Learning Objectives / COI

- Gain general knowledge of the technology available for drug testing along with each technology’s benefits and limitations
- Understand how drug concentration is impacted by the testing matrix (or specimen type), biological clearance rates, and dose vs. collection time
- Understanding and interpreting lab results when they are inconsistent with expectations

- No conflicts to disclose
10 Minute Topics

Laboratory Methods
- Immunoassays
- Mass spectrometry
- Strengths and Limitations

Screen vs. Confirm
- Differences between screen and confirm results
- When to screen and when to go straight to confirm
- Benefits and Limitations

Benzodiazepines Case Study
- Metabolism pathways
- Result patterns and interpretations
- Screen results vs. confirm results

Opioids Case Study
- Metabolism pathways
- Result patterns and interpretations
- Screen results vs. confirm results

Amphetamine Case Study
- Metabolism pathways
- Amphetamine False Positive
- Unexpected Negative Results

Timing and Types of Sample Collection
- Mini-review on pharmacokinetics
- Detection windows
- Sample type

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Laboratory Methods to Support Pain Management Testing
Commonly Used Laboratory Methods

- Immunoassays
- Enzymatic assays
- GC-MS
- LC-MS
- LC-MS/MS
- LC-TOF MS

Enzyme

Antibody

Substrate

Product

Collision induced dissociation

$m/z$ 256

$m/z$ 207

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Immunoassays

- Simplified Components

Reagent Antibodies

Drugs in Sample

- Amphetamine
- Methamphetamine
- Bupropion
- Morphine

Signal

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Immunoassays - Animation

• Simplified Components

Drugs in Sample
- Amphetamine
- Methamphetamine
- Bupropion
- Morphine
# Product Insert – Cross Reactivity

## Key Points

- Cutoff is based on a “representative” compound
- Cross-reactivity allows for structurally related compound detection
- Cross-reactivity allows for false positives

## Table 7 — Concentrations (ng/mL) of Opiate Compounds That Produce a Result Approximately Equivalent to the 300 ng/mL Cutoff

<table>
<thead>
<tr>
<th>Compound</th>
<th>Concentration (ng/mL) at 300 ng/mL Cutoff</th>
</tr>
</thead>
<tbody>
<tr>
<td>Codeine</td>
<td>102–306</td>
</tr>
<tr>
<td>Dihydrocodeine</td>
<td>291</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>247</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>498</td>
</tr>
<tr>
<td>Levallorphan</td>
<td>&gt;7500*</td>
</tr>
<tr>
<td>Levorphanol</td>
<td>1048</td>
</tr>
<tr>
<td>Meperidine</td>
<td>&gt;50000*</td>
</tr>
<tr>
<td>6-Acetylmorphine</td>
<td>435</td>
</tr>
<tr>
<td>Morphine-3-Glucuronide</td>
<td>626</td>
</tr>
<tr>
<td>Nalorphine</td>
<td>9862*</td>
</tr>
<tr>
<td>Naloxone</td>
<td>828139</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>2550</td>
</tr>
<tr>
<td>Oxymorphone</td>
<td>&gt;20000</td>
</tr>
</tbody>
</table>

Therapeutic doses of ofloxacin (Floxicin) or levofloxacin (Levaquin), non-opiates, may produce positive results with this assay. A positive result from an individual taking ofloxacin or levofloxacin should be interpreted with caution and confirmed by another method.
Key Points about Immunoassays

- Good & Bad Cross-reactivity (*sensitivity*)
- *Can be different with different vendors*

Amphetamine
Methamphetamine
Bupropion

Morphine

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Commonly Used Laboratory Methods

- Immunoassays
- Enzymatic assays
  - GC-MS
  - LC-MS/MS
  - LC-TOF MS

[Diagram showing enzyme, antibody, substrate, and product with m/z values 256 and 207 and collision induced dissociation note]

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Key Concepts

1. Everything starts at the same time
2. Mobile phase moves in one direction
3. Compounds repeatedly “choose” mobile phase or stationary phase
4. Less stationary phase interaction results in early elution
5. More stationary phase interaction results in late elution
Mass Spectrometry

Selective for $m/z$ 256

Key Concepts
1. Gas phase ions a must
2. Ion Flight Stabilization

From LC or GC
Tandem Mass Spectrometry

Key Concepts
1. Precursor and Product Ion Flight Stabilization
2. Only subsets of ions get through

From LC or GC

Precursor \( m/z \) 256
Product \( m/z \) 207
Collision induced dissociation

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Key Concepts
1. Also based on $m/z$
2. Everything starts at the same time
3. Everything gets the same amount of “push”
4. Smaller goes faster
5. Bigger goes slower
6. Everything (eventually) gets to the detector
Strengths & Weaknesses

• Immunoassay

**Good**
- Detects classes of compounds
- Signal is a combination of all compounds detected – can boost sensitivity
- Fast
- Relatively inexpensive
- Point of Care Testing possible

**Bad**
- Cross-reactivity with unrelated compounds
- Inability to differentiate detected compounds
- Usually qualitative
- Results can differ between vendors
### Strengths & Weaknesses

<table>
<thead>
<tr>
<th><strong>GC or LC-MS/MS</strong></th>
<th><strong>Good</strong></th>
<th><strong>Bad</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Individual compounds identified</td>
<td>• Longer TAT</td>
<td></td>
</tr>
<tr>
<td>• Quantitation is possible</td>
<td>• Interferences can still occur</td>
<td></td>
</tr>
<tr>
<td>• High Specificity</td>
<td>• Relatively more expensive</td>
<td></td>
</tr>
<tr>
<td>• High Sensitivity</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>LC-TOF MS</strong></th>
<th><strong>Good</strong></th>
<th><strong>Bad</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Individual compounds identified</td>
<td>• Longer TAT</td>
<td></td>
</tr>
<tr>
<td>• High Specificity</td>
<td>• Interferences can still occur</td>
<td></td>
</tr>
<tr>
<td>• High Sensitivity</td>
<td>• Relatively more expensive</td>
<td></td>
</tr>
<tr>
<td>• Reduces need for reflexive confirmation</td>
<td>• Not available for all sample types – yet!</td>
<td></td>
</tr>
</tbody>
</table>

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Timing and Types of Sample Collection
## Sample Types and Uses

### Urine

<table>
<thead>
<tr>
<th>Good</th>
<th>Bad</th>
</tr>
</thead>
<tbody>
<tr>
<td>Naturally concentrated</td>
<td>Easier to adulterate</td>
</tr>
<tr>
<td>Metabolites can enhance detection</td>
<td>Dose determination NOT possible</td>
</tr>
<tr>
<td>Longer window of detection</td>
<td>Not appropriate for dialysis patients</td>
</tr>
</tbody>
</table>

### Serum/Plasma

<table>
<thead>
<tr>
<th>Good</th>
<th>Bad</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parent drugs often present</td>
<td>More invasive</td>
</tr>
<tr>
<td>Pharmacokinetics can be determined</td>
<td>Collection timing is critical</td>
</tr>
<tr>
<td>Difficult to adulterate</td>
<td>Shorter window of detection</td>
</tr>
<tr>
<td>Equates dose with effect</td>
<td></td>
</tr>
<tr>
<td>Appropriate for dialysis patients</td>
<td></td>
</tr>
</tbody>
</table>
Pharmacokinetics: What the body does to a drug

- Oxidation
- Reduction
- O-Demethylation
- N-Demethylation
- Deacetylation
- Glucuronidation

- Age
- Co-medications
- Genetics
- Clinical status
- Dosing pattern
- Drug delivery mechanism
- Food-drug interactions

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## Detection Windows

<table>
<thead>
<tr>
<th>Drug</th>
<th>Plasma half-life</th>
<th>Urine Detection Window</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphetamine</td>
<td>7 to 34 hours</td>
<td>3 to 5 days</td>
</tr>
<tr>
<td>Codeine</td>
<td>1.9 to 3.9 hours</td>
<td>2 to 3 days</td>
</tr>
<tr>
<td>Amobarbital</td>
<td>15 to 40 hours</td>
<td>4 to 6 days</td>
</tr>
<tr>
<td>Clonazepam</td>
<td>19 to 60 hours</td>
<td>2 to 4 days</td>
</tr>
<tr>
<td><em>7-aminoclonazepam</em></td>
<td>30 to 92 hours</td>
<td></td>
</tr>
<tr>
<td>THC (metabolite)</td>
<td>4 to 12 hours</td>
<td>1 to 45 days</td>
</tr>
</tbody>
</table>

Usually measured in **HOURS**

Usually measured in **DAYS**

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Screen vs. Confirm
Typical Testing Workflow

Sample Collected

Screen w/ reflex ordered

Positive

Mass Spec confirmation

Positive

Report out Positive

Negative

Report out Negative

Negative

Stop

Report out Negative
Screening assays

- Often immunoassay based
  - *Single representative compound as target*
- Qualitative
  - *Positive or Negative Only*
- Compound classes reported

**Example Results: UDS**

<table>
<thead>
<tr>
<th>Substance</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMPHETAMINE</td>
<td>NEGATIVE</td>
</tr>
<tr>
<td>BARBITURATES</td>
<td>NEGATIVE</td>
</tr>
<tr>
<td>BENZODIAZEPINES</td>
<td>NEGATIVE</td>
</tr>
<tr>
<td>COCAINE</td>
<td>NEGATIVE</td>
</tr>
<tr>
<td>OPIATES</td>
<td>H POSITIVE</td>
</tr>
<tr>
<td>PCP</td>
<td>NEGATIVE</td>
</tr>
<tr>
<td>PROPOXYPHENE</td>
<td>NEGATIVE</td>
</tr>
</tbody>
</table>

**Possible Interpretations**

- Morphine
- Codeine
- Hydrocodone
- Heroin
- Levofloxacin (Levaquin)
“Which Lab” makes a big difference!

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Lab “L”, Drug Abuse Profile</th>
<th>Lab “M”, Drug of Abuse Screen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marijuana</td>
<td>Marijuana</td>
<td>Marijuana</td>
</tr>
<tr>
<td>Cocaine</td>
<td>Cocaine</td>
<td>Cocaine</td>
</tr>
<tr>
<td>Opiates</td>
<td>Opiates</td>
<td>Opiates</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>Oxycodone</td>
<td>Phencyclidine</td>
</tr>
<tr>
<td>Phencyclidine</td>
<td>Phencyclidine</td>
<td>Phencyclidine</td>
</tr>
<tr>
<td>Amphetamines</td>
<td>Amphetamines</td>
<td>Amphetamines</td>
</tr>
<tr>
<td>MDMA (Ecstasy)</td>
<td>MDMA (Ecstasy)</td>
<td>MDMA (Ecstasy)</td>
</tr>
<tr>
<td>Barbiturates</td>
<td>Barbiturates</td>
<td>Barbiturates</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>Benzodiazepines</td>
<td>Benzodiazepines</td>
</tr>
<tr>
<td>Methadone</td>
<td>Methadone</td>
<td>Methadone</td>
</tr>
<tr>
<td>Propoxyphene</td>
<td>Propoxyphene</td>
<td>Propoxyphene</td>
</tr>
</tbody>
</table>

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Confirmation Assays

- Different method than the method used to screen the specimen
- Different aliquot of the same sample
- Typically Quantitative
- Mass spectrometry most common (LC-MS/MS)

Example Results: Urine Opioid Confirmation

<table>
<thead>
<tr>
<th>Substance</th>
<th>Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrocodone</td>
<td>897 ng/mL</td>
</tr>
<tr>
<td>Hydromorphone (free)</td>
<td>6 ng/mL</td>
</tr>
<tr>
<td>Dihydrocodeine</td>
<td>(qualitative only)</td>
</tr>
</tbody>
</table>

Unable to identify Oxycodone (free) due to interfering substances in the specimen

Possible Interpretations

- ✓ Hydrocodone
- ✓ Codeine
Is Confirmation Testing Needed?

- **Screen alone**
  - Sometimes concentration is not needed
  - False positives are low
  - Results consistent with expectations

- **Screen w/ Reflex to Quantitative confirmation**
  - Opiates and oxycodone
  - Benzodiazepines
  - Screen results unexpected

- **Drugs not included in screening panel**
  - Buprenorphine
  - Fentanyl

Tests that usually don’t require confirmation:
- Amp w/o meth
- Barbs
- Cocaine
- Marijuana
- Methadone
- Meth w/ amp
- PCP
- Propoxyphene
- TCAs

Context

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Benzodiazepine Case Study
Benzodiazepine Case Study Details

- Age: 61
- Gender: F
- Relevant medications
  - Clonazepam

Problem
Repeatedly NEGATIVE urine screens for benzos
What could a negative result mean?

**Compliance**
- Drug wasn’t taken
- Drug taken wrong
- Adulteration

**Physiology**
- Drug not absorbed
- Fast metabolizer

**Testing**
- Specimen timing wrong
- Specificity/Sensitivity inadequate
- Mix-up

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Screening Assay Problems

- ARUP
  - EMIT II Plus Benzodiazepine
  - Lormetazepam as representative target
  - 200ng/mL cutoff

Clonazepam Facts
- Detection Time of 1 – 10 days in Urine
- Predominately excreted as 7-aminoclonazepam
- Little to no clonazepam excreted

The Benzodiazepine Assay has two cutoffs: 200 ng/mL and 300 ng/mL Lormetazepam.

Positive – The drugs listed are in ng/mL at which they will cross-react equivalent to the Lormetazepam cutoff.

<table>
<thead>
<tr>
<th>Drug</th>
<th>200 Cutoff</th>
<th>300 Cutoff</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alprazolam</td>
<td>65</td>
<td>79</td>
</tr>
<tr>
<td>7-Aminoclonazepam</td>
<td>5700</td>
<td>11000</td>
</tr>
<tr>
<td>7-Aminoflunitrazepam</td>
<td>590</td>
<td>1400</td>
</tr>
<tr>
<td>7-Aminonitrazepam</td>
<td>365</td>
<td>1000</td>
</tr>
<tr>
<td>Bromazepam</td>
<td>630</td>
<td>1400</td>
</tr>
<tr>
<td>Chlordiazepoxide</td>
<td>3300</td>
<td>7800</td>
</tr>
<tr>
<td>Clobazam</td>
<td>260</td>
<td>350</td>
</tr>
<tr>
<td><strong>Clonazepam</strong></td>
<td><strong>260</strong></td>
<td><strong>500</strong></td>
</tr>
<tr>
<td>Clorazepate</td>
<td>#</td>
<td>#</td>
</tr>
<tr>
<td>Clotiazepam</td>
<td>250</td>
<td>420</td>
</tr>
</tbody>
</table>
Final Interpretation

☑ Multiple negative benzo screens
  • Consistent with assay performance
  • Assay looking for clonazepam
  • Urine likely contains 7-aminoclonazepam
Potential Solutions

1. Skip the screen and go straight to confirm
   - More specific assay
   - 7-aminoclonazepam measured directly
   - More sensitive

2. Order screen and benzo confirm regardless of screen result
   - Same reasons as #1
   - Identify abused drugs if clinical suspicion is high

3. Test blood
   - More likely to find parent drug
   - ARUP assay is directed against clonazepam

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Opioids Case Study
Opiate Case Study Details

- Age: 53
- Gender: M
- Relevant medications
  - Percocet (Oxycodone w/ Acetaminophen)

Problems

- 1st urine screen POSITIVE for opiates
- Reflex confirm POSITIVE for hydrocodone, hydromorphone, dihydrocodeine
- 2nd urine screen NEGATIVE for opiates
What could a positive result mean?

Compliance
• Drug was taken
• Drug added to urine
• Drug abuse
• Incorrect prescription

Physiology
• Drug is a metabolite of the prescribed medication
• Fast metabolizer

Testing
• Specimen timing wrong
• Specificity inadequate
• Mix-up
Opiate & Opioid Metabolism

- Buprenorphine
  - Norbuprenorphine

- Fentanyl
  - Norfentanyl

- Propoxyphene
  - Norpropoxyphene

- Codeine
  - Norcodeine
  - Hydrocodone
    - Norhydrocodone
    - Dihydrocodeine
    - Hydromorphone

- Morphine
  - 6-acetylmorphine
    - Heroin
  - Normorphine
  - Morphine Glucuronide

- Oxycodone
  - Oxymorphone
    - Noroxycodone
  - Normethadol
  - EMDP
    - EDDP
      - Methadone
        - Methadol
          - Normethadolin
          - EMDP
  - 6-oxymorphol
1st Opiate Screen and Confirm

- **ARUP**
  - EMIT II Plus Opiate
  - Morphine as representative target
  - 300ng/mL cutoff

What lab performed the screen?

Confirm Results - ARUP

Positive – The drugs listed are in ng/mL at which they will cross-react equivalent to the morphine cutoff.

<table>
<thead>
<tr>
<th>Drug</th>
<th>300 Cutoff</th>
<th>2000 Cutoff</th>
</tr>
</thead>
<tbody>
<tr>
<td>6-Acetylmorphine</td>
<td>435</td>
<td>4182</td>
</tr>
<tr>
<td>Codeine</td>
<td>102–306</td>
<td>660–1980</td>
</tr>
<tr>
<td>Dihydrocodeine</td>
<td>291</td>
<td>1872</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>247</td>
<td>1545</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>498</td>
<td>5349</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>125000</td>
<td>–</td>
</tr>
<tr>
<td>Levorphanol</td>
<td>1048</td>
<td>4700</td>
</tr>
<tr>
<td>Morphine-3-Glucuronide</td>
<td>626</td>
<td>6167</td>
</tr>
<tr>
<td>Nalorphine</td>
<td>5540</td>
<td>(see below)</td>
</tr>
<tr>
<td>Naloxone</td>
<td>11000</td>
<td>(see below)</td>
</tr>
<tr>
<td>Normorphine</td>
<td>1200</td>
<td>–</td>
</tr>
<tr>
<td>Ofloxacin</td>
<td>330</td>
<td>–</td>
</tr>
<tr>
<td><strong>Oxycodone</strong></td>
<td>1500</td>
<td>(see below)</td>
</tr>
<tr>
<td>Pholcodine</td>
<td>320</td>
<td>1400</td>
</tr>
</tbody>
</table>

Confirmed POSITIVE by LC-MS/MS for the following opiates:
- Oxycodone = 897 ng/mL
- Hydromorphone (free) = 6 ng/mL
- Dihydrocodeine (qualitative only)
- Unable to identify Oxycodone (free) due to interfering substance(s) in the specimen.

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What could a negative result mean?

**Compliance**
- Drug wasn’t taken
- Drug taken wrong
- Adulteration

**Physiology**
- Drug not absorbed
- Fast metabolizer

**Testing**
- Specimen timing wrong
- Specificity/Sensitivity inadequate
- Mix-up

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2nd Opiate Screen

- ARUP
  - EMIT II Plus Opiate
  - Morphine as representative target
  - 300ng/mL cutoff

What lab performed the screen?

Positive – The drugs listed are in ng/mL at which they will cross-react equivalent to the morphine cutoff.

<table>
<thead>
<tr>
<th>6-Acetylmorphine</th>
<th>300 Cutoff</th>
<th>2000 Cutoff</th>
</tr>
</thead>
<tbody>
<tr>
<td>Codeine</td>
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</tr>
<tr>
<td></td>
<td>102–306</td>
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<tr>
<td>Dihydrocodeine</td>
<td>291</td>
<td>1872</td>
</tr>
<tr>
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<td>247</td>
<td>1545</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>498</td>
<td>5349</td>
</tr>
<tr>
<td>Levofoxacin</td>
<td>125000</td>
<td></td>
</tr>
<tr>
<td>Levorphanol</td>
<td>1048</td>
<td>4700</td>
</tr>
<tr>
<td>Morphine-3-Glucuronide</td>
<td>626</td>
<td>6167</td>
</tr>
<tr>
<td>Nalorphine</td>
<td>5540</td>
<td>(see below)</td>
</tr>
<tr>
<td>Naloxone</td>
<td>11000</td>
<td>(see below)</td>
</tr>
<tr>
<td>Normorphine</td>
<td>1200</td>
<td></td>
</tr>
<tr>
<td>Ofloxacine</td>
<td>330</td>
<td></td>
</tr>
<tr>
<td><strong>Oxycodone</strong></td>
<td><strong>1500</strong></td>
<td>(see below)</td>
</tr>
<tr>
<td>Pholcodine</td>
<td>320</td>
<td>1400</td>
</tr>
</tbody>
</table>

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Final Interpretation

✓ 1st screen w/ reflex confirmation
  • Inconsistent w/ Oxycodone ingestion alone
  • Ingestion of hydrocodone containing product highly likely

✓ 2nd screen
  • Incorrect screening test most likely (Oxycodone might be there but the ordered test couldn’t find it)
Potential Solutions

1. Ensure drug screen is targeted to drugs of interest
   • Opiate screen will not reliably find oxycodone
   • Separate oxycodone screening assay is needed

2. Order oxycodone screen alone
   • No clinical concern for abuse of other drugs

3. Order opiate & opioid confirmation directly
   • Provides individual drugs with quantitation
   • No clinical concern for abuse of other drugs

4. Counsel/confront patient and provide an opportunity for re-testing with a new sample to avoid the possibility of sample mix-up
Amphetamine Case Study
Amphetamine Case Study Details

• Age: 64
• Gender: F
• Relevant medications
  ▪ Tylenol w/ Codeine, Wellbutrin (Bupropion)

Problem

POSITIVE amphetamine screen w/ negative confirmation
What could a positive result mean?

**Compliance**
- Drug was taken
- Drug added to urine
- Drug abuse
- Incorrect prescription

**Physiology**
- Drug is a metabolite of the prescribed medication
- Fast metabolizer

**Testing**
- Specimen timing wrong
- Specificity inadequate
- Mix-up
Amphetamine & Stimulant Metabolism

- Methamphetamine
  - Amphetamine
- MDMA
  - MDA
- Methylphenidate
  - Ritalinic acid
- Cocaine
  - Benzoylcegonine
  - m-hydroxy benzoylcegonine
  - + Ethanol
    - Cocaethylene

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**Screening Assay Problems**

- **ARUP**
  - EMIT II Plus Amphetamines
  - d-Methamphetamine as representative target
  - 300ng/mL cutoff

### The Amphetamines Assay has three cutoffs: 300 ng/mL, 500 ng/mL, and 1000 ng/mL
d-Methamphetamine.

<table>
<thead>
<tr>
<th>Drug</th>
<th>300 Cutoff</th>
<th>500 Cutoff</th>
<th>1000 Cutoff</th>
</tr>
</thead>
<tbody>
<tr>
<td>d,l-Amphetamine</td>
<td>625</td>
<td>1050</td>
<td>2150</td>
</tr>
<tr>
<td>l-Amphetamine</td>
<td>3450</td>
<td>3750</td>
<td>11500</td>
</tr>
<tr>
<td>Benzphetamine</td>
<td>400</td>
<td>700</td>
<td>1000</td>
</tr>
<tr>
<td>d,l-Methamphetamine</td>
<td>450</td>
<td>700</td>
<td>2100</td>
</tr>
<tr>
<td>l-Methamphetamine</td>
<td>725</td>
<td>1325</td>
<td>3650</td>
</tr>
<tr>
<td>MDA (Methylenedioxoamphetamine)</td>
<td>1100</td>
<td>1700</td>
<td>(see below)</td>
</tr>
<tr>
<td>MDEA (Methylenedioxoethylamphetamine)</td>
<td>4400</td>
<td>6800</td>
<td>(see below)</td>
</tr>
<tr>
<td>MDMA (Methylenedioxymethamphetamine)</td>
<td>5200</td>
<td>9150</td>
<td>(see below)</td>
</tr>
<tr>
<td>Phenmetrazine</td>
<td>2300</td>
<td>3500</td>
<td>13000</td>
</tr>
<tr>
<td>Selegiline</td>
<td>#</td>
<td>#</td>
<td>#</td>
</tr>
</tbody>
</table>

**Common Issues**
- Vicks inhaler
- D/L isomers
- Selegiline metabolite
  - AMP/MAMP
- Adderall
- Vyvanse

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## Undesired Cross-reactivity

### Negative — Structurally Related

The drugs listed are in µg/mL at which they will cross-react equivalent to the d-Methamphetamine cutoff.

<table>
<thead>
<tr>
<th>Drug</th>
<th>300 Cutoff</th>
<th>500 Cutoff</th>
<th>1000 Cutoff</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bupropion</td>
<td>250</td>
<td>500</td>
<td>2220</td>
</tr>
<tr>
<td>Cathinone</td>
<td>&gt;100</td>
<td>&gt;100</td>
<td>&gt;100</td>
</tr>
<tr>
<td>4-Chloramphetamine</td>
<td>2.6</td>
<td>4.5</td>
<td>12.2</td>
</tr>
<tr>
<td>Chloroquine</td>
<td>2100</td>
<td>2200</td>
<td>4500</td>
</tr>
<tr>
<td>l-Ephedrine</td>
<td>400</td>
<td>800</td>
<td>3500</td>
</tr>
<tr>
<td>Fenfluramine</td>
<td>25</td>
<td>40</td>
<td>150</td>
</tr>
<tr>
<td>MDA (Methylenedioxyamphetamine)</td>
<td>(see above)</td>
<td>(see above)</td>
<td>6.5</td>
</tr>
<tr>
<td>MDEA (Methylenedioxyethylamphetamine)</td>
<td>(see above)</td>
<td>(see above)</td>
<td>27.2</td>
</tr>
<tr>
<td>MDMA (Methylenedioxymethamphetamine)</td>
<td>(see above)</td>
<td>(see above)</td>
<td>34.3</td>
</tr>
<tr>
<td>Mephentermine</td>
<td>8</td>
<td>15</td>
<td>60</td>
</tr>
<tr>
<td>Methcathinone</td>
<td>&gt;100</td>
<td>&gt;100</td>
<td>&gt;100</td>
</tr>
<tr>
<td>Methoxyphenamine</td>
<td>90</td>
<td>160</td>
<td>360</td>
</tr>
<tr>
<td>Phentermine</td>
<td>5.8</td>
<td>9</td>
<td>25</td>
</tr>
<tr>
<td>Phenylpropanolamide</td>
<td>700</td>
<td>1000</td>
<td>2000</td>
</tr>
<tr>
<td>PMA (p-Methoxyamphetamine)</td>
<td>4</td>
<td>7</td>
<td>34</td>
</tr>
<tr>
<td>PMMA (p-Methoxymethamphetamine)</td>
<td>8</td>
<td>14</td>
<td>81</td>
</tr>
<tr>
<td>Propranolol</td>
<td>100</td>
<td>125</td>
<td>500</td>
</tr>
<tr>
<td>d,l-Pseudoephedrine</td>
<td>1400</td>
<td>2600</td>
<td>8300</td>
</tr>
<tr>
<td>nor-Pseudoephedrine</td>
<td>40</td>
<td>70</td>
<td>170</td>
</tr>
<tr>
<td>Quinacrine</td>
<td>2500</td>
<td>3800</td>
<td>16500</td>
</tr>
<tr>
<td>Tranylcypromine</td>
<td>30</td>
<td>60</td>
<td>200</td>
</tr>
<tr>
<td>Tyramine</td>
<td>150</td>
<td>200</td>
<td>600</td>
</tr>
</tbody>
</table>

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Final Interpretation

- Positive amphetamine screen
  - Consistent w/ bupropion ingestion

- Negative amphetamine confirmation
  - Consistent w/ bupropion ingestion

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Potential Solutions

1. Expect the amphetamine positive and ignore
   • Low clinical suspicion of abuse

2. Skip the screen and go straight to confirm for opiates/opioids and/or amphetamines
   • More specific assay
   • Methamphetamine and amphetamine do not interfere with opioid confirm
   • Codeine (and metabolites) measured directly

3. Order screen and amphetamine confirm regardless of screen result
   • Same reasons as #2
   • Identify abused drugs if clinical suspicion is high

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