



## New High-Resolution Targeted Stimulant & Phencyclidine (PCP) Screen

Superior Sensitivity and Specificity to Evaluate Adherence to Prescribed Stimulant Therapy

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## Disclosures

- None

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## Objectives

- Describe the clinical utility of prescription stimulant drugs.
- Identify the advantages and limitations of urine drug tests used to support adherence monitoring or detection of abuse for these controlled substances:
  - Traditional laboratory or point-of-care based amphetamine/methamphetamine immunoassays
  - Mass spectrometry-based targeted screening assays
- Compare the effectiveness of immunoassays and mass spectrometry-based targeted screening assays to identify phencyclidine (PCP) abuse.
- Differentiate how Mayo Clinic's targeted stimulant and PCP test, as well as the controlled substance monitoring panel helps clinicians correctly interpret test results.

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## Central Nervous System (CNS) Stimulants

- Large class of drugs (legal & illicit) which enhance the activity of the brain chemicals dopamine and norepinephrine.
- Most prescription stimulants come in tablet, capsule, or liquid form, which a person takes by mouth. When misusing a prescription stimulant, a person can swallow, snort, smoke, or inject the drug.

Health Effects	Toxicity/Overdose Effects
Increased alertness, attention, and energy	Irregular heartbeat; heart disease/heart attack
Increased blood pressure/heart rate	Seizures
Increased blood glucose	Psychosis; paranoia
Opens up breathing passages; increased respiration	Dangerously high body temperatures

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## Examples of CNS Stimulants

- Prescription drugs include:
  - Amphetamine (Adderall<sup>®</sup>, Dexedrine<sup>®</sup>, Vyvanse<sup>®</sup>)
  - Methamphetamine (Desoxyn<sup>®</sup>)
  - Methylphenidate (Ritalin<sup>®</sup>, Concerta<sup>®</sup>)
- Diet aids:
  - Phentermine (Adipex-P<sup>®</sup>, Fastin<sup>®</sup>)
- Illicit drugs:
  - Methamphetamine (Speed, Uppers, Crank, Meth)
  - Methylenedioxymethamphetamine; MDMA (Ecstasy, Molly)

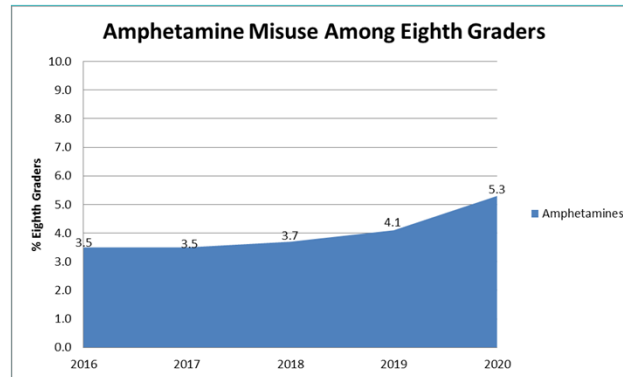
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## Simulant Statistics

In the United States, ~6.6% adults (16 million) use prescription stimulants

- ~4.5% (11 million) use appropriately
- ~2.1% (5 million) misuse
- ~0.2% (0.4 million) had stimulant use disorders

## 2020 Monitoring the Future Survey Results:



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## CNS Stimulants (Prescription/Rx)

- Amphetamine (Rx):
  - FDA approved uses:
    - Attention deficit hyperactivity disorder (ADHD); ages 3+
    - Narcolepsy
    - Simple obesity (short-term; adjunctive use)
- Methamphetamine (Rx):
  - FDA approved use:
    - Attention deficit hyperactivity disorder (ADHD); ages 6+
- Methylphenidate (Rx):
  - FDA approved uses:
    - Attention deficit hyperactivity disorder (ADHD); ages 6+
    - Narcolepsy

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## Stimulants (Rx and/or Over-the-Counter; OTC\*)

OTC\*=Non-prescription, but behind pharmacy counter

- Phentermine (Rx):
  - FDA approved use:
    - Obesity or overweight with at least one weight-related comorbidity (short-term; adjunctive use)
- Ephedrine (Rx/OTC\*):
  - FDA approved use:
    - Hypotension in setting of anesthesia
    - Symptoms of mild, intermittent asthma (bronchodilator)
- Pseudoephedrine (Rx/OTC\*):
  - FDA approved use:
    - Nasal/sinus congestion

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## Dissociative Anesthetic

- Phencyclidine (PCP):
  - Illegal drug abused for its hallucinogenic effects
    - Street names:
      - Angel dust
      - Embalming fluid
      - Killer weed
      - Rocket fuel
    - Effects:
      - Distortion of sights, sounds, colors, self, and one's environment (hallucinations)
      - Numbness of extremities, slurred speech and loss of coordination
      - Sense of strength/invulnerability
      - Blank stare; rapid involuntary eye movements
      - Acute anxiety, paranoia, and hostility

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## PCP Abuse is Highly Regional



Thombs DL: A review of PCP abuse trends and perceptions. Public Health Reports 1989; 104:325-328.

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## Laboratory Testing for CNS Stimulant Use/Misuse & PCP Abuse



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## Screening Assays for CNS Stimulants & PCP

- Types:

- Traditional screen immunoassays:
  - Point-of-collection tests (POCT)
  - Laboratory-based (commercial immunoassays)
- Targeted screening assays:
  - Laboratory-developed tests (LDTs) using mass spectrometry (LC-MS/MS or TOF-MS)

Test	Advantages	Disadvantages
POCT	Fastest TAT CLIA-waived versions available Instant result to review/discuss with patient Great if patient resides far from care Good for high-risk patient	Limited sensitivity Higher cutoffs Limited specificity Maintain inventory/regulatory compliance Higher cost
Immunoassay-lab based	Automated CLIA environment Most economic Larger test menu	Limited sensitivity Limited specificity
Targeted screen	Better sensitivity Better specificity Broadest test menu	Limited availability

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## Amphetamine Immunoassays & Cross-Reactivity Issues

- Urine amphetamine/methamphetamine immunoassays commonly calibrated with:
  - d-methamphetamine
- Concentrations required to trigger a “positive” amphetamine result:

Drug	500 ng/mL cutoff	% Cross reactivity
d-Amphetamine	494 ng/mL	101%
d-Methamphetamine	488 ng/mL	102%
Methylenedioxymethamphetamine (MDMA)	196 ng/mL	255%
Methylenedioxyamphetamine (MDA)	394 ng/mL	127%
Methylenedioxyethylamphetamine (MDEA)	668 ng/mL	75%
Phentermine	123,457 ng/mL	0.41%
d-Pseudoephedrine	112,613 ng/mL	0.44%
l-Ephedrine	141,643 ng/mL	0.35%

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## Clinical Case Study #1

- Case History:
  - 16-year-old male
- Medical History:
  - Attention deficit hyperactivity disorder (ADHD)
  - Patient currently reports cough & congestion in chest
- Medications:
  - Methylphenidate (Ritalin®); 20 mg BIG
  - OTC cough & cold medicine (Delsym® Cough + Chest Congestion)
- Clinical Evaluation:
  - ADHD well controlled
  - Grades in school are above average
  - Orders urine drug testing (UDT) to monitor compliance/adherence and identify any misuse

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## Clinical Case #1 Continued

- Routine Laboratory or POCT-based Urine Immunoassay results:
  - January 2021

Immunoassay Screening Test	Urine Cutoff	Result
Amphetamine/Methamphetamine	500 ng/mL	Negative
Barbiturates	200 ng/mL	Negative
Benzodiazepines	100 ng/mL	Negative
Cocaine Metabolite	150 ng/mL	Negative
Phencyclidine (PCP)	25 ng/mL	Presumptive Positive
THC (Marijuana)	50 ng/mL	Negative
Opiates	300 ng/mL	Negative

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## Is the Patient Compliant Based on the Urinary Test Results?

- Patient prescribed Methylphenidate (Ritalin®)
- Patient Urine Amphetamine/Methamphetamine & PCP Immunoassay Result:

Screening Test	Urine Cutoff	Result
Amphetamine/ Methamphetamine	500 ng/mL	Negative
Phencyclidine (PCP)	25 ng/mL	Presumptive Positive

- Remember cross-reactivity w/ Amphetamine/Methamphetamine Immunoassay:

Drug	500 ng/mL Cutoff	% Cross reactivity
Methylphenidate	NA	<0.14% @ 1 mg/mL
Ritalinic acid	NA	NA

- Methylphenidate appears in the urine largely (60-81%) as the metabolite (rialinic acid)

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## Clinical Case #1 Continued

### Physician Adds on Confirmation Test for Methylphenidate & Metabolite

- Methylphenidate & Metabolite, Confirmation Test (Urine)

Analyte	Urine Detection Limit	Result
Methylphenidate	10 ng/mL	152 ng/mL
Ritalinic acid	50 ng/mL	8,425 ng/mL

- **Conclusion:**
  - Patient is taking Methylphenidate (Ritalin®)

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## What about the “Presumptive Positive” PCP Test Result?

- PCP is an illicit drug
- Remember cross-reactivity w/ PCP Immunoassay:

Immunoassay Test	Other drugs that can give a positive result
Phencyclidine (PCP)	Chlorpromazine Dextromethorphan Ibuprofen Tramadol Venlafaxine

- PCP confirmation (GC-MS) test was ordered:

Drug	Detection Limit	Result
Phencyclidine	10 ng/mL	Negative

- **Final conclusion:**

- Patient is taking Methylphenidate (Ritalin®); PCP was a false-positive screening result

## Mayo Clinic’s New High Resolution Targeted Stimulant & PCP Screen (TSPU)

## 2017 AACC Academy LMPG Evidence-based Recommendation: Definitive Testing

Table 4: Summary of Evidence-based LMPG Recommendations

#	Recommendation	Grading : Strength of recommendation, Quality of evidence	Target Group		
			Lab	Clinician	Policy <sup>‡</sup>
1	Qualitative definitive tests should be used over immunoassays since they are more effective at identifying relevant over-the-counter medications, prescribed and non-prescribed drugs, and illicit substances in pain management patients.	A, II	X	X	X

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## High-Resolution Targeted Stimulant & PCP Screen TSPU/Targeted Stimulant Screen, Urine

- Features and benefits:
  - Uses high-resolution accurate mass spectrometry to identify 10 different stimulants and/or metabolites along with PCP where immunoassays are not adequate
  - Lower detection limits (improved sensitivity)

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## Drugs Detected in the High-Resolution Targeted Stimulant & PCP Screen

Analyte	Cutoff	Analyte	Cutoff
Amphetamine	100 ng/mL	Ephedrine	100 ng/mL
Methamphetamine	100 ng/mL	Pseudoephedrine	100 ng/mL
Methylenedioxymethamphetamine (MDMA)	100 ng/mL	Phentermine	100 ng/mL
Methylenedioxyamphetamine (MDA)	100 ng/mL	Methylphenidate	20 ng/mL
Methylenedioxyethylamphetamine (MDEA)	100 ng/mL	Ritalinic acid	100 ng/mL
Phencyclidine (PCP)	20 ng/mL		

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  - Improved test utilization without compromising turn-around-times
  - Significantly reduced need for confirmatory testing required with traditional immunoassay screens (~90% PCP & ~20% Amphetamine positive immunoassays are false-positives)

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## Common False-Positive Results Reported with Immunoassays

Screening Immunoassay (drug class)	Drugs that can give a positive result
Amphetamine/Methamphetamine	Bupropion Chlorpromazine (metabolite) Pseudoephedrine Ranitidine Trazodone (metabolite)
Phencyclidine (PCP)	Chlorpromazine Dextromethorphan Ibuprofen Tramadol Venlafaxine

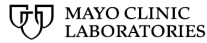
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  - Available with enhanced reports with interpretative comments

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## Example of Enhanced Report for Case Study #1



1-800-533-1711  
TSPU

Targeted Stimulant Screen, Urine

Patient ID SAMPLE	Patient Name PATIENT, TEST	Birth Date 1990-08-23	Gender F	Age 30
Order Number SAMPLE	Client Order Number SAMPLE	Ordering Physician SAMPLE	Report Notes Sample Report	
Account Information SAMPLE		Collected 28 Sep 2020 14:45		

List prescribed stimulants  
Methylphenidate (U) SOL

**ADDITIONAL INFORMATION**  
Accuracy and completeness of declared medications on reports solely dependent on information submitted by client.

**Stimulants Interpretation** (U) SOL  
Test detected the presence of methylphenidate and its metabolite (ritalinic acid). Suspect use of methylphenidate within the past three days.

Drug	Result	Cutoff	Drug	Result	Cutoff
Methylphenidate Ritalin, Concerta	Present	20 ng/mL	3,4-methylenedioxymethamphetamine (MDMA)	Not Detected	100 ng/mL
Ritalinic acid Metabolite of methylphenidate	Present	100 ng/mL	3,4-methylenedioxy-N-ethylamphetamine (MDEA) Also a metabolite of MDMA and/or MDEA	Not Detected	100 ng/mL
Methamphetamine Desoxyn	Not Detected	100 ng/mL	3,4-methylenedioxyamphetamine (MDA) Also a metabolite of MDMA and/or MDEA	Not Detected	100 ng/mL
Amphetamine Diprivel XR, Adderall ER, Adderall, Vyvanse, Also a metabolite of methamphetamine	Not Detected	100 ng/mL	Ephedrine	Not Detected	100 ng/mL
			Pseudoephedrine Sudafed	Not Detected	100 ng/mL
			Phentermine Adipex-P, Lomaira, Orymia	Not Detected	100 ng/mL
			Phencyclidine (PCP)	Not Detected	20 ng/mL



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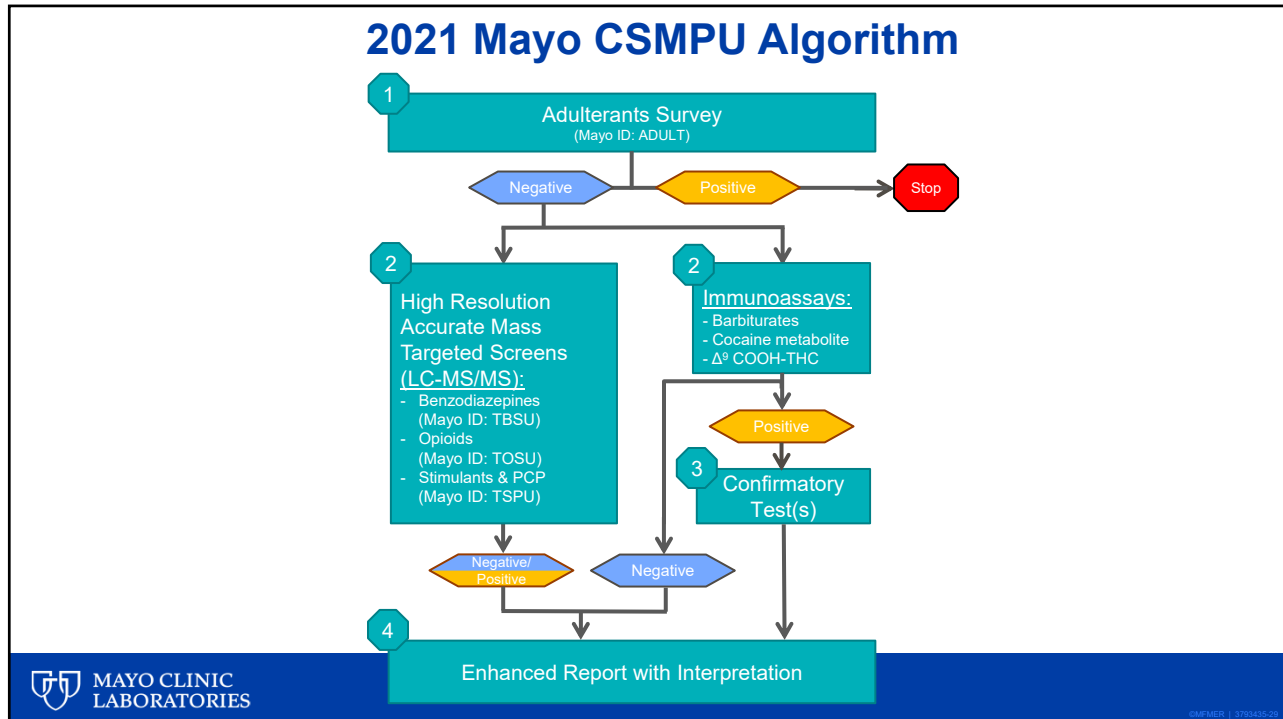
## Controlled Substance Monitoring Panel (CSMPU)

- Profile:
  - Adulterant Testing:
    - Creatinine, Specific gravity, pH, Oxidant/Nitrite
  - Targeted Opioid, Benzodiazepine, & Stimulant High-Resolution LC-MS/MS Screen:
    - 33 Opioids (parent/metabolites)
    - 27 Benzodiazepines (parent/metabolites)
    - 10 Stimulants & PCP
  - Immunoassay Screens:
    - Barbiturates (Cutoff: 200 ng/mL)
    - Cocaine metabolite (Benzoylecgonine, Cutoff: 150 ng/mL)
    - Tetrahydrocannabinol metabolite; Δ<sup>9</sup> COOH-THC (Cutoff: 50 ng/mL)



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## Summary

- Objective measures like laboratory tests are needed to:
  - Identify and evaluate recent drug use/abuse
  - Set and monitor clinical goals/expectations
- The new high-resolution targeted stimulant & PCP assay:
  - Identifies 10 different stimulants & PCP where immunoassays are not adequate
  - Has lower detection limits (improved sensitivity)
  - Reduces need for unnecessary confirmatory testing required with traditional immunoassay screens (improved specificity; less false-positives)
  - Improves test utilization
  - Available with enhanced reports and interpretive comments
- UDT results need to be interpreted in the context of the test, drug(s) prescribed, specimen type, specimen validity test results, and the patient. Unexpected/unexplained results should be discussed with the patient/laboratory, and additional testing performed if needed

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**THANK YOU**