TOXICOLOGY

Drugs of Abuse Overview

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DRUGS OF ABUSE OVERVIEW

Drug Categorization

Drug Classification

- A drug is a substance that produces a physiological effect when ingested or introduced into the body

- Drugs can be categorized in several different ways, mainly by
  - Their effects
  - Their controlled status
  - Drug family

Categorization of Drugs by Effect

CATEGORY	DESCRIPTION
CNS Depressants	Slow down the functions of the brain and body (Alcohol, barbiturates, benzodiazepines, tranquilizers, anti-depressants)
CNS Stimulants	Accelerate heart rate and “speed up”/stimulate the body (Cocaine, amphetamine, methamphetamine)
Hallucinogens	Change perception from reality (PCP, LSD, psilocybin)
Dissociative Anesthetics	Inhibit pain by dissociating the brain’s perception of pain (PCP)
Narcotic Analgesics	Relieve pain by inducing euphoria and creating mood changes (Morphine, codeine, hydrocodone, hydromorphone, oxycodone, heroin, methadone, fentanyl, meperidine)
Inhalants	Breathable substances which produce mind-altering effects (Toluene, paint thinners, gasoline, anesthetic gases)
Cannabis	Cannabinoids and synthetics (THC)

CNS = Central Nervous System

Categorization of Drugs by Controlled Status

DRUG ENFORCEMENT ADMINISTRATION (DEA)*

SCHEDULE	DESCRIPTION
I	Drugs with **no currently accepted medical use and a high potential for abuse** (Heroin, LSD, marijuana , MDMA, methaqualone)
II	Drugs with a **high potential for abuse**, with use **potentially leading to severe psychological or physical dependence** (Cocaine, methamphetamine, methadone, hydromorphone, meperidine, oxycodone, fentanyl)
III	Drugs with a **moderate to low potential for physical and psychological dependence** (Anabolic steroids, ketamine)
IV	Drugs with a **low potential for abuse and low risk of dependence** (Carisoprodol, tramadol, zolpidem, benzodiazepines)
V	Drugs **with lower potential for abuse than Schedule IV** and consist of preparations containing limited quantities of certain narcotics (Cough preparations containing not more than 200 milligrams of codeine per 100 milliliters or per 100 grams - Robitussin AC®)

*Schedules listed on this slide are US definitions only and may differ in different regions

Categorization of Drugs by Family

Family	Drugs in the family
Amphetamines	Stimulants (Amphetamine, methamphetamine, MDMA, MDA, phentermine)
Barbiturates	Sedatives, CNS depressants (Phenobarbital, secobarbital, butalbital, pentobarbital, amobarbital)
Benzodiazepines	Tranquilizers, anti-anxiety drugs (Diazepam, temazepam, oxazepam, alprazolam, clonazepam, lorazepam)
Opiates/Opioids	Natural and synthetic substances bind to the opioid receptors controlling pain • Opiates: Drugs from the poppy plant: heroin, morphine, codeine • Synthetic Opioids: Hydrocodone, oxycodone, hydromorphone, fentanyl, methadone, meperidine, tramadol
Tricyclic Antidepressants (TCAs)	Antidepressants and anxiolytics (Amitriptyline, nortriptyline, desipramine, imipramine, trimipramine)

DRUGS OF ABUSE OVERVIEW

Common Testing Matrices

Drug Tests

- An examination of biological material (such as urine, hair, saliva or sweat) to detect the presence or absence of specific parent drugs or their metabolites

- Drug tests can be used to detect illegal drug use as well as the use of drugs and substances not permitted in specific occupations or athletic competitions

- A positive drug test is an indication that an individual was exposed to the drug, which could be from an illegal use of the drug or the use of a prescribed drug. It does not prove they have abused the drug

Drug Testing – Sample Type

POST-MORTEM TOXICOLOGY

- Blood
- Urine
- Vitreous Fluid
- Tissue (Liver, brain)
- Gastric Contents
- Hair/Nails

HUMAN PERFORMANCE

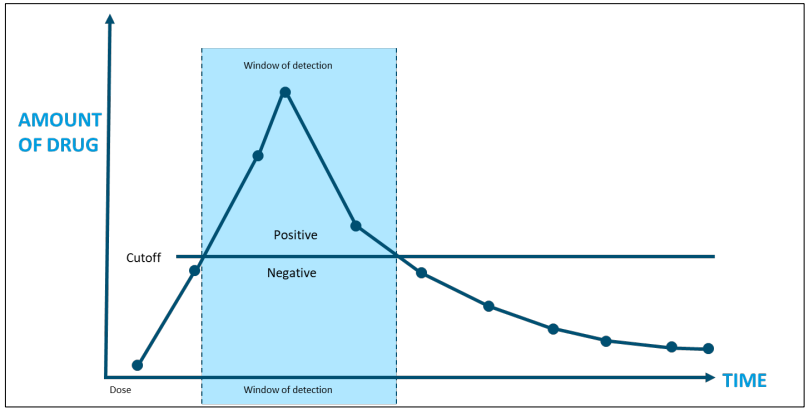
- Blood
- Urine
- Oral Fluid (Saliva)
- Hair

FORENSIC DRUG TESTING

- Urine
- Oral Fluid (Saliva)
- Hair
- Nails
- Sweat

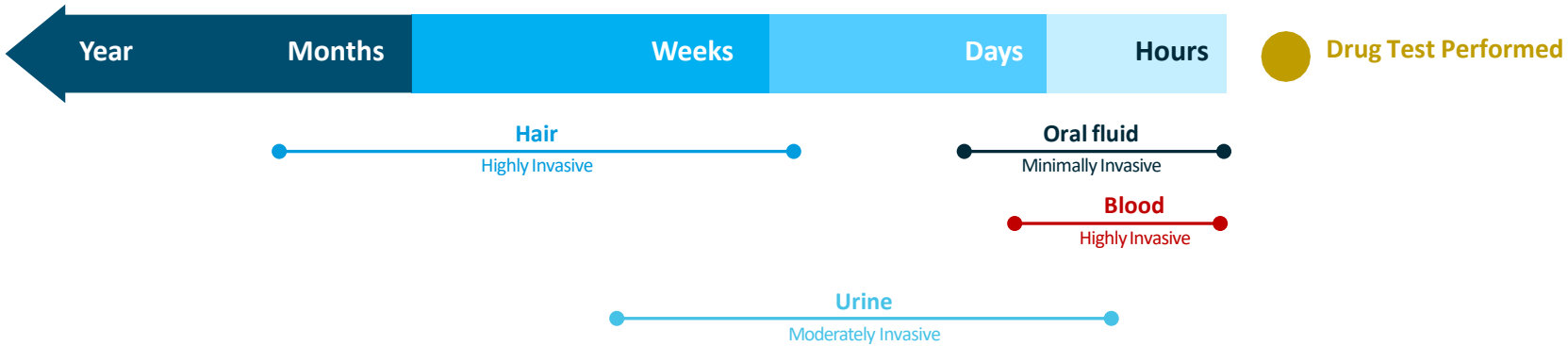
Cutoff and Window of Detection

- The point that segregates a test result as being either positive or negative
- The cutoff is given as a defined drug concentration
- It is important to note that a negative sample does not mean it is drug free
  - It may contain a drug at the concentration below the cutoff
- The time that a drug will remain detectable in an individual's sample depends on:
  - The amount of drug and frequency of use
  - The nature of the drug itself
  - An individual's metabolism and general health
  - The amount of fluids taken and exercise
  - Tolerance of the individual to the drug
  - Genetic variations that affect a response to drugs



Toxicology Matrix Comparison

DETECTION WINDOW COMPARISON FOR DIFFERENT SPECIMEN TYPES[1]



1. Detection time of any specific drug depends on multiple factors including the drug's chemical properties, quantity and frequency of use, individual metabolism and test cutoffs.

Drug Testing Sample Types

BLOOD

- Detection period: 0-2 days for most drugs
- Used for Therapeutic Drug Monitoring (TDM) and human performance (Roadside) testing

ORAL FLUID (SALIVA)

- Lower levels of drugs are present in saliva than in urine
- Detection period: hours to 1-2 days
- Used in workplace, roadside testing, criminal justice (CJ), TDM

URINE

- Drug concentrations are higher in urine than in blood, saliva or sweat – easier to detect
- Urine is aqueous - simpler testing matrix
- Large amount of data
- Detection period: typically few days to weeks depending on drug and frequency of use
- Used in workplace, CJ

HAIR

- Detection period: may range from a week to years, depending on the length of the hair tested
- Used in workplace, CJ

Drug Testing

- For many years, urine was the only biological specimen used for drug testing and is still the most widely adopted
  - Workplace
  - Pain management clinics/compliance testing
  - Criminal Justice
- Other matrices have been suggested:
  - Oral fluid
  - Hair
  - Sweat
  - Blood
- Oral fluid is increasingly important in all these areas of drug testing

Urine vs. Oral fluid

- Both can be used for the detection of illegal and prescription drugs
- The choice of sample type depends on the testing and program requirements

ORAL FLUID

- Short window of detection provides recent use information
- Detection of recent drug use makes it a suitable sample type for drug detection in a variety of settings including
  - Roadside testing (DUID)
  - For-cause or post-accident testing
  - Treatment monitoring
  - Workplace
  - Criminal justice

URINE

- Longer window of detection provides historical use information
- Urine testing has been well regulated and commonly used in
  - Workplace settings
  - Treatment monitoring
  - Criminal justice settings

Urine: Benefits and Limitations

BENEFITS

- Most commonly used matrix
- Wide range of technologies and support resources available
- Longer window of detection providing valuable historical use information
- Wide selection of drug test panels
- Scientifically reliable and legally defensible data

LIMITATIONS

- Gender specific collection challenges if observed
- Can be subject to adulteration
- Donor and collector user experience not ideal
- Reliance on ability of donor to be able to provide sample (shy bladder)

Oral Fluid: Benefits and Limitations

BENEFITS

- Adulteration difficult
- Simple, rapid, minimally-invasive collection
- Parent drugs present in higher concentration than metabolites
- Potentially shows recent ingestion
- Ideal for post-accident or for-cause testing
- Designated collection facility not required
- Easier implementation of random testing

LIMITATIONS

- Low concentrations of drug present
- Limited or unknown sample size in some devices
- Low specimen volume may limit drug test panel
- Window of detection usually shorter than urine

DRUGS OF ABUSE OVERVIEW

Drug Screening Principles

Screening vs. Confirmation

DRUG SCREENING

- Detects drug groups present in a sample
- Qualitative or semi-quantitative
- Screening can be performed as Point- of-Care Testing (POCT) and/or in the reference laboratory
- Samples are screened for a group of drugs including the parent compound, metabolites and structurally similar compounds
- Any positive screening test should be confirmed
- Positives are considered presumptive until confirmed

DRUG CONFIRMATION AND QUANTITATION

- Detects and identifies the actual drug compound present in a sample
- Quantifies the amount of target compound present in a sample
- Performed using gas chromatography mass spectrometry (GC-MS) or liquid chromatography-tandem mass spectrometry (LC-MS/MS)

Screening vs. Confirmation Cutoff

In general, screening cutoffs are higher than those used in confirmation via GC-MS, LC-MS or equivalent.

SCREENING

During screening, samples are screened for a group of drugs including structurally similar compounds.

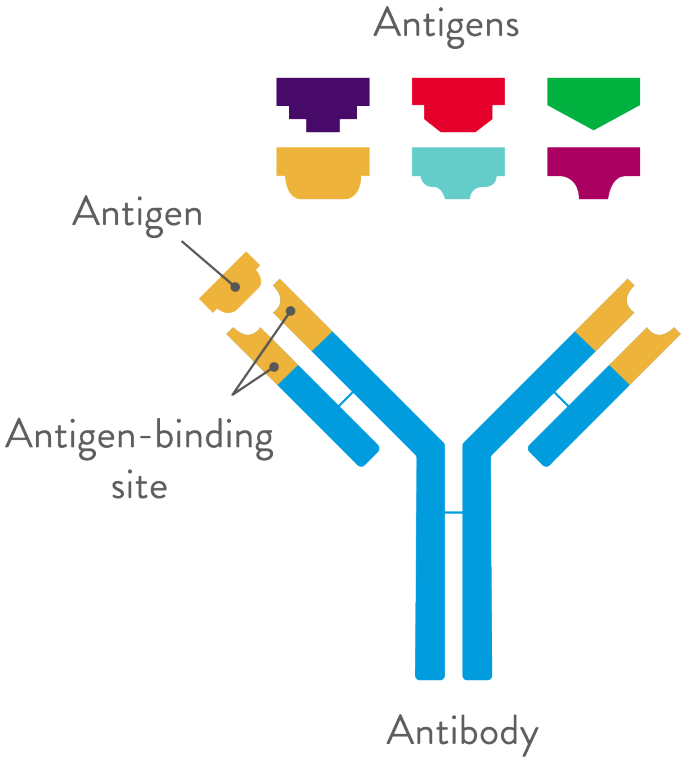
CONFIRMATION

During confirmation, individual compounds are being tested resulting in a much lower cutoff.

For example, following consumption of heroin, a screening test would detect the combined presence of morphine, 6-AM and other metabolites. However, a confirmation test would specifically identify how much of each compound was present in the sample.

How Does a Screening Test Work?

- Uses the lock and key principle (antibody: antigen)
- The key (drug) has a distinct shape which will only fit into a suitably matched lock (antibody)
- Antibodies bind to the antigen by recognizing a distinct three-dimensional shape



How Does a Screening Test Work?

- Screening tests detect part of the drug molecule.
- Cross reactivity occurs when structurally similar compounds are able to bind with the antibody.
- The antibody will react with a particular group of drugs which are different but have similar structures.

- Some molecules have similar structures so screening tests can detect more than one substance.
- Prescription and over the counter medications may give a non-negative result (e.g. codeine will give a non-negative opiate test as will heroin)

DRUGS OF ABUSE OVERVIEW

Sample Adulteration

Adulterants

WHAT IS ADULTERATION?

- Adulteration is the tampering of a urine sample with the intention of altering test results
- The use of adulterants can cause false negative results

This could include:

- Adding adulterants to the sample to mask the presence of drugs
- Replacing the sample with another liquid
- Diluting the sample

Adulterants

HOUSEHOLD SUBSTANCES/CHEMICALS

- Water
- Bleach
- Detergent
- Baking soda
- Vinegar
- Hydrogen peroxide

COMMERCIAL SUBSTANCES

- Nitrite
- Acid
- Detergent
- Glutaraldehyde
- Oxidizing reagents
- Mixed reagents

Tests commonly used by a laboratory to detect possible adulteration include tests for: creatinine, specific gravity, pH, or nitrites

DRUGS OF ABUSE OVERVIEW

Confirmation Testing

Confirmation Testing

- GC-MS and LC-MS/MS
  - Combination of two techniques, chromatography and mass spectrometry, to form a single method of analyzing chemicals in a mixture or sample
- Both are widely used for analysis of drugs and other small molecules in biological and non-biological samples and considered confirmatory techniques
  - GC-MS is comprised of a gas chromatograph coupled to a mass spectrometer
  - LC-MS/MS is comprised of a liquid chromatograph coupled with a tandem mass spectrometer
- Both methods separate chemicals by chromatography first, then further examine and identify them by mass spectrometry

DRUGS OF ABUSE OVERVIEW

Drug Information

DRUG INFORMATION

CNS Depressants

Barbiturates

- Barbiturates are a class of sedative-hypnotics introduced to treat seizures, induce anesthesia and manage increased intracranial pressure
- Barbiturates typically are present in oral fluid within 15 - 60 minutes after use and in urine within 2 hours
- The average detection time in oral fluid for many barbiturates is 1-2 days
- Due to decreased rates of barbiturate use, there is limited literature involving barbiturates in oral fluid

Fritch D, Blum K, Nonnemacher S, Kardos K, Buchhalter AR, Cone EJ. Barbiturate detection in oral fluid, plasma, and urine. Therapeutic Drug Monitoring. 2011;33(1):72-79. doi:10.1097/ftd.0b013e3182018151

Coulter CA, Moore CM. Analysis of drugs in oral fluid using LC-MS/MS. Methods in Molecular Biology. 2018:237-259. doi:10.1007/978-1-4939-8823-5_22

Common Barbiturates

Common names, routes of administration, and common analytical targets in oral fluid and urine

	COMMON NAME(S)*	ROUTE(S) OF ADMINISTRATION	TARGETS IN ORAL FLUID	TARGETS IN URINE
Butalbital	Axocet, Fioricet	Oral tablet/capsule; injection	Butalbital	Butalbital
Pentobarbital	Nembutal	Oral tablet/capsule; injection	Pentobarbital	3’-hydroxypentobarbital, pentobarbital
Phenobarbital	Luminal	Oral tablet/capsule; injection	Phenobarbital	p-hydroxyphenobarbital, glucuronides, phenobarbital
Secobarbital	Seconal	Oral tablet/capsule; injection	Secobarbital	Secodiol, 3’-hydroxysecobabital, secobarbital

Fritch D, Blum K, Nonnemacher S, Kardos K, Buchhalter AR, Cone EJ. Barbiturate Detection in Oral Fluid, Plasma, and Urine. Therapeutic Drug Monitoring. 2011;33(1):72-79. doi:https://doi.org/10.1097/ftd.0b013e3182018151

Baselt RC. Disposition of Toxic Drugs and Chemicals in Man. 8th ed. Canton, Conn: Biomedical Publ; 2008.

*Registered Product Name – United States

Benzodiazepines

- One of the most commonly prescribed medications
- Used to treat anxiety and depression
- Also act as an anti-convulsant
- Introduced as a safer alternative to barbiturates
- Usually classified by how long their effects last
  - Ultra-short acting – midazolam, triazolam
  - Short-acting – alprazolam, lorazepam
  - Long acting – chlordiazepoxide, diazepam
- Oral administration is most common but crushed tablets in solution can be injected

Moore C, Coulter C, Crompton K, Zumwalt M. Determination of benzodiazepines in oral fluid using LC-MS-MS. Journal of Analytical Toxicology. 2007;31(9):596-600. doi:10.1093/jat/31.9.596

Smink BE, Mathijssen MP, Lusthof KJ, de Gier JJ, Egberts AC, Uges DR. Comparison of urine and oral fluid as matrices for screening of thirty-three benzodiazepines and benzodiazepine-like substances using immunoassay and LC-MS(-MS). Journal of Analytical Toxicology. 2006;30(7):478-485. doi:10.1093/jat/30.7.478

Coulter CA, Moore CM. Analysis of drugs in oral fluid using LC-MS/MS. Methods in Molecular Biology. 2018:237-259. doi:10.1007/978-1-4939-8823-5_22

Common Benzodiazepines

Common names, routes of administration, and common analytical targets in oral fluid and urine

	COMMON NAME(S)*	ROUTE(S) OF ADMINISTRATION	TARGETS IN ORAL FLUID	TARGETS IN URINE
Alprazolam	Xanax	Oral tablet/capsule	Alprazolam	4-hydroxyalprazolam, α-hydroxyalprazolam, alprazolam
Diazepam	Valium	Oral tablet/capsule; injection	Diazepam, nordiazepam, oxazepam	Nordiazepam, oxazepam, temazepam
Clonazepam	Klonopin, Clonopin	Oral tablet/capsule	Clonazepam	7-aminoclonazepam and 7-acetamidoclonazepam
Lorazepam	Ativan	Oral tablet/capsule; injection	Lorazepam	Lorazepam-glucuronide
Midazolam	Versed	Oral tablet/capsule; injection	Midazolam	α-hydroxymidazolam
Chlordiazepoxide	Librium	Oral tablet/capsule; injection	Chlordiazepoxide, norchlordiazepoxide	Norchlordiazepoxide, demoxepam, nordiazepam, oxazepam

*Registered Product Name – United States

Zolpidem and Z-Drugs

- Zolpidem, zopiclone, and zaleplon are often referred to as “Z-Drugs”
- Non-benzodiazepine drugs designed to induce and maintain sleep, typically in those with insomnia
- Ingested orally as a tablet or capsule
- Zolpidem (Ambien®)
- Zopiclone (Imovane®)
- Zaleplon (Sonata®)

Baselt RC. Disposition of Toxic Drugs and Chemicals in Man. 8th ed. Canton, Conn: Biomedical Publ; 2008.

Gunja N. The clinical and forensic toxicology of Z-Drugs. Journal of Medical Toxicology. 2013;9(2):155-162. doi:10.1007/s13181-013-0292-0

Lewis JH, Vine JH. A Simple and Rapid Method for the Identification of Zolpidem Carboxylic Acid in Urine. Journal of Analytical Toxicology. 2007;31(4):195-199. doi:https://doi.org/10.1093/jat/31.4.195

GHB

GAMMA-HYDROXYBUTYRATE

- Referred to as “liquid X” or “XTC”, “salt water”, “Georgia Home Boy”, “Gamma-OH”
- GHB is naturally occurring within the body so appropriate analytical cutoffs are critical to determine GHB use/misuse
- Oral administration of a liquid or a white “soap-like” powder is typical, but IV is possible
- GHB is very rapidly metabolized in the body making analysis challenging
- In urine, GHB, can be targeted, but only for ~12 hours after use
- In oral fluid, GHB can be detected for ~5 hours, but sample collection must occur soon after administration

Moore C, Coulter C, Crompton K, Zumwalt M. Determination of benzodiazepines in oral fluid using LC-MS-MS. Journal of Analytical Toxicology. 2007;31(9):596-600. doi:10.1093/jat/31.9.596

Smink BE, Mathijssen MP, Lusthof KJ, de Gier JJ, Egberts AC, Uges DR. Comparison of urine and oral fluid as matrices for screening of thirty-three benzodiazepines and benzodiazepine-like substances using immunoassay and LC-MS(-MS). Journal of Analytical Toxicology. 2006;30(7):478-485. doi:10.1093/jat/30.7.478

Coulter CA, Moore CM. Analysis of drugs in oral fluid using LC-MS/MS. Methods in Molecular Biology. 2018:237-259. doi:10.1007/978-1-4939-8823-5_22

DRUG INFORMATION

CNS Stimulants

Cocaine

- Main psychoactive product from the coca plant
- Two main forms
  - Cocaine hydrochloride
    - Insufflation or injection
  - Cocaine base
    - Inhalation
- Stimulant effects with euphoria, increased alertness and confidence, increased heart rate/breathing/body temperature

Cone EJ, Oyler J, Darwin WD. Cocaine disposition in saliva following intravenous, intranasal, and smoked administration. Journal of Analytical Toxicology. 1997;21(6):465-475. doi:10.1093/jat/21.6.465

Dams R, Choo RE, Lambert WE, Jones H, Huestis MA. Oral fluid as an alternative matrix to monitor opiate and cocaine use in substance-abuse treatment patients. Drug and Alcohol Dependence. 2007;87(2-3):258-267. doi:10.1016/j.drugalcdep.2006.08.020

Cocaine

URINE

- Cocaine may be present in very low concentrations but is typically undetectable in urine
- Benzoylecgonine (BE) is the primary urinary metabolite
  - Average detection window is dependent upon history of use, but may be detected for 1-6+ days in chronic users

ORAL FLUID

- Cocaine and BE may be detected following exposure
  - Average window of detection: 12+ hours depending on history of use
- Anhydroecgonine methyl ester is a unique metabolite detected only in oral fluid after smoking

Dams R, Choo RE, Lambert WE, Jones H, Huestis MA. Oral fluid as an alternative matrix to monitor opiate and cocaine use in substance-abuse treatment patients. Drug and Alcohol Dependence. 2007;87(2-3):258-267. doi:10.1016/j.drugalcdep.2006.08.020

Cone EJ, Oyler J, Darwin WD. Cocaine disposition in saliva following intravenous, intranasal, and smoked administration. Journal of Analytical Toxicology. 1997;21(6):465-475. doi:10.1093/jat/21.6.465

Verstraete AG. Detection times of drugs of abuse in blood, urine, and oral fluid. Therapeutic Drug Monitoring. 2004;26(2):200-205. doi:10.1097/00007691-200404000-00020

Allen KR. Screening for drugs of abuse: Which matrix, oral fluid or urine? Annals of Clinical Biochemistry: International Journal of Laboratory Medicine. 2011;48(6):531-541. doi:10.1258/acb.2011.011116

Stimulant Drugs

METHAMPHETAMINE

- Can appear as light brown powder, tablet or capsule, crystalline
  - "Desoxyn", "crystal", "ice", "rock candy", "crank"
- General effects may include feelings of physical and/or mental well-being, exhilaration and mental and physical stimulation
- Powder and crystalline form can be snorted or smoked, dissolved in solution and injected, or pressed into a tablet and taken orally
- Metabolizes to amphetamine which also has psychoactive activity

Huestis MA, Cone EJ. Methamphetamine disposition in oral fluid, plasma, and urine. Annals of the New York Academy of Sciences. 2007;1098(1):104-121. doi:10.1196/annals.1384.038

Terminology and Information on Drugs. United Nations Office on Drugs and Crime. https://www.unodc.org/documents/scientific/Terminology_and_Information_on_Drugs-E_3rd_edition.pdf. Published March 2016.

Stimulant Drugs

METHAMPHETAMINE

URINE

- Excreted mostly unchanged or as amphetamine
  - Average detection time is 1-4 days
- Appearance of amphetamine is delayed
  - Detected 1-3 days following exposure

ORAL FLUID

- Average detection times may be similar to those in urine

Huestis MA, Cone EJ. Methamphetamine disposition in oral fluid, plasma, and urine. Annals of the New York Academy of Sciences. 2007;1098(1):104-121. doi:10.1196/annals.1384.038

Verstraete AG. Detection times of drugs of abuse in blood, urine, and oral fluid. Therapeutic Drug Monitoring. 2004;26(2):200-205. doi:10.1097/00007691-200404000-00020

Schepers RJ, Oyler JM, Joseph RE, Cone EJ, Moolchan ET, Huestis MA. Methamphetamine and amphetamine pharmacokinetics in oral fluid and plasma after controlled oral methamphetamine administration to human volunteers. Clinical Chemistry. 2003;49(1):121-132. doi:10.1373/49.1.121

Drummer OH, Gerostamoulos D, Chu M, Swann P, Boorman M, Cairns I. Drugs in oral fluid in randomly selected drivers. Forensic Science International. 2007;170(2-3):105-110. doi:10.1016/j.forsciint.2007.03.028 .

Stimulant Drugs

AMPHETAMINE

- Prescribed for attention deficit hyperactivity disorder, narcolepsy and appetite suppression
  - Adderall®, Dexedrine®
- In urine, 30-50% is excreted unchanged
  - 50% is excreted in the urine as metabolites
- Average detection times in urine and oral fluid are 1-4 days

Schepers RJ, Oyler JM, Joseph RE, Cone EJ, Moolchan ET, Huestis MA. Methamphetamine and amphetamine pharmacokinetics in oral fluid and plasma after controlled oral methamphetamine administration to human volunteers. Clinical Chemistry. 2003;49(1):121-132. doi:10.1373/49.1.121

Allen KR. Screening for drugs of abuse: Which matrix, oral fluid or urine? Annals of Clinical Biochemistry: International Journal of Laboratory Medicine. 2011;48(6):531-541. doi:10.1258/acb.2011.011116

Santagati NA, Ferrara G, Marrazzo A, Ronsisvalle G. Simultaneous determination of amphetamine and one of its metabolites by HPLC with electrochemical detection. Journal of Pharmaceutical and Biomedical Analysis. 2002;30(2):247-255. doi:10.1016/s0731-7085(02)00330-8

MDMA

3,4-METHYLENEDIOXYMETHAMPHETAMINE

- Compound with stimulant and potential hallucinogenic properties
  - Often called the “hug drug” for entactogenic effects
- “Ecstasy”, “E”, “Love Drug”, “X”, “M&M”
- Routes of Administration
  - Oral ingestion
  - Insufflation of crushed tablet
  - Intravenous or intramuscular injection of dissolved tablet
- Metabolizes into 3,4-methylenedioxyamphetamine (MDA) which also has psychoactive properties

Couper, FJ, Logan, BK. Drugs and human performance fact sheets (Revised 2013). Washington, DC: National Highway Traffic Safety Administration; 2004. DOT HS 809 725.

Poyatos L, Papaseit E, Olesti E, et al. A comparison of acute pharmacological effects of methylone and MDMA administration in humans and oral fluid concentrations as biomarkers of exposure. Biology. 2021;10(8):788. doi:10.3390/biology10080788

MDMA

3,4-METHYLENEDIOXYMETHAMPHETAMINE

URINE

- MDMA detectable for 1-2 days following exposure
  - Other metabolites found in urine include MDA, HMMA, HHMA, HMA and HHA

ORAL FLUID

- Average detection in oral fluid is 24 hours
- Concentration of MDMA in oral fluid can depend heavily on oral fluid pH

Verstraete AG. Detection times of drugs of abuse in blood, urine, and oral fluid. Therapeutic Drug Monitoring. 2004;26(2):200-205. doi:10.1097/00007691-200404000-00020

Choo RE, Huestis MA. Oral fluid as a diagnostic tool. Clinical Chemistry and Laboratory Medicine (CCLM). 2004;42(11). doi:10.1515/cclm.2004.248

Krotulski AJ, Mohr AL, Fogarty MF, Logan BK. The detection of novel stimulants in oral fluid from users reporting ecstasy, Molly and MDMA ingestion. Journal of Analytical Toxicology. 2018;42(8):544-553. doi:10.1093/jat/bky051

Mitragynine

- Primary psychoactive component of kratom
- Stimulant effects have been reported following small doses, while opioid-like effects have been reported following higher doses
- Often used to treat pain, anxiety, depression, and opioid or alcohol withdrawal
- Widely available in the forms of powder, dried leaves, capsules, tablets, extract, or tea leaves
- Not currently under federal control in the U.S. but some states have legislation to control it

Schimmel J, Amioka E, Rockhill K, et al. Prevalence and description of kratom (mitragyna speciosa) use in the United States: A cross-sectional study. Addiction. 2020;116(1):176-181. doi:10.1111/add.15082

Eggleston W, Stoppacher R, Suen K, Marraffa JM, Nelson LS. Kratom use and toxicities in the United States. Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy. 2019;39(7):775-777. doi:10.1002/phar.2280

Kerrigan S, Basiliere S. Kratom: A systematic review of toxicological issues. WIREs Forensic Science. 2021;4(1). doi:10.1002/wfs2.1420

DRUG INFORMATION

Hallucinogens

LSD

LYSERGIC ACID DIETHYLAMIDE

- First synthesized in the 1930s from naturally occurring lysergic acid
- “acid”, “blotter”, “window panes”, “microdots”
- Available in liquid, powder, tablet, capsule
  - Liquid forms are generally sprayed or soaked onto some kind of substrate such as paper, stickers, candy, or even sugar cubes
  - Can also be inhaled, injected, or administered transdermally
- Targets of analysis in urine and oral fluid are LSD and 2-oxo-3OH-LSD (OH-LSD)
  - In oral fluid, LSD and small amounts of OH-LSD were detected up to 12 hours after ingestion
  - Detectable in urine on average 24 hours

Baselt RC. Disposition of Toxic Drugs and Chemicals in Man. 8th ed. Canton, Conn: Biomedical Publ; 2008.

Couper, FJ, Logan, BK. Drugs and human performance fact sheets (Revised 2013). Washington, DC: National Highway Traffic Safety Administration; 2004. DOT HS 809 725.lsd

Verstraete AG. Detection Times of Drugs of Abuse in Blood, Urine, and Oral Fluid. Therapeutic drug monitoring. 2004;26(2). doi:https://doi.org/10.1097/00007691-200404000-00020

DRUG INFORMATION

Dissociative Anaesthetics

Phencyclidine

- Phencyclidine (PCP) is a dissociative anesthetic that can cause lethargy, disorientation, hallucinations and loss of coordination
- “Angel dust”, “supergrass”
- PCP is typically inhaled by smoking plant material sprayed with liquid drug
  - Can also be administered intranasally, intravenously and orally
- The average detection window in urine varies significantly, ranging from 2-30 days
- In oral fluid, PCP is the primary analyte of interest

Couper, FJ, Logan, BK. Drugs and human performance fact sheets (Revised 2013). Washington, DC: National Highway Traffic Safety Administration; 2004. DOT HS 809 725.

Cone EJ, Huestis MA. Interpretation of Oral Fluid Tests for Drugs of Abuse. Annals of the New York Academy of Sciences. 2007;1098(1):51-103. doi:https://doi.org/10.1196/annals.1384.037

Baselt RC. Disposition of Toxic Drugs and Chemicals in Man. 8th ed. Canton, Conn: Biomedical Publ; 2008.

Ketamine

- A derivative of phencyclidine
- Used to treat psychiatric disorders, act as an anesthetic in veterinary medicine as well as a sedative in emergency medicine
- The liquid form of ketamine can be injected or sprayed over plant material and smoked
- The powder form can be insufflated or pressed into a pill form to be ingested orally
  - Onset of effects can occur within minutes

Corkery JM, Hung W-C, Claridge H, Goodair C, Copeland CS, Schifano F. Recreational ketamine-related deaths notified to the national programme on Substance Abuse Deaths, England, 1997–2019. Journal of Psychopharmacology. 2021;35(11):1324-1348. doi:10.1177/02698811211021588 .

Morgan CJ, Curran HV. Ketamine use: A Review. Addiction. 2011;107(1):27-38. doi:10.1111/j.1360-0443.2011.03576.x

Edinoff AN, Sall S, Koontz CB, et al. Ketamine evolving clinical roles and potential effects with cognitive, motor and driving ability. Neurology International. 2023;15(1):352-361. doi:10.3390/neurolint15010023

Couper, FJ, Logan, BK. Drugs and human performance fact sheets (Revised 2013). Washington, DC: National Highway Traffic Safety Administration; 2004. DOT HS 809 725.

Ketamine

TARGETS OF ANALYSIS

- Other names include Special K, Vitamin K, Jet, Ketalar, Bump, Super Acid, and Cat Valium
- Ketamine metabolizes to norketamine (an active compound) and dehydronorketamine (an inactive compound)
- In urine, norketamine is the primary marker of use with concentrations typically higher than those of ketamine
  - Dehydronorketamine can also be present but at low concentrations
- In oral fluid, concentrations of ketamine are significantly higher than those of norketamine and dehydronorketamine

Morgan CJ, Curran HV. Ketamine use: A Review. Addiction. 2011;107(1):27-38. doi:10.1111/j.1360-0443.2011.03576.x

Tsui TK, Chan AS, Lo CW, Wong A, Wong RC, Ho CS. Performance of a point-of-care device for oral fluid ketamine evaluated by a liquid chromatography-tandem mass spectrometry method. Journal of Analytical Toxicology. 2012;36(3):210-216. doi:10.1093/jat/bks006

Couper, FJ, Logan, BK. Drugs and human performance fact sheets (Revised 2013). Washington, DC: National Highway Traffic Safety Administration; 2004. DOT HS 809 725.

DRUG INFORMATION

Narcotic Analgesics

Opiates/Opioids

- A group of drugs produced from naturally-occurring alkaloids found in the poppy plant
- Opiate and opioid are often used interchangeably
  - Opioids are not derived from natural opium
- Both act on the opioid receptors in the body
- Compounds include morphine, codeine, heroin and others

Morphine

- A powerful painkiller with high potential for addiction
- “MS-Contin”, “Duramorph”, “Morphine sulfate”
- Effects can include analgesia, sedation, cough-suppression and euphoria
- Routes of administration
  - Injection of liquid morphine or crushed tablets in solution
  - Oral ingestion of tablets

ORAL FLUID

- May indicate recent use
- Average detection window is 12-24 hours

URINE

- Morphine3-glururonide and morphine-6-glucuronide metabolites are the most detected analytes in urine
- Provides a longer detection window with an average of 1-3 days

Verstraete AG. Detection times of drugs of abuse in blood, urine, and oral fluid. Therapeutic Drug Monitoring. 2004;26(2):200-205. doi:10.1097/00007691-200404000-00020
De Gregori S, De Gregori M, Ranzani GN, Allegri M, Minella C, Regazzi M. Morphine metabolism, transport and brain disposition. Metabolic Brain Disease. 2011;27(1):1-5. doi:10.1007/s11011-011-9274-6
Baselt RC. Disposition of Toxic Drugs and Chemicals in Man. 8th ed. Canton, Conn: Biomedical Publ; 2008.

Codeine Detection

- Codeine is typically administered orally in syrup or as a coating for tablet forms of other medications
- Metabolized to morphine and norcodeine
- Present in heroin and poppy seeds
- In oral fluid, codeine and norcodeine are detectable following use
- Norcodeine is the primary analyte in urine, but small amounts of codeine can be found
- Dihydrocodeine is a form of codeine used to treat pain
  - Free and conjugated parent drug and metabolites (nordihydrocodeine) appear in urine
  - Dihydrocodeine is primary analyte in oral fluid.

Coulter CA, Moore CM. Analysis of Drugs in Oral Fluid Using LC-MS/MS. Methods in Molecular Biology. Published online October 13, 2018:237-259. doi:https://doi.org/10.1007/978-1-4939-8823-5_22

Baselt RC. Disposition of Toxic Drugs and Chemicals in Man. 8th ed. Canton, Conn: Biomedical Publ; 2008.

Heroin

- Heroin is the name for illicit diamorphine
- “Diacetylmorphine”, “smack”, “China White”, “H”
  - More potent than morphine
  - Metabolizes quickly to 6-acetylmorphine (6AM) then rapidly to morphine
- Effects may include euphoria, sedation, analgesia, respiratory depression, and a higher risk of addiction
- May be dissolved in solution and injected, snorted as a powder or inhaled via smoking
- The pharmaceutical preparation diamorphine is use in palliative care and sometimes post-operative pain relief

Terminology and Information on Drugs. United Nations Office on Drugs and Crime. https://www.unodc.org/documents/scientific/Terminology_and_Information_on_Drugs-E_3rd_edition.pdf. Published March 2016.
Drummer OH. Review: Pharmacokinetics of illicit drugs in oral fluid. Forensic Science International. 2005;150(2-3):133-142. doi:10.1016/j.forsciint.2004.11.022

Heroin Detection

- In urine, it is difficult to distinguish heroin use from morphine
- In oral fluid, the parent drug and early metabolites can be detected very shortly following exposure
  - Heroin detected almost immediately after administration
  - 6-acetylmorphine (also known as 6-monoacetylmorphine, or 6-MAM) is a unique metabolite of heroin detectable a few hours after administration
  - Morphine detectable hours to days after administration

Allen KR. Screening for drugs of abuse: Which matrix, oral fluid or urine? Annals of Clinical Biochemistry: International Journal of Laboratory Medicine. 2011;48(6):531-541. doi:10.1258/acb.2011.011116

Drummer OH. Review: Pharmacokinetics of illicit drugs in oral fluid. Forensic Science International. 2005;150(2-3):133-142. doi:10.1016/j.forsciint.2004.11.022

Verstraete AG. Detection times of drugs of abuse in blood, urine, and oral fluid. Therapeutic Drug Monitoring. 2004;26(2):200-205. doi:10.1097/00007691-200404000-00020

Poppy Seeds and Opioids

- Obtained from dried seed pods of the poppy plant
- It is possible that after the ingestion of poppy seeds, morphine and codeine can be detectable
- There is no indication that eating poppy seeds as a normal part of the diet has any impairing effects on an individual
- Screening results should be confirmed
- Interpretation of opiate confirmation results relating to poppy seed use is complex and should be carried out by experienced toxicologists

Carisoprodol and Meprobamate

- Carisoprodol is a skeletal muscle relaxant also known as “Soma”
- Carisoprodol is metabolized to meprobamate, an anti-anxiety medication
- Both drugs are administered orally as a tablet or capsule
- Carisoprodol is excreted in urine as a glucuronide conjugate of parent drug and meprobamate
  - Hydroxycarisoprodol and hydroxymeprobamate are also potential urinary targets
- In oral fluid, carisoprodol and meprobamate are the primary markers for analysis

Coulter C, Garnier M, Tuyay J, Orbita J, Moore C. Determination of carisoprodol and meprobamate in oral fluid. Journal of Analytical Toxicology. 2012;36(3):217-220. doi:10.1093/jat/bks009
Couper, FJ, Logan, BK. Drugs and human performance fact sheets (Revised 2013). Washington, DC: National Highway Traffic Safety Administration; 2004. DOT HS 809 725.
Cone EJ, Huestis MA. Interpretation of oral fluid tests for drugs of abuse. Annals of the New York Academy of Sciences. 2007;1098(1):51-103. doi:10.1196/annals.1384.037

DRUG INFORMATION

Cannabis

Marijuana

- "Cannabis" describes products that come from any subspecies of the Cannabis sativa plant
  - Herb: green or brown dried material from the plant
  - Resin or "Hash": the dried secretion obtained from the flowering tops or herbal material of the plant
  - Oil or "Hash Oil": the extract obtained from the crude plant material or resin using organic solvent
- One of the most used/abused substances worldwide
- Delta-9 tetrahydrocannabinol (Δ9-THC) is the primary effect-causing compound in cannabis
- Δ9-THC content can vary based on cultivation and preparation techniques

Terminology and Information on Drugs. United Nations Office on Drugs and Crime. https://www.unodc.org/documents/scientific/Terminology_and_Information_on_Drugs-E_3rd_edition.pdf. Published March 2016.

Sharma P, Murthy P, Bharath MM. Chemistry, metabolism, and toxicology of cannabis: clinical implications. Iran J Psychiatry. 2012;7(4):149-156.

Cannabis Detection

ORAL FLUID

- Δ9-THC is the parent compound whose presence in oral fluid indicates recent use
- Carboxylic acid metabolite (THC-COOH) is not a suitable metabolite for oral fluid
- Screening tests in oral fluid should target the most readily available compound, Δ9-THC

URINE

- Primary analytes in urine are THC-COOH and glucuronide conjugates
- Longer window of detection
  - Very minimal amounts of THC can be detected

Hoffman MA, Hubbard JA, Sobolesky PM, et al. Blood and oral fluid cannabinoid profiles of frequent and occasional cannabis smokers. Journal of Analytical Toxicology. 2021;45(8):851-862. doi:10.1093/jat/bkab078

Sharma P, Murthy P, Bharath MM. Chemistry, metabolism, and toxicology of cannabis: clinical implications. Iran J Psychiatry. 2012;7(4):149-156.

Verstraete AG. Detection times of drugs of abuse in blood, urine, and oral fluid. Therapeutic Drug Monitoring. 2004;26(2):200-205. doi:10.1097/00007691-200404000-00020

Desrosiers NA, Huestis MA. Oral Fluid Drug Testing: Analytical approaches, issues and interpretation of results. Journal of Analytical Toxicology. 2019;43(6):415-443. doi:10.1093/jat/bkz048

Cannabis

PASSIVE VS ACTIVE EXPOSURE

- It is often questioned whether presence of Δ9-THC in oral fluid could be due to active or passive exposure
- It is unlikely that passive exposure will cause an individual to screen positive on a drug test
- In confirmation, the presence of THC-COOH in conjunction with Δ9-THC in oral fluid may indicate recent active exposure

Desrosiers NA, Huestis MA. Oral Fluid Drug Testing: Analytical approaches, issues and interpretation of results. Journal of Analytical Toxicology. 2019;43(6):415-443. doi:10.1093/jat/bkz048

Röhrich J, Schimmel I, Zörntlein S, et al. Concentrations of delta9-tetrahydrocannabinol and 11-nor-9-carboxytetrahydrocannabinol in blood and urine after passive exposure to Cannabis smoke in a coffee shop. J Anal Toxicol. 2010;34(4):196-203

Synthetic Cannabinoids

IMPACT OF THE 2018 FARM BILL

The Agriculture Improvement Act of 2018 removed hemp and hemp products containing less than 0.3% Δ^9-THC from the legal definition of marijuana. Hemp products include "all derivatives, extracts, cannabinoids, isomers, acids, salts and salts of isomers" from hemp such as cannabidiol (CBD) and potentially Δ^8-THC

Δ^8-THC has a pharmacological profile similar to Δ^9-THC and can be derived from CBD

Whether Δ^8-THC is considered a hemp derivative or a synthetic cannabinoid due to its cyclization from CBD is still debated

Dubrow GA, Pawar RS, Srigley C, et al. A survey of cannabinoids and toxic elements in hemp-derived products from the United States marketplace. Journal of Food Composition and Analysis. 2021;97:103800. doi:10.1016/j.jfca.2020.103800

Tagen M, Klumpers LE. Review of delta-8-tetrahydrocannabinol (Δ 8 -THC): Comparative Pharmacology with Δ 9 -THC. British Journal of Pharmacology. 2022;179(15):3915-3933. doi:10.1111/bph.15865

DRUG INFORMATION

New Psychoactive Substances (NPS)

NPS

- NPS category includes substances often referred to as “designer drugs” or “legal highs”
- May also be labeled as “not for human consumption” to avoid legal control
- Discarded pharmaceutical substances or substances designed to evade current drug control laws and mimic the pharmacological effects of existing drugs of abuse
- UNODC listed 964 NPS as of 2019 with the majority falling into synthetic cathinone and synthetic cannabinoid categories

Leaflet: New psychoactive substances-2020. United Nations : Office on Drugs and Crime. https://www.unodc.org/unodc/en/scientists/leaflet_-new-psychoactive-substances-2020.html. Published February 2020.

NPS

CONSUMPTION AND TESTING

- Routes of administration may include snorting of a powder, consumption of tablets or pills orally, or intravenous use which is not as common
- Oral fluid as a matrix is useful for identifying emerging NPS due to the greater prevalence of parent compounds
- By 24 hours post ingestion, parent drugs are present at much lower levels
- Urine as a matrix provides a longer window of detection, however, metabolites are more common than parent drugs
- As many NPS metabolic pathways are unknown, this presents a greater challenge in detecting and identifying NPS use in urine

Pascual-Caro S, Borrull F, Aguilar C, Calull M. Determination of synthetic cathinones in urine and oral fluid by liquid chromatography high-resolution mass spectrometry and low-resolution mass spectrometry: A method comparison. Separations. 2020;7(4):53. doi:10.3390/separations7040053

Karila L, Megarbane B, Cottencin O, Lejoyeux M. Synthetic cathinones: A new public health problem. Current Neuropharmacology. 2015;13(1):12-20. doi:10.2174/1570159x13666141210224137

Prosser JM, Nelson LS. The toxicology of bath salts: A review of Synthetic Cathinones. Journal of Medical Toxicology. 2011;8(1):33-42. doi:10.1007/s13181-011-0193-z

NPS

SYNTHETIC CATHINONES

- Synthetic cathinones are substances derived from cathinone, a natural alkaloid of Catha edulis, with stimulant and other psychoactive effects
- These compounds are often sold as “bath salts,” “plant food,” or “research chemicals” in order to evade legal control
- Typically, they are snorted or swallowed in a crystal or tablet form
- Effects are classified on the similarity to other known drugs of abuse such as cocaine, MDMA, methamphetamine and pyrovalerone
- Recent examples of synthetic cathinones include methedrone, mephedrone, pentylone, eutylone, N,N-dimethypentylone, methcathinone (“MCAT”), MDPV, and α-PVP (“Flakka")
- Common street names include Blue Silk, Cloud Nine, Drone, Ivory Wave, Meow Meow, Vanilla Sky and Stardust

Poyatos L, Papaseit E, Olesti E, et al. A comparison of acute pharmacological effects of methylone and MDMA administration in humans and oral fluid concentrations as biomarkers of exposure. Biology. 2021;10(8):788. doi:10.3390/biology10080788

Baumann MH, Walters HM, Niello M, Sitte HH. Neuropharmacology of synthetic cathinones. New Psychoactive Substances. 2018;252:113-142. doi:10.1007/164_2018_178

Schifano F, Napoletano F, Arillotta D, et al. The clinical challenges of synthetic cathinones. British Journal of Clinical Pharmacology. 2020;86(3):410-419. doi:10.1111/bcp.14132

NPS

SYNTHETIC CANNABINOIDS

- First identified in 2008
- A structurally diverse group of synthetic substances that target the same receptors as THC
- Some originally developed as alternatives to THC for use in pharmaceutical research
- Effects include euphoria, elevated mood, relaxation, and appetite stimulation
- Unwanted side effects may include hallucinations, delusions or psychosis, and bizarre behavior
- Effects may be much more potent than typical cannabis use
- Generally consumed by smoking plant material sprayed with synthetic cannabinoids
- Common names include K2/Spice, Blaze, Potpourri, Serenity, Fire, Dream, Genie, Ninja, and Black Magic
- There are many synthetic cannabinoids such as: JWH-018, JWH-073, HU-210, HU-211
- The rapidly changing landscape of synthetic cannabinoids presents challenges for screening and requires laboratory analysis

Roque-Bravo R, Silva RS, Malheiro RF, et al. Synthetic cannabinoids: A pharmacological and toxicological overview. Annual Review of Pharmacology and Toxicology. 2023;63(1):187-209. doi:10.1146/annurev-pharmtox-031122-113758

Spaderna M, Addy PH, D'Souza DC. Spicing things up: Synthetic cannabinoids. Psychopharmacology. 2013;228(4):525-540. doi:10.1007/s00213-013-3188-4

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Drugs of Abuse, A DEA Resource Guide. https://www.dea.gov/sites/default/files/sites/getsmartaboutdrugs.com/files/publications/DoA_2017Ed_Updated_6.16.17.pdf. Published 2017.


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