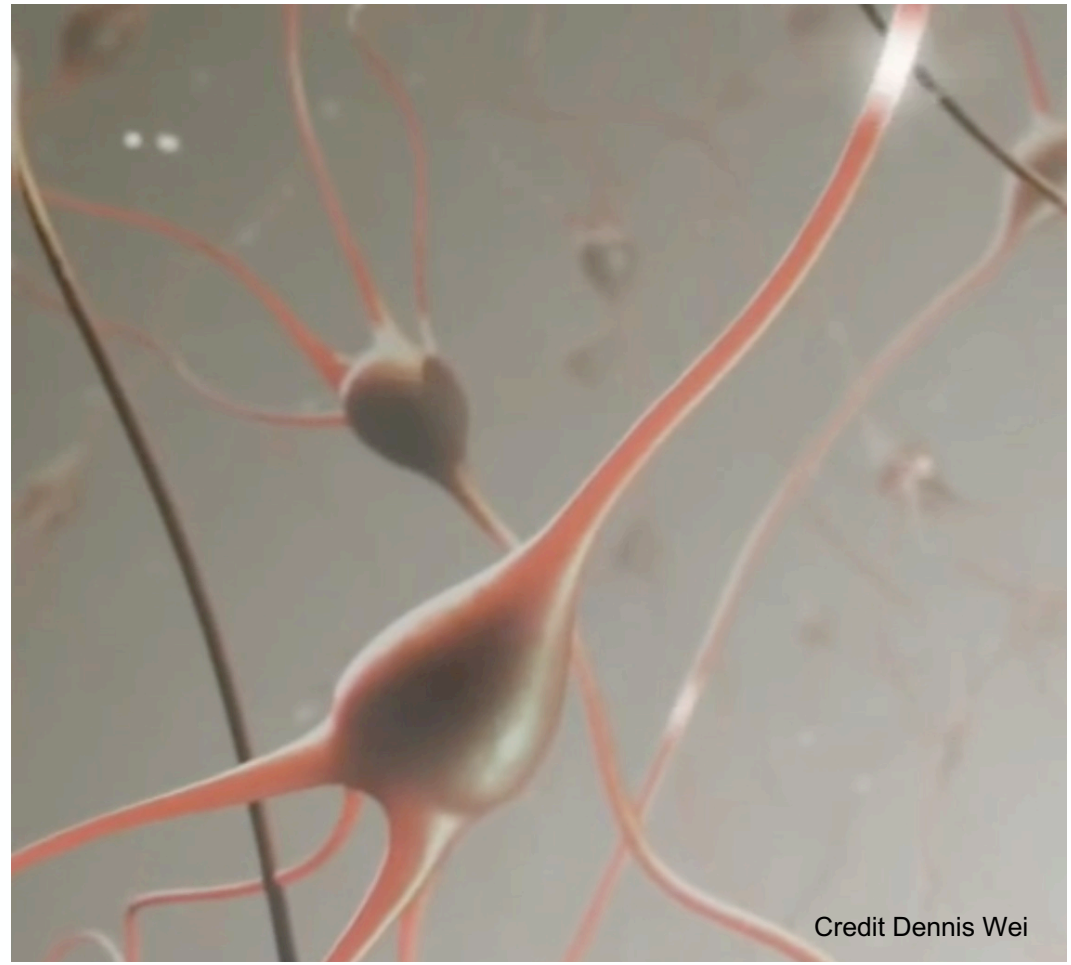
- Medications for Alcohol Dependence
  - Naltrexone: (ReVia®, Vivitrol®, Depade ®)
  - Disulfiram: (Antabuse®)
  - Acamprosate: (Campral®)
- Medications for Opioid Dependence
  - Methadone:
  - Buprenorphine: (Suboxone® and Subutex®)
  - Naltrexone: (ReVia®, Vivitrol®, Depade ®)

What is Naltrexone?

- belongs to a class of drugs known as opiate antagonists
- block the brain's neurotransmitters
- displaces opiates from their binding site
- diminishes physical effects of opiates
- will naltrexone test positive on an opiate drug test?

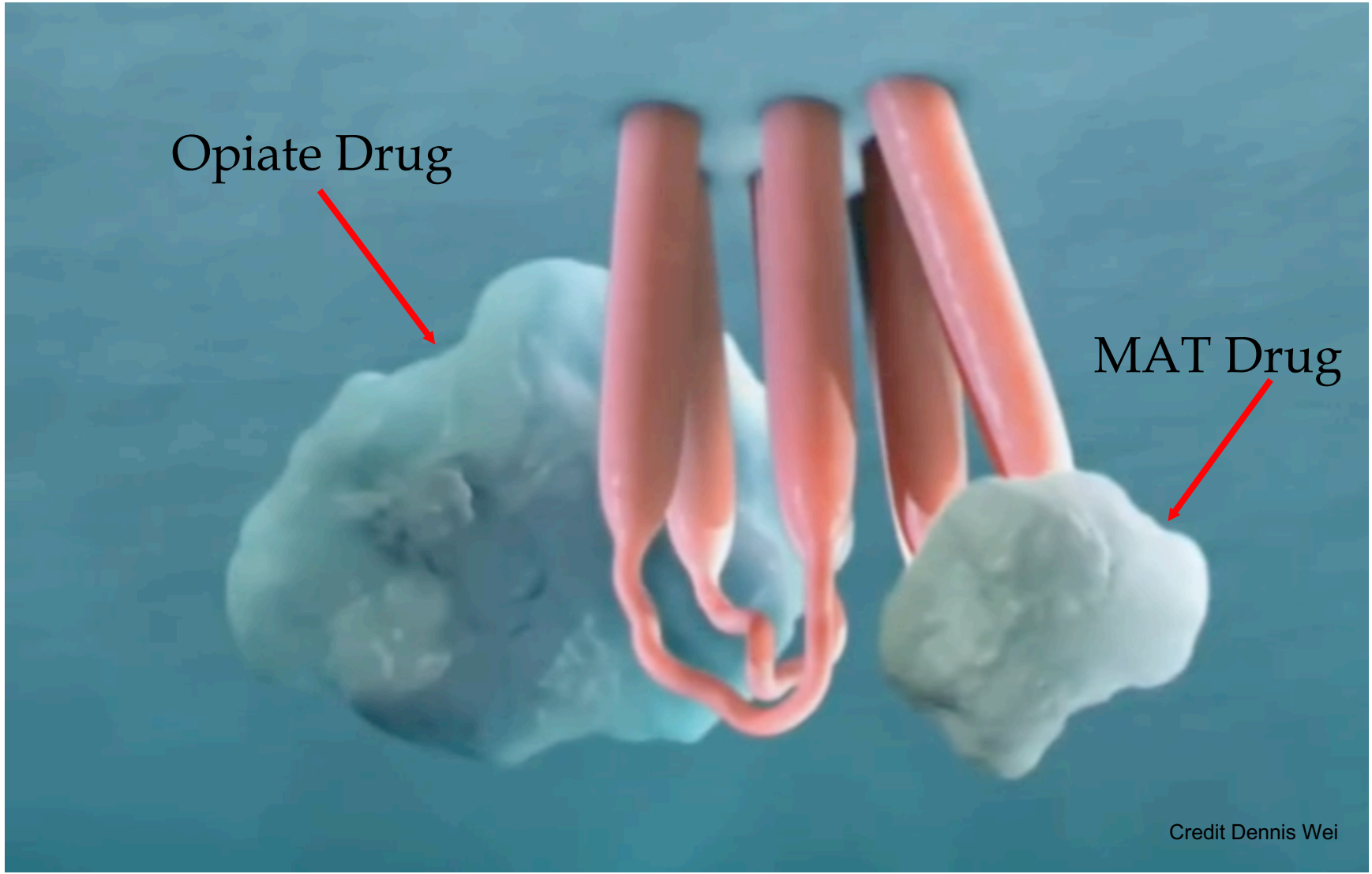
Neuron Transmission





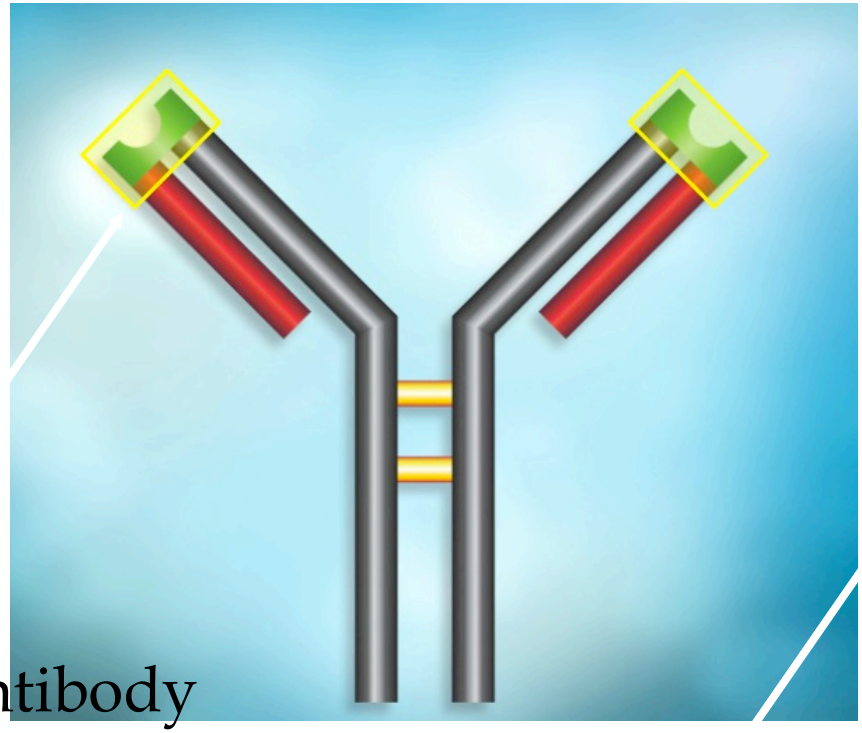
Neural Surface Membrane

Ligand (MAT drug) Binds to Receptor

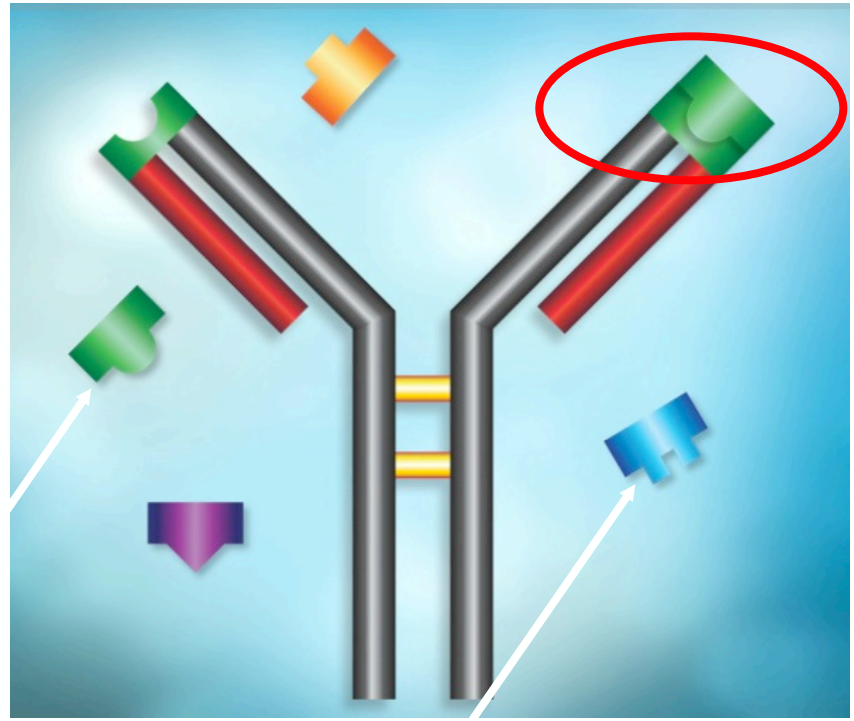


Drug tests & cross reactivity:

Immunoassay screening tests



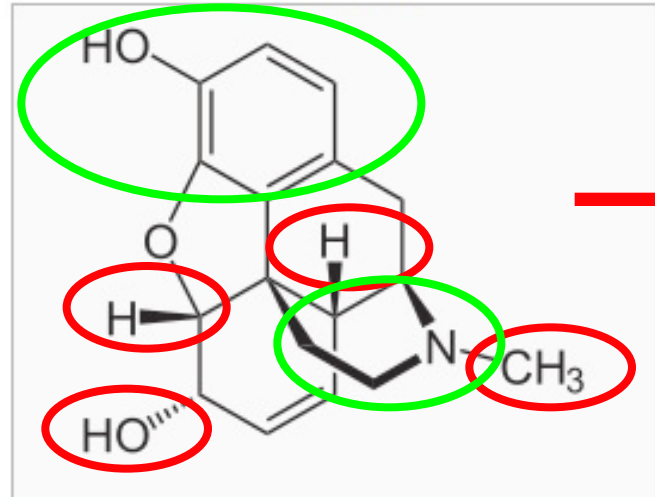
opiates antibody

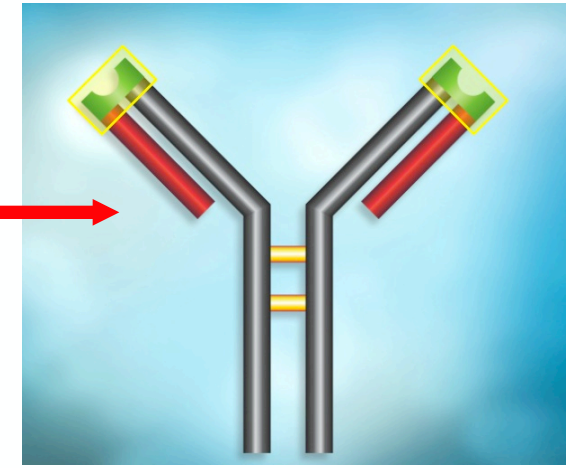


opiates fit = positive test

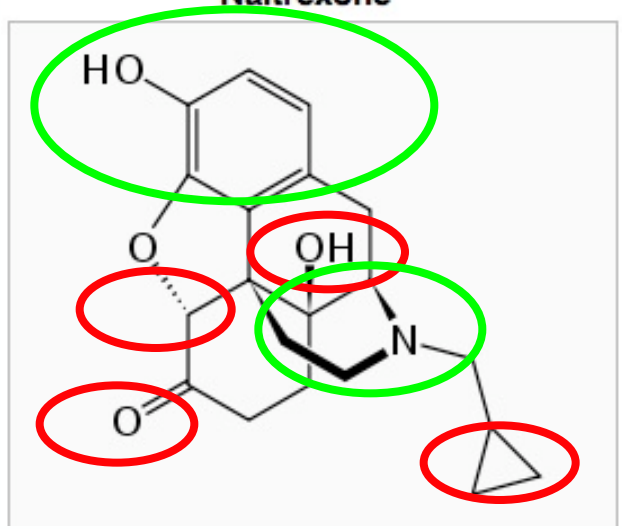
methadone doesn't fit = negative test

Morphine

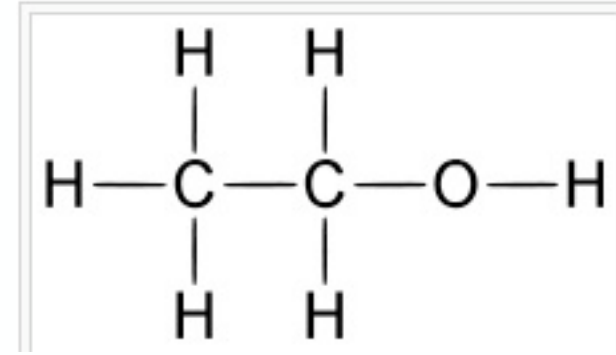




Naltrexone



Ethanol



EMIT® II Plus – Opiate

Negative

The compounds below were negative for the Opiate 300 and 2000 cutoffs at the concentrations shown except where noted. Concentrations listed are in µg/mL.

Acetaminophen	1000
Acetylsalicylic Acid	1000
Albuterol	1000
Alendronate	1000
Alprazolam	1000
5-Aminosalicyclic Acid	1000
Amitriptyline @ 300	500
Amitriptyline @ 2000	1000
Amlodipine	1000
Amoxicillin	1000
d-Amphetamine	1000
Atomoxetine	1000
Atorvastatin	1000
Azithromycin	1000
AZT (Zidovudine)	2000
Benazepril	1000
Benzoylecgonine	1000
Buprenorphine	1000
Bupropion	1000
Caffeine	1000
Carisoprodol	1000
Celecoxib	1000
Cephalexin	1000
Cetirizine	1000
Chlorpheniramine	1000
Chlorpromazine	125
Cimetidine	1000
Ciprofloxacin	1000
Citalopram	1000
Clomipramine	2.5
Clonazepam	1000
Clonidine	1000
Clopidogrel Hydrogen Sulfate	1000
Clotrimazole	1000
Cotinine	100
Cyclobenzaprine	63
Desipramine	800
Dextromethorphan	63
Dezocine	1000
Diazepam	1000
Diclofenac	1000
Dihydroergotamine	1000
Diltiazem	1000
Diphenhydramine	1000
Dothiepin	100
Doxepin	10
Doxycycline	1000
Doxylamine	500
Droperidol	1000
EDDP 2-Ethylidene-1, 5-dimethyl-3, 3-diphenylpyrrolidine	1000
EMDP	100
Enalapril Maleate	1000
Ephedrine	1000
Escitalopram	1000
Escomeprazole	1000
Eszopiclone	1000
Ezetimibe	1000
Fentanyl	1000
Fexofenadine	1000
Fluoxetine	900
Fluticasone Proprionate	1000
Furosemide	1000
Gabapentin	1000
Glutethimide	500
Glyburide	1000
Goldenseal	tea solution
Griseofulvin	1000
Hydrochlorothiazide	1000
Ibuprofen	1000
d,l-Isoproterenol	1000
Isoxsuprine	1000
Ketamine	100
Ketoprofen	1000
Ketorolac Tromethamine	1000
LAAM (l-α-Acetylmethadol)	25
dinor LAAM (α-Acetyl-N, N-dinormethadol)	25
Lamotrigine	1000
Lansoprazole	1000
Lidocaine	1000
Lisinopril	1000
Loperamide	1000
Lormetazepam	1
LSD (Lysergic acid diethylamide)	0.01
MDA (Methylenedioxyamphetamine)	5
MDMA (Methylenedioxymeth ampheamine)	200
Meloxicam	1000
Meprobamate	1000
Metaproterenol	1000
Metformin	1000
Methadone	100
d-Methamphetamine	35
Methaqualone	1500
Metoprolol Tartrate	1000
Metronidazole	1000
Myoglobin	287
Naltrexone	1000
NAPA (N-Acetylprocainamide)	400
Naproxen	1000
Netazodone	1000
Nortriptyline	250
Nylidrin	1000

Siemens EMIT Assay Cross-Reactivity Data

Myoglobin	287
Naltrexone	1000
NAPA (N-Acetylprocainamide)	400
Naproxen	1000

= 1,000,000 ng/mL

ThermoFisher SCIENTIFIC

The world leader in serving science

CEDIA® Opiate Cross-Reactivity Table
For catalog #s 100089, 100098 & 1661248

POSITIVE COMPOUNDS

The following compounds tested POSITIVE on the CEDIA® DAU Opiate assay at the 300 ng/mL cutoff.

Positive Compounds	Trade Name	Concentration Tested (ng/mL)
6-Monoacetylmorphine		370
Clomipramine HCl	Anafranil	500,000
Codeine		240
Cyclazocine		500,000
Cyamemazine		31,125
Diacetylmorphine	Heroin	570
Dihydrocodeine	DHC Plus, Synalgos-DC	600
Hydrocodone	Lortab, Vicodin	625
Hydromorphone	Dilaudid	530
Levorphanol tartrate	Levo-Dromoran	100,000
Morphine		300
Morphine SO4	MS Contin, MSIR, Oramorph SR, Roxanol	100,000
Morphine-3-glucuronide		370
Morphine-6-glucuronide		640
Nalorphine HCl		100,000
Naloxone	Narcan	6,000
Naltrexone HCl	Depade, ReVia	50,000
Ofloxacin	Floxin	100,000
Oxycodone	OxyContin	320,000
Pholcodine		500
Rifampin	Rifadin	65,000
Thebaine		1,250

Abstract: A clinical evaluation of the naltrexone, a biodegradable sustained-release dosage was carried out in 4 healthy normal males.

Subjects were given an intravenous dose of 10 mg naltrexone and approximately 1 week later a 63-mg dose of naltrexone by subcutaneous administration.

Urine levels for naltrexone were 79-215 ng/mL.

Naloxone	Narcan	6,000
Naltrexone HCl	Depade, ReVia	50,000
Ofloxacin	Floxin	100,000

MAT Drugs

- Medications for Alcohol Dependence
  - Naltrexone: False Positive with Opiate Assay - NO!
  - Disulfiram: (Antabuse®)
  - Acamprosate: (Campral®)
- Medications for Opioid Dependence
  - Methadone:
  - Buprenorphine: (Suboxone® and Subutex®)
  - Naltrexone: False Positive with Opiate Assay - NO!

chet1

Why does naltrexone post a positive opiate result on a UA test?

Posted: 4 Nov 2010 by chet1

Topics: naltrexone, opiate

does naltrexone cause a positive opiate or benzo result on a UA test?

Question is Closed

Report Favorite

Responses (1)

Marvell

5 Nov 2010

Because naltrexone is actually a special narcotic drug that blocks the effects of other narcotic medicines and alcohol. That's why it comes up in a urinary analysis as an opiate.

http://www.drugs.com/mtm/naltrexone.html

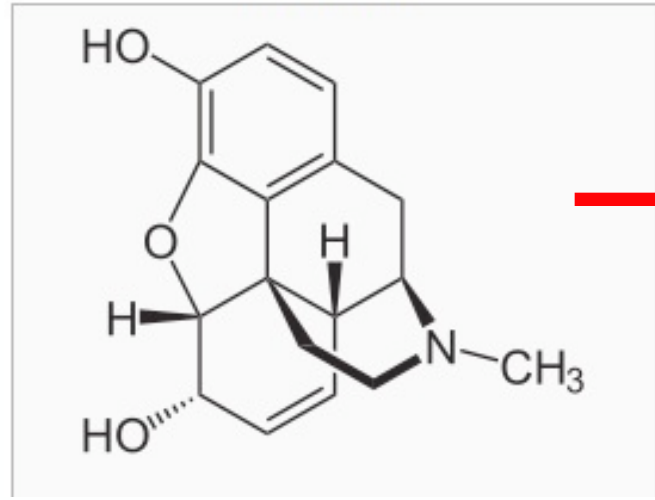
Votes: +0

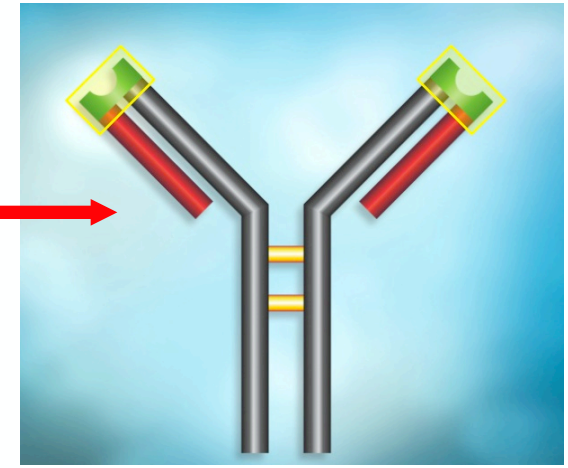
Vote up Report

Opiates - Results Interpretation

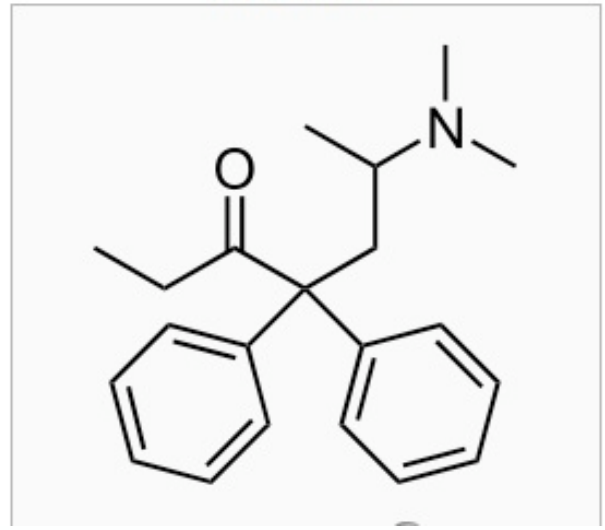
- all opiates are narcotic analgesics
  - relieve pain & controlled substances
- not all narcotic analgesics are opiates
  - meperidine (Demerol®)
  - propoxyphene (Darvon®)
  - methadone
  - pentazocine (Talwin®)
  - fentanyl (Sublimaze®)
  - buprenorphine: (Suboxone®)
  - naltrexone: (ReVia®, Vivitrol®, Depade ®)

Morphine

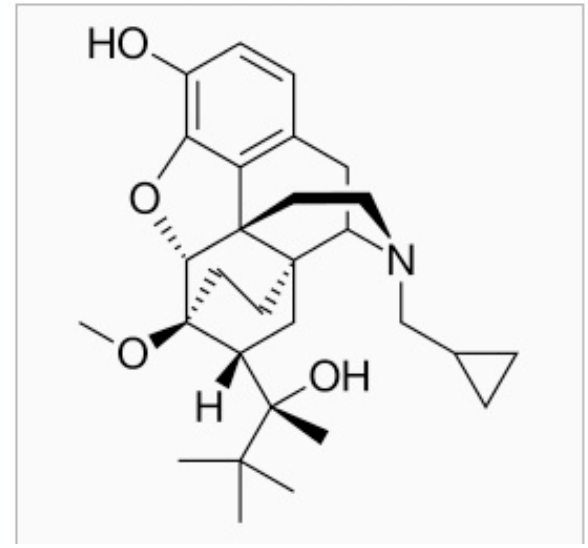




Methadone



Buprenorphine



Siemens Negative Reactivity Data

Azithromycin	1000
AZT (Zidovudine)	2000
Benazepril	1000
Benzoylecgonine	1000
Buprenorphine	1000
Bupropion	1000
Caffeine	1000

Thermo-Fisher Negative Reactivity Data

Negative Compounds	Trade Name	Concentration Tested (ng/mL)
Bromocriptine mesylate	Ergoset, Parlodel	500,000
Brompheniramine	Dimetane, Dimetapp, Nasahist, ND-Stat, Oraminic II	500,000
Bupivacaine	Marcaine, Sensorcaine	500,000
Buprenorphine	Buprenex	100,000
Bupropion	Wellbutrin, Zyban	100,000

Siemens Negative Reactivity Data

Metaproterenol	1000
Metformin	1000
Methadone	100
d-Methamphetamine	35
Methaqualone	1500

Thermo-Fisher Negative Reactivity Data

Metaproterenol hemisulfate salt	Alupent, Metaprel	500,000
Metaraminol bitartrate	Aramine	500,000
Methadone HCl	Dolophine	500,000
Methamphetamine	Desoxyn	500,000
Methaqualone HCl	Normi-Nox, Pallidan, Somnomed, Quaalude	100,000

MAT Drugs

- Medications for Alcohol Dependence
  - Naltrexone: False Positive with Opiate Assay - NO!
  - Disulfiram: (Antabuse®)
  - Acamprosate: (Campral®)
- Medications for Opioid Dependence
  - Methadone: NO! with Opiate Assay
  - Buprenorphine: NO! with Opiate Assay
  - Naltrexone: False Positive with Opiate Assay - NO!

Search History (3 searches) *(close)*

View Saved

	# ▲	Searches	Results	Search Type	Actions
☐	1	Disulfiram/ or Disulfiram.mp.	3835	Advanced	Display More »
☐	2	Substance Abuse Detection/ or drug testing.mp.	8883	Advanced	Display More »
☐	3	1 and 2	9	Advanced	Display More »

Remove Selected | Save Selected | Combine selections with: And | Or | RSS

Save Search History

Basic Search | Find Citation | Search Tools | Search Fields | **Advanced Search** | Multi-Field Search

1 Resource selected | Hide | Change

Ovid MEDLINE(R) and Ovid OLDMEDLINE(R) 1946 to Present with Daily Update

Enter keyword or phrase (* or $ for truncation)

◉ Keyword ○ Author ○ Title ○ Journal

Search

Limits *(close)*

☑ Map Term to Subject Heading

☐ Abstracts	☐ Structured Abstracts	☐ English Language
☐ Local Holdings	☐ Evidence Based Medicine Reviews	☐ Article Reviews (ACP Journal Club)
☐ Full Text	☐ Review Articles	☐ Article Reviews (DARE)
☐ Humans	☐ Topic Reviews (Cochrane)	☐ Core Clinical Journals (AIM)
☐ Latest Update	☐ Pharmacologic Actions	

Publication Year – – –

Additional Limits | Edit Limits

Ovid®

Wolters Kluwer

My Account | Ask a Librarian | Support & Training | Help | Logoff

Search | Journals | Books | Multimedia | My Workspace

Search History (3 searches) *(close)*

View Saved

	# ▲	Searches	Results	Search Type	Actions
☐	1	Acamprosate.mp.	686	Advanced	Display More »
☐	2	Substance Abuse Detection/ or drug testing.mp.	8883	Advanced	Display More »
☐	3	1 and 2	1	Advanced	Display More »

Remove Selected | Save Selected | Combine selections with: And | Or | RSS

Save Search History

Basic Search | Find Citation | Search Tools | Search Fields | **Advanced Search** | Multi-Field Search

1 Resource selected | Hide | Change

Ovid MEDLINE(R) and Ovid OLDMEDLINE(R) 1946 to Present with Daily Update

Enter keyword or phrase (* or $ for truncation)

◉ Keyword ○ Author ○ Title ○ Journal

Search

Limits *(close)*

☑ Map Term to Subject Heading

☐ Abstracts
☐ Local Holdings
☐ Full Text
☐ Humans
☐ Latest Update
☐ Structured Abstracts
☐ Evidence Based Medicine Reviews
☐ Review Articles
☐ Topic Reviews (Cochrane)
☐ Pharmacologic Actions
☐ English Language
☐ Article Reviews (ACP Journal Club)
☐ Article Reviews (DARE)
☐ Core Clinical Journals (AIM)

Publication Year - -

Additional Limits | Edit Limits

MAT Drugs

- Medications for Alcohol Dependence
  - Naltrexone: False Positive with Opiate Assay - NO!
  - Disulfiram: NO! with drug tests reviewed
  - Acamprosate: NO! with drug tests reviewed
- Medications for Opioid Dependence
  - Methadone: NO! with Opiate Assay
  - Buprenorphine: NO! with Opiate Assay
  - Naltrexone: False Positive with Opiate Assay - NO!

Result Interpretation for Therapeutic/OTC Drugs

Very Difficult Task

- not all drug tests are created equal
  - laboratory-based tests (numerous products)
  - on-site, instant, POC tests (dozens of products)
  - each test has unique selectivity (i.e. ability to distinguish between similar compounds
- hundreds of therapeutic drugs
- hundreds of OTC medications

Court's Obligation

- limit use of therapeutic drugs
  - court must be notified
- prohibit the use of OTC medications without prior approval
- prohibit the use of dietary supplements, energy drinks, homeopathic substances, herbal products, sports nutrition powders, anything not regulated by FDA (anything from GNC)

An Interpretational Gift!

Opiate Metabolites

Parent Drug: Codeine
Metabolites: Norcodeine,Morphine,
(hydrocodone potential minor metabolite in high codeine doses)

Parent Drug: Morphine
Metabolites: Normorphine

Parent Drug: Heroin
Metabolites: 6-monoacetyl morphine (6-AM), Normorphine, Morphine

Parent Drug: Oxycodone
Metabolites: Oxymorphone, Noroxycodone, Noroxymorphone

Opiate Metabolites

Parent Drug: Hydrocodone
Metabolites: Hydromorphone, Norhydrocodone

Parent: Hydromorphone (may only as parent drug)
Metabolites: undetectable conjugated metabolites

Benzo Metabolites

Parent: Alprazolam
Metabolites: alpha-hydroxyalprazolam

Parent: Lorazepam
Metabolites: Detected as parent drug; undetectable metabolites

Parent: Clonazepam
Metabolites: 7-aminoclonazepam

Parent: Diazepam
Metabolites: Temazepam, Nordiazepam, Oxazepam

Benzo Metabolites

Parent: Temazepam
Metabolites: Oxazepam

Parent: Chlordiazepoxide
Metabolites: Norchlordiazepoxide, Nordiazepam, Oxazepam

Parent: Triazolam
Metabolites: only as parent drug; undetectable metabolites

Parent: Clorazepate
Metabolites: Nordiazepam, Oxazepam

Therapeutic/OTC Drugs

Drug/Class	Potential F/P Results
antihistamines/decongestants	amphetamines
Adderall	amphetamines
◆ confirm by GC/MS - ensure no methamphetamine	
chlordiazepoxide	benzodiazepine
◆ confirm by GC/MS - look for other benzos not metabolites of chlordiazepoxide	
dextromethorphan	phencyclidine (PCP)
l-methamphetamine (OTC nasal inhaler) Vick's	amphetamines
diet pills (eg, clobenzorex, fenproporex)	amphetamines
quinolone antibiotics (eg, levofloxacin)	opiates
antidepressants (Stertraline)	benzodiazepine

How to Drive a Toxicologist Crazy

My client claims he is testing positive for THC because he takes ibuprofen (Advil).

REVIEW

Urine Drug Screening: Practical Guide for Clinicians

KAREN E. MOELLER, PHARMD, BCPP; KELLY C. LEE, PHARMD, BCPP; AND JULIE C. KISSACK, PHARMD, BCPP

Drug testing, commonly used in health care, workplace, and criminal settings, has become widespread during the past decade. Urine drug screens have been the most common method for analysis because of ease of sampling. The simplicity of use and access to rapid results have increased demand for and use of immunoassays; however, these assays are not perfect. False-positive results of immunoassays can lead to serious medical or social consequences if results are not confirmed by secondary analysis, such as gas chromatography–mass spectrometry. The Department of Health and Human Services' guidelines for the workplace require testing for the following 5 substances: amphetamines, cannabinoids, cocaine, opiates, and phencyclidine. This article discusses potential false-positive results and false-negative results that occur with immunoassays of these substances and with alcohol, benzodiazepines, and tricyclic antidepressants. Other pitfalls, such as adulteration, substitution, and dilution of urine samples, are discussed. Pragmatic concepts summarized in this article should minimize the potential risks of misinterpreting urine drug screens.

Mayo Clin Proc. 2008;83(1)66-76

Our goal is to provide clinically relevant information that can be used to interpret urine drug screens (UDSs) for commonly abused drugs (ie, alcohol, amphetamines, benzodiazepines, opioids, marijuana, cocaine, phencyclidine [PCP], and tricyclic antidepressants [TCAs]). Proper evaluation of urine specimens, including detection times, are discussed, as well as false-positive results and potential false-negative results. Interpretation of tests for performance-enhancing drugs is beyond the scope of this article and is not discussed.

METHODS OF DRUG TESTING

Urine, blood, hair, saliva, sweat, and nails (toenails and fingernails) are some biological specimens used to perform laboratory drug testing, and they provide different levels of

TABLE 3. **Summary of Agents Contributing to Positive Results by Immunoassay[a]**

Substance tested via immunoassay	Potential agents causing false-positive result	Substance tested via immunoassay	Potential agents causing false-positive result
Alcohol[20]	Short-chain alcohols (eg, isopropyl alcohol)	Cannabinoids[1,8,43-48]	Dronabinol
			Efavirenz
Amphetamines[21-40]	Amantadine		Hemp-containing foods
	Benzphetamine		NSAIDs
	Bupropion		Proton pump inhibitors
	Chlorpromazine		Tolmetin

43. Protonix [package insert]. Philadelphia, PA: Wyeth; 2007.

44. la Porte CJ, Droste JA, Burger DM. False-positive results in urine drug screening in healthy volunteers participating in phase 1 studies with efavirenz and rifampin [letter]. *Ther Drug Monit*. 2006;28(2):286.

45. Leson G, Pless P, Grotenhermen F, Kalant H, ElSohly MA. Evaluating the impact of hemp food consumption on workplace drug tests. *J Anal Toxicol*. 2001;25(8):691-698.

46. Rollins DE, Jennison TA, Jones G. Investigation of interference by nonsteroidal anti-inflammatory drugs in urine tests for abused drugs. *Clin Chem*. 1990;36(4):602-606.

47. Rossi S, Yakub T, Bentley H, van den Brande G, Grant I, Ellis R. Characterization of interference with 6 commercial delta9-tetrahydrocannabinol immunoassays by efavirenz (glucuronide) in urine [letter]. *Clin Chem*. 2006;52(5):896-897.

48. Steinagle GC, Upfal M. Concentration of marijuana metabolites in the urine after ingestion of hemp seed tea. *J Occup Environ Med*. 1999;41(6):510-513.

ity in a case of fatal tramadol overdose. *Am J Forensic Med Pathol*. 2006; 27(4):359-362.

69. Khajawall AM, Simpson GM. Critical interpretation of urinary phencyclidine monitoring. *Adv Alcohol Subst Abuse*. 1984 Spring;3(3):65-73.

70. Sena SF, Kazimi S, Wu AH. False-positive phencyclidine immunoassay results caused by venlafaxine and O-desmethylvenlafaxine [letter]. *Clin Chem*. 2002;48(4):676-677.

71. Al-Mateen CS, Wolf CE II. Falsely elevated imipramine levels in a patient taking quetiapine [letter]. *J Am Acad Child Adolesc Psychiatry*. 2002;41(1):5-6.

72. Chattergoon DS, Verjee Z, Anderson M, et al. Carbamazepine interference with an immune assay for tricyclic antidepressants in plasma. *J Toxicol Clin Toxicol*. 1998;36(1-2):109-113.

73. Dasgupta A, Wells A, Datta P. False-positive serum tricyclic antidepressant concentrations using fluorescence polarization immunoassay due to the presence of hydroxyzine and cetirizine. *Ther Drug Monit*. 2007;29(1):134-

CLIN. CHEM. 36/4, 602–606 (1990)

Investigation of Interference by Nonsteroidal Anti-Inflammatory Drugs in Urine Tests for Abused Drugs

Douglas E. Rollins,[1] Thomas A. Jennison,[2] and Graham Jones[3]

Anecdotal and uncontrolled studies have suggested that nonsteroidal anti-inflammatory drugs produce false-positive results in immunoassay urine tests for some drugs of abuse. This study was performed in 60 volunteers who took ibuprofen as either a single 400-mg dose, or 200 mg three times a day, or 400 mg three times a day, and in 42 patients taking ibuprofen, naproxyn, or fenoprofen in therapeutic regimens for more than 30 days. Of the 510 urines collected from 102 individuals during these dosage regimens, two gave false-positive tests for cannabinoid by enzyme-mediated immunoassay (EMIA), one after 1200 mg of ibuprofen in three divided doses for one day and one in a patient taking naproxyn on a chronic basis; none was falsely positive for

falsely positive report.

Conversely, adulterants (e.g., acids or bases or substances with a high ionic strength) added to a urine specimen may give falsely negative immunoassay results (*1*). Moreover, the excretion of drugs, drug metabolites, or food substances in the urine could also interfere with immunoassays and cause a false-positive or false-negative result for a urine drug assay. Ibuprofen and other commonly used nonsteroidal anti-inflammatory drugs (NSAIDs) reportedly cause false-positive test results with the EMIA (EMIT™; Syva Co., Palo Alto, CA) for cannabinoids (*2–4*), false-negative mass-spectrometric confirmation for cannabinoids (*5*), and false-positive results for barbiturates and benzodiazepines by the FPIA (TDx™; Abbott

oid tests (*14*).

Brunk (*5*) describes a false-negative GC/MS cannabinoid confirmation caused by high concentrations of urinary ibuprofen that competed with the analyte for the cannabinoid-derivatizing reagent. This is an unlikely explanation for the data presented in this study. In his GC/MS tests, Brunk extracted 10 mL of urine, which would contain large amounts of potentially competing substances. He used tetramethyl ammonium hydroxide as a derivatizing reagent, and did not use a deuterated internal standard. For cannabinoid confirmation in this study we used only 1 mL of urine, hexafluoroisopropanol and pentafluoropropionic anhydride as the derivatizing reagents, and deuterated COOH-THC as an internal standard. If competition between ibuprofen and COOH-THC for the derivatizing reagents had occurred, no peak for the internal standard would have been observed—a situation that did not occur for any specimen in this study.

In conclusion, these data demonstrate that ibuprofen taken as either a single dose or in acute multiple doses or ibuprofen, naproxyn, or fenoprofen taken as chronic doses is unlikely to result in a positive immunoassay test for urine cannabinoids, benzodiazepines, or barbiturates. All positive immunoassay results should be considered as presumptively positive. A second chemical test such as GC/MS, performed properly, will markedly reduce the possibility of falsely accusing of substance abuse someone who was taking NSAIDs.

Partial support for this study came from Abbott Laboratories, Diagnostic Division, Abbott Park, IL.

1. Article used by the Mayo paper claiming ibuprofen could cause a false positive cannabinoid test is 25 years old.
2. Even though the Rollins paper is 25 years old, it concludes “unlikely”.
3. Assay used to conduct the 25-year old paper has not been available commercially for two decades
4. Confirmation testing resolves potential “false positive” concerns.
5. Doesn’t prohibit Mayo from publishing a misleading paper.

Commonly prescribed medications and potential false-positive urine drug screens

NANCY C. BRAHM, LYNN L. YEAGER, MARK D. FOX, KEVIN C. FARMER, AND TONY A. PALMER

Purpose. The implications of potential false-positive urine drug screen (UDS) results for patients receiving commonly prescribed medications were evaluated.

Summary. A comprehensive literature review was conducted to identify false-positive UDSs associated with all clinic formulary medications, as well as common nonprescription medications. The references of each report describing a medication whose use was associated with false-positive UDS results were also reviewed. If a class effect was suspected, additional agents in the category were searched. A total of 25 reports of false-positive UDS results were identified. Categories of medications included antihistamines, antidepressants, antibiotics, analgesics, antipsychotics, and nonprescription agents. Reports of false-positive results were found for the following formulary and nonprescription medications: brompheniramine, bupropion, chlorpromazine, clomipramine, dextromethorphan, diphenhydramine, doxylamine, ibuprofen, naproxen, promethazine, quetiapine, quinolones (ofloxacin and gatifloxacin), ranitidine, sertraline, thioridazine, trazodone, venlafaxine, verapamil, and a nonprescription nasal inhaler. False-positive results for amphetamine and methamphetamine were the most commonly reported. False-positive results for methadone, opioids, phencyclidine, barbiturates, cannabinoids, and benzodiazepines were also reported in patients taking commonly used medications. The most commonly used tests to screen urine for drugs of abuse are immunoassays, even though false-positive results for drugs of abuse have been reported with a number of these rapid-screening products. Results from such tests should be confirmed using additional analytical methods, including gas chromatography–mass spectrometry.

Conclusion. A number of routinely prescribed medications have been associated with triggering false-positive UDS results. Verification of the test results with a different screening test or additional analytical tests should be performed to avoid adverse consequences for the patients.

Index terms: Drug abuse; Drugs, over the counter; Drugs; False positive reactions; Tests, laboratory; Urine levels

Am J Health-Syst Pharm. 2010; 67:1344-50

The potential for false-positive urine drug screen (UDS) results for substances of abuse presents a therapeutic selection dilemma for the treating health care professional. While this problem is reported with specific medications, the extent of the problem in a clinic serving indigent patients and the medically underserved has not been evaluated. In particular, the use of medications with the potential for false-positive UDS results may present a significant liability for individuals required to undergo random or periodic UDSs as a component of a recovery or court-ordered monitoring program[1,2] or as a condition of employment.[1,3,4] In addition, false-positive UDS results may affect the clinician–patient relationship by raising issues of trust.[5] This article identifies commonly used medications associated with reports of false-positive UDSs.

Literature review

A comprehensive literature review

NANCY C. BRAHM, PHARM.D., M.S., is Clinical Associate Professor, Department of Pharmacy Practice: Clinical and Administrative Sciences, College of Pharmacy; LYNN L. YEAGER, M.L.I.S., is Assistant Professor, College of Medicine; MARK D. FOX, M.D., PH.D., M.P.H., is Associate Dean for Community Health and Research Development, School of Community Medicine, College of Medicine; KEVIN C. FARMER, PH.D., is Associate Professor, Department of Pharmacy Practice: Clinical and Administrative Sciences, College of Pharmacy; and TONY A. PALMER, B.S.PHARM., M.B.A., is Clinical Associate Professor, Department of Pharmacy Practice: Clinical and Administrative Sciences, College of Pharmacy, University of Oklahoma, Tulsa.

Address correspondence to Dr. Brahm at the Department of Pharmacy Practice: Clinical and Administrative Sciences, College of Pharmacy, University of Oklahoma, 4502 East 41st Street, 2H17, Tulsa, OK 74135-2512 (nancy-brahm@ouhsc.edu).

The authors have declared no potential conflicts of interest.

DOI 10.2146/ajhp090477

Table 1.

Reports of False-Positive Results of Urine Drug Screens for Selected Formulary Agents[6-30]

Medication	False-Positive Result						
	Amphetamine or Methamphetamine	Phencyclidine	Methadone	Opiates	Benzodiazepines	Cannabinoids	Barbiturates
Antihistamines/decongestants							
Brompheniramine	X						
Diphenhydramine			X				
Doxylamine			X				
Phenylpropanolamine	X						
Nonprescription nasal inhaler	X						
Antidepressants							
Bupropion	X						
Clomipramine			X				
Sertraline					X		
Trazodone	X						
Venlafaxine		X					
Antibiotics							
Quinolones (selected agents)				X			
Analgesics							
Ibuprofen		X				X	X
Naproxen						X	X
Antipsychotics							
Chlorpromazine	X		X				
Promethazine	X						
Quetiapine			X				
Thioridazine			X				
Other agents							
Dextromethorphan		X					
Ranitidine	X						
Verapamil			X				

References

1. Baden LR, Horowitz G, Jacoby H et al. Quinolones and false-positive urine screening for opiates by immunoassay technology. *JAMA*. 2001; 286:3115-9.
2. Lichtenwalner MR, Mencken T, Tully R et al. False-positive immunochemical screen for methadone attributable to metabolites of verapamil. *Clin Chem*. 1998; 44:1039-41.
3. Zacher JL, Givone DM. False-positive urine opiate screening associated with fluoroquinolone use. *Ann Pharmacother*. 2004; 38:1525-8.
4. Rollins DE, Jennison TA, Jones G. Investigation of interference by nonsteroidal anti-inflammatory drugs in urine tests for abused drugs. *Clin Chem*. 1990; 36:602-6.
5. Cherwinski K, Petti TA, Jekelis A. False methadone-positive urine drug screens in patients treated with quetiapine. *J Am Acad Child Adolesc Psychiatry*. 2007; 46:435-6.

Confirmation: Best Practice

- gas or liquid chromatography-mass spectrometry - GC/MS or LC/MS/MS
  - drug molecules separated by physical characteristics
  - identified based on chemical "finger-print"
  - considered "gold standard"
- refer to NADCP Adult Drug Court Best Practice Standards - Volume II

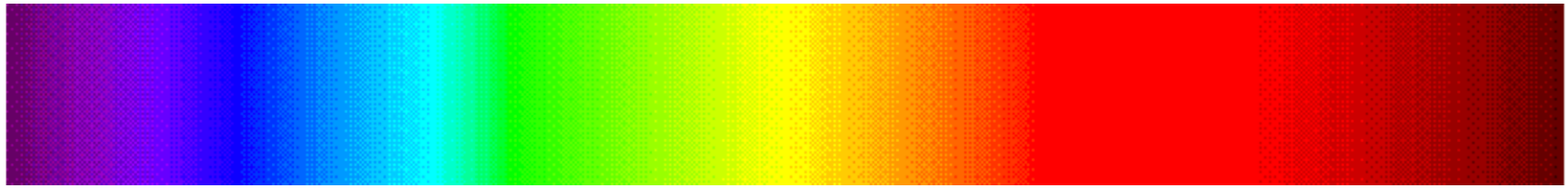
No Substitute for Knowledge/Expertise

- unethical to adjudicate based upon misinformation - violation of due process
- develop a relationship with your laboratory
- develop a relationship with your on-site device vendor
- don't be afraid to "call the company"
- seek expert advice

Prescription Drugs

Challenge with Prescription Drugs

- therapeutic use versus abuse



therapeutic use

various stages of misuse

abuse

Drug testing is an excellent tool for the abstinence monitoring of court clients, however it provides limited information for the differentiation between the appropriate therapeutic use of prescribed medications and the misuse/abuse of those same drugs - regardless of the specimen tested.

Client Signed Releases

- doctors
- dentists
- other healthcare professionals
- pharmacies

I (client name), am a participant in drug court. This program is a court monitored recovery program for addicts. As a result, I am subject to frequent and random drug testing. Therefore, I must report to the court my visit today. As I am in recovery, I would respectfully request that you take this into consideration and offer non-narcotic medications, if possible, when drugs are necessary for my medical treatment.

Physician (Name) _____
Physician (Signature) _____

If you have any questions or concerns, please feel free to call the court and talk to my case specialists.
If this patient fails to present this form to the nurse and physician prior to receiving medication or a prescription for medication, please notify the court.

Please list the medications prescribed today:

Other Control Strategies

- search & seizure (client contract)
  - car, home, possessions
- pill counts
- no out-of-state prescriptions
- use of specified pharmacies
- loss of completion credits/time while on certain prescription meds

Drug Testing is a *TOOL*!

- drug testing, as an abstinence monitoring strategy, is just one assessment option
- don't become myopic regarding drug testing results
- consider all of the client behavioral data
- consider the therapeutic ramifications of results & adjudicate to support recovery

email address:

- carypl@health.missouri.edu

Speaker Evaluations

Please fill out our speaker evaluations at the link below:

http://bit.ly/2qR37MR