

# Medication Monitoring; Drug Testing in Clinical Practice (urine, blood, saliva, hair)

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# Objectives

- Learn the principles of urinary, blood, saliva and hair drug testing
- Understand clinical interpretation of the tests
- Grow insight into period of detection of various substances
- Build awareness of samples alteration to combat deception

# Federally Regulated Urine Drug Testing

- \* Most established use of UDTs “Federal Five”
  - \* marijuana (THC)
  - \* cocaine
  - \* opiates
  - \* phencyclidine (PCP)
  - \* amphetamine/methamphetamine
- \* Mandated cutoff concentrations too high to be of value in clinical practice
- \* Requirements of federally regulated testing not always applicable to clinical practice

\*Shults TF. Medical Review Officer Handbook. 8th ed. 2002. Gourlay DL, et al. Urine Drug Testing in Clinical Practice: Dispelling the Myths & Designing Strategies [monograph]. 2004

# Scope of abuse

- Unexpected toxicology results demonstrated in about 50% of patients in treatment with controlled substances\*
- Recent study of 200,000 urine specimens showed that 60% of results were inconsistent with prescribed regiments\*\*
  - Different drugs found 15%
  - Additional drugs found 20%
  - No drugs found 25%
  - Illicit drugs found 11-24%

\* Clarke JJ1, Lawlor TE, Madraymootoo W, et al. Summary of in vitro genetic toxicology assay results: expected and unexpected effects of recent study design modifications. Environ Mol Mutagen. 2012 Oct;53(8):631-5.

\*Michna E, Jamison RN, Pham LD et al. Urine toxicology screening among chronic pain patients on opioid therapy: frequency and predictability of abnormal findings. Clin J Pain. 2007;23(2):173-9

\*Quest Diagnostics Health Trends: Prescription Drug Monitoring Report 2013

[www.questdiagnostics.com/dms/Documents/health-trends/2013\\_health\\_trends\\_prescription\\_drug\\_misuse.pdf](http://www.questdiagnostics.com/dms/Documents/health-trends/2013_health_trends_prescription_drug_misuse.pdf)

# Drug Screening is a Standard of Care

- Recommended by Institute of Medicine, DEA, American Pain Society, American Academy of Pain Management, American Society of Interventional Pain Physicians, American Society of Addiction Medicine, Federation of State Medical Boards and Indiana Medical Licensing Board
- Only 8% of patients in primary care opioid treatment complete Urine Drug Screening (UDS)

\*Indiana Pain Management Prescribing Final Rule (updated October, 2016)

\* Starrels JL, Becker WC, Weiner MG et al. Low use of opioid risk reduction strategies in primary care even for high risk patients with chronic pain. J Gen Intern Med. 2011;26(9):958-64

# Who Should Be Tested?

- Katz study: 27% of patients with NO behavioral signs suggestive of opioid abuse present with positive urine results\*
- No relationship could be established with any variables including sex, pain site, type of opioid, opioid dose, number of opioids prescribed, prescribing physician and type of abnormal toxicology result.\*\*

\* Katz NP, Adams EH, Benneyan JC et al. Foundations of opioid risk management. Clin J Pain 2007;23(2):103-18

\*\* \* Michna E, Jamison RN, Pham LD et al. Urine toxicology screening among chronic pain patients on opioid therapy: frequency and predictability of abnormal findings. Clin J Pain. 2007;23(2):173-9

# Indiana Pain Management Prescribing

- \* Drug Monitoring Tests (Effective Jan. 1, 2015)
- \* At any time the physician determines that it is medically necessary, whether at the outset of the treatment plan, or any time thereafter, a prescribing physician shall perform or order a drug monitoring test that must include a confirmatory test using a method selective enough to differentiate individual drugs within a drug class.
- \* <https://www.ismanet.org/pdf/legal/IndianaPainManagementPrescribingFinalRuleSummary.pdf>  
(accessed Sept 29, 2018)

# The rule applies to:

| Drug Dose Duration   | Dose                                 | Duration              |
|--|--------------------------------------|-----------------------|
| Transdermal opioid patch   | Any                                  | >3 consecutive months |
| Any opiate ER medication not in abuse - deterrent form if an FDA-abuse deterrent form is available | Any                                  | Day 1                 |
| Tramadol   | >60 mg MED/day                       | >3 consecutive months |
| Any other opioid-containing controlled substance   | >60 pills/month<br>OR >15 mg MED/day | >3 consecutive months |



# Exclusions

1. Patients with a terminal medical condition (Refer to definitions section.)
2. Residents of an Indiana-licensed health facility (as defined by state law)
3. Patients enrolled in an Indiana-licensed hospice program (as defined by state law)
4. Patients enrolled in an inpatient or outpatient palliative care program of an Indiana-licensed hospital or hospice (as defined by state law)

# When to test?

- At initial appointment
- At least once every 3-6 months for low risk patients
- More frequently in high risk patients
- At least once a year confirmatory testing
- At any time the physician determines that it is medically necessary

\*<https://www.ismanet.org/pdf/legal/IndianaPainManagementPrescribingFinalRuleSummary.pdf>  
(accessed Sept 29, 2018)

\* Chou R., Fanciullo GJ, Fine PG, et al. Opioid treatment guidelines: clinical guidelines for the use of chronic opioid therapy in chronic noncancer pain J. Pain. 2009;10(2):113-30

# When to test?

## Patient

- Is on a controlled substance
- Medication regimen is changing
- Resistant to evaluation
- Requests a specific drug
- Displays aberrant behavior
- In a recovery program
- Declines in function
- 18 factors as per Indiana Pain Management Prescribing Rule

\*<https://www.ismanet.org/pdf/legal/IndianaPainManagementPrescribingFinalRuleSummary.pdf> (accessed Sept 29, 2018)

\*Compton P. The role of urine toxicology in chronic opioid analgesic therapy Pain Manag Nurs 2007;8(4):166-72

\*Gourlay DL, et al. Urine Drug Testing in Clinical Practice: Dispelling the Myths & Designing Strategies [monograph]. 2004.

# Randomization



# Summary: Interpretation of UDS Results

## Requires that you know

- How specimen is collected
- What is prescribed
- Retention times
- Alternative medical explanations
- Metabolism of drugs
- Scams
- Laws, regulations & guidelines

# Specimen Collection in Clinical Practice

- Random collection preferred
  - Adulterants, substituted specimens
- Unobserved usually acceptable
- Collection facility
  - No basin
  - Pigmented toilet water
- If tampering suspected, check
  - Temperature 90°F-100°F – pH 4.5-8.0
  - Creatinine >20 mg/dL – Color

\* Cook JD, et al. *J Anal Toxicol*. 2000;24:579-88.

\*\* Galloway JH, et al. *J Clin Pathol*. 1999;52:713-8.

\*\*\* Gourlay DL, et al. *Urine Drug Testing in Clinical Practice: Dispelling the Myths & Designing Strategies* [monograph]. 2004.

# Specimen Validity

| Analyte          | Normal range |
|------------------|--------------|
| Creatinine       | >2 mg/dl     |
| Specific gravity | >1.0020      |
| pH               | 3.5-9.0      |
| Nitrites         | <200 mcg/ml  |
| Chromates        | <50 mcg/ml   |

# Creatinine Interpretation

| Concentration | Specimen    | Possible reasons                          |
|---------------|-------------|---|
| 100 mg/dl     | Average     |   |
| <20 mg/dl     | Dilute      | Adulteration;<br>increase water<br>intake |
| <2 mg/dl      | Substituted | Not urine                                 |



# Specific Gravity Interpretation

| Value   | Specimen      | Possible reasons   |
|---------|---------------|--|
| >1.04   | Concentrated  | Disease state;<br>adulteration with<br>salt or other<br>compound |
| 1.0200  | Average urine |  |
| <1.0020 | Dilute        | Adulteration;<br>increased water<br>intake                       |
| <1.0010 | Substituted   | Not urine  |

# Urine Drug Screening Process

## 1. **Immunoassay** screening

- Laboratory-based or at point of care
- Classify substances as present or absent
- Presumptive positives

## 2. **Confirmatory** & quantitative

- Laboratory-based specific drug identification
- GC/MS standard
- **No** correlation between urine drug concentration & dose

Use a reputable laboratory (DHHS or CAP certified)

GC/MS=gas chromatography/mass spectrometry; DHHS=Department of Health & Human Services; CAP=College of American Pathologists

\*Pesce A,,West C, Egan K, et al, Interpretation of Urine Drug Testing in Pain PatientsPain Medicine, Volume 13, Issue 7, 1 July 2012, Pages 868–885.

\*Shults TF. *Medical Review Officer Handbook*. 8th ed. 2002.

\*Braithwaite RA, et al. *Ann Clin Biochem*. 1995;32:123-53.

# Immunoassay

- Based on competitive binding to antibody to a target substance
- If a drug has a similar structure to a target analyte, it may trigger false positive result
- Sometimes a drug without structural similarity may bind to antibody (false positive)
- Lack of cross reactivity across a class may result in false negatives
- Qualitative result only (or semi-qualitative)
- Rapid result

\*Jagerdeo E, Schaff JE. UPLC-Orbitrap® Screening for over 35 Drugs of Abuse and Metabolites in Biological Fluids in Under 10 min. *Methods Mol Biol.* 2018;1810:75-87

\*DePriest AZ1, Black DL2, Robert TA. Immunoassay in healthcare testing applications. *J Opioid Manag.* 2015 Jan-Feb;11(1):13-25

\*\*Gourlay DL, Heit HA, Caplan YH. *Urine drug testing in clinical practice: the art and science of patient care.* 5th ed. Baltimore, MD; The Johns Hopkins University School of Medicine; 2012:1-20

\*Hetsley R, Zichterman A, Black DL, et al. Urine drug testing of chronic pain patients. II. Prevalence patterns of prescription opiates and metabolites. 2010;34(1):32-8

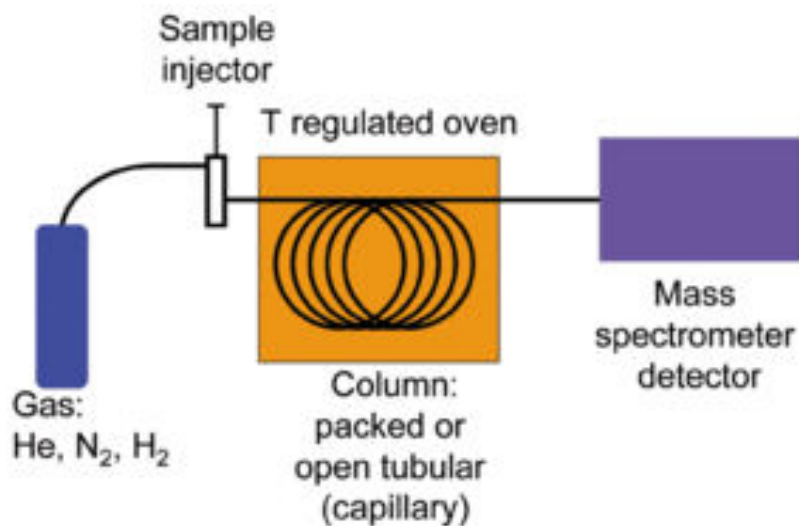
\*DePriest A, Heltsley R, BlackDL, et al. Urine drug testing of chronic pain patients. III. No rmetabolites as biomarkers of synthetic opioid use. *J Anal Toxicol.* 2010;34:444-9



# False Positives on Immunoassay

| Immunoassay     | Manchicanti et al. (2011)<br>% | Passik at al. (2013)<br>% |
|-----------------|--------------------------------|---------------------------|
| Amphetamines    | 52.9                           | 21.4                      |
| Barbiturates    | -----                          | 21.5                      |
| Benzodiazepines | -----                          | 11.4                      |
| Cocaine         | 0.0                            | 12.3                      |
| Marijuana       | 38.7                           | 21.3                      |
| Methadone       | 18.3                           | 45.3                      |
| Opiates         | 3.6                            | 22.4                      |
| Oxycodone       | 38.8                           | 41.3                      |
| MDMA/Meth       | 85.7                           | 99.5                      |
| PCP             | -----                          | 100                       |
| TCA             | -----                          | 76.2                      |

# Gas Chromatography/Mass Spectrometry (GC/MS)



- Specialized personnel.
- Quantitative
- Drug is identified based on the molecular mass and ion ratios



Abe H, Takei C, Sakakura M, et al. Comprehensive Drug Screening by Thermal Desorption and Pyrolysis Combined with Direct Analysis in Real Time-Mass Spectrometry (TDP/DART-MS). *Methods Mol Biol.* 2018;1810:115-124

# False Positives on Gas Chromatography/Mass Spectrometry (GC/MS)

- Technical errors
- Clerical errors
- Poor laboratory methods
- Contaminants

# Emerging Technologies for Drug Testing

## Saliva

### Advantages

- Collection ease
- Minimal invasiveness
- Close supervision
- Limited preanalytical manipulation

### Disadvantages

- Shorter retention, lower levels than typically in urine

## Hair

### Advantage

- Long-term measure related to hair length

### Disadvantages

- Dark hair greater capacity to bind drug
- Irregular growth
- Accessibility
- Labor-intensive sample preparation

\*Wong JKY, Choi TLS, Kwok KY, et al. Doping control analysis of 121 prohibited substances in equine hair by liquid chromatography-tandem mass spectrometry. *J Pharm Biomed Anal.* 2018 Sep 5

\*Shults TF. *Medical Review Officer Handbook*. 8th ed. 2002. Wolff K, et al. *Addiction.* 1999;94:1279-98. Braithwaite RA, et al. *Ann Clin Biochem.* 1995;32:123-53. Kintz P, et al. *Ther Drug Monit.* 2002;24:239-46. Caplan YH, et al. *J Anal Toxicol.* 2001;25:396-9.

# Emerging Technologies for Drug Testing

## Sweat

### Advantage

- Noninvasive, cumulative measure over days to weeks

### Disadvantages

- Varying sweat production
- Risk of accidentally removing/contaminating collection device

## Blood

### Advantage

- Reduced chance of patients influencing test results

### Disadvantages

- Not amenable to rapid screening
- Low concentration
- Invasive collection

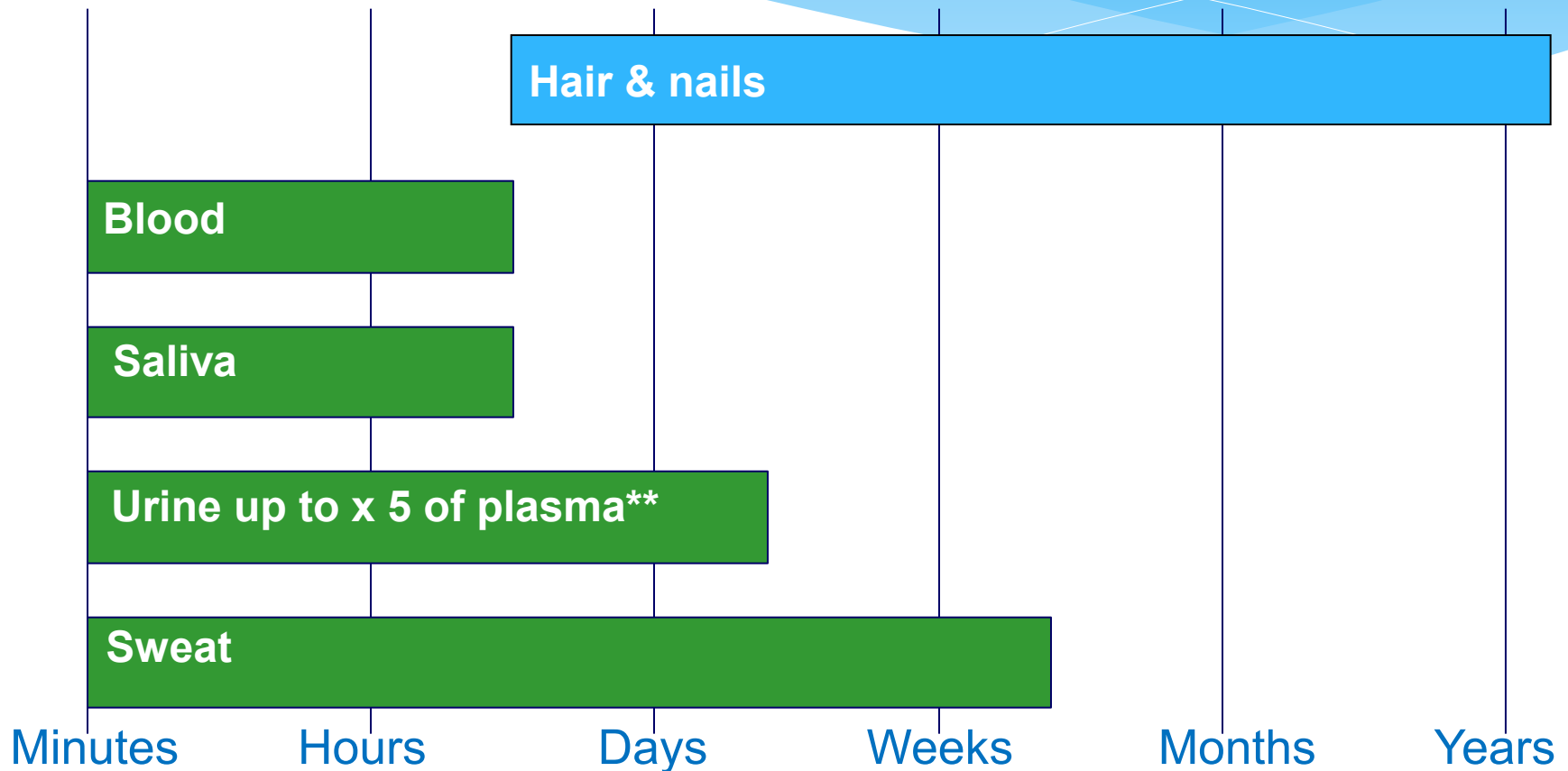
\*Wagner E, Raabe F, Martin G et al. Concomitant drug abuse of opioid dependent patients in maintenance treatment detected with a multi-target screening of oral fluid. *Am J Addict.* 2018 May 24

\*Braithwaite RA, et al. *Ann Clin Biochem.* 1995;32:123-53.

\*Wolff K, et al. *Addiction.* 1999;94:1279-98. Caplan YH, et al. *J Anal Toxicol.* 2001;25:396-9.



# Relative Drug Detection Times in Biologic Specimens\*



\*Caplan YH, et al. *J Anal Toxicol.* 2001;25:396-9.

\*\*Katz N, Fanciullo Gj. Role of urine toxicology testing in the management of chronic opioid therapy. *Clin J Pain.* 2002;18S76-b82

# Drug-Class–Specific Windows of Detection in Urine

| Drug   | Federal immunoassay cutoff (ng/mL) | Days       |
|--|------------------------------------|------------|
| • Amphetamine (misuse)                           | 1000                               | ≤5         |
| • Cannabinoids, 1 cigarette<br>– Chronic smoker  | 50                                 | 2-4<br>≤30 |
| • Benzoyllecgonine after street doses of cocaine | 300                                | ≤7         |
| • Opiates (morphine, codeine)                    | 2000                               | 1-2        |
| • Phencyclidine<br>– Chronic user                | 25                                 | 8<br>≤30   |

\*Shults TF. *Medical Review Officer Handbook*. 8th ed. 2002.

\*Vandevenne M, et al. *Acta Clinica Belgica*. 2000;55:323-33.

\*Wolff K, et al. *Addiction*. 1999;94:1279-98.

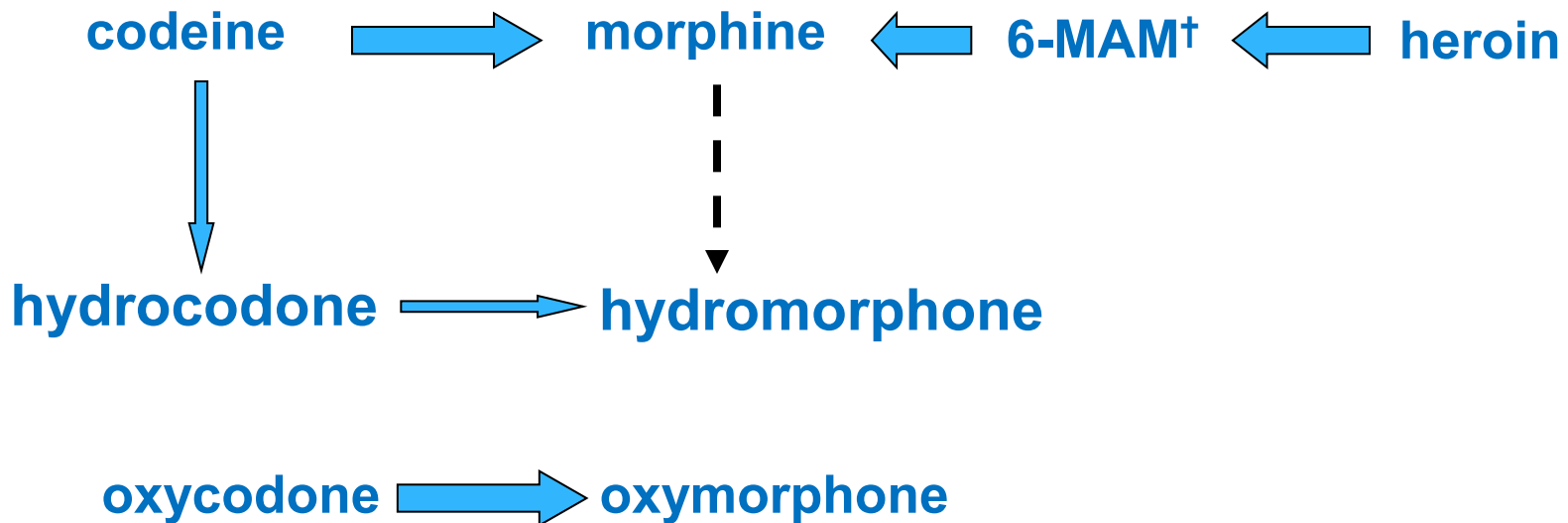
# Thresholds used

| Drug Class      | Workplace screening<br>(ng/ml ) | Pain management<br>(ng/ml) |
|-----------------|---------------------------------|----------------------------|
| Amphetamines    | 500-1000                        | 100-250                    |
| Barbiturates    | 300                             | 100-200                    |
| Benzodiazepines | 300                             | 50                         |
| Cocaine         | 150-300                         | 50                         |
| Marijuana       | 50                              | 5                          |
| Opiates         | 300-2000                        | 50-100                     |

# Interpretation of UDT Results

|                 | Patient has taken drug | Patient has not taken drug |
|-----------------|------------------------|----------------------------|
| Positive result | True positive          | False positive             |
| Negative result | False negative         | True negative              |

# Metabolism of Opioids



Not comprehensive pathways, but may explain the presence of apparently unprescribed drugs

<sup>†</sup>6-MAM=6-monoacetylmorphine, an intermediate metabolite

# False-Positive Results

- Technician or clerical error
- Cross-reaction with other compounds in urine
  - May be structurally unrelated; e.g., quinolone antibiotics can cause positive opiate results
  - GC/MS not influenced by cross-reacting compounds

GC/MS=gas chromatography/mass spectrometry

\*Brahm NC, Yeager LL, Fox MD. Commonly prescribed medications and potential false-positive urine drug screens. *Am J Health Syst Pharm*. 2010 Aug 15;67(16):1344-50

\*Shults TF. *Medical Review Officer Handbook*. 8th ed. 2002.

\*Baden LR, et al. *JAMA*. 2001;286:3115-9.

\*Zacher JL, et al. *Ann Pharmacother*. 2004;38:1525-8.

# False-Positive Results

- In OxyContin - 1% of hydrocodone is allowed
- Hydromorphone – hydrocodone and morphine allowed
- Contaminated herbal supplements – about 25% contain diuretics, benzodiazepines, steroids and amphetamines
- In pharmacies pill counters are rarely cleaned other than after dispensing sulfa or penicillin drugs

\* Haddox JD, Kupper RJ, Cone EJ Clinical considerations for interpretation of unexpected results from UDS. Pain Med. 2010

\*\*FDA Consumer Update: Beware of fraudulent weight-loss dietary supplements. March 15, 2011 [www.fda.gov/ForConsumers/ConsumerUpdates/ucm246742.htm](http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm246742.htm)

# UDS Results Reported as “None Detected”

- May mean any of following
  - Patient
    - Does not use drug
    - Has not recently used drug
    - Excretes drug/metabolite faster than normal
  - UDS used not sufficiently sensitive to detect drug at concentration present
    - Ask for “no threshold” testing
  - Clerical error
- In adherence testing, may raise concerns about misuse/diversion

\*Wolff K, et al. *Addiction*. 1999;94:1279-98.

\*Gourlay DL, et al. *Urine Drug Testing in Clinical Practice: Dispelling the Myths & Designing Strategies* [monograph]. 2004.



# False-Negative Results

- Technical or clerical error
- Tampering with urine sample
  - Dilution
  - Substitution
  - Adulteration

1. Feldhammer M, Saitman A, Nguyen L, Milstid B. Dilution of Urine Followed by Adulteration in an Attempt to Deceive the Laboratory. *J Anal Toxicol*. 2018 Sep 6

2. Shults TF. *Medical Review Officer Handbook*. 8th ed. 2002.  
Wolff K, et al. *Addiction*. 1999;94:1279-98.

# Dilution

- Most common method – many “cleansing” teas and products available on line, including Vit B to restore color to avoid diluted appearance
- 40oz of water intake under 3h
- 8oz of water under 30min
- Measure Cr
- Measure specific gravity



Moeller KE, Lee KC, Kissack JC.

Urine drug screening: practical guide for clinicians.

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

# Substitution

- Another person's urine
- Synthetic urine
- Animal urine



# Whizzinator

AVAILABLE IN :



**WHITE**

**TAN**

**LATINO**

**BROWN**

**BLACK**





# Adulteration



- Adding chemicals to a urine sample after voiding to mask the presence of illicit or prescription drugs
- Household products: bleach, vinegar, lemon juice, dish soap, drain cleaners, ammonia, hydrogen peroxide, Visine, table salt, pectin
- Commercial products: glutaraldehyde, sodium and potassium nitrate, peroxide and peroxidase, pyridinium chlorochromate (PCC)
- Marijuana is the most masked ingredient

\*Murnion BP, Granot R, Day RO. Utility of urine drug screening: a clinical audit. Emerg Med A 2007 Jun;19(3):246-52.

\*Moeller KE, Lee KC, Kissack JC. Urine drug screening: practical guide for clinicians. Mayo Clin 2008 Jan;83(1):66-76



# Adulteration Products Are Many

- Klear, Whizzies, Urine Luck – not detected by traditional specimen integrity tests
- Mary Jane SuperClean 13, Instant Clean ADD-IT-ive
- UrinAid, Amber 13, THC-Free, Randy's Clear
- LL418, Sweet Pee's Spoiler, Stealth





# False-Positive Results on Screening

- **Marijuana** - PPIs (especially pantoprazole -Protonix), ASA, baby wash/soaps, ibuprofen, naproxen
- **Opioids** - quinolone antibiotics (levofloxacin, ofloxacin), verapamil, procaine, rifampin and tonic water (quinine), dextromethorphan, diphenhydramine
- **Tramadol** - venlafaxine (Effexor)
- **PCP** – lamotrigine, tramadol, venlafaxine
- Craven C, Fileger M, Woster P. Demystifying benzodiazepine urine drug screen results, Pract Pain Manage. 2014;14(1):38-41
- Saitman A, Park HD, Fitzgerald RL. False-positive interferences of common urine drug screen immunoassays: a review. J Anal Toxicol. 2014;38(7):387-396

# False-Positive Results on Screening

- **Amphetamines** – amantadine, bupropion, desipramine, ephedrine, Vicks inhaler, metronidazole, selegiline, ranitidine, promethazine, trazodone
  - **Benzodiazepines** – chlorpromazine, fenoprofen, flurbiprofen, indomethacin, sertraline, efavirenz
  - **Barbiturates** – ibuprofen, naproxen, phenytoin
  - **Fentanyl** – trazodone
- 
- Craven C, Fileger M, Woster P. Demystifying benzodiazepine urine drug screen results, Pract Pain Manage. 2014;14(1):38-41
  - Saitman A, Park HD, Fitzgerald RL. False-positive interferences of common urine drug screen immunoassays: a review. J Alal Toxicol.2014;38(7):387-396



# False-Positive Results on Screening

- **Methadone** – clomipramine, chlorpromazine, diphenhydramine, olanzapine, quetiapine, tapentadol, verapamil, thioridazine
- **Phencyclidine (PCP)** – dextromethorphan, diphenhydramine, ibuprofen, imipramine, ketamine, lamotrigine, meperidine, thioridazine, tramadol, venlafaxine
- **Tricyclic Antidepressants** – carbamazepine, cyclobenzaprine, cyproheptadine, diphenhydramine, hydroxyzine, promethazine, quetiapine

# False-Positive Results on Screening

## References

- Snozek CLH, Kaleta EJ, Jannetto PJ, et al. False-positive amphetamine results on several drug screening platforms due to mexiletine. Clin Biochem. 2018 Aug;58:125-127
- Gourlay DL, Heit HA, Caplan YH. Urine drug testing in clinical practice: the art and science of patient care. 5th ed. Baltimore, MD; The Johns Hopkins University School of Medicine; 2012:1-20
- Allen KR. Interference by venlafaxine ingestion in the detection of tramadol by liquid chromatography linked to tandem mass spectrometry for the screening of illicit drugs in human urine Clin Toxicol (Phila) 2006;44(2)
- Moeller KE, Lee KC, Kissack JC Urine drug screening: practical guide for clinicians. Mayo Clin Proc 2008;83(1)66-76
- Reisfield GM, Goldenberg BA, Bertholf RL 'False-positive' and 'false-negative' test results in clinical urine drug testing. Bioanalysis 2009;1(5):937-52
- Brahm NC, Yeager LL, Fox MD, et al. Commonly prescribed medications and potential false-positive urine drug screens. Am J Health-Sys Pharm. 2010;67:1344-50
- Christo PJ, Manchikanti L, Ruan X et al. Urine drug testing in chronic pain. Pain Physician 2011;14:175-87

# Interpretation of Dose Compliance

- Studies repeatedly demonstrated that urine drug concentrations MAY NOT be interpreted to determine the amount of drug taken, when the last dose was administered or the source of the drug
- UDS cannot reliably determine whether a pt. is abusing the prescribed medication, has reached a toxic level, has hoarded or binged, taken more than prescribed, or diverted the prescription while taking a few doses before the test

\*Katz N, Fanciullo Gj. Role of urine toxicology testing in the management of chronic opioid therapy. Clin J Pain.2002;18S76-b82

\*\*Gourlay DL, et al. Urine Drug Testing in Clinical Practice: Dispelling the Myths & Designing Strategies [monograph]. 2004

\*\*\* Cone EJ, Caplan YH. Urine toxicology testing in chronic pain management Postgrad Med . 2009;121(4):91-102

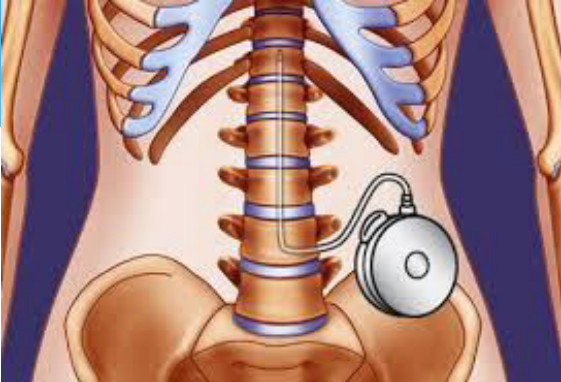
# Therapeutic blood levels are not established for BZs and opiates

- Pharmacokinetics (what the body does to the drug) and pharmacodynamics (what the drug does to the body) are too complex
- Blood level does not correlate with therapeutic response
- Serum blood levels do not correlate with CNS levels
- Genetic variations in receptor subtypes and P-450 system
- P- Glycoprotein transporter activity
- Drug tolerance

\*Lotsch J Pharmacokinetic-pharmacodynamic modeling of opioids J Pain Symptom Manag 2005;29(5S):S90-103

\*Levy S, Harris SK, Sherritt L, et al. Drug testing of adolescents in ambulatory medicine: physician practices and knowledge. Arch Pediatr Adolesc Med. 2006 Feb;160(2):146-50

# Testing for Intrathecal Drug Administration



- Morphine blood levels are very low due to its hydrophilicity
- Morphine drug testing in urine is, as a rule below 100mg/ml cut off
- Morphine in oral fluid is even lower

\*Ready Lb. Regional analgesia with intraspinal opioids. In: Loeser JD, et al. eds. Bonica's Management of Pain. Philadelphia: Lippincott Williams & Wilkins; 2001;1953-66

# Testing for Benzodiazepines

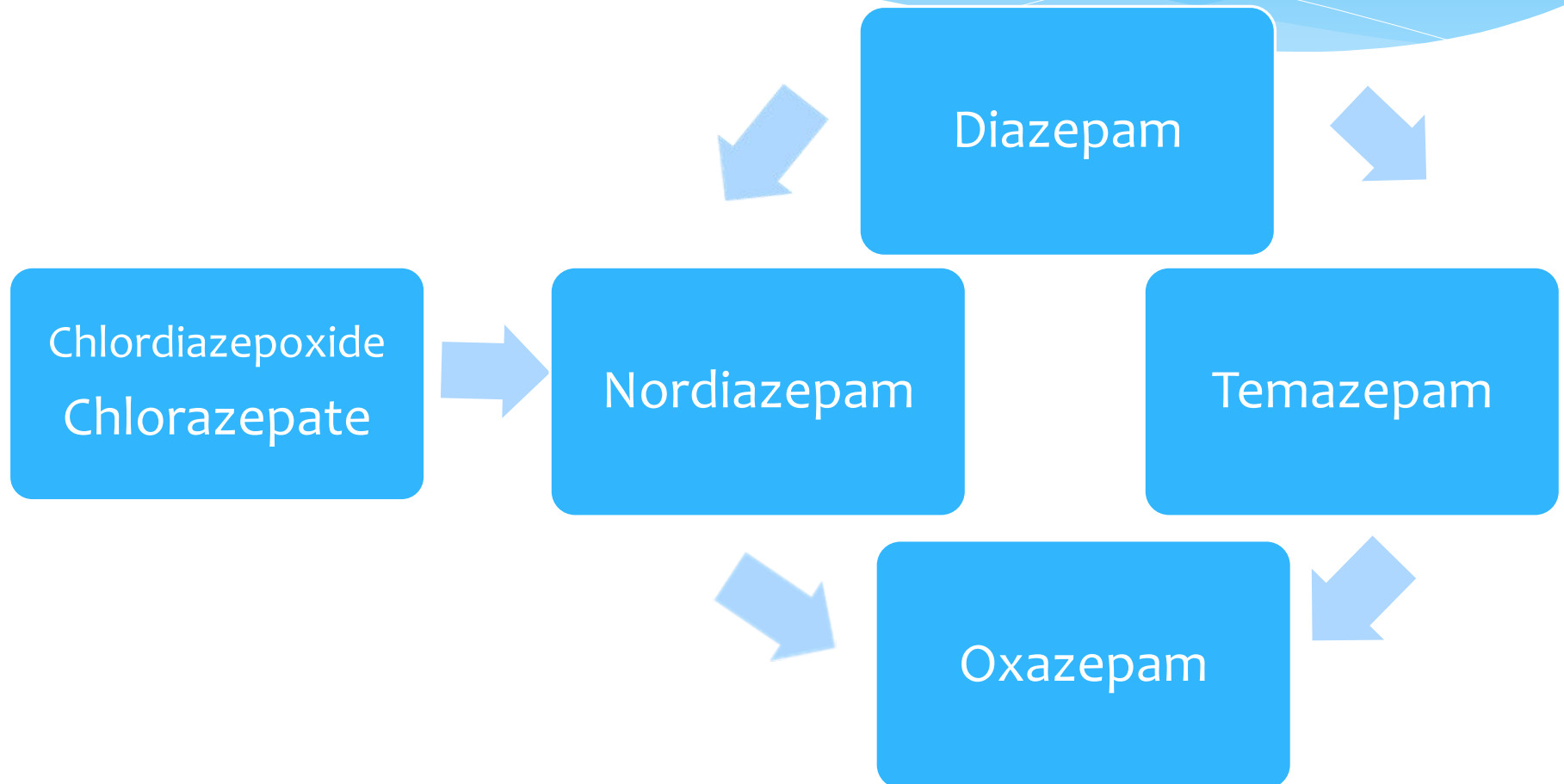


Parental drug frequently is not detectable in the urine due to metabolism, so frequently it is impossible to say which BZ was ingested

| Parent Drug           | Metabolite               |
|-----------------------|--------------------------|
| Alprazolam (Xanax)    | alpha-hydroxy-alprazolam |
| Clonazepam (Klonopin) | 7-amino-clonazepam       |
| Flurazepam (Dalmane)  | 2-hydrohethyl-flurazepam |
| Lorazepam (Ativan)    | Lorazepam glucoronige    |

\*Substance Abuse and Mental Health Service Administration, Drug Testing Advisory Board meeting. October 2012. National Forensic Laboratory Information System (NFLIS) reports

# Benzodiazepines' Metabolism



# Testing for Alcohol



- Majority of ethanol testing is done in blood
  - Ethanol in urine 7-8h
  - Maybe positive due to post collection fermentation (diabetes, Candida) – up to 1/3 of positives caused
  - UDS is not admissible as legal evidence of intoxication due to lack of correlation between amount ingested and urine concentration
  - Ethyl Glucuronide (EtG) and Ethyl Sulfate (EtS) are metabolites – in urine in 1h and up to 1-5 days
- 
- Foley KF. A Positive Urine Alcohol with Negative Urine Ethyl-Glucuronide. Lab Med. 2018 Jul 5;49(3):276-279
  - Crews B, West R, Gutierrez R, et al. An improved method of determining ethanol use in chronic pain population. J Opioid Manage. 2011;7(1):27-34
  - Kissak JC, Bishop J, Leatherwood Roper A., Ethylglucuronide as a biomarker for ethanol detection. Pharmacother. 2008;28(6):769-81



# Testing for Alcohol

- Hand sanitizer does not contribute to EtS levels above 100ng/ml
- Ingestion of an active baker's yeast combined with sugar may result in high EtS and EtG concentration
- 2l apple juice, 1,320g sauerkraut, 690g bananas – produce levels below 500ng/ml of EtS and EtG
- Mouthwash – produce level below 500ng/ml of EtS and EtG
- Grape juice contains EtS and ethanol
- Nonalcoholic beverages contain alcohol (up to 0.5 vol %)

\* Reisfield GM, Goldberger BA, Crews BO, et al, Ethyl glucuronide, ethyl sulfate, and ethanol in urine after sustained exposure to an ethanol based hand sanitizer. J Anal Toxicol 2011;35:85-91

\* Thierauf A, Wolhlfarth A, Auwarter V, et al. Urine tested positive for ethyl glucuronide and ethyl sulfate after the consumption of yeast and sugar. Forensic Sci Int 2010;202:e45-47

\* Mussloff F, Albermann E, Madea B. Ethyl glucuronide and ethyl sulfate in urine after consumption of various beverages and food-misleading results? Int J Legal Med 2010;124:623-30

# Testing for Marijuana



- Before passive exposure could result in positive urine tests, the atmosphere has to become so saturated with marijuana smoke that subjects have to wear goggles to protect their eyes; the smoke is also strongly irritating the nose and throat.
- Ventilation of any sort prevents positive tests for passive subjects.
- Such an exposure is not “passive” as individuals must actively force themselves to remain in the smoke saturated atmosphere to test positive.
- The same works for oral fluid

\*Lee D1, Huestis MA. Current knowledge on cannabinoids in oral fluid. Drug Test Anal. 2014 Jan-Feb;6(1-2):88-111

\*MuleSL, Lomax P, Gross SJ. Active and realistic passive marijuana exposure tested by three immunoassays and GC/MS in urine J Anal Toxicol. 1988;12(3):113-6

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# Testing for Synthetic Cannabinoids



- A myriad of synthetic compounds which are active at cannabinoid receptors
- Introduced in 2004, first reported in the US in 2008, not scheduled before 2011, smoked or ingested, frequently contaminated
- Structurally unrelated to marijuana
- High number of compounds and ever-changing nature of these substances results in detection of some, but not all spice products
- Bonaccorso S, Metastasio A, Ricciardi A, et al. Synthetic Cannabinoid use in a Case Series of Patients with Psychosis Presenting to Acute Psychiatric Settings: Clinical Presentation and Management Issues. Brain Sci. 2018 Jul 14;8(7).
- Drugs of Abuse 2017 edition . A DEA Resource Guide. [https://www.dea.gov/pr/multimedia-library/publications/drug\\_of\\_abuse.pdf](https://www.dea.gov/pr/multimedia-library/publications/drug_of_abuse.pdf)

# Testing for Synthetic Cathinones



Gundersen POM, Spigset O, Josefsson M. Screening, quantification, and confirmation of synthetic cannabinoid metabolites in urine by UHPLC-QTOF-MS.

Drug Test Anal. 2018 Jul 11

# Testing for Synthetic Cathinones (Bath Salts)

- Inhalation, oral ingestion, or injections
- Sold under the guise of plant food, jewelry cleaner, etc.
- Derivatives of khat, East African plant
- Abused in Europe since 2009 and the US since 2010
- Stimulants similar to cocaine, methamphetamine and ecstasy
- False positive for meth on immunoassays
- Period of detection in urine 5 days

\* DrugFacts: Synthetic Cathinones (“Bath Salts”). NIH National Institute of Drug Abuse.  
[www.drugabuse.gov/publications/drugfacts/synthetic-cathinones-bath-salts](http://www.drugabuse.gov/publications/drugfacts/synthetic-cathinones-bath-salts)

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# Testing for Cotinine (Nicotine Metabolite)



- In blood 1-3 days depending on usage
- $T_{1/2}$  18-20h (vs. 2-4h of nicotine)
- In urine 2-4 days and longer
- Not quantitative
- Passive exposure gives concentration below 500ng/ml

\* JarvisMJ, Russell MAH, Benowitz NL, et al. Elimination of cotinine from body fluids: implications of noninvasive measurement of tobacco smoke exposure. Am J Publ Health. 1988;78(6):696-8



Thank You

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