Urine Drug Screening (UDS) - Frequently Asked Questions (FAQ)

"I do this routinely for all my patients when prescribing opioids for chronic pain."

A) Why bother with urine drug screening (UDS)?

- To improve patient care and communication by managing the misuse and diversion risks associated with select medications.
- To help verify self-report of medication history. Is a prescribed drug present? Is anything else unexpectedly present?
- To encourage or reinforce healthy behavioral change, sometimes as a requirement of continued treatment. UDS is commonly included in a treatment agreement outlining both patient's and health care professional's responsibilities for safe medication use.

B) How often should we monitor for compliance using UDS?[1]

- Consider risk for opioid misuse or addiction, aberrant drug-related behaviours & availability. [See ORT tool.[2]] Monitor more frequently in those at higher risk or exhibiting behavioural issues (e.g. q2-4wks); others less frequently (e.g. random, 1-4 times per year).
- Random testing (for high risk): select dates & have receptionist call patient on date; allow ≤ 24hrs for patient to come in.

C) What are the types of UDS?[1,3]

Types of UDS	When to test?	Benefits	Limitations & Comments
Point-of-care (POC) Testing Enzyme Immunoassay (EIA) (e.g. ELISA, EMIT)	o When immediate results are desired (not too commonly done as relatively non-specific for drug class only)	o Urine sample collected & tested at the physician's office/clinic o Results are immediate for a drug class (e.g. opiate) o Portable o Identify illicit drug use in a timely fashion	o Cost of POC test kits & dipsticks o Less sensitive & specific than laboratory tests o Will not identify specific drug or metabolites o Subjective nature of the qualitative assays o Lacks adequate quality assurance & control (e.g. integrity of the test reagents following transportation & storage) o Data management issues. Limited menu of drugs offered o POC devices lack evidence to improve patient outcomes
Laboratory Testing – Immunoassay	o Useful for initial screening (rapid & inexpensive)	o Detects drugs for a longer time than chromatography (5-7 days vs 1-2 days for chromatography)	o Does not distinguish between different types of opioids o Often misses semi-synthetic/synthetic opioids e.g. fentanyl, hydromorphone, oxycodone, meperidine & methadone o Shows false positives (poppy seeds, quinolone antibiotics)
Lab. Testing – Chroma-tography or Mass spectrometry (MS) see comment on right	o To specifically confirm presence of a given drug o To identify drugs not included in an immunoassay test, when result contested	o More accurate for semi-synthetic & synthetic opioids. o Differentiates: codeine, morphine, oxycodone, hydrocodone, hydromorphone, heroin (monoacetylmorphine), etc. o Doesn't react to poppy seeds	o More expensive & may take longer to get results o Requires caution in interpretation: e.g. codeine metabolized to morphine
Strips Temperature-test		o Detects tampering/dilution	o Must be read within minutes; sample cools quickly. Costly.
Urine Creatinine level: Detects sample dilution (urine creatinine < 2-3 mmol/L is non-physiologic & suggests dilution)			

Mass spectrometry (used at SK Provincial Lab) gives better specificity as opposed to chromatography. Combination & tandem testing also used when more specific detection & quantification needed [e.g. gas or liquid chromatography + mass spectrometry (GC-MS, LC-MS); or tandem MS].

ELISA=enzyme linked immunosorbent assay EMIT=enzyme multiplied immunoassay GC=gas chromatography LC=liquid chromatography MS=mass spectrometry POC=point of care

D) What are the detection times for immunoassay and chromatography?[1,3] → for most drugs: 1 to 3 days

- Long-term use of lipid soluble drugs {eg. marijuana, diazepam, ketamine, or phencyclidine (PCP)} may extend detection to a week or more
- Immunoassay's ability to detect drugs will vary according to the drug's concentration in urine & the assay's cutoff concentration

Drug	Immunoassay (days detected)	GC, LC or MS
Amphetamines	Up to 2-5 days {caution with false positives from interfering agents; see "G".}	
Benzodiazepines (regular use)	1-7 days for short-acting benzo's; 20+ days if long-acting e.g. diazepam regular use. Does not differentiate benzo's. Intermediate-acting (eg. clonazepam) may not be detected.	Varies; identifies specific agents
Cannabis/THC (depends on grade & frequency of use)	Single use – 1-3 days. Moderate use: 5-7 days. Chronic use – up to 30 days. Nabilone (Cesamet®) does not contain THC & never detected in urine. Dronabinol (Marinol®), & Sativex® will produce positive results.	Varies
Cocaine + metabolite	1-4 days (metabolite=benzoylecgonine confirmatory test) {Note: no structural similarity to other "caine"s}	1-2 days
Gabapentin	-	1-2+ days if used in high doses
Heroin & 6-MAM monoacetylmorphine	Heroin rarely detected (half-life =3-5 minutes). {Heroin → 6-MAM → morphine} 6-MAM difficult to detect (half-life=25-30 min) –detection within a few hours.	
Meperidine	1 day; but often missed; (can be specifically requested)	1 day
Methadone & EDDP	Often missed. Up to 3 days. {Up to 6 days with EDDP (methadone metabolite)}	
Opioids, various	<2-5 days: codeine, hydrocodone, hydromorphone, morphine Often missed: fentanyl, oxycodone (can be specifically requested), methadone	1-2 days. ♣

♣ Metabolism note: codeine will be metabolized to both morphine & ~ hydrocodone/hydromorphone. Morphine high dose may be partly metabolized to hydromorphone.

ROUTINE TESTS - RUN BY SK PROVINCIAL LAB (Regina): Alprazolam & mets, Amphetamine, Benzoylecgonine, Clonazepam & mets, Cocaine, Codeine, Diazepam, Diphenhydramine, EDDP, Fentanyl & mets, Flunitrazepam, Flurazepam & mets, Gabapentin, Hydrocodone, Hydromorphone, Ketamine, Lorazepam, MDA, MDEA, MDMA, Meperidine & mets,Methadone ,Methamphetamine, Methylphenidate, Morphine, Oxazepam, Oxycodone, PCP, Pseudoephedrine, Ritalinic acid, Temazepam, THC, Triazolam. **NOT TESTED UNLESS SPECIFICALLY ORDERED:** barbiturates, buprenorphine & mets, cocaethylene, bromazepam, ethanol, GHB gammahydroxybutyrate. Other: chloral hydrate.

E) Prior to doing a UDS

- Inform the patient of the routine nature of test (e.g. "I do this routinely for all of my patients on opioids…")
- Take a careful history of medication use in the past week. May ask "what should I expect to see in the results?"
- Collect the sample in the physician office & ensure proper labeling. Consider who will be using the information.

F) How do we interpret unexpected results and what can we do?[1,4,5]

⇨**CAUTION: Goal is to improve communication and <u>not</u> to police! Remember result could be false.**

⇨Give opportunity for patient to address the report & suggest a repeat UDS if results are plausibly false. Clinician must be willing to change treatment plan if an abuse/diversion issue arises. This could include: 1) tightening boundaries with ↑ emphasis on holisitic, non-drug treatment; 2) referral to addiction services; 3) discontinue drug with or without a taper. Seek confirmatory testing if necessary. Detox services help & introduce recovery processes & services.

Results	Possible explanation	Actions for the Physician or Allied Health Professional
UDS negative for prescribed opioid Clonazepam & lorazepam may test <u>negative</u> in benzodiazepine EIAs!	• False negative • Non-compliance (e.g. if patient binging on opioid, then running out) • Diversion (suspect especially if repeatedly negative)	• Repeat test using chromatography; specify the drug of interest (e.g. oxycodone, fentanyl, methadone often missed by immunoassay) • Take a detailed history of medication use for the preceding 7 days (e.g. could learn that patient ran out several days prior) • Ask patient if they have given the drug to others • Monitor compliance with pill counts • Review/revise treatment agreement (tighten boundaries)
UDS positive for non-prescribed opioid or benzodiazepines	• False positive (e.g. poppy seeds) • Patient acquired opioids from other sources (double-doctoring, "street")	• Repeat UDS regularly • Ask the patient if they accessed opioids from other sources • Assess for opioid misuse/addiction; may refer to addiction tx program • Review/revise treatment agreement (tighten boundaries)
UDS positive for illicit drugs (e.g. cocaine, cannabis/THC)	• False positive • Patient occasionally using or addicted to the illicit drug • Cannabis is positive for patients taking dronabinol (Marinol®), THC:CBD (Sativex®) or using medical marijuana	• Repeat UDS regularly • Assess for abuse/addiction and refer to addiction treatment program as appropriate • Ask about medical prescription of dronabinol, THC:CBD or medical marijuana access program
Urine creatine is <2-3 mmol/L suggesting dilution	• Patient added water to sample • Patient added an acid to sample (may detect by ordering pH)	• Repeat UDS (Note, some labs can test for common adulterants if suspected) • Consider supervised collection or temperature testing • Take a detailed history of medication use for the preceding 7 days • Review/revise treatment agreement (tighten boundaries)
Urine sample is cold	• Delay in handling sample (urine cools within minutes) • Patient added water to sample	• Repeat UDS, consider supervised collection or temperature testing • Take a detailed history of the patient's med use for the preceding 7 days • Review/revise treatment agreement (tighten boundaries)

G) What are some examples of cross-reacting compounds for certain immunoassays? [2, 6]

Interfering agent	Immunoassay affected	Interfering agent	Immunoassay affected
Codeine {codeine metabolizes to morphine; will produce a morphine:codeine ratio of <2:1. a ratio >2:1 suggests non-codeine source (e.g. heroin, morphine; also poppy seeds if low morphine level but high ratio}	Codeine, morphine, hydrocodone (NOT likely hydromorphone)	Morphine	Morphine, Hydromorphone
Diet pills (e.g. clobenzorex, fenproporex)	Amphetamine	Pantoprazole possibly other PPI?	THC
Efavirenz, baby shampoo/soap	THC	Poppy Seeds [c]	Morphine -will produce high ratio (>19:1) of morphine:codeine with very small amounts of morphine (<2000ng/ml)
Amantadine, Bupropion, Desipramine, Doxepin, Labetalol, Pseudoephedrine, Ranitidine	Amphetamine	Aripiprazole, Promethazine	Amphetamine
Hydrocodone	Hydromorphone	Quetiapine	Methadone, TCAs depression
l-methamphetamine (Vicks® Inhaler in USA only)	Amphetamine	Sertraline	Benzodiazepine
Levofloxacin & some other fluoroquinolones	Opiates	Trazodone	Fentanyl,amphetamine
		Venlafaxine, desvenlafaxine	Phencyclidine,amphetamine

NOTES: [a] Cocaine is very reliable and has low cross-reactivity with other agents. [b] A minor metabolite should not be in excess of its parent. Clarify any unexplained test results with someone with expertise in the area. Quantitative testing (GC & MS) may be performed in some cases for confirmatory testing. [c] Poppy seed & heroin EIAs can be very similar (very high morphine:codeine ratio >2:1) but absolute levels of morphine & codeine are typically lower with poppy seed. To distinguish, avoid poppy seed ingestion; alternately if test for 6-MAM is positive, this proves hx of heroin use (but short t ½ of 6-MAM makes difficult to get +'ve test).

Acknowledgements: We would like to thank those who contributed to the development, review for this chart: *M. Markentin, Dr. L. Lanoie, Dr. P. Butt, Dr. B. Fern, Jeff Eichorst (SK Provincial Lab).* *Prepared by: Margaret Jin PharmD, L Regier BSP.*

References

Remember, it's OK to say "no".

[1] National Opioid Use Guideline Group (NOUGG). Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-Cancer Pain. Part B: Recommendations for Practice. April 30, 2010. Version 5.6. http://nationalpaincentre.mcmaster.ca/opioid/
[2] Opioid Risk Tool: http://nationalpaincentre.mcmaster.ca/opioid/cgop_b_app_b02.html
[3] Gourlay DL, Heit, Caplan YH. Urine Drug Testing in Clinical Practice. The art and science of patient care. Edition 4. May 31, 2010
[4] Gourlay DL, Heit HA. Universal precautions revisited: managing the inherited pain patient. Pain Med. 2009 Jul;10 Suppl 2:S115-23.
[5] Regier L. Substance Abuse / Addiction Chart in RxFiles Drug Comparison Charts –8th Ed. Accessed on line at: http://www.rxfiles.ca/rxfiles/uploads/documents/CHT-Substance-Abuse.pdf

[6] Tenore PL. Advanced urine toxicology testing. J Addict Dis. 2010. Oct;29(4):436-48.

Additional references:
Cotten SW, Duncan DL, Burch EA, Seashore CJ, Hammett-Stabler CA. Unexpected interference of baby wash products (soaps/shampoo) with a cannabinoid (THC) immunoassay. Clin Biochem. 2012 Jun;45(9):605-9.
FDA Mar/12 False-positive urine immunoassay screening tests for phencyclidine (PCP) and amphetamine have been reported in patients taking desvenlafaxine.
Kaplan J, Shah P, Faley B, Siegel ME. Case Reports of Aripiprazole Causing False-Positive Urine Amphetamine Drug Screens in Children. Pediatrics. 2015 Nov 2.
Oral R et al. Illicit drug exposure in patients evaluated for alleged child abuse and neglect. Pediatr Emerg Care 2011 Jun; 27:490.

Gerostamoulos D. Abnormal Laboratory Results: Urinary Drug Screening. Australian Prescriber 2013;36:62-4. Accessed 05Apr 2013 @ http://www.australianprescriber.com/magazine/36/2/62/4