

MRO'ing Prescription Drugs

Presented by:

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Why Dr. Swotinsky?

- Typical occupational doc, wear many hats.
- MRO assistant wears many hats, too
- Mostly non-DOT. Lots of POCT. Some hair. 5, 7, and 10 panels. A few clients have added oxycodone.
- Most clients are small employers. They ask MRO assistant and other staff, and sometimes me, for advice.

My presentation

- MRO, employer, and regulatory beliefs about workplace drug testing.
- Why test for prescription drugs?
Which drugs?
- Complexities of interpreting prescription drug positives.
- Consequences of testing positive.

MROs:

- Follow the rules and guidance. Cite them if challenged.
- Get nervous when test outcome is a judgment call.
- When in doubt, cancel or downgrade to negative.
- Know MRO'ing illegal drugs is easy, but MRO'ing prescription drugs is hard and can claim innocent victims.

Employers Believe:

- Drug testing weeds out bad employees.
- Policies should be flexible.
- Acceptability of explanations is up to the MRO.
- Extended drug panels generally better than 5 panels.
- Treat all positives the same.

Testing Trends

- '70s military testing programs targeted soldiers to help steer them to treatment.
- '80's Federal workplace testing of illicit drugs to deter illegal use.
- '90s DOT authorizes MROs to inform employers of safety info related to Rx drug use.
- '90s Growth of testing by pain clinics and impaired professional testing to monitor compliance, abstinence.

Testing Trends

- Future target – workplace testing for prescription drugs? Without suspicion? If so, why?
 - Safety?
 - Deterrence (social engineering)?
 - Identification, referral to treatment?

What to Test For?

Q. Would you test for this drug?

Manufacturer's Warning:

When using this product do not use more than directed. Marked drowsiness may occur. Avoid alcoholic drinks. Alcohol, sedatives, and tranquilizers may increase drowsiness. Be careful when driving a motor vehicle or operating machinery.

What to Test For?

- >700 drugs in *PDR* with impairment warnings
- Paucity of evidence of increased crash rate from use of *any* of these drugs.
 - One study suggests higher rate in drivers on opioids.
 - A few studies show impaired simulator performance after one dose of Schedule II opiates.
- FMCSA prohibits commercial driving and methadone use. Other Rx drugs are ok if prescriber says so.
- Is this all about hydrocodone and oxycodone?
- What about alcohol?

Interpretation is complex

- Some metabolic pathways are complex.
- Ambiguity about medicine that is:
 1. Borrowed
 2. Foreign
 3. Off-label
 4. Obtained by Internet
 5. Self-prescribed
 6. Used other than as prescribed
 - a. Old/used for different problem
 - b. Taken in excess

Benzodiazepine Metabolism

Drug	Functionalization	Oxidation*
Mediazepam (Nobrium)	Diazepam (Valium)	Temazepam (Restoril) → Oxazepam (Serax)
Clorazepate (Tranxene)	Desmethyldiazepam (nordiazepam)	Oxazepam (Serax)
Halazepam	Desmethyldiazepam (nordiazepam)	Oxazepam (Serax)
Prazepam (Centrax)	Desmethyldiazepam (nordiazepam)	Oxazepam (Serax)
Chlordiazepoxide (Librium)	Desmethylchlordiazepoxide → Demoxepam → Desmethyldiazepam (nordiazepam)	Oxazepam (Serax)
Flurazepam (Dalmane)	N-OH-ethylflurazepam → N-desalkyl-flurazepam	3-OH-flurazepam
Quazepam (Doral)	2-oxo-quazepam → N-desalkyl-flurazepam	3-OH-flurazepam
Quazepam (Doral)	2-oxo-quazepam	2-oxo-3-OH-quazepam
Estazolam (ProSom)		3-OH-estazolam
Alprazolam (Xanax)	α-hydroxyalprazolam	
Midazolam (Versed)	α-hydroxymidazolam	
Triazolam (Halcion)	α-hydroxytriazolam	
Clonazepam (Clonopin)	7-aminoclonazepam	7-acetamidoclonazepam
Clonazepam (Clonopin)	7-aminoclonazepam	
Lorazepam (Ativan)		

*Oxidative products are conjugated by glucuronidation

Opiate and Opioid Metabolism

Drug	Process	Metabolite 1	Metabolite(s) 2	Metabolite(s) 3
Codeine		Hydrocodone	Norhydrocodone 6-Hydrocodol Hydromorphone	
Codeine	O-demethylation	Morphine	Normorphine Morphine glucuronide Hydromorphone	
Codeine	N-demethylation	Norcodeine		
Diacetylmorphine	Hydrolysis	6-Acetylmorphine	Morphine	Normorphine Morphine glucuronide
Methadone		Methadol	Normethadol	
Methadone		EDDP	EMDP	
Oxycodone		Glucuronides		
Oxycodone	O-demethylation	Oxymorphone	6-Oxymophol	Glucurondides
Oxycodone	N-demethylation	Noroxycodone	Glucuronides	
Meperidine		Normeperidine		
Propoxyphene		Norpropoxyphene		

Interpretation is Complex

- Metabolic pathways can be complex
- Knowledge base is relatively scant and evolving, e.g.,
 - Codeine ➡ hydrocodone (2000)
 - Morphine ➡ hydromorphone (2006)
- Can't correlate urine levels with dose or impairment

MRO'ing medicine that is...

Borrowed

Jill tests positive for hydrocodone. Jill tells the MRO she had a root canal and her roommate gave her a Vicodin.

MRO's Determination:

x Positive

Negative

MRO'ing medicine that is...

Borrowed (aka spousal use)

- If a donor says the positive result is from use of someone else's medicine, is that a valid explanation? (DOT says, No.)
- Borrowed controlled substance use:
 - Is illegal.
 - Is a common explanation for Rx positives.
- Is deterrence of spousal use a valid target?

MRO'ing medicine that is...

Foreign

- *Jack tests positive for codeine. He tells the MRO a clinic gave him codeine when he burst his ear drum scuba diving in Cancun two days before the test. He forgets the clinic's name.*

MRO's Determination:

Positive

x Negative

MRO'ing of medicine that is...

Foreign

- If a donor got the medicine abroad, is that a valid medical explanation?
 - Regulatory guidance says ok to use abroad and to bring back and use in US for up to 30 days.
 - Some people buy medicine abroad to save money.
- Hard to corroborate drugs obtained abroad.
- Is deterrence of bringing prescription drugs into the US a valid target?

MRO'ing medicine that is...

Off-Label

- *Joe tests positive for marijuana. He has a dronabinol prescription, which he says he takes for chronic pain.*

MRO's Determination:

Positive

x Negative

MRO'ing medicine that is...

Off Label

- If a donor took a medicine for a non- FDA approved condition, is it a valid medical explanation?
- MROs say, “Yes.”
- Off label prescribing is common, not illegal.
- Is deterrence of off label prescription drug use a valid target?

MRO'ing medicine that is...

Obtained by Internet

- *Jess takes Adderall. His doctor prescribed it 4 yrs ago for ADD. Jess started getting it over the Internet after he moved away to college. His preemployment test is amphetamine-positive.*

MRO's Determination:

Positive ? Negative

MRO'ing medicine that is...

Obtained by Internet

- If a donor obtained medicine over the Internet, is that a valid medical explanation? DOT says, No, unless prescribed by treating physician.
- Common source of drugs for legitimate and illegitimate purposes
- Is deterrence of Internet drugs a valid target?

MRO'ing medicine that is...

Self-Prescribed

- *Dr. John tests positive for a oxazepam. He has a prescription for Serax that he wrote for his wife, and says he took some before his redeye flight from California just before his drug test.*

MRO's Determination:

x Positive

Negative

MRO'ing medicine that is...

Self-Prescribed

- If a physician (or NP or PA) took a self-prescribed medicine, is that a valid medical explanation?
- Prohibited or discouraged in some states.
- What if physician has multiple state licenses?
- Is deterrence of self-prescribing a valid target?

MRO'ing medicine that is...

Old

- *Jane tested positive for oxycodone. She faxes the Percocet prescription label to the MRO. It's 3 years old.*

MRO's Determination:

Positive

?

Negative

MRO'ing medicine that is...

Old

- If a donor took a medicine that was prescribed long ago, is that a valid explanation?
- Expiration dates refer to shelf life. It's not illegal to take one's old medicine.
- What's in *your* medicine cabinet?
- Drug abusers use, don't store, drugs.
- Is one prescription for oxycodone a license for lifelong abuse of oxycodone?
- Is deterrence of use of old prescription drugs a valid target?

MRO'ing medicine that is...

Taken in Excess

Jeff tests positive for morphine at 30,000 ng/mL. He has a prescription for MSIR, and says he takes it as needed for chronic low back pain

MRO's Determination:

Positive

x Negative

MRO'ing medicine that is...

Taken in Excess

- If a donor took a medicine at a dose higher than prescribed, is that a valid medical explanation?
- Typical of prescription opiate abuse. Most recreational users of prescription drugs get them from physicians or family members.
- MROs will accept the explanation and, if applicable, alert the employer to safety concerns.
- Is deterrence of excess prescription drug use a valid (or viable) target?

Interpretation is complex

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Consequences of Testing Positive

- Employers treat all positives the same.
- What would be the rationale for removing someone from safety sensitive duty based on a positive result for prescription drugs?
- What kind of treatment is appropriate for someone who tests positive for a prescription drug and believes he/she took it for medical reasons?
- Would the courts say prescription drug testing without individualized suspicion is reasonable?

Why an MRO?

- MROs directly encounter the casualties of prescription drug testing.
- Physicians realize that prescription drug “abuse” is ill defined – a continuum. Illegal drug seems relatively black/white.
- MROs want to do good, and do it well.
- If HHS starts targeting prescription drugs, please give MROs clear standards and guidelines on alternative explanations.

Questions?

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