

# A Toxicologists View of Addiction

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# AGENDA

Background :Addiction

Toxicology 101

Drug testing 101

Question and Answer Session

# ADDICTION

- Four in five new heroin users started out misusing prescription painkillers.

# ADDICTION

- **How one family used an obituary to lay out the reality of opioid addiction**

After Madelyn Ellen Linsenmeir died on 7 October, Kate O'Neill penned a now-viral obituary on her sister's addiction battle as 'an authentic authoring of her life'

# ADDICTION

- Linsenmeir tried OxyContin for the first time at a high school party when she was 16. By 18, she was using heroin.
- Living in and out of rehab, losing custody of her son, and ultimately dying in a hospital while in police custody, Linsenmeir's story is a raw one, felt and known by millions of Americans who struggle with addiction amid America's opioid crisis.

# ADDICTION



# ADDICTION



# ADDICTION

- <https://www.theguardian.com/us-news/2018/oct/19/madelyn-ellen-linsenmeir-obituary-opioid-addiction-response-family>

# Drug Comparison

The amount of  
drug necessary to  
KILL an average  
size adult male

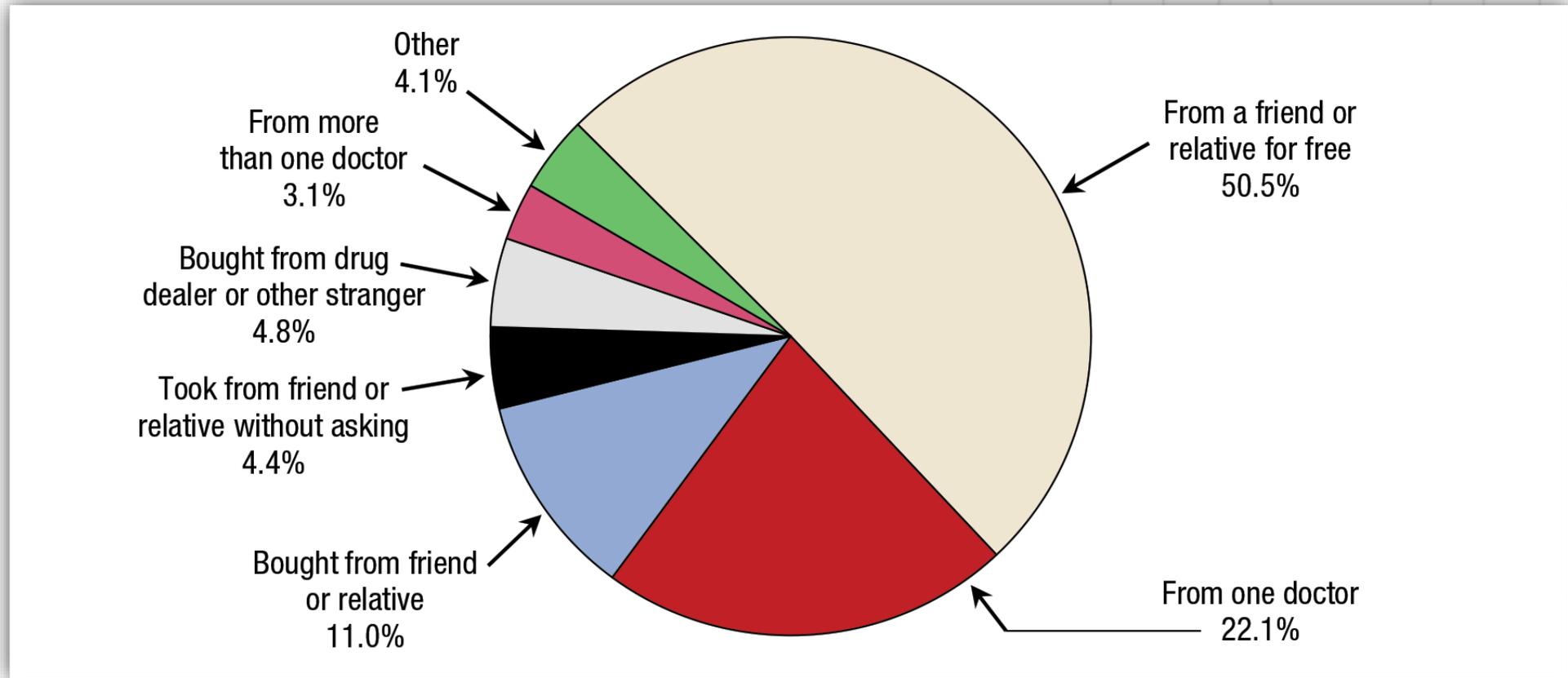


# The Source of the Problem

- Drug Diversion
- Drug Importation
- Counterfeit Oxycontin contains Fentanyl



# The Source of the Problem



Source: [https://www.samhsa.gov/data/sites/default/files/report\\_2686/ShortReport-2686.html](https://www.samhsa.gov/data/sites/default/files/report_2686/ShortReport-2686.html) January 12 2017 SAMHSA Publication

# Toxicology 101

# ADME

Absorption

Distribution

Metabolism

Excretion

# Absorption

DRUGS ARE ABSORBED THROUGH  
VARIOUS MEANS

# Distribution

DRUGS ARE DISTRIBUTED THROUGHOUT  
THE BODY

# Metabolism

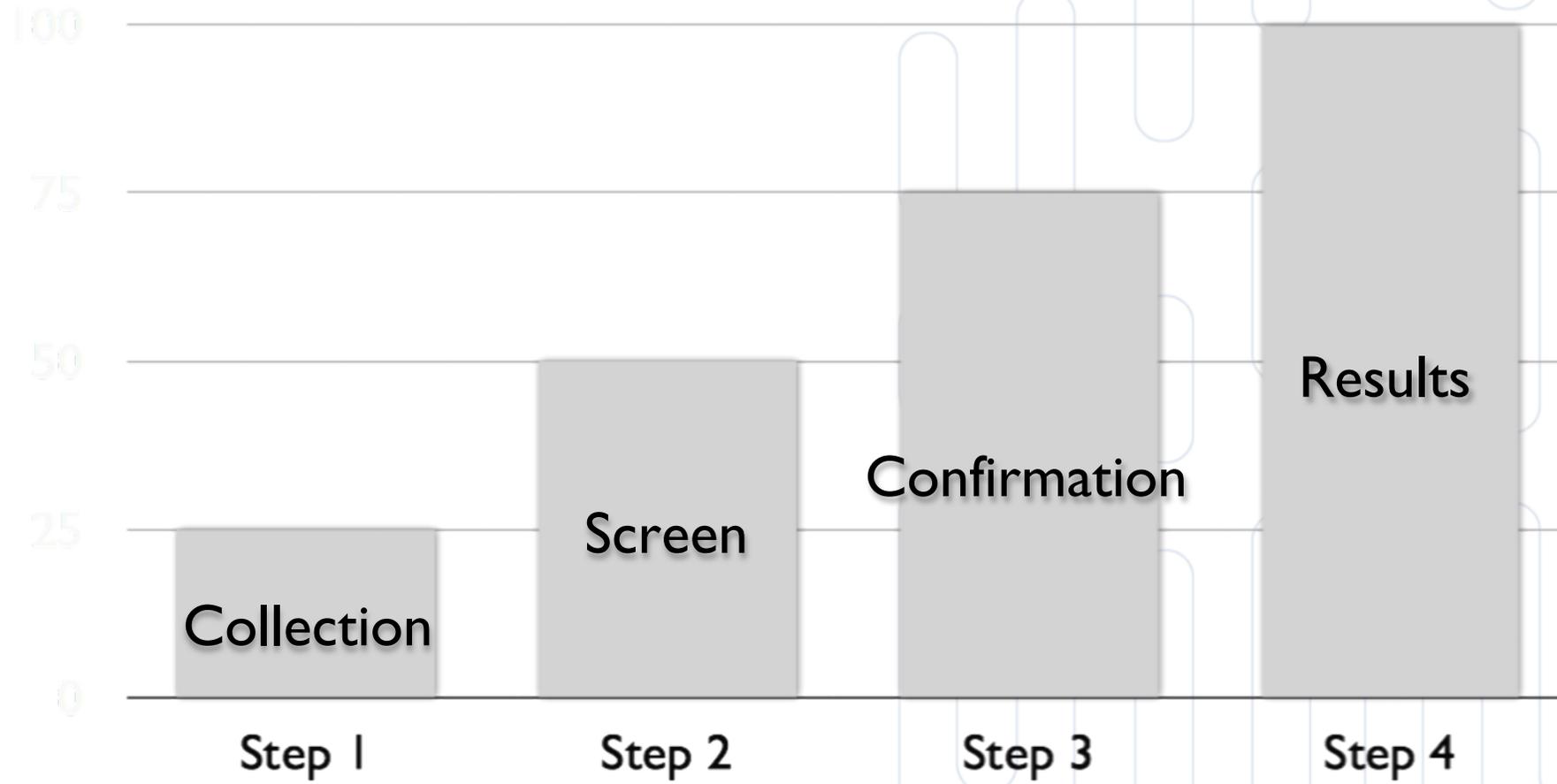
DRUGS ARE METABOLIZED PRIMARILY IN  
THE LIVER

# Excretion

DRUGS ARE EXCRETED THROUGH  
VARIOUS MEANS

# Drug Testing 101

# Urine Drug Testing Process



# Collection

# Is the sample urine?

- Temperature
- Observed
- Donor cannot produce a sample
- Specimen Validity Testing

# Screening

# POCT Immunoassay

# How does immunoassay work?

- **Immunoassay:** initial screening test
- **Advantage:** ability to simultaneously and rapidly test for drugs in urine
- **Disadvantage:** vary in the range of compounds detected, some detecting specific drugs others recognize classes of drugs. Ability to detect drugs varies according to the drug's concentration in the urine and the assay's cutoff concentration.
- **Check the package insert**

# Interpretation

- **Presumptive Positive:**

Screening – Cup or Instrument

- **Subject to cross-reactivity:**

Substances with similar, and sometimes dissimilar, chemical composition may cause a test to appear positive for the target drug.

- **Sensitivity and Specificity:**

Negative may not be the absence of drugs. Positive may not be the presence of a drug.

Drug Group	Cross Reactivity (Product Insert)	Cross Reactivity
Cannabinoids	Dronabinol (Marinol) Synthetic Delta 9 THC	NSAIDs, Efavirenz (Sustiva), Hemp Seed Oil (Cannabis seed) Pantoprazole (Protonix), Nexium, Prilosec
Opiates	Morphine, Codeine and Heroin(6-acetylmorphine), Dihydrocodeine Hydrocodone, Hydromorphone,	<b>Poppy Seeds</b> , Levorphanol, Meperidine*, Nalorphine*, Oxycodone*, Oxymorphone*
Amphetamines	Dextroamphetamine + amphetamine (Adderall) d-Methamphetamine d-Amphetamine Chloroquine (Aralen) Desoxyephedrine MDMA (Ecstasy), MDA, MDEA, d,l-amphetamine., d,l-methamphetamine Methamphetamine (Desoxyn)	Chloramphetamine, Benzphetamine, Bupropion, Chloroquine, Donepezil, l-Ephedrine, Fenfluramine, Isometheptene, Mephentermine, Methoxyphenamine, Nor-pseudoephedrine, , Phenmetrazine, Phentermine, Phenylpropanolamine, Propranolol, d,l-pseudoephedrine, Quinacrine, Tyramine, Vicks Vapor Spray.
PCP	Other PCP derivatives PCDE, PCM, PCPy, TCM, TCP, TCPy	Meperidine, <b>Dextromethorphan</b> , Dextrophan, Mesoridazine
Benzodiazepine	Alprazolam, Clonazepam* Flurazepam, Diazepam, Flunitrazepam, Halazepam, Medazepam, Midazolam, Oxazepam, Temazepam, Nordiazepam	Oxaprozin (Daypro) Some herbal agents
Cocaine	Benzoylecgonine Ecgonine Ecgonine Methyl Ester	
ETOH	None	Urine exogenous production
Methadone	None	Propoxyphene Seroquel

# Confirmation



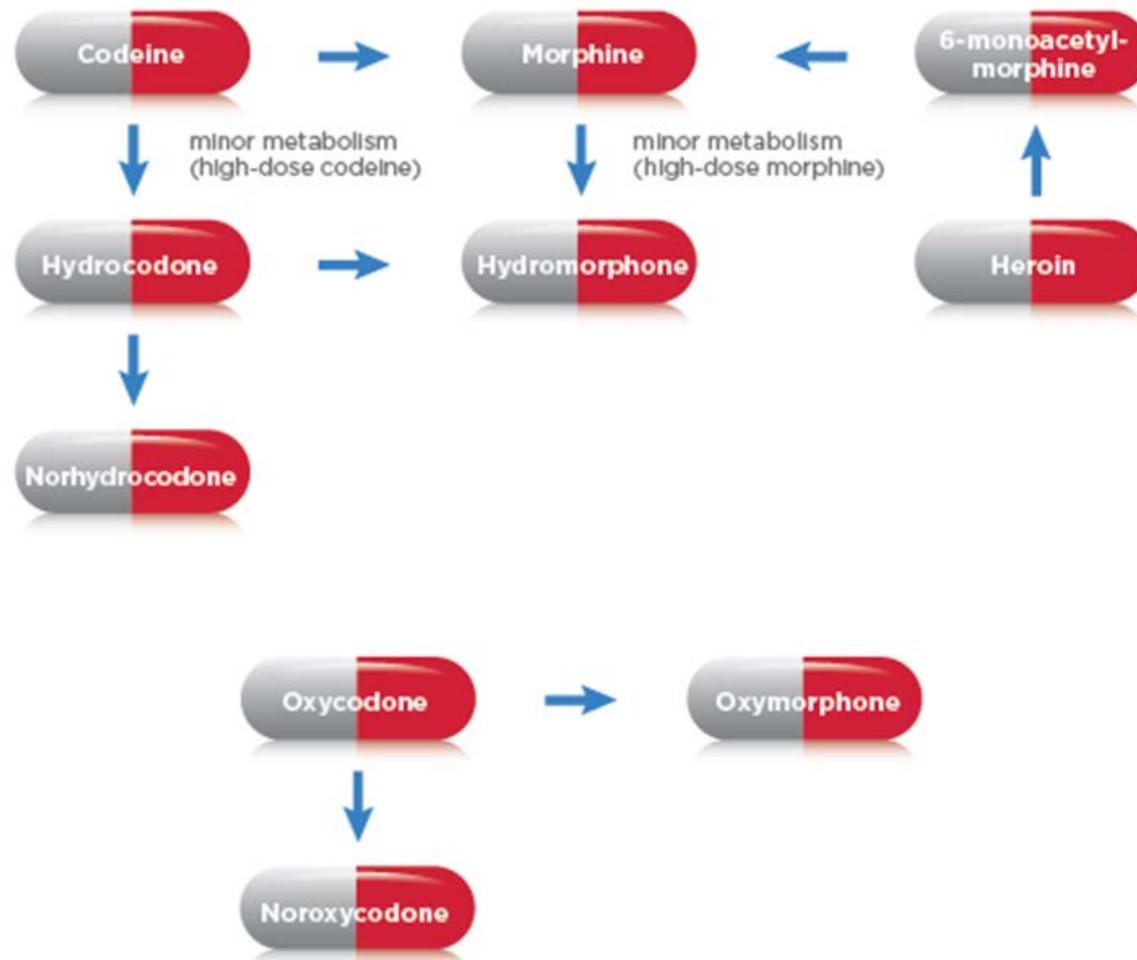
# Fundamentals of Urine Drug Testing

Why confirm?

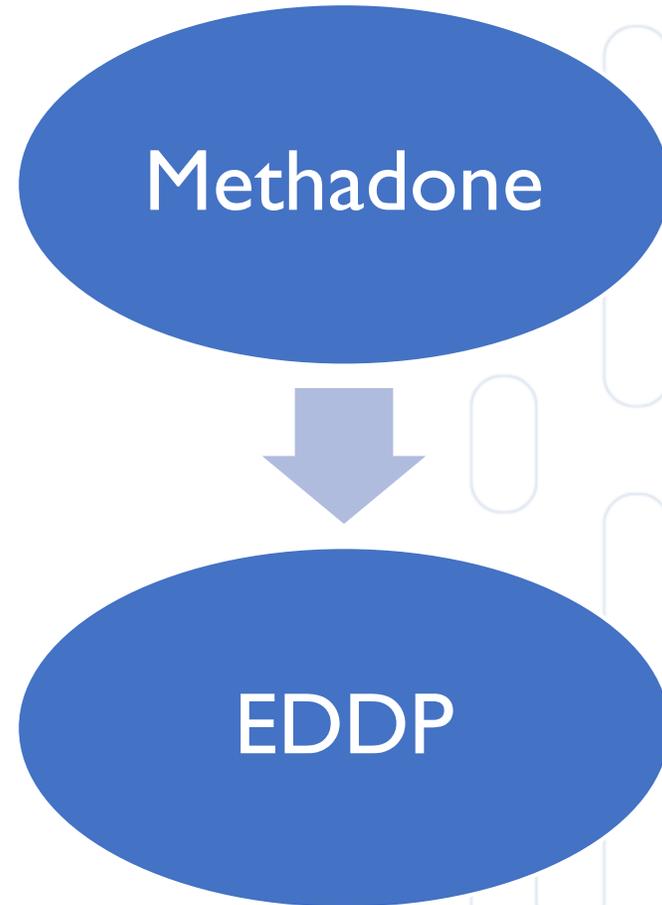
Interpreting UDT  
Results

# Metabolites

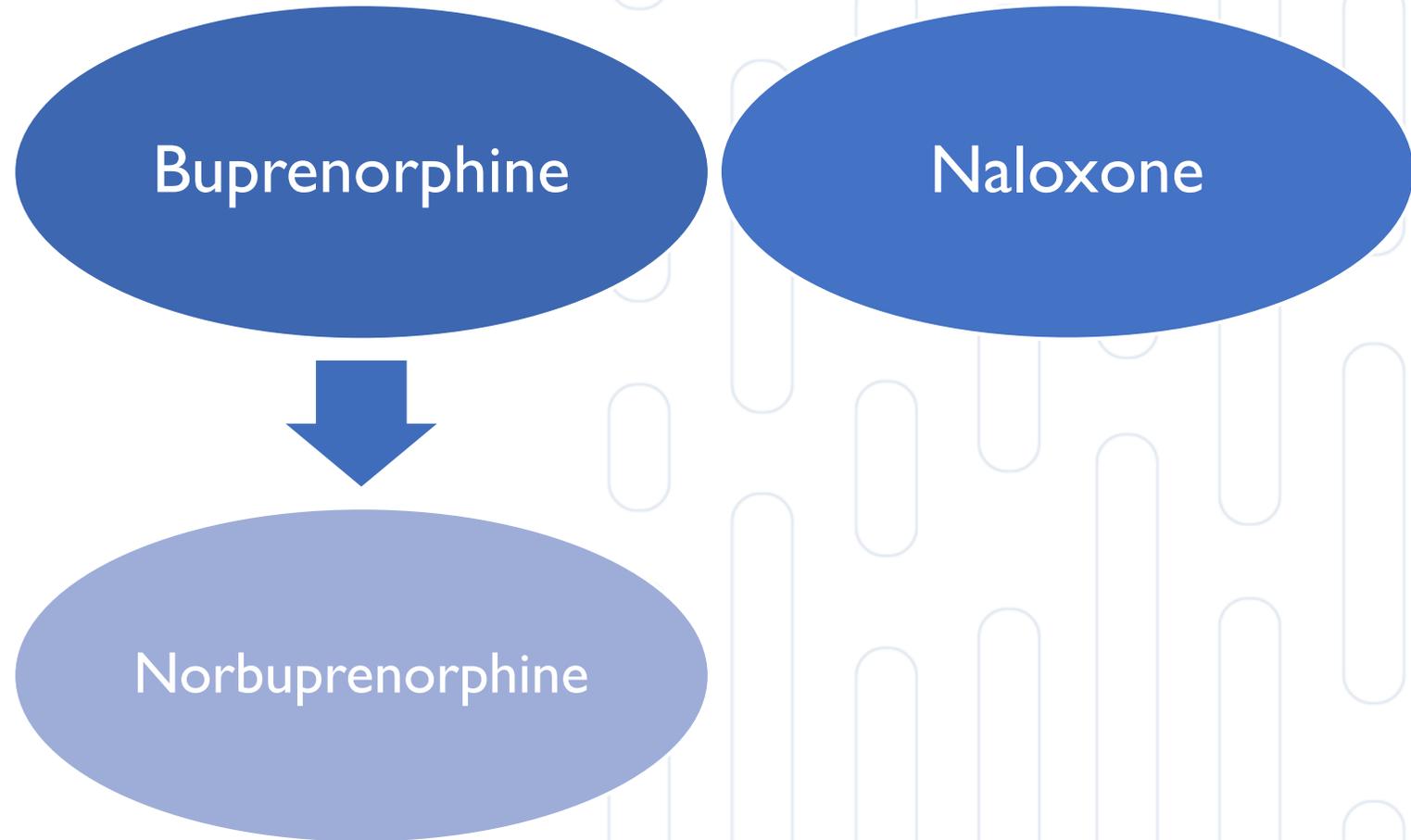
# MAJOR AND MINOR METABOLIC PATHWAYS FOR OPIATES AND OPIOIDS



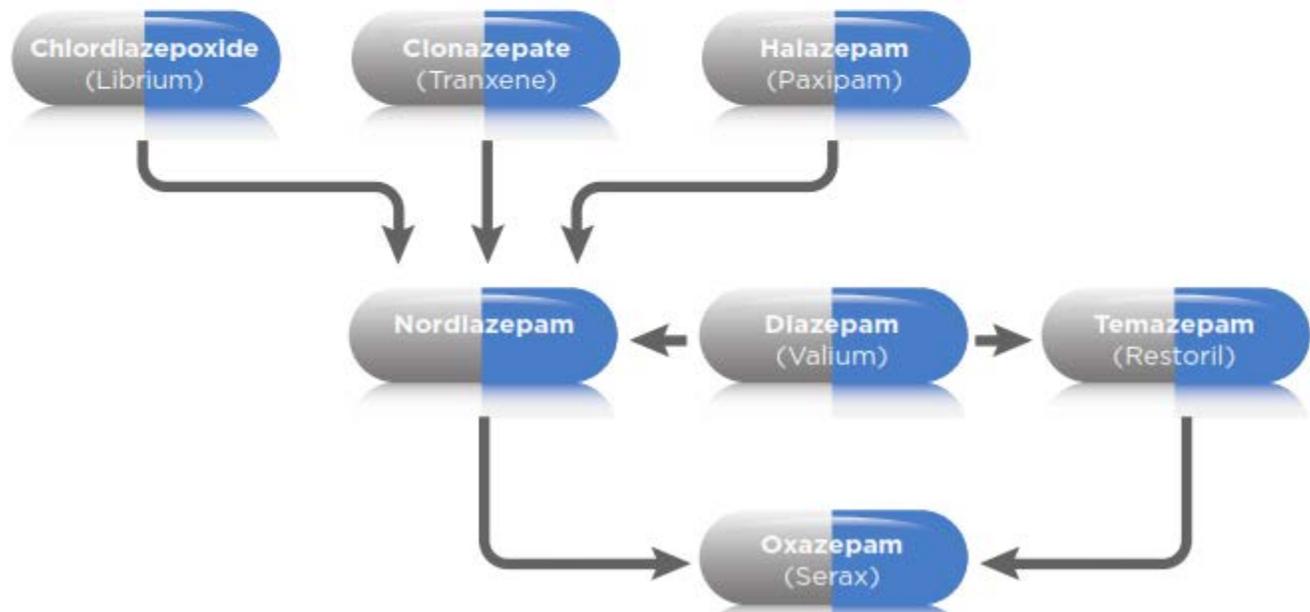
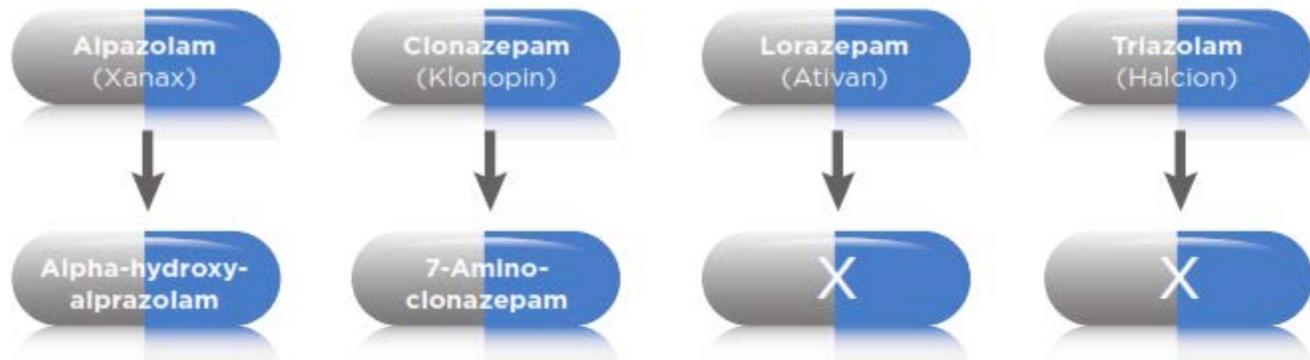
# Methadone



# Suboxone



# METABOLISM OF BENZODIAZEPINES



# Process Impurities



# Acceptable Opioid Process Impurities In Commercial Drug Substances

New Methods Eliminate These Impurities for Hydrocodone and Hydromorphone; Both Varieties Are Currently Available

Commercial active Pharmaceutical Ingredient (API)	Process Impurities	Allowable Limit (%)	Typical Observed (%)
Codeine	Morphine	0.15	0.01 – 0.1
Hydrocodone	Codeine	0.15	0 – 0.1
Hydromorphone	Morphine	0.15	0 – 0.025
	Hydrocodone	0.1	0 – 0.025
Morphine	Codeine	0.5	0.01 – 0.05
Oxycodone	Hydrocodone	1.0	0.02 – 0.12
Oxymorphone	Hydromorphone	0.15	0.03 – 0.1
	Oxycodone	0.5	0.05 – 0.4

Information from API Manufacturers' Certificates of Analysis MRO Advisory <https://www.aamro.com/docs/news/18.pdf>

# Methamphetamine

# CHIRAL METHAMPHETAMINE INTERPRETATION

## METHAMPHETAMINE ANALYSIS

**A chiral analysis will report the percentage of the *d*-form of methamphetamine. A result of less than 20% *d*-methamphetamine of the total is consistent with the following:**

1. Use of Vicks Vapor Inhaler containing *l*-Methamphetamine (also known as levo-methamphetamine).
2. A prescription for Selegiline which is prescribed for treating Parkinson's disease and major depressive disorder. Selegiline is metabolized by the body to produce *l*-Methamphetamine.

**A result of greater than 20% *d*-methamphetamine of the total is consistent with the following:**

1. A prescription for Desoxyn or Methedrine.
2. A prescription for Benzphetamine. This drug is marketed as Didrex, and is prescribed for obesity. Benzphetamine is metabolized by the body to produce *d*-Methamphetamine.
3. The *d*-Methamphetamine is from an illicit production source (i.e. crystal meth).

Reference: Evaluation of the 20% D-Methamphetamine Requirement for Determining Illicit Use of Methamphetamine in Urine. Journal of Analytical Toxicology (2012) 36 (6): 399-404

DOI: <https://doi.org/10.1093/jat/bks042>

# Urine Alcohol

- Ethanol
  - Caution in interpretation
  - Diabetics

# EtG – Ethyl Glucuronide

- EtG
  - Direct metabolite of ethanol
  - Window of detection up to 80 hours
    - Depends on use patterns and metabolism

# PEth

- Phosphatidyl Ethanol
- Direct Ethanol Biomarker
- 2-4 week window of detection
- Blood Test

# Adulterated Sample

# Adulterated Sample

TESTS PERFORMED		*Units for Cut Off and Value are in ng/mL		
Test Name	Test Result	Value*	Cut Off *	Note
<b>Amphetamines [1]</b>	Negative		300	
<b>Benzodiazepines [1]</b>	Negative		50	
<b>Buprenorphine/Naloxone</b>				
Buprenorphine [1]	Negative		5	
<b>Cannabinoids</b>				
Marijuana Metabolite [1]	Negative		20	
<b>Cocaine Metabolites [1]</b>	Negative		150	
<b>ETG/ETS [1]</b>	Negative		100	
<b>Fentanyl</b>				
Fentanyl [1]	Negative		2	
<b>Methadone</b>				
Methadone [1][3]	Positive	>8000	150/100	
Methadone Metabolite (EDDP) [1] [3]	Negative		150/100	
<b>Opiates - Basic [1]</b>	Negative		100	
<b>Oxycodone/Oxymorphone [1]</b>	Negative		100	

# Adulterated Sample

## SUMMARY RESULTS

Please review this report carefully; results are noted below and include the following:

Test Name	Prescribed	Outcome	Reported Value	Comment
Amphetamine	Yes	Consistent	682.6 ng/mL	Prescribed drug was detected.
<b>Alprazolam Metabolite</b>	<b>Yes</b>	<b>INCONSISTENT</b>	<b>Negative</b>	<b>Prescribed drug was not detected.</b>
Tramadol	Yes	Consistent	2320 ng/mL	Prescribed drug was detected.
<b>O-Desmethyl Tramadol</b>	<b>Yes</b>	<b>INCONSISTENT</b>	<b>Negative</b>	<b>Prescribed drug metabolite was not found.</b>
Oxycodone	Yes	Consistent	2637 ng/mL	Prescribed drug was detected.
<b>Noroxycodone</b>	<b>Yes</b>	<b>INCONSISTENT</b>	<b>Negative</b>	<b>Prescribed drug metabolite was not found.</b>
<b>Oxymorphone</b>	<b>Yes</b>	<b>INCONSISTENT</b>	<b>Negative</b>	<b>Prescribed drug metabolite was not found.</b>

# Dilute Urine – always a red flag

The LC/MS/MS and GC/MS tests are high complexity laboratory developed tests and their performance characteristics determined by DRUGSCAN.

## VALIDITY TESTING

Test Name	Screening Range	Result	Units	Method	Comment
Creatinine	>20.00	<b>15.7</b>	mg/dL	Colorimetric	<b>Dilute</b>
Nitrite	<200	28.3 Normal	mcg/mL	Colorimetric	
pH	4.50 - 9.00	6.8 Normal		Colorimetric/pH Meter	
Specific Gravity	1.0010 - 1.020	1.0024 Normal		Refractometer	

# Dilute Urine

Adding water to a sample

Taking diuretics

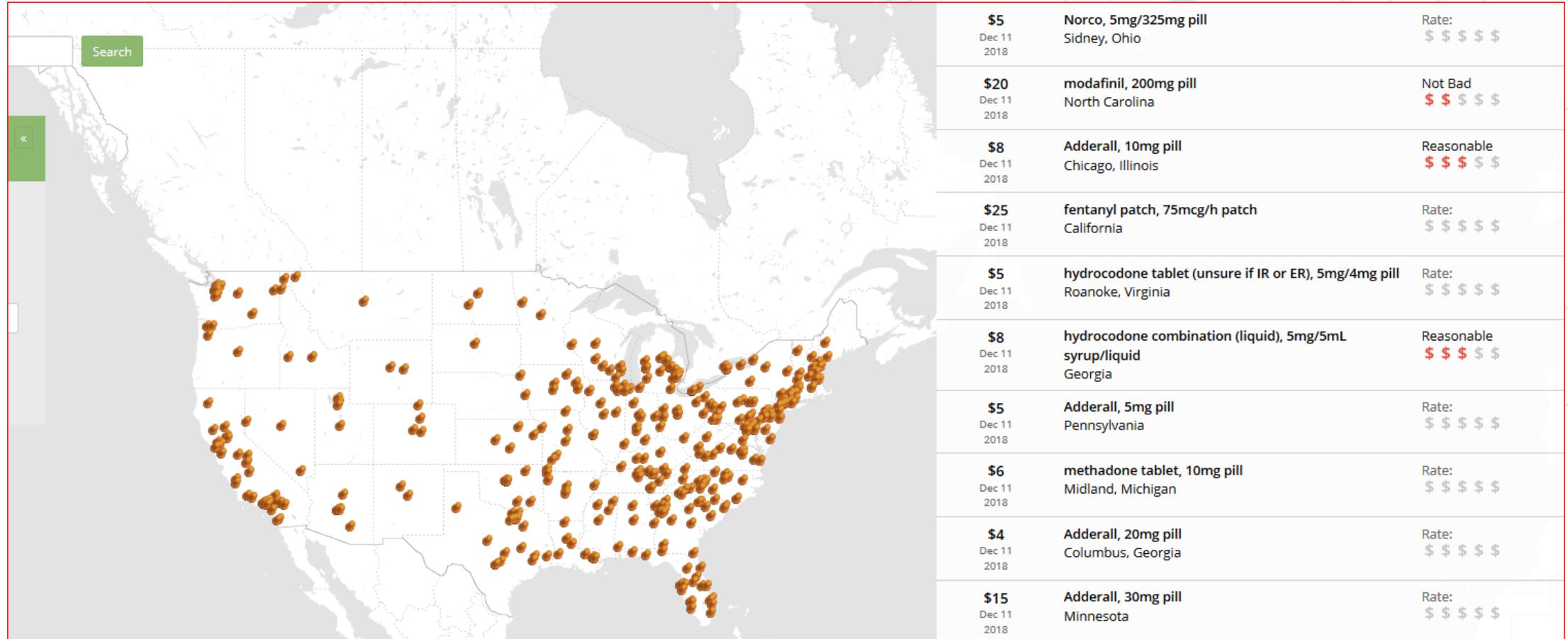
Substituting another  
product for urine

Legitimate or another  
reason for dilute urine

# StreetRx

- The StreetRx Program captures the “black market” or “street price” of prescription drugs by employing crowdsourcing principles.

# StreetRx – 12/11/2018



# Websites

- [www.BlueLight.org](http://www.BlueLight.org)
- [www.Streetrx.com](http://www.Streetrx.com)
- [www.Erowid.org](http://www.Erowid.org)

# QUESTIONS

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