# **Illicit Drugs: A Comprehensive Analysis of Health Consequences, Societal Impacts, and Emerging Threats**

## **1. Introduction**

### **Defining Illicit Drugs and the Public Health Challenge**

Illicit drugs, defined as substances whose use, possession, manufacture, or distribution is prohibited by law, represent a significant and multifaceted public health challenge globally.1 These substances are frequently associated with severe health risks, a high potential for addiction, and considerable societal harm. The global drug problem is intricate, impacting not only individual health and safety but also contributing to the proliferation of criminal networks involved in their production and trafficking, and imposing substantial economic and social costs on communities.3 The United Nations Office on Drugs and Crime (UNODC) World Drug Report 2024 underscores the escalating scale of this issue, revealing that the number of individuals using drugs worldwide reached 292 million in 2022, marking a 20% increase over the preceding decade.6 This escalating prevalence highlights the urgent need for comprehensive understanding and effective intervention strategies.

### **Overview of the Evolving Drug Landscape**

The contemporary illicit drug landscape is undergoing a rapid and perilous transformation. A dominant trend is the significant shift from plant-based drugs, such as heroin and cocaine derived from natural sources, towards highly potent synthetic drugs, particularly fentanyl and methamphetamine. These synthetic substances are now identified as the primary drivers of fatal drug poisonings in numerous regions, including the United States.4 This transition is largely driven by the fact that synthetic drugs can often be produced more cheaply, are easier to smuggle due to smaller volumes for equivalent psychoactive effect, and can be manufactured anywhere with the requisite chemical precursors and knowledge, bypassing traditional agricultural constraints.5

Simultaneously, New Psychoactive Substances (NPS) continue to emerge at an alarming rate. These substances are often designed with minor chemical modifications to mimic the effects of controlled illicit drugs while attempting to circumvent existing drug laws.9 The constant influx of NPS, many with unknown pharmacological and toxicological profiles, presents a formidable challenge to public health systems and regulatory bodies.8 The dynamic nature of the NPS market reflects an ongoing interplay between clandestine chemists seeking to innovate and authorities striving to identify and control these novel threats. This necessitates agile and adaptive public health surveillance and law enforcement strategies capable of responding to a constantly changing chemical landscape.

A particularly concerning development is the widespread adulteration of the illicit drug supply. Fentanyl and its potent analogues are increasingly detected in a variety of illicit drugs, including heroin, cocaine, methamphetamine, and counterfeit pills, often without the user's knowledge.4 This practice dramatically increases the risk of unintentional overdose, as users may be unaware of the true composition or extreme potency of the substances they are consuming. This trend means that individuals who use non-opioid drugs are now also at significant risk of fatal opioid overdose, a danger not as prevalent before the widespread infiltration of fentanyl into diverse drug markets. Consequently, harm reduction efforts, including naloxone distribution and drug checking services, must be broadened to reach all populations who use illicit substances.

Furthermore, novel drug administration routes and the increasing potency of available substances, such as the dabbing of high-THC cannabis concentrates, introduce new health risks and complicate prevention and treatment efforts.16 The rise of polysubstance use, frequently unintentional due to adulterated drug supplies, also significantly complicates clinical management of intoxication, withdrawal, and overdose, as the interaction of multiple substances can produce unpredictable and more severe health outcomes.4 Overdose response protocols may also be less effective; for instance, naloxone is ineffective against respiratory depression caused by benzodiazepines, which are increasingly found in combination with opioids.

## **2. Major Illicit Drug Classifications & Profiles**

The following table provides a summary of major illicit drug classes, offering a comparative overview of their characteristics and risks. Detailed profiles for each class follow.

**Table 1: Summary of Major Illicit Drug Classes**

| **Drug Class** | **Examples** | **Common Street Names** | **Primary Methods of Use** | **Key Acute Effects (Desired/Adverse)** | **Major Long-Term Risks** | **Addiction Potential** |
| --- | --- | --- | --- | --- | --- | --- |
| **Opioids** | Heroin, Fentanyl, Prescription Opioids (misused) | H, Smack, China White, Apache, Percs, Vikes | Injecting, snorting, smoking, oral | Euphoria, pain relief, drowsiness; Nausea, respiratory depression, confusion, constipation | Addiction, organ damage (liver, kidney, brain via hypoxia), infectious diseases (HIV/hepatitis via injection), chronic constipation, mental health disorders (depression), sexual dysfunction | Very High |
| **Stimulants** | Cocaine (powder & crack), Methamphetamine, Amphetamine | Coke, Crack, Snow, Meth, Ice, Speed, Uppers | Snorting, smoking, injecting, oral | Euphoria, increased energy/alertness, talkativeness; Anxiety, paranoia, psychosis, aggression, rapid heart rate, hypertension, hyperthermia, seizures | Addiction, cardiovascular damage (heart attack, stroke), neurological damage (cognitive impairment, movement disorders), severe dental problems (meth), malnutrition, skin sores, mental health disorders (psychosis, depression, anxiety) | Very High |
| **Hallucinogens** | LSD, Psilocybin (Mushrooms), PCP, Ketamine (illicit use) | Acid, Shrooms, Angel Dust, Special K | Oral, snorting, smoking, injecting | Altered perception, hallucinations, mood swings, euphoria, spiritual experiences; "Bad trips" (fear, panic, paranoia), risky behavior, nausea, increased heart rate | HPPD (flashbacks), persistent psychosis, potential for triggering/exacerbating mental illness, memory problems (PCP, Ketamine), urinary tract issues (Ketamine) | Low to Moderate (psychological for some) |
| **Depressants** | Barbiturates, Benzodiazepines (illicit/non-medical use) | Barbs, Benzos, Downers, Tranks, Xanax, Valium | Oral, injecting (less common) | Sedation, anxiety relief, muscle relaxation, euphoria; Drowsiness, impaired coordination/judgment, memory loss, slurred speech, respiratory depression | Addiction, severe withdrawal (can be life-threatening), cognitive impairment, increased risk of accidents, organ damage with chronic high-dose use, exacerbation of mental health issues | High to Very High |
| **Cannabis (High-THC/Illicit)** | Marijuana (high potency), Hashish, Dabs (Wax, Shatter, BHO) | Weed, Pot, Bud, Hash, Wax, Shatter | Smoking, vaping, dabbing, oral (edibles) | Euphoria, relaxation, altered perception; Anxiety, paranoia, impaired coordination/memory, increased heart rate, psychosis (especially with high THC/dabs) | Cannabis Use Disorder, respiratory issues (smoking), cardiovascular risks, mental health disorders (psychosis, depression, anxiety, especially with early/heavy use), cognitive impairment (especially adolescent onset), CHS, contaminant exposure | Moderate to High |
| **Inhalants** | Solvents, Aerosols, Gases (e.g., nitrous oxide), Nitrites | Huff, Rush, Whippets, Poppers | Inhaling vapors | Euphoria, dizziness, loss of inhibition; Slurred speech, nausea, loss of coordination, confusion, delirium, headache | Severe organ damage (brain, heart, liver, kidneys, lungs), neurological damage (cognitive impairment, paralysis), hearing loss, bone marrow damage, addiction, "Sudden Sniffing Death" | Moderate |

### **2.1 Opioids**

Opioids are a class of drugs that interact with opioid receptors located in the brain, spinal cord, and other organs. They are primarily known for their potent analgesic (pain-relieving) properties but also carry a significant risk of misuse, addiction, and overdose.2 This class includes natural opiates derived from the opium poppy (e.g., morphine, codeine), semi-synthetic opioids created from opiates (e.g., heroin, oxycodone), and fully synthetic opioids manufactured in laboratories (e.g., fentanyl, methadone).2

The primary mechanism of action involves binding to mu-opioid receptors (MORs). This binding modulates pain perception, can induce euphoria by stimulating dopamine release in the brain's reward pathways, and can also depress respiratory function by affecting neurochemical activity in the brain stem.2 The intensity and duration of effects vary depending on the specific opioid, the dose, and the route of administration.

General risks associated with opioid use are substantial. They possess a very high potential for addiction, with tolerance developing rapidly, often leading to dose escalation.2 Physical dependence is common, resulting in a severe and distressing withdrawal syndrome upon cessation or reduction of use. The most life-threatening acute risk is respiratory depression, which can lead to hypoxia, brain damage, and death, particularly in overdose situations.2 The danger of overdose is significantly amplified when opioids are used concurrently with other central nervous system depressants, such as alcohol or benzodiazepines.27

The landscape of opioid misuse has evolved dramatically. Initially, the crisis was largely driven by the misuse of prescription opioids. As regulations tightened and formulations changed, many individuals transitioned to heroin. More recently, the illicit drug market has been inundated with illegally manufactured fentanyl (IMF) and its even more potent analogues. These synthetic opioids are often mixed into or sold as other drugs, frequently without the user's knowledge, leading to a surge in overdose fatalities.3 This dynamic nature of the opioid market necessitates adaptive public health strategies that address the entire class of opioids and the evolving patterns of use and adulteration.

#### **2.1.1 Heroin**

Heroin is a semi-synthetic opioid derived from morphine, a natural substance extracted from the seed pod of the opium poppy plant.25 It typically appears as a white or brownish powder, or a black, sticky substance known as "black tar heroin".25 Common street names include "H," "horse," "smack," and "junk".25

Methods of Use and Mechanism of Action:

Heroin is most commonly administered via intravenous injection, which delivers the drug to the brain very rapidly, contributing to its high addictive potential. Other methods include sniffing, snorting, or smoking the substance.25 Once in the brain, heroin is converted into morphine and binds to opioid receptors, particularly mu-opioid receptors, which are involved in the perception of pain and reward.23 This binding triggers a cascade of neurochemical events, including a surge in dopamine, leading to the drug's characteristic effects.

Acute Effects:

Users typically report an intense surge of pleasure, or a "rush," shortly after administration.25 This is often accompanied by a warm flushing of the skin, dry mouth, and a heavy feeling in the extremities.23 Following the initial euphoria, users typically experience a period of drowsiness and clouded mental functioning, sometimes referred to as being "on the nod".25 Adverse acute effects can include nausea, vomiting, and severe itching.25 A critical acute risk is respiratory depression, where breathing slows significantly.30

Long-Term Health Consequences:

Chronic heroin use is associated with a wide array of severe health problems:

* **Physical:** Repeated intravenous use often leads to collapsed veins, abscesses (swollen tissue filled with pus), and infections of the skin, heart lining and valves (endocarditis).25 Sharing contaminated injection equipment significantly increases the risk of contracting blood-borne viruses such as HIV and hepatitis (B and C).25 Other physical consequences include chronic constipation, liver and kidney disease, and lung complications like pneumonia, exacerbated by the drug's depressive effect on respiration and the user's often poor overall health.23
* **Neurological:** Prolonged heroin use can lead to deterioration of the brain's white matter, which may impair decision-making abilities, the capacity to regulate behavior, and responses to stressful situations.30 Hypoxia resulting from repeated non-fatal overdoses can cause permanent brain damage.25
* **Mental:** Mental health disorders such as depression and antisocial personality disorder are commonly observed in individuals with long-term heroin use.23

Addiction, Dependence, and Withdrawal:

Heroin is exceptionally addictive, regardless of the method of administration, though rapid delivery routes like injection and smoking increase the risk of developing heroin use disorder.25 Tolerance develops quickly, meaning users require progressively larger or more frequent doses to achieve the desired effects and avoid withdrawal.31 Physical dependence is a hallmark of regular heroin use. Withdrawal symptoms typically begin within a few hours after the last dose and can be intensely uncomfortable. These include restlessness, severe muscle and bone pain, insomnia, diarrhea, vomiting, cold flashes with goose bumps ("cold turkey"), and uncontrollable leg movements ("kicking the habit").25 Severe heroin cravings are also a prominent feature of withdrawal. While major withdrawal symptoms peak between 24 to 48 hours and generally subside after about a week, some individuals may experience persistent withdrawal signs for many months.25

Overdose Risks and Emergency Interventions:

Heroin overdose is a medical emergency, primarily caused by severe respiratory depression, where breathing becomes shallow or stops, leading to hypoxia (insufficient oxygen to the brain).25 This can rapidly progress to coma, irreversible brain damage, and death.25 The risk of overdose is heightened by the unknown purity and composition of street heroin, which may be "cut" with other substances, including highly potent opioids like fentanyl. Co-administering heroin with other depressants such as alcohol or benzodiazepines further increases this risk. Naloxone is an opioid antagonist medication that can rapidly reverse a heroin overdose by blocking the effects of opioids at their receptor sites, restoring normal breathing if administered in time.25 Due to the increasing presence of fentanyl in the heroin supply, multiple doses of naloxone may sometimes be necessary.

#### **2.1.2 Fentanyl (Illicitly Manufactured Fentanyls - IMFs)**

Fentanyl is a potent synthetic opioid, approximately 50 to 100 times stronger than morphine.26 While pharmaceutical fentanyl has legitimate medical uses for severe pain management and anesthesia 34, the primary concern in the illicit drug landscape is illegally manufactured fentanyl (IMF) and its analogues. These substances are major contributors to the ongoing overdose crisis.7

Forms and Street Names:

IMFs are clandestinely produced and often appear as powders, which can be white, off-white, or colored. They are frequently pressed into counterfeit pills designed to mimic legitimate prescription opioids (like oxycodone or hydrocodone) or other drugs such as alprazolam (Xanax®).7 IMFs can also be found dropped on blotter paper or in liquid form in eye droppers or nasal sprays.26 Due to its high potency, fentanyl is often mixed with or used to replace other illicit drugs like heroin, cocaine, and methamphetamine, frequently without the end-user's knowledge.4

Methods of Use:

IMFs can be snorted, smoked, injected, or taken orally when in pill form.26 The route of administration can influence the speed of onset and intensity of effects.

Mechanism of Action:

Like other opioids, fentanyl exerts its effects by binding to mu-opioid receptors in the brain, particularly in areas controlling pain and emotions.26 Its high potency means that even small amounts can produce strong opioid effects.

Acute Effects:

The acute effects of fentanyl are similar to other opioids but can be far more intense and rapid in onset due to its potency. These include:

* **Desired:** Extreme euphoria, significant pain relief, relaxation, and sedation.26
* **Adverse:** Drowsiness, nausea, confusion, constipation, and severe respiratory depression, which can quickly become life-threatening.26 Unconsciousness and coma can also occur.

Long-Term Health Consequences:

Chronic exposure to fentanyl and other potent opioids leads to significant health problems:

* **Physical:** Beyond the immediate risks, long-term use can cause chronic constipation, gastrointestinal issues, and potential damage to organs like the liver and kidneys due to sustained toxicity or impurities.26 Immune system suppression and hormonal imbalances (e.g., reduced testosterone, irregular menses) are also reported.38
* **Neurological:** Repeated episodes of hypoxia from non-fatal overdoses can result in irreversible brain damage.26 Long-term opioid use is associated with structural brain changes, including reduced gray matter, and cognitive impairments such as memory problems, difficulty concentrating ("brain fog"), and impaired decision-making abilities.26
* **Mental:** Addiction (Opioid Use Disorder) is a primary long-term consequence. Users may also experience or exacerbate existing mental health conditions like depression, anxiety, and anhedonia (inability to feel pleasure from non-drug related activities).26 An increased risk of suicide has also been noted.39

Addiction, Dependence, and Withdrawal:

Fentanyl's high potency contributes to a rapid development of tolerance and profound physical dependence.26 Addiction (Opioid Use Disorder) is a common outcome of repeated use. Withdrawal symptoms are severe and can begin within hours of the last dose. These include intense muscle and bone pain, sleep disturbances, diarrhea and vomiting, cold flashes with goose bumps, uncontrollable leg movements, and overwhelming cravings for the drug.26

Overdose Risks and Emergency Interventions:

The risk of overdose with IMFs is exceptionally high due to their extreme potency and the frequent unknown presence or variable concentration in illicitly sold drugs.26 Even a few milligrams, equivalent to a few grains of salt, can be lethal.34 Respiratory depression is the primary cause of fentanyl overdose deaths, leading to hypoxia, coma, and death.26 Naloxone is an opioid antagonist that can reverse a fentanyl overdose, but due to fentanyl's potency and binding affinity, multiple or higher doses of naloxone may be required compared to overdoses involving other opioids.26 Prompt emergency medical intervention is critical.

The widespread adulteration of various illicit drugs with fentanyl has significantly broadened the population at risk of accidental opioid overdose. Individuals who primarily use stimulants like cocaine or methamphetamine, or those purchasing counterfeit pills, may unknowingly ingest lethal doses of fentanyl.4 This necessitates expanded harm reduction strategies, including widespread naloxone availability and drug checking services, to reach beyond traditional opioid-using populations.

#### **2.1.3 Misuse of Prescription Opioids**

The non-medical use of prescription opioids, such as oxycodone (e.g., OxyContin®), hydrocodone (e.g., Vicodin®), morphine, and codeine, remains a significant public health concern.35 These medications are legitimately prescribed for pain relief but are often diverted and misused for their psychoactive effects.

Forms and Methods of Misuse:

Prescription opioids are typically manufactured as tablets or capsules for oral administration. However, when misused, they may be taken in higher doses than prescribed, taken by someone other than the person for whom they were prescribed, or administered via alternative routes to achieve a more rapid and intense effect. This can include crushing pills to snort the powder or dissolving them in water to inject the solution.40

Risks and Consequences:

The risks associated with misusing prescription opioids are similar to those for other opioids, including the development of tolerance, dependence, and addiction (Opioid Use Disorder).22 Overdose is a major risk, particularly when high doses are taken, when they are combined with other central nervous system depressants like alcohol or benzodiazepines, or when the method of administration is altered to increase the speed of absorption.29

A significant trend observed is the progression from prescription opioid misuse to the use of heroin or illicitly manufactured fentanyl.22 This transition may occur as individuals develop tolerance to prescription opioids, find their prescriptions are no longer available or affordable, or seek a more potent high. The illicit market often provides cheaper and more readily available alternatives, albeit with much greater risks due to unknown purity and the potential presence of dangerous adulterants like fentanyl.

Prevalence:

According to the 2021 National Survey on Drug Use and Health (NSDUH), an estimated 3.1% of people aged 12 or older (approximately 8.7 million individuals) reported misusing prescription pain relievers in the past year. Among adolescents, misuse rates for specific prescription opioids like OxyContin and Vicodin were also noted, though generally lower than among young adults.40

### **2.2 Stimulants**

Stimulants are a class of psychoactive drugs that increase activity in the central nervous system, leading to heightened alertness, attention, energy, and elevated physiological markers such as blood pressure, heart rate, and respiration.41 This category includes illicit drugs like cocaine and methamphetamine, as well as prescription medications such as methylphenidate (Ritalin®) and amphetamine (Adderall®) when misused.

General Mechanism of Action:

Stimulants typically exert their effects by increasing the levels of certain neurotransmitters in the brain, particularly dopamine and norepinephrine.43 Dopamine is a key neurotransmitter involved in the brain's reward system, movement, and motivation, while norepinephrine influences alertness, arousal, and attention. By amplifying the effects of these neurochemicals, stimulants produce their characteristic effects.

General Risks:

The use of stimulants carries significant risks, including a high potential for addiction, cardiovascular complications (such as rapid or irregular heartbeat, heart attack, and stroke), and severe psychological effects like anxiety, paranoia, psychosis, and aggression.41

An emerging and particularly dangerous trend is the co-use of stimulants and opioids. This can occur intentionally, as in "speedballing" (cocaine and heroin), or unintentionally when stimulants like cocaine or methamphetamine are adulterated with fentanyl.4 This combination is hazardous because the stimulating effects of one drug can mask the depressant effects of the other. For instance, a user might not realize the extent of opioid-induced respiratory depression because the stimulant effects keep them feeling alert. When the stimulant's effects wear off, which often happens more quickly than the opioid's effects, the full impact of the opioid's respiratory depression can manifest, leading to a delayed and often unexpected overdose. This dynamic underscores the critical need for harm reduction messaging and naloxone availability to extend to stimulant users, who may unknowingly be exposed to potent opioids.

#### **2.2.1 Cocaine**

Cocaine is a powerfully addictive stimulant drug derived from the leaves of the coca plant (Erythroxylon coca), native to South America.46 It is a Schedule II drug, indicating a high potential for abuse but with accepted medical uses, such as local anesthesia for certain surgeries.46

Forms and Street Names:

Cocaine is typically encountered in two main forms:

* **Cocaine hydrochloride:** A fine, white, crystalline powder. Common street names include "Coke," "Snow," "Powder," and "Blow".35 This form is often "cut" (diluted) with substances like cornstarch, talcum powder, or other drugs such as procaine or amphetamine.46
* **Crack cocaine:** The freebase form of cocaine, which looks like small, irregularly shaped white rocks. It is named for the crackling sound it makes when heated and smoked.35 A dangerous combination known as a "Speedball" involves mixing cocaine with heroin.46

Methods of Use:

Cocaine hydrochloride powder is typically snorted (intranasally) or dissolved in water and injected intravenously.46 It can also be rubbed onto the gums (orally).47 Crack cocaine is smoked, allowing for very rapid absorption into the bloodstream via the lungs.46

Mechanism of Action:

Cocaine primarily exerts its effects by interfering with the reuptake of dopamine in the brain's mesolimbic reward pathway.46 Normally, after dopamine is released into the synapse and binds to receptors, it is recycled back into the transmitting neuron by a dopamine transporter. Cocaine blocks this transporter, causing dopamine to accumulate in the synapse and repeatedly stimulate receiving neurons. This amplified dopamine signal contributes significantly to the drug's euphoric and reinforcing effects.46 Chronic use leads to neuroadaptations in brain pathways, including those involving glutamate and stress hormones, and can impair functioning in the orbitofrontal cortex, affecting decision-making and self-insight.47

Acute Effects:

The effects of cocaine appear almost immediately and can last from a few minutes to an hour, depending on the route of administration.46 Smoking or injecting produces a faster, more intense, but shorter-lasting high compared to snorting.46

* **Desired Effects (typically with smaller amounts):** Intense euphoria, increased energy, talkativeness, mental alertness, and hypersensitivity to sight, sound, and touch. It may also temporarily decrease the need for food and sleep.46
* **Adverse Physical Effects:** Constricted blood vessels, dilated pupils, increased body temperature, heart rate, and blood pressure.46
* **Adverse Psychological/Cognitive Effects (especially with larger amounts or prolonged use):** Restlessness, irritability, anxiety, panic attacks, paranoia, tremors, vertigo, and muscle twitches. Large amounts can lead to bizarre, erratic, and violent behavior.46 In some cases, acute psychosis with hallucinations and delusions can occur.47

Long-Term Health Consequences:

Chronic cocaine use can lead to severe health problems affecting multiple organ systems:

* **Physical:**
  + *Cardiovascular:* Disturbances in heart rhythm (arrhythmias), heart attacks, inflammation of the heart muscle (myocarditis), deterioration of the heart's ability to contract, and aortic ruptures.47
  + *Respiratory (from smoking crack):* Lung damage, worsened asthma.47
  + *Nasal (from snorting):* Loss of sense of smell, nosebleeds, problems with swallowing, hoarseness, and chronic irritation/inflammation of the nasal septum.47
  + *Gastrointestinal:* Reduced blood flow leading to intestinal tears and ulcerations; malnutrition and significant weight loss due to appetite suppression.47
  + *Infectious Diseases (from injecting):* Increased risk of HIV, hepatitis C, and other infections.47
* **Neurological:** Increased risk of strokes, seizures, and headaches. Movement disorders, including Parkinson's disease, may develop after many years of use. Chronic exposure can impair cognitive functions like attention, memory, and decision-making.47
* **Mental:** Increased irritability, restlessness, panic attacks, paranoia, and psychosis, which may include auditory and visual hallucinations. Cocaine use disorders often co-occur with other mental health conditions, including stress-related disorders and mood disorders.47

Addiction, Dependence, and Withdrawal:

Cocaine is highly addictive.46 Tolerance to the euphoric effects can develop, leading users to take higher or more frequent doses.47 Conversely, sensitization to some adverse effects like anxiety or convulsions can also occur, increasing risks.47 While a classic, physically pronounced withdrawal syndrome like that seen with opioids is less common, cessation of regular cocaine use can lead to significant psychological withdrawal symptoms, including depression, fatigue, increased appetite, unpleasant dreams, psychomotor retardation or agitation, and intense cravings.47

Overdose Risks:

Cocaine overdose can be life-threatening and may result in cardiac arrest, seizures, stroke, or respiratory failure.46 The risk of overdose is increased by high doses, high purity, or the concurrent use of other substances, particularly alcohol (which forms cocaethylene, a cardiotoxic metabolite) or opioids like fentanyl, which are increasingly found as adulterants in the cocaine supply.14

#### **2.2.2 Methamphetamine**

Methamphetamine is a potent and highly addictive synthetic stimulant that affects the central nervous system.43 It is classified as a Schedule II drug by the U.S. Drug Enforcement Administration (DEA), meaning it has some limited medical use (e.g., for ADHD, narcolepsy) but a high potential for abuse.41

Forms and Street Names:

Methamphetamine typically appears as a white, odorless, bitter-tasting crystalline powder that dissolves easily in water or alcohol.45 It can also be found in pill form or as crystal-like rocks, which is known as "crystal meth," "ice," or "Tina".35 Other street names include "meth," "speed," and "crank".41

Methods of Use:

Methamphetamine can be administered in several ways:

* **Smoking:** This is a common method, especially for crystal meth, leading to rapid absorption and an intense rush.43
* **Snorting:** The powder form can be inhaled through the nose.43
* **Injecting:** The powder can be dissolved in a liquid and injected intravenously, also producing a rapid and intense effect.43
* **Oral Ingestion:** Taken as pills or by swallowing the powder.43
* **Rectal Administration:** Less common but also reported.45 The method of use influences the speed and intensity of the drug's effects, with smoking and injecting producing the quickest and most intense euphoria, which also contributes to its high addictive potential.45

Mechanism of Action:

Methamphetamine primarily acts by increasing the release and blocking the reuptake of dopamine in the brain, particularly in the reward pathways.43 This results in a significant accumulation of dopamine in the synapse, leading to intense euphoria and reinforcement of drug-using behavior. It also affects other neurotransmitters like norepinephrine and serotonin.

Acute Effects:

The effects of methamphetamine can be felt almost immediately, especially when smoked or injected, and can last for several hours.45

* **Desired Effects:** A temporary sense of heightened euphoria, increased alertness, wakefulness, energy, talkativeness, confidence, increased sex drive, and decreased appetite.43
* **Adverse Physical Effects:** Increased blood pressure and body temperature, faster breathing, rapid or irregular heartbeat, loss of appetite, disturbed sleep patterns, and nausea.43
* **Adverse Psychological/Cognitive Effects:** Paranoia, anxiety, aggression, irritability, mood disturbances, and hallucinations. Even small amounts can lead to erratic or violent behavior.43 High doses can lead to convulsions and cardiovascular collapse.41

Long-Term Health Consequences:

Chronic methamphetamine use can lead to severe and lasting health problems:

* **Physical:**
  + *Cardiovascular:* Permanent damage to the heart and brain, high blood pressure leading to heart attacks, strokes, and death.43
  + *Organ Damage:* Liver, kidney, and lung damage.43
  + *Dental Problems:* Severe tooth decay and loss, commonly known as "meth mouth".43
  + *Skin:* Intense itching leading to skin sores from scratching.43
  + *Other:* Premature osteoporosis, weight loss, decreased sexual function in men.43 Increased risk of contracting HIV and hepatitis B and C, especially among those who inject the drug or engage in risky sexual behaviors.45
* **Neurological:** Changes in brain structure and function, including damage to dopamine and serotonin neurons. This can lead to memory loss, impaired verbal learning, reduced motor speed, and difficulties with emotional regulation and cognitive tasks.45 Some brain changes may persist long after drug use stops.
* **Mental:** Chronic anxiety, confusion, insomnia, and mood disturbances. Severe psychiatric symptoms, including paranoia, hallucinations (visual and auditory), delusions (e.g., the sensation of insects crawling under the skin, known as formication), and violent behavior. These psychotic symptoms can sometimes last for months or even years after cessation of use and may resemble schizophrenia.43

Addiction, Dependence, and Withdrawal:

Methamphetamine is extremely addictive due to its unique properties and intense euphoric effects.45 Tolerance develops quickly, leading to users taking higher doses or using more frequently in a "binge and crash" pattern.

* **Dependence:** Physical and psychological dependence are common.
* **Withdrawal Symptoms:** Upon stopping use, individuals often experience a withdrawal syndrome characterized by depression, anxiety, fatigue, paranoia, aggression, intense cravings, sleep problems, and difficulty concentrating.41

Overdose Risks:

Methamphetamine overdose can be fatal and is often associated with stroke, heart attack, or multiple organ problems caused by overheating (hyperthermia).41 The risk of overdose is significantly increased by the common practice of adulterating methamphetamine with fentanyl, often unbeknownst to the user.15 The rate of fatal overdoses involving methamphetamine and other stimulants has increased significantly.43

#### **2.2.3 Misuse of Prescription Stimulants (e.g., Adderall®, Ritalin®)**

Prescription stimulants, such as amphetamine (e.g., Adderall®) and methylphenidate (e.g., Ritalin®, Concerta®), are primarily used for the treatment of Attention-Deficit/Hyperactivity Disorder (ADHD) and narcolepsy.41 While beneficial when used as prescribed, these medications have a potential for misuse and addiction due to their stimulant effects.

Forms and Methods of Misuse:

These medications are typically available as tablets or capsules intended for oral administration.41 Misuse can involve taking someone else's medication, taking the medication in higher doses or more frequently than prescribed, or using alternative routes of administration such as crushing pills to snort the powder or dissolving them for injection, to achieve a more rapid and intense effect.41 Street names for these drugs can include "Speed," "Uppers," "Bennies," or specific brand names.41

Reasons for Misuse:

Non-medical use of prescription stimulants is often driven by a desire to enhance academic or athletic performance (due to increased focus and alertness), to experience euphoria ("get high"), or for weight loss (due to appetite suppression).41

Mechanism of Action:

Like other stimulants, prescription amphetamines and methylphenidate primarily work by increasing the levels of dopamine and norepinephrine in the brain, which affects attention, impulse control, and wakefulness.44

Acute Effects and Risks of Misuse:

When misused, especially in high doses, prescription stimulants can produce effects similar to illicit stimulants, including:

* **Desired:** Increased alertness, attention, energy, and euphoria.41
* **Adverse:** Increased blood pressure and heart rate, dangerously high body temperature (hyperthermia), irregular heartbeat, potential for seizures, and cardiovascular failure. Psychological effects can include anxiety, paranoia, hostility, aggression, and psychosis (hallucinations, delusions).41

Long-Term Health Consequences of Misuse:

Chronic misuse of prescription stimulants can lead to:

* **Physical:** Malnutrition, weight loss, cardiovascular problems.
* **Neurological:** Impairments in cognitive function.
* **Mental:** Dependence, addiction (stimulant use disorder), anxiety, paranoia, psychosis, and mood disturbances.41

Addiction, Dependence, and Withdrawal:

Regular misuse can lead to tolerance, where higher doses are needed to achieve the desired effects, and physical and psychological dependence.41 Abrupt cessation after prolonged misuse can result in withdrawal symptoms such as fatigue, depression, anxiety, drug cravings, and sleep disturbances ("crash").41

Prevalence of Misuse:

According to the 2021 National Survey on Drug Use and Health, an estimated 1.8% of people aged 12 or older (approximately 5.1 million individuals) reported misusing prescription stimulants in the past year.40 Misuse is particularly noted among young adults and adolescents for perceived academic or performance enhancement.40 For example, in 2021, an estimated 3.4% of 12th graders reported misusing Adderall® in the past 12 months.40

### **2.3 Hallucinogens**

Hallucinogens are a diverse group of drugs that profoundly alter a person's perception, thoughts, and feelings.51 They can cause users to experience hallucinations—seeing, hearing, or feeling things that seem real but are not—or significant distortions of reality.51 This class is broadly divided into classic hallucinogens (like LSD and psilocybin) and dissociative drugs (like PCP and ketamine).51

General Risks:

The effects of hallucinogens are often unpredictable and can vary significantly based on the substance, dose, individual's personality, mood, expectations, and environment ("set and setting").51 A common risk is experiencing a "bad trip," characterized by intense fear, panic, paranoia, and disturbing hallucinations.51 During intoxication, impaired judgment can lead to risky behaviors and accidental injuries.54 While classic hallucinogens are not typically associated with compulsive drug-seeking addiction, psychological dependence on the experiences can occur.56 A rare but serious long-term risk associated with some hallucinogens is Hallucinogen Persisting Perception Disorder (HPPD), commonly known as "flashbacks," where individuals re-experience perceptual distortions long after the drug's effects have worn off.51 Hallucinogens can also trigger or exacerbate underlying mental health conditions, particularly psychotic disorders.51

The recent resurgence of interest in the potential therapeutic uses of certain psychedelics, often termed a "psychedelic renaissance," warrants careful consideration.6 While research explores these substances in controlled clinical settings for conditions like depression or PTSD, this increased visibility might inadvertently normalize or encourage recreational use. Unsupervised use of illicitly sourced hallucinogens carries significantly different risks than controlled therapeutic administration, including unknown potency, potential contaminants, and lack of psychological support during intense experiences. Public health messaging must clearly differentiate these contexts to prevent misinterpretation of safety and efficacy.

#### **2.3.1 LSD (Lysergic Acid Diethylamide)**

LSD is one of the most potent mood- and perception-altering classic hallucinogens.51 It is a synthetic chemical derived from lysergic acid, found in ergot, a fungus that grows on rye and other grains.51

Forms and Street Names:

LSD is typically odorless, colorless, and has a slightly bitter taste.55 It is most commonly distributed on "blotter" paper—absorbent paper perforated into small squares, each representing a dose, often decorated with designs.51 Other forms include tablets ("microdots"), thin squares of gelatin ("window panes"), liquid LSD (which can be dropped onto sugar cubes or other items), and, rarely, capsules.51 Street names include "Acid," "Blotter," "Dots," "Mellow Yellow," "Window Pane," "Sunshine," and "Zen".54

Methods of Use:

LSD is almost always taken orally, by ingesting the blotter paper, tablet, gelatin, or liquid.55

Mechanism of Action:

LSD primarily interacts with serotonin (5-hydroxytryptamine, 5-HT) receptors in the brain, particularly the 5-HT2A subtype.51 Its effects are most prominent in the prefrontal cortex, an area involved in mood, cognition, and perception, as well as other regions regulating arousal and stress responses.51

Acute Effects:

The effects of LSD typically begin within 20 to 90 minutes of ingestion and can last for 6 to 12 hours.51 Experiences are highly variable and subjective.

* **Perceptual Changes:** Vivid visual and auditory hallucinations (seeing, hearing things that aren't there, or distortions of existing stimuli), synesthesia ("seeing" sounds or "hearing" colors), altered sense of time and space, intensified sensory experiences (brighter colors, sharper sounds).51
* **Psychological/Emotional Effects:** Rapid and intense emotional swings (euphoria to fear/despair), feelings of heightened understanding or spiritual insight, impulsiveness, depersonalization (feeling detached from oneself), derealization (feeling that one's surroundings are not real).51 A "bad trip" can involve terrifying thoughts, severe anxiety, panic, paranoia, and fear of losing control or going insane.51
* **Physical Effects:** Dilated pupils, increased heart rate, elevated blood pressure, increased body temperature, sweating, loss of appetite, sleeplessness, dry mouth, and tremors.51

**Long-Term Health Consequences:**

* **Hallucinogen Persisting Perception Disorder (HPPD):** Commonly known as "flashbacks," HPPD involves the spontaneous recurrence of some of the perceptual distortions experienced during an LSD trip, such as visual trails, halos around objects, or intensified colors. These can occur days, weeks, months, or even years after the last use and can be distressing or impairing.51
* **Persistent Psychosis:** In rare cases, LSD use may trigger prolonged psychotic episodes or worsen pre-existing psychotic disorders like schizophrenia. Symptoms can include visual disturbances, disorganized thinking, paranoia, and mood disturbances.51
* **Tolerance:** Tolerance to LSD develops rapidly with repeated use, requiring higher doses to achieve the same effects. However, this tolerance also diminishes quickly after a few days of abstinence. Cross-tolerance occurs with other classic hallucinogens like psilocybin and mescaline.51

Addiction, Dependence, and Withdrawal:

LSD is not considered to be physically addictive in the way that opioids or stimulants are; it does not typically lead to compulsive drug-seeking behavior or strong physical cravings.51 Physical withdrawal symptoms are generally not experienced upon cessation of use.51 However, psychological dependence on the experience or perceived insights from LSD use can occur.56

Overdose Risks:

While a fatal overdose directly from the pharmacological effects of LSD is extremely rare, significant psychological harm can occur, especially with high doses, leading to prolonged and intense "bad trips," severe anxiety, panic, or psychosis.54 The primary danger associated with LSD use comes from impaired judgment and distorted perceptions, which can lead to accidents, self-injury, or other risky behaviors while intoxicated.54

#### **2.3.2 Psilocybin (Magic Mushrooms)**

Psilocybin is a naturally occurring psychedelic compound produced by numerous species of mushrooms, often referred to as "magic mushrooms" or "shrooms".53 These mushrooms have a long history of use in traditional spiritual and healing ceremonies.65

Forms and Street Names:

Psilocybin-containing mushrooms are typically consumed in their dried form, either whole or powdered.65 The powder can be put into capsules or tablets.66 Common street names include "Magic Mushrooms," "Shrooms," "Mushies," and names specific to mushroom species.

Methods of Use:

The most common method of use is oral ingestion: eating the dried or fresh mushrooms, brewing them into a tea, or mixing the powder into food or drinks.66 Psilocybin powder can also be snorted, though this is less common.66 Intravenous injection of mushroom material is extremely dangerous and has been associated with severe medical complications, including septic shock and organ failure.66

Mechanism of Action:

After ingestion, psilocybin is converted in the body to psilocin, which is the primary psychoactive compound.61 Psilocin primarily interacts with serotonin receptors in the brain, particularly the 5-HT2A subtype, similar to LSD.53 This interaction alters normal brain activity and communication patterns between different brain regions, leading to changes in perception, mood, and thought.65 Research suggests psilocybin can temporarily disrupt the default mode network, a brain network active during self-reflection, potentially leading to feelings of openness and connectedness.65

Acute Effects:

The effects of psilocybin typically begin within 15-45 minutes of ingestion and can last for 4 to 6 hours.60 The intensity and nature of the experience are highly dependent on the dose, the specific mushroom species (potency can vary greatly), the individual's mindset ("set"), and the environment ("setting").53

* **Perceptual Changes:** Altered perception of reality, visual and auditory hallucinations (e.g., seeing geometric patterns, intensified colors, sounds seeming clearer or distorted), synesthesia (e.g., "seeing" music), and a distorted sense of time and space.60
* **Psychological/Emotional Effects:** Experiences can range from euphoria, heightened emotions, creativity, laughter, and a sense of mental clarity or spiritual insight to anxiety, fear, panic attacks, paranoia, confusion, and disorientation. "Bad trips" involving frightening hallucinations or overwhelming negative emotions are possible, especially at higher doses.53
* **Physical Effects:** Nausea (common), vomiting, muscle weakness or twitches, increased heart rate and blood pressure, dilated pupils, dizziness, drowsiness, numbness (especially in the face), sweating, increased body temperature followed by chills.61

**Long-Term Health Consequences:**

* **Hallucinogen Persisting Perception Disorder (HPPD):** As with LSD, there is a risk, though considered rare, of developing HPPD, characterized by persistent or recurring visual disturbances ("flashbacks") after the drug's effects have worn off.53
* **Psychiatric Conditions:** For individuals with a predisposition to or existing psychiatric conditions (e.g., schizophrenia, bipolar disorder), psilocybin use may trigger or exacerbate symptoms. However, the overall risk of long-term psychiatric problems from supervised use in clinical research appears low.53 The long-term effects of repetitive recreational use are not well studied.66
* **Personality Changes:** Some users report positive long-term changes in personality, such as increased openness and a greater sense of spirituality, while others might experience negative effects.61

Addiction, Dependence, and Withdrawal:

Current evidence suggests that psilocybin has a low potential for physical or psychological dependence in the traditional sense of addiction.65 Compulsive drug-seeking behavior is not typical. Tolerance to the effects of psilocybin can develop rapidly with repeated use over several days, meaning higher doses are needed to achieve the same effect. This tolerance also diminishes quickly upon cessation of use.66 There is no well-defined withdrawal syndrome associated with stopping psilocybin use.

Overdose Risks:

A fatal overdose directly from the toxicity of psilocybin is considered extremely unlikely due to its low toxicity.53 However, significant risks are associated with its use:

* **"Bad Trips" and Psychological Distress:** High doses can lead to intensely frightening and overwhelming experiences, including severe anxiety, panic, paranoia, and temporary psychosis.53
* **Risky Behavior:** Impaired judgment and distorted perception during intoxication can lead to accidents, injuries, or other dangerous behaviors.53
* **Accidental Poisoning:** A significant risk is the misidentification of mushrooms. Consuming poisonous mushrooms mistaken for psilocybin-containing varieties can lead to severe illness or death.53
* **Contaminated Products:** Illegally sold products marketed as psilocybin (e.g., candies, chocolates) may contain other, potentially more dangerous, synthetic drugs or contaminants.53
* **Cardiovascular Risks:** The increase in blood pressure and heart rate could pose a risk to individuals with pre-existing heart conditions.53

#### **2.3.3 PCP (Phencyclidine)**

Phencyclidine, commonly known as PCP, is a powerful dissociative anesthetic that was originally developed in the 1950s for surgical anesthesia but was discontinued for human use due to its severe postoperative side effects, including delirium and hallucinations.52 It is now primarily found on the illicit drug market.

Forms and Street Names:

PCP is most commonly encountered as a white crystalline powder or a liquid.68 It can also be found in tablet or capsule form.68 Common street names include "Angel Dust," "Hog," "Ozone," "Rocket Fuel," "Shermans," "Wack," "Crystal," and "Embalming Fluid".52 When PCP is applied to plant material like marijuana or tobacco for smoking, it may be called "Killer Joints," "Super Grass," "Fry," "Lovelies," "Wets," or "Waters".68 A "dipper" refers to a marijuana joint or cigarette dipped in liquid PCP.68

Methods of Use:

The most common method of PCP use is smoking, where the liquid or powder form is applied to leafy materials (e.g., mint, parsley, oregano, tobacco, or marijuana) and then smoked.52 It can also be snorted (insufflated) as a powder or swallowed in tablet, capsule, or liquid form.52 Injection is less common but possible.

Mechanism of Action:

PCP is classified as a dissociative drug with hallucinogenic effects.68 It primarily acts as an N-methyl-D-aspartate (NMDA) receptor antagonist, interfering with the action of the neurotransmitter glutamate.53 Glutamate is involved in pain perception, learning, memory, and emotion. By blocking NMDA receptors, PCP disrupts normal brain function, leading to its characteristic dissociative and hallucinogenic effects. It also affects dopamine pathways, contributing to its abuse potential.71

Acute Effects:

The effects of PCP are dose-dependent and can vary significantly among users. Onset is rapid when smoked (2-5 minutes) and slower when ingested orally (30-60 minutes).68 Intoxication can last 4-8 hours, with some subjective effects lingering for 24-48 hours.68

* **Psychological/Cognitive Effects:** Feelings of detachment from reality and oneself (dissociation), distorted perceptions of sight and sound, confusion, disorientation, hallucinations (especially at higher doses), euphoria, feelings of invulnerability and superhuman strength, agitation, anxiety, paranoia, and panic. Users may exhibit bizarre, unpredictable, or violent behavior.52 Speech may be slurred or incoherent.68 Memory impairment and difficulty concentrating are common.69
* **Physical Effects:** Numbness (especially in extremities), loss of coordination, blank stare, rapid and involuntary eye movements (nystagmus), catatonic posturing, muscle rigidity, increased blood pressure, rapid and shallow breathing, elevated heart rate, and elevated body temperature.52 Analgesia (inability to feel pain) is a prominent effect, which can lead to users sustaining severe injuries without realizing it.69

Long-Term Health Consequences:

Chronic PCP use can lead to severe and persistent health problems:

* **Neurological:** Memory loss, difficulties with speech (slurring, stuttering) and thinking, cognitive impairment, and potential for permanent brain damage.52
* **Mental:** Persistent anxiety, depression, social withdrawal, paranoia, and chronic psychosis resembling schizophrenia. Suicidal thoughts and attempts are also associated with long-term use.52 Flashbacks, similar to those experienced with LSD, can occur.72
* **Physical:** Weight loss, poor hygiene, and potential for cardiovascular issues due to chronic elevation of heart rate and blood pressure.72

Addiction, Dependence, and Withdrawal:

PCP has a high potential for abuse and can lead to psychological dependence.68 Tolerance can develop, leading users to take higher doses.

* **Withdrawal Symptoms:** Upon cessation of chronic use, a withdrawal syndrome can occur, typically beginning within 8 to 24 hours of the last dose and potentially lasting for weeks or months.68 Symptoms include intense cravings, depression, anxiety, panic attacks, irritability, mood swings, confusion, disorientation, hallucinations, paranoia, suicidal thoughts, excessive sweating, muscle aches, tremors, headaches, nausea, vomiting, diarrhea, rapid eye movements, and increased blood pressure and heart rate.70 Some psychological symptoms like depression and memory issues can persist for an extended period.71

Overdose Risks:

High doses of PCP can lead to severe and life-threatening complications. While the DEA factsheet 68 does not detail specific overdose symptoms, other sources and the nature of the drug suggest risks include seizures, coma, respiratory depression, dangerously high fever (hyperthermia), stroke, and death, often resulting from accidents, violence, or suicide during acute intoxication or psychosis.69 The dissociative and analgesic effects can also lead to users ignoring severe injuries.

#### **2.3.4 Ketamine (Illicit Use)**

Ketamine is a dissociative anesthetic medically approved for use in humans and animals.73 However, it is also illicitly manufactured and abused for its hallucinogenic and dissociative effects.73 Esketamine, a form of ketamine, is FDA-approved as a nasal spray for treatment-resistant depression.74

Forms and Street Names:

Illicit ketamine is typically sold as a clear liquid or an off-white powder.73 Common street names include "Special K," "K," "Super K," "Vitamin K," "Cat Valium," "Kit Kat," "Purple," and "Jet K".73

Methods of Use:

Ketamine can be injected (intramuscularly or intravenously), snorted (insufflated as a powder), smoked (often by lacing it with marijuana or tobacco), or ingested orally (e.g., mixed into drinks).73

Mechanism of Action:

Ketamine is a noncompetitive N-methyl-D-aspartate (NMDA) receptor antagonist, similar to PCP, which disrupts the neurotransmitter glutamate.53 This action is primarily responsible for its anesthetic and dissociative effects. It also interacts with other receptor systems, including opioid, dopamine, and serotonin receptors, which may contribute to its complex psychoactive profile and antidepressant effects.76

Acute Effects:

The effects of ketamine are dose-dependent and can vary widely. Onset is rapid, especially when injected or snorted.

* **Desired Effects (Lower Doses):** Dream-like state, feelings of floating or detachment from the body, euphoria, relaxation, altered sensory perceptions (distorted sights and sounds), increased sociability.73
* **Dissociative Effects (Higher Doses):** Profound detachment from one's body and reality, sometimes described as an "out-of-body" experience or a "near-death experience." This state is often referred to as a "K-hole".73 Users may feel unable to move or speak.73
* **Adverse Physical Effects:** Nausea, vomiting, dizziness, slurred speech, impaired motor coordination, numbness, blurred vision, rapid eye movements (nystagmus), muscle rigidity, increased heart rate and blood pressure.73
* **Adverse Psychological/Cognitive Effects:** Confusion, disorientation, agitation, anxiety, panic, paranoia, hallucinations, amnesia, difficulty speaking or thinking clearly, impaired judgment.73

Long-Term Health Consequences:

Chronic or heavy ketamine use is associated with several serious long-term health problems:

* **Physical:**
  + *Urinary Tract Issues:* "Ketamine bladder syndrome" or ketamine-induced ulcerative cystitis, characterized by frequent and painful urination, blood in urine, and incontinence. In severe cases, this can lead to irreversible bladder damage requiring surgical removal.73
  + *Gastrointestinal Problems:* Abdominal pain, often referred to as "K-cramps".75
  + *Liver Damage:* Potential for liver dysfunction with chronic use.
* **Neurological:** Memory problems (particularly spatial memory), cognitive impairments affecting attention and executive function, and potential for lasting changes in brain structure and function.73
* **Mental:** Depression, anxiety, and psychosis. Frequent recreational use can lead to persistent delusions.73

Addiction, Dependence, and Withdrawal:

While ketamine may not cause the same degree of physical dependence as opioids, psychological dependence is common, with users developing cravings and compulsive use patterns.73 Tolerance to ketamine's effects can build quickly, leading to dose escalation.73

* **Withdrawal Symptoms:** Upon cessation, users may experience primarily psychological withdrawal symptoms, including anxiety, depression, intense cravings, agitation, confusion, psychosis (delusions, hallucinations), fatigue, insomnia, and shakes. Physical symptoms like nausea, rapid heart rate, and rapid breathing can also occur. A particularly severe, though rare, symptom is excitotoxicity, which involves nerve cell damage due to overexposure to neurotransmitters.76 Withdrawal symptoms typically begin 24-72 hours after the last dose and can last from days to weeks.76

Overdose Risks:

Ketamine overdose can occur, especially with high doses or when combined with other substances like alcohol or depressants.73 Symptoms of overdose include severe confusion, unconsciousness, dangerously slowed breathing (respiratory depression), irregular heartbeat, chest pain, high blood pressure, vomiting, and convulsions or hallucinations.73 While rarely fatal on its own, overdose can lead to life-threatening situations, particularly due to respiratory depression or accidents occurring while intoxicated.73 There is no specific antidote for ketamine overdose; treatment is supportive.

### **2.4 Depressants (Illicit/Non-Medical Use)**

Central nervous system (CNS) depressants are substances that slow down brain activity. This action can produce effects such as drowsiness, relaxation, decreased inhibition, and anesthesia. While many depressants have legitimate medical uses (e.g., for anxiety, insomnia, seizures), they are also commonly misused for their intoxicating effects. This section focuses on the illicit or non-medical use of barbiturates and benzodiazepines.

General Risks:

The primary risks associated with depressant misuse include profound sedation, impaired coordination and judgment, memory problems, and, critically, respiratory depression, which can lead to coma and death, especially when taken in high doses or combined with other depressants like alcohol or opioids.78 These substances carry a high potential for physical and psychological dependence, and abrupt withdrawal after prolonged use can be severe and even life-threatening, often requiring medical supervision.27

A significant and growing concern in the illicit depressant market is the presence of counterfeit pills and adulteration with highly potent substances. Pills sold as common benzodiazepines like Xanax® or Valium® may actually contain novel designer benzodiazepines, which can be far more potent and unpredictable, or even fentanyl.12 This dramatically increases the risk of accidental overdose for individuals seeking these drugs on the illicit market, as they are often unaware of the true chemical composition and dosage of what they are consuming. This underscores the danger that the user may not only be taking a different substance than intended but also one for which standard overdose reversal agents (like naloxone for opioids) may be ineffective or only partially effective if multiple depressants are involved.

#### **2.4.1 Barbiturates**

Barbiturates are a class of sedative-hypnotic drugs derived from barbituric acid. They were widely prescribed in the past for anxiety, insomnia, and seizure disorders but have largely been replaced by benzodiazepines due to their higher risk of overdose and dependence.79

Forms and Street Names:

Barbiturates are typically available as pills or capsules for oral use, or in liquid form for injection.79 Prescribed names include Fiorinal® (often contains butalbital), Pentothal® (thiopental, an anesthetic), Seconal® (secobarbital), and Nembutal® (pentobarbital).79 Common street names include "Barbs," "Block Busters," "Christmas Trees," "Goof Balls," "Pinks," "Red Devils," "Reds & Blues," and "Yellow Jackets".35

Methods of Use:

When misused, barbiturates are typically swallowed as pills or, less commonly, the liquid form is injected.79 They are often abused to reduce anxiety, decrease inhibitions, or counteract the effects of stimulant drugs.79

Mechanism of Action:

Barbiturates are CNS depressants that enhance the action of gamma-aminobutyric acid (GABA), the primary inhibitory neurotransmitter in the brain.83 By increasing GABA's effects, they reduce neuronal excitability, leading to sedation, hypnosis, and anticonvulsant activity.

Acute Effects:

The effects of barbiturates are dose-dependent:

* **Desired/Mild Effects (Lower Doses):** Mild euphoria, relaxation, reduced anxiety, disinhibition, and drowsiness.79
* **Adverse Effects (Higher Doses or Misuse):** Impaired memory, judgment, and coordination; slurred speech; confusion; irritability; paranoia; and suicidal ideation.79

Long-Term Health Consequences:

Chronic misuse of barbiturates can lead to significant and severe health problems:

* **Physical:** Chronic fatigue, gastrointestinal disturbances, weakened immune function, and respiratory problems due to chronic CNS depression.83
* **Neurological:** Persistent cognitive impairment, including difficulties with memory (especially short-term), learning, concentration, reasoning, and decision-making. Slurred speech and impaired motor coordination may also become chronic.83
* **Mental:** Emotional instability, mood swings, increased irritability, depression, and exacerbation of underlying mental health conditions.83

Addiction, Dependence, and Withdrawal:

Barbiturates have a very high potential for both physical and psychological dependence, developing even with therapeutic use if prolonged.79 Tolerance develops rapidly, requiring users to take increasingly higher doses to achieve the desired effects, which significantly increases the risk of overdose.83

* **Withdrawal Symptoms:** Abrupt cessation or significant reduction in dosage after dependence has formed can trigger a severe and potentially life-threatening withdrawal syndrome. Symptoms include anxiety, restlessness, insomnia, tremors, muscle twitching, nausea, vomiting, abdominal cramps, increased heart rate, sweating, agitation, confusion, hallucinations, and grand mal seizures.79 Barbiturate withdrawal requires careful medical management, often involving a gradual tapering of the dose.

Overdose Risks and Emergency Interventions:

Barbiturate overdose is extremely dangerous due to their narrow therapeutic index (small difference between a therapeutic dose and a toxic dose).83 Overdose leads to profound CNS depression, resulting in severely decreased respiration, slowed heart rate, dangerously low blood pressure, decreased body temperature, loss of consciousness, coma, and potentially death.79 The risk of fatal overdose is dramatically increased when barbiturates are combined with other CNS depressants, such as alcohol or opioids.83 There is no specific antidote for barbiturate overdose; treatment is supportive and aimed at maintaining vital functions.

#### **2.4.2 Benzodiazepines (Illicit/Non-Medical Use of Xanax®, Valium®, etc.)**

Benzodiazepines are a class of psychoactive drugs widely prescribed for anxiety, insomnia, seizures, muscle spasms, and alcohol withdrawal.27 Common examples include diazepam (Valium®), alprazolam (Xanax®), lorazepam (Ativan®), and clonazepam (Klonopin®).27 While medically useful, they are frequently misused for their sedative and euphoric effects.

Forms and Street Names:

Benzodiazepines are typically manufactured as tablets or capsules for oral use.27 Some are available in injectable forms or syrups.27 Common street names include "Benzos," "Downers," "Nerve Pills," "Tranks," and often brand names like "Xanax" or "Valium" are used illicitly.27

Methods of Use:

The most common route of illicit use is oral ingestion of tablets or capsules.78 Some users may crush tablets to snort the powder for a faster onset of effects.78 Injection is less common but occurs. Misuse often involves taking higher doses than prescribed, using them without a prescription, or combining them with other substances, particularly opioids or alcohol, to enhance euphoria or modulate other drug effects.27

Mechanism of Action:

Benzodiazepines are CNS depressants that enhance the effect of the neurotransmitter gamma-aminobutyric acid (GABA) at GABA-A receptors in the brain.27 GABA is the primary inhibitory neurotransmitter, and by increasing its effects, benzodiazepines reduce neuronal excitability, leading to their sedative, anxiolytic (anti-anxiety), muscle-relaxant, and anticonvulsant properties.81

**Acute Effects:**

* **Desired Effects:** Feelings of calm, relaxation, sedation, reduced anxiety, and mild euphoria.27
* **Adverse Physical Effects:** Drowsiness, dizziness, slurred speech, impaired coordination (ataxia), muscle weakness, and decreased reflexes.27
* **Adverse Cognitive/Psychological Effects:** Confusion, memory impairment (anterograde amnesia), impaired judgment, difficulty concentrating, restlessness, delirium, vivid or disturbing dreams. Paradoxical effects like hostility, irritability, aggression, and paranoia can also occur, especially with high doses or when combined with alcohol.27

Long-Term Health Consequences:

Chronic misuse of benzodiazepines can lead to various long-term problems:

* **Physical:** Persistent fatigue, gastrointestinal disturbances, and potentially a weakened immune system.80
* **Neurological:** Significant cognitive decline, particularly affecting short-term memory, attention, and processing speed. These impairments can sometimes persist even after discontinuation.80
* **Mental:** Increased risk or worsening of anxiety and depression, emotional blunting or instability, and personality changes. Prolonged use can exacerbate underlying mental health disorders.80

Addiction, Dependence, and Withdrawal:

Benzodiazepines have a high potential for physical and psychological dependence, which can develop even within a few weeks of regular use, including therapeutic use.27 Tolerance to the sedative and euphoric effects occurs, often leading to dose escalation.27

* **Withdrawal Symptoms:** Abrupt cessation or rapid dose reduction after prolonged use can trigger a severe and potentially life-threatening withdrawal syndrome. Symptoms include rebound anxiety, insomnia, irritability, agitation, tremors, sweating, muscle pain and stiffness, palpitations, headache, perceptual disturbances (e.g., hypersensitivity to light and sound), dysphoria, nausea, vomiting, and in severe cases, hallucinations, delirium, and seizures.27 Benzodiazepine withdrawal should be medically supervised, often involving a gradual tapering schedule.

Overdose Risks and Emergency Interventions:

Benzodiazepine overdose is a serious concern, especially when taken in large quantities or combined with other CNS depressants like alcohol or opioids.27 Symptoms of overdose include extreme drowsiness, confusion, impaired coordination, significantly decreased reflexes, slurred speech, respiratory depression, hypotension, coma, and potentially death.78 The co-ingestion of benzodiazepines and opioids is a major contributor to fatal drug overdoses, as the combination synergistically depresses respiration.15 Flumazenil is a benzodiazepine receptor antagonist that can be used in hospital settings to reverse the sedative effects of benzodiazepine overdose, but its use is complex and requires careful medical assessment due to risks like precipitating seizures in dependent individuals.27

The emergence of novel designer benzodiazepines (covered in the NPS section) in the illicit drug supply, often sold as counterfeit versions of pharmaceutical benzodiazepines or as adulterants in other drugs, has further increased these risks due to their often higher potency and unknown pharmacological profiles.12

### **2.5 Cannabis and Concentrates (Illicit/High-Potency Context)**

Cannabis, derived from the *Cannabis sativa* or *Cannabis indica* plants, is one of the most widely used psychoactive substances globally.18 While its legal status varies significantly across jurisdictions, this section focuses on the risks associated with high-potency cannabis products, illicit market concerns, and emerging consumption trends like dabbing, which align with the user's query about "new trending things." The primary psychoactive compound in cannabis is delta-9-tetrahydrocannabinol (THC).17

Forms and Street Names:

Cannabis is available in various forms:

* **Dried plant material (marijuana):** Consists of dried leaves, flowers, stems, and seeds. Street names include "weed," "pot," "bud," "grass," "herb".16
* **Hashish:** A concentrated resin derived from the plant.17
* **Cannabis Concentrates:** Highly potent extracts with significantly elevated THC levels. These include oils, "wax" (a soft, opaque substance), "shatter" (a brittle, glass-like substance), Butane Hash Oil (BHO), and "live resin" (extracted from fresh, frozen plants to preserve terpenes).88 Potency of concentrates can range from 50% to over 90% THC, compared to traditional marijuana flower which, while increasing in potency, typically ranges from less than 5% historically to around 20% or higher in current regulated markets.92

**Methods of Use:**

* **Smoking:** Marijuana is commonly smoked in hand-rolled cigarettes ("joints"), cigars refilled with cannabis ("blunts"), or in pipes or water pipes ("bongs").18 Hashish can also be smoked.
* **Vaping:** Cannabis oils or dried flower can be vaporized using electronic devices (vape pens, vaporizers).96
* **Dabbing:** This method involves vaporizing and inhaling highly concentrated cannabis extracts (dabs) using a specialized apparatus (dab rig) or vape pen. Dabbing allows for the rapid delivery of very high doses of THC.96
* **Edibles:** Cannabis can be infused into foods or drinks (e.g., cookies, brownies, candies, teas).18

Mechanism of Action:

THC and other cannabinoids exert their effects by interacting with the body's endocannabinoid system, primarily binding to cannabinoid receptors (CB1 and CB2).17 CB1 receptors are abundant in the brain and influence pleasure, memory, thinking, concentration, sensory and time perception, and coordination. CB2 receptors are more prevalent in the immune system. THC's psychoactive effects are largely mediated through its action on CB1 receptors.17

Acute Effects:

The acute effects of cannabis vary depending on the dose of THC, route of administration, individual factors (e.g., tolerance, genetics), and setting. Effects from smoking or vaping are typically felt within minutes, while edibles have a delayed onset (30 minutes to 2 hours or more) and can lead to more prolonged and sometimes unexpectedly intense effects.17

* **Desired Psychoactive Effects:** Euphoria, relaxation, altered sensory perception (e.g., brighter colors, enhanced taste), increased appetite ("munchies"), and increased talkativeness or giggling.17
* **Adverse Physical Effects:** Increased heart rate (tachycardia), dry mouth, red eyes, impaired coordination and balance, dizziness.101
* **Adverse Cognitive/Psychological Effects:** Impaired short-term memory, attention, and concentration; difficulty with problem-solving and decision-making; altered perception of time.101 High doses or high-potency products, particularly concentrates used in dabbing, can induce more severe adverse effects, including anxiety, fear, panic attacks, paranoia, and acute psychosis (hallucinations, delusions).101

Long-Term Health Consequences:

Regular, long-term cannabis use, especially starting in adolescence and involving high-potency products, is associated with a range of health risks:

* **Physical:**
  + *Respiratory System:* Chronic smoking of cannabis is linked to airway inflammation, chronic bronchitis, cough, and phlegm production, similar to tobacco smoke as it contains many of the same toxins and carcinogens.96 Dabbing may also pose respiratory risks due to high temperatures and potential inhalation of contaminants or byproducts like methacrolein and benzene.106
  + *Cardiovascular System:* Cannabis use can acutely increase heart rate and blood pressure. Some research suggests a long-term increased risk of heart attack and stroke, though more research is needed to fully understand this link.16
  + *Cannabinoid Hyperemesis Syndrome (CHS):* A condition characterized by recurrent nausea, vomiting, and abdominal pain in long-term, heavy cannabis users.16
* **Neurological and Cognitive:**
  + *Adolescent Brain Development:* The adolescent brain is particularly vulnerable to the effects of THC. Early and regular use can disrupt brain development, potentially leading to lasting impairments in cognitive functions such as memory, learning, attention, processing speed, and executive functions (e.g., decision-making, impulse control).16 Some studies suggest a potential for permanent IQ loss with early, heavy use.18
  + *Lasting Brain Changes:* Chronic THC exposure may lead to alterations in brain structure and function, including changes in cannabinoid receptor density and connectivity in brain regions critical for cognition and emotional regulation.112
* **Mental Health:**
  + *Cannabis Use Disorder (CUD):* See addiction/dependence section below.
  + *Psychotic Disorders:* Cannabis use, particularly high-potency cannabis and early-onset use, is associated with an increased risk of developing psychotic disorders like schizophrenia, especially in vulnerable individuals.16 It can also worsen the course of existing psychotic illnesses.100
  + *Depression and Anxiety:* Studies have linked cannabis use to an increased risk of depression, anxiety disorders, and suicidal ideation and behavior, particularly with heavy or early use.16 However, the causal relationship is complex and may involve self-medication of pre-existing symptoms.128

Addiction/Dependence Potential (Cannabis Use Disorder - CUD):

Cannabis use can lead to the development of Cannabis Use Disorder (CUD), a medical condition characterized by the inability to stop using cannabis despite it causing health and social problems.19

* **Prevalence:** Approximately 3 in 10 people who use cannabis may have CUD.20 The risk is higher for those who start using cannabis during youth or adolescence and who use it frequently.17
* **Influence of Potency:** Higher THC concentrations are associated with a greater likelihood of cannabis use progressing to CUD.16 The increasing availability of high-potency concentrates used in dabbing is a significant concern in this regard.91
* **Diagnostic Criteria (DSM-5 for SUD, adaptable for CUD):** Includes impaired control (using more/longer than intended, inability to cut down, cravings), social impairment (failure to fulfill obligations, continued use despite social problems), risky use (use in hazardous situations), and pharmacological criteria (tolerance, withdrawal).130

Withdrawal Symptoms:

When individuals with CUD stop or reduce cannabis use, they may experience withdrawal symptoms, including:

* Irritability, anger, or aggression
* Anxiety or nervousness
* Sleep difficulties (insomnia, disturbing dreams)
* Decreased appetite or weight loss
* Restlessness
* Depressed mood
* Physical discomfort such as abdominal pain, shakiness/tremors, sweating, fever, or chills
* Headache
* Intense cravings for cannabis .17 Symptoms typically peak within the first week of cessation and can last up to two weeks.17

Overdose Risks:

A fatal overdose solely from cannabis is highly unlikely.96 However, consuming high doses of THC, especially via edibles (due to delayed onset leading to overconsumption) or high-potency concentrates like dabs, can lead to severe acute adverse reactions, sometimes referred to as "greening out" or cannabis poisoning.96 Symptoms can include:

* Extreme confusion, anxiety, panic, and paranoia
* Delusions or hallucinations
* Rapid heart rate and increased blood pressure
* Severe nausea and vomiting These effects can lead to unintentional injuries, such as falls or motor vehicle crashes if driving while impaired.20

Contaminants in Cannabis Concentrates:

A significant emerging risk, particularly with dabbing, is exposure to contaminants from the illicit production of cannabis concentrates. These can include:

* **Residual Solvents:** Solvents like butane, propane, or ethanol used in extraction processes may not be fully purged, and their inhalation can be harmful. Butane inhalation, for example, can cause organ damage.102 The manufacturing process itself, especially amateur BHO extraction, carries risks of fires and explosions.135
* **Pesticides:** Cannabis plants can accumulate pesticides from cultivation. When concentrated, these pesticide residues can also become concentrated. Some pesticides, like myclobutanil, can release toxic gases (e.g., hydrogen cyanide) when heated/combusted during dabbing or smoking, posing severe respiratory and systemic health risks.136
* **Heavy Metals:** Cannabis is a known hyperaccumulator of heavy metals (e.g., lead, cadmium, arsenic, mercury) from soil, water, or fertilizers. These metals can be present in the plant material and become concentrated in extracts. Inhalation of heavy metals is linked to cancer, neurological, renal, cardiovascular, and hepatic damage.108
* **Thermal Degradation Products:** Heating terpenes (aromatic compounds in cannabis) to high temperatures during dabbing can degrade them into harmful byproducts like methacrolein and benzene, which are pulmonary irritants and carcinogens.106

The trend towards high-THC cannabis products, especially concentrates for dabbing, amplifies many known cannabis-related risks and introduces new ones tied to contaminants and the intensity of THC exposure. This underscores the need for robust public health messaging that differentiates the risks of these products from lower-potency cannabis flower, further research into their long-term effects, and stringent regulatory oversight for legal cannabis markets concerning potency and contaminant testing.20

### **2.6 Inhalants**

Inhalants are a broad category of volatile substances found in common household, industrial, and medical products that produce chemical vapors. When inhaled, these vapors can induce psychoactive, or mind-altering, effects.145 Due to their easy accessibility, low cost, and ease of concealment, inhalants are often among the first substances abused by young adolescents.145

Categories and Forms:

Inhalants are generally grouped into four main categories:

* **Volatile Solvents:** Liquids that vaporize at room temperature. Examples include paint thinners and removers, degreasers, dry-cleaning fluids, gasoline, lighter fluid, and glues (e.g., model airplane glue, rubber cement).145
* **Aerosols:** Sprays that contain propellants and solvents. Examples include spray paints, deodorant and hair sprays, vegetable oil sprays for cooking, and fabric protector sprays.145
* **Gases:** Include medical anesthetics as well as gases used in household or commercial products. Examples include ether, chloroform, halothane, nitrous oxide ("laughing gas," found in whipped cream dispensers or "whippets," and used as an anesthetic), butane (from lighters), and propane (from tanks).145 Helium is also sometimes abused.
* **Nitrites:** A special class of inhalants that act primarily as vasodilators and are used mainly to enhance sexual experience rather than for their intoxicating effects. Amyl nitrite ("poppers") is a common example. While often grouped with other inhalants, their mechanism and primary effects differ.145

Street Names:

Common street names for inhalants in general include "Huff," "Rush," and "Whippets" (specifically for nitrous oxide canisters).146 Specific products may also be referred to by their brand names or contents.

Methods of Use:

Users inhale the chemical vapors directly from containers ("sniffing" or "snorting"), by spraying aerosols directly into the nose or mouth, or by placing an inhalant-soaked rag in the mouth ("huffing"). Another common method is "bagging," which involves sniffing or inhaling fumes from substances sprayed or deposited inside a plastic or paper bag held over the mouth and nose.145 Some volatile substances release intoxicating vapors when heated.145

Mechanism of Action:

Most inhalants (excluding nitrites) act as central nervous system depressants, slowing down brain activity.146 The chemicals are rapidly absorbed through the lungs into the bloodstream and quickly distributed to the brain and other organs.146 Their effects are often similar to those of alcohol or anesthetics, producing a rapid high.

Acute Effects:

The effects of inhalants are typically rapid in onset but short-lived, often lasting only a few minutes. This can lead users to inhale repeatedly over several hours to prolong the high, a particularly dangerous practice.146

* **Desired Effects (Initial):** Slight stimulation, euphoria, excitement, disinhibition, giddiness, and a feeling of light-headedness or a "head rush".145
* **Adverse Physical Effects:** Slurred speech, dizziness, drowsiness, lethargy, impaired coordination and motor control, muscle weakness, nausea, vomiting, headaches, wheezing, and loss of sensation (numbness).145
* **Adverse Cognitive/Psychological Effects:** Impaired judgment, confusion, disorientation, distorted perceptions of reality and spatial relations, delirium, agitation, and irritability.145 High doses can lead to loss of consciousness.146

Long-Term Health Consequences:

Chronic abuse of inhalants can cause severe and often irreversible damage to major organ systems:

* **Neurological:** Significant brain damage is a primary concern. This can include damage to the cerebral cortex (affecting personality, memory, learning) and the cerebellum (affecting balance and coordination).145 Specific solvents like toluene can damage the myelin sheath, the protective covering around nerve fibers, leading to conditions similar to multiple sclerosis. Cognitive impairments can range from mild attention and memory problems to severe dementia.146 Damage to the peripheral nervous system can result in numbness, tingling, and paralysis.145 Hearing loss due to damage to the acoustic nerve can also occur.145
* **Cardiovascular:** Chronic exposure can damage the heart muscle and lead to arrhythmias.145
* **Respiratory:** Repeated irritation of the airways can lead to chronic lung problems and impaired breathing.145
* **Hepatic (Liver):** Liver damage, including fatty liver, can result from the toxic effects of chemicals like toluene and trichloroethylene.145
* **Renal (Kidneys):** Kidney damage, including impaired ability to control blood acid levels and kidney stones, can occur.145
* **Hematological (Blood):** Some chemicals, like benzene (found in gasoline), can damage bone marrow and cause leukemia.145 Others can inhibit the oxygen-carrying capacity of the blood.145
* **Musculoskeletal:** Muscle wasting and reduced muscle tone and strength.145
* **Dermatological:** A characteristic "glue sniffer's rash" around the nose and mouth can occur.145
* **Mental Health:** Long-term use is strongly associated with personality disorders, mood disorders (including major depression), and anxiety disorders.146 Users often exhibit inattentiveness, irritability, and general apathy.146

Addiction, Dependence, and Withdrawal:

While not all inhalants are considered highly addictive in the same way as opioids or stimulants, many users report a strong need or compulsion to continue using them, particularly after prolonged periods.146 Tolerance can develop, requiring more of the substance to achieve the desired effects.130

* **Withdrawal Symptoms:** After cessation of regular, heavy use, a withdrawal syndrome can occur within hours to a few days. Symptoms include irritability, anxiety, drug cravings, sweating, rapid pulse, hand tremors, insomnia, nausea, vomiting, physical agitation, and, in severe cases, hallucinations and grand mal seizures.130

Overdose Risks and Emergency Interventions:

Inhalant overdose is a serious medical emergency and can be fatal, even from a single session of use.

* **Sudden Sniffing Death (SSD) Syndrome:** This is a primary cause of death from inhalant abuse, resulting from cardiac arrhythmia (irregular heartbeat) leading to heart failure. It can occur within minutes of inhalation, especially if the user is startled or engages in sudden physical activity after inhaling, which can trigger an adrenaline surge.145 SSD is particularly associated with butane, propane, and aerosol propellants.
* **Asphyxiation/Suffocation:** Death can occur from displacement of oxygen in the lungs by high concentrations of inhaled fumes, or by suffocation if inhaling from a plastic bag placed over the head.146
* **Choking:** Users may choke on vomit after inhaling substances.146
* **Other Risks:** Seizures, coma, and accidents due to impaired judgment and coordination.145 Emergency intervention involves removing the person from the source of fumes, ensuring an open airway, providing oxygen if available, and seeking immediate medical attention (e.g., calling emergency services).

The widespread availability and low cost of many inhalable products make them a persistent threat, especially to young adolescents who may be unaware of their severe and often irreversible health consequences. The profound neurological damage, including cognitive decline and potential for addiction, underscores the critical importance of targeted prevention programs and public awareness campaigns for this vulnerable age group. The difficulty in restricting access to these everyday products means that education and community-based interventions are paramount.

## **3. Emerging Drug Trends and New Psychoactive Substances (NPS)**

The illicit drug landscape is characterized by its dynamic nature, with continuous evolution in the types of substances available, methods of their production and distribution, and patterns of use. A dominant feature of this evolution is the proliferation of New Psychoactive Substances (NPS) and the increasing adulteration of traditional illicit drugs with highly potent synthetic compounds.

### **The NPS Phenomenon: An Overview**

New Psychoactive Substances (NPS) are defined by the United Nations Office on Drugs and Crime (UNODC) as "substances of abuse, either in a pure form or a preparation, that are not controlled by the 1961 Single Convention on Narcotic Drugs or the 1971 Convention on Psychotropic Substances, but which may pose a public health threat".9 The term "new" does not necessarily imply a novel chemical invention but rather indicates substances that have recently become available or prominent on the illicit market.9 These substances are often marketed under misleading names such as "legal highs," "designer drugs," "research chemicals," "herbal incense," or "bath salts" in an attempt to circumvent existing drug control laws and appeal to users seeking alternatives to controlled substances.9

The rapid emergence and chemical diversity of NPS present significant challenges to public health, law enforcement, and regulatory agencies worldwide.8 Many NPS have limited or no established pharmacological or toxicological profiles in humans, meaning their acute and long-term health effects are often unknown or unpredictable.9 This lack of information complicates prevention efforts, clinical management of intoxication and overdose, and the development of effective treatment strategies. The UNODC and the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) are key international bodies that monitor NPS trends, with the EMCDDA tracking over 950 NPS by the end of 2023, 26 of which were first reported in Europe that year.9 This constant evolution reflects a "cat-and-mouse game" where clandestine chemists modify molecular structures to create new compounds that are not yet legally controlled, thereby staying one step ahead of legislation. This dynamic creates a persistent threat, as new, untested, and potentially highly dangerous substances can quickly penetrate the illicit market, often with users being unaware of the true nature or potency of the products they consume.

The following table provides a high-level overview of major NPS categories and their general associated risks.

**Table 2: Major NPS Categories and General Risks**

| **NPS Category** | **Common Examples/Sub-types** | **General Desired Effects** | **Key Associated Risks/Harms** |
| --- | --- | --- | --- |
| **Synthetic Cannabinoids** | Spice, K2, JWH-018, AM-2201, MDMB-4en-PINACA, ADB-BUTINACA | Mimic THC effects (euphoria, relaxation, altered perception) | Severe anxiety, paranoia, psychosis, hallucinations, agitation, tachycardia, seizures, kidney damage, addiction, death. Effects often stronger/unpredictable than cannabis. |
| **Synthetic Cathinones** | Mephedrone (Meow Meow), MDPV, Methylone, Eutylone ("Bath Salts") | Stimulant effects (euphoria, energy, alertness, empathy) | Agitation, paranoia, hallucinations, psychosis, aggression, violence, tachycardia, hypertension, hyperthermia, seizures, cardiac arrest, addiction, death. |
| **Novel Synthetic Opioids** | Fentanyl Analogues (Carfentanil, Acetylfentanyl), Nitazenes (Isotonitazene, Protonitazene) | Opioid effects (euphoria, pain relief, sedation) | Extreme potency, high risk of rapid respiratory depression, overdose, and death, even in minute amounts. Rapid tolerance and dependence. |
| **Novel Benzodiazepines** | Etizolam, Flualprazolam, Clonazolam, Bromazolam ("Designer Benzos") | Anxiolytic, sedative, muscle relaxant effects | CNS depression, loss of motor coordination, respiratory depression (especially with opioids), memory loss, blackouts, dependence, severe withdrawal. Potency often unknown. |
| **Phenethylamines** | 2C-series (2C-B, 2C-I), NBOMes (25I-NBOMe) | Hallucinogenic, stimulant, empathogenic effects | Intense hallucinations, anxiety, paranoia, agitation, tachycardia, hypertension, seizures, hyperthermia, cardiovascular complications, neurotoxicity, death (especially NBOMes). |
| **Piperazines** | BZP (Benzylpiperazine), mCPP, TFMPP ("Party Pills") | Stimulant, entactogenic effects (mimicking MDMA) | Tachycardia, hypertension, anxiety, insomnia, seizures, serotonin syndrome (mCPP). Risks increased with polydrug use. |
| **Tryptamines (Synthetic)** | AMT (Alpha-methyltryptamine), 5-MeO-DIPT ("Foxy Methoxy") | Hallucinogenic effects | Hallucinations, psychosis, visual/auditory distortions, nausea, emotional distress, cardiovascular effects, potential for neurotoxicity with chronic use. |
| **Plant-Based NPS** | Kratom, Salvia divinorum (though Salvia is often considered separately) | Stimulant/opioid-like (Kratom), dissociative/hallucinogenic (Salvia) | Kratom: dependence, withdrawal, liver toxicity, psychosis. Salvia: intense, short-lived dissociative/hallucinogenic effects, potential for dysphoria. |

### **3.1 Key NPS Categories**

#### **3.1.1 Synthetic Cannabinoids (e.g., Spice, K2)**

Synthetic cannabinoids (SCs) are a large and chemically diverse group of man-made substances designed to mimic the effects of THC, the main psychoactive component of cannabis.10 They are not derived from the cannabis plant itself but are sprayed onto dried plant material (often marketed as "herbal incense" or "potpourri") or sold as liquids for use in vaporizers or e-cigarettes.152 Common street names include "Spice," "K2," "Skunk," "Black Mamba," "Bonzai," and "Jamaika".152

**Mechanism of Action:** SCs bind to the same cannabinoid receptors (CB1 and CB2) in the brain and body as THC. However, many SCs are full agonists at these receptors and bind with much higher affinity and potency than THC (which is a partial agonist).153 This difference often results in more intense, unpredictable, and dangerous effects.

**Acute Effects:** While users may seek effects similar to cannabis, such as euphoria, relaxation, and altered perception, SCs frequently produce severe adverse reactions.10 These can include:

* **Psychological:** Extreme anxiety, paranoia, agitation, confusion, terrifying hallucinations, acute psychosis, and violent behavior.
* **Physical:** Tachycardia (rapid heart rate), hypertension (high blood pressure), chest pain, palpitations, seizures, tremors, vomiting, diaphoresis (profuse sweating), and loss of consciousness.
* **Other:** Numbness, tingling, and pallor.

**Long-Term Health Consequences and Risks:** The long-term effects of many SCs are not well understood due to their relatively recent emergence and constantly changing chemical structures. However, reported consequences include:

* **Addiction and Dependence:** Regular use can lead to dependence and a withdrawal syndrome characterized by headaches, anxiety, depression, and irritability.153
* **Cardiovascular problems:** Including heart attacks.
* **Kidney damage:** Acute kidney injury has been reported.
* **Severe psychiatric effects:** Persistent psychosis and worsening of underlying mental health conditions.
* **Deaths:** Fatalities have been linked to SC use, often due to cardiovascular events or accidents resulting from severe intoxication.153

A significant emerging trend is the adulteration of low-THC cannabis products (hemp) with SCs, and the appearance of SCs in edible products, which poses a high risk, particularly to unsuspecting users or young people.151 The marketing of these substances as "synthetic marijuana" or "legal highs" is dangerously misleading, as their effects and risk profiles are vastly different and often more severe than those of natural cannabis.152

#### **3.1.2 Synthetic Cathinones (e.g., "Bath Salts")**

Synthetic cathinones, commonly known as "bath salts," are a class of NPS that are chemically related to cathinone, a naturally occurring stimulant found in the khat plant.13 These substances are designed to mimic the effects of illicit stimulants like amphetamine, cocaine, and MDMA (ecstasy).35

**Forms and Street Names:** Synthetic cathinones are typically sold as white or brown crystalline powders, but can also be found as small chunky crystals, capsules, or, less commonly, tablets.148 They are often deceptively marketed as "bath salts," "plant food," "glass cleaner," or "research chemicals," and labeled "not for human consumption" to evade drug laws.35 Common street names include "Bliss," "Blue Silk," "Cloud Nine," "Drone," "Energy-1," "Ivory Wave," "Lunar Wave," "Meow Meow" (mephedrone), "Ocean Burst," "Pure Ivory," "Purple Wave," "Red Dove," "Snow Leopard," "Stardust," "Vanilla Sky," "White Dove," "White Knight," and "White Lightning".148 Examples of specific synthetic cathinones include mephedrone (4-MMC), methylone, MDPV (3,4-methylenedioxypyrovalerone), and eutylone.156

**Methods of Use:** The most common methods of use are insufflation (snorting the powder) and oral ingestion (swallowing pills or capsules).148 They can also be smoked or dissolved in a solution and injected.148 Effects are typically felt within minutes to 45 minutes, depending on the route, and usually last for 2-4 hours.157

**Mechanism of Action:** Synthetic cathinones act as central nervous system stimulants, primarily by increasing the levels of monoamine neurotransmitters such as dopamine, norepinephrine, and serotonin in the brain, similar to amphetamines.35 This leads to their characteristic stimulant and, for some, empathogenic effects.

**Acute Effects:** Users often seek synthetic cathinones for their purported euphoric and stimulant effects.148

* **Desired Effects:** Euphoria, increased energy and alertness, talkativeness, increased empathy or openness, and heightened libido.148
* **Adverse Physical Effects:** Rapid heartbeat (tachycardia), hypertension, hyperthermia (elevated body temperature), prolonged pupil dilation, muscle tension (especially jaw clenching), tremors, sweating, headaches, palpitations, chest pain, nausea, vomiting, skin rashes, and seizures.148
* **Adverse Psychological/Cognitive Effects:** Confusion, agitation, anxiety, panic attacks, paranoia, hallucinations (visual and auditory), delusions, aggression, combativeness, violent and self-destructive behavior, and acute psychosis.148 Users may also experience memory loss, blurred vision, and a distorted sense of time.157 A strong urge to re-dose is common.157

**Long-Term Health Consequences and Risks:** The long-term health effects of many synthetic cathinones are not well understood. However, chronic use is associated with:

* **Addiction and Dependence:** These substances have a high potential for abuse and dependence.156
* **Cardiovascular Complications:** Persistent tachycardia and hypertension can lead to serious heart problems.156
* **Neurological Damage:** Irreversible central nervous system damage has been reported.156
* **Psychiatric Disorders:** Chronic use can lead to or exacerbate anxiety, depression, paranoia, and psychosis.156
* **Overdose:** Overdoses can be severe and life-threatening, characterized by hyperthermia, seizures, cardiac arrest, and multi-organ failure. Deaths associated with synthetic cathinone use have been reported.148 Mixing with other drugs, such as opioids or other stimulants, significantly increases these risks.157

The EMCDDA monitors synthetic cathinones as the second largest category of NPS, highlighting their significant presence in the European drug market.158 There are indications of large-scale production and trafficking, with some substances becoming established in stimulant markets.155

#### **3.1.3 Novel Synthetic Opioids (Fentanyl Analogues, Nitazenes)**

This category of NPS is of extreme concern due to their exceptionally high potency and the severe risk of fatal overdose they pose. They are often found as adulterants in other illicit drugs, unbeknownst to the user.

##### **3.1.3.1 Fentanyl Analogues (NPS)**

Fentanyl analogues are synthetic opioids that are structurally similar to fentanyl but have been illicitly manufactured, often with minor chemical modifications to evade drug laws or, in some cases, to further increase potency.36 These are distinct from pharmaceutical fentanyl used legitimately in medicine.

**Forms and Names:** Illicit fentanyl analogues are typically found as powders (which can be white, off-white, or colored).36 They are frequently pressed into counterfeit pills designed to look like legitimate prescription opioids (e.g., oxycodone, alprazolam) or other street drugs.14 They can also be found on blotter paper or as liquids.36 Examples include carfentanil (one of the most potent opioids known, estimated to be 10,000 times more potent than morphine and intended for large animal tranquilization), acetylfentanyl, butyrfentanyl, furanylfentanyl, and ocfentanil.36 Street names often overlap with fentanyl itself (e.g., "China White," "Apache") or may be specific to the analogue if known, though users are often unaware they are consuming an analogue.161

**Methods of Use:** Similar to illicit fentanyl, analogues can be injected, snorted, smoked, or taken orally if pressed into pills.36

**Mechanism of Action:** Fentanyl analogues are potent agonists at mu-opioid receptors, the same receptors targeted by morphine, heroin, and fentanyl.36 Their effects are similar to other opioids but are often vastly magnified due to their extreme potency.

**Acute Effects and Risks:** The acute effects mirror those of fentanyl but are typically much more intense and carry a significantly higher risk profile.36

* **Desired effects:** Potent analgesia, euphoria, sedation.
* **Adverse effects:** Rapid and profound respiratory depression, extreme drowsiness, confusion, nausea, pupillary constriction, loss of consciousness, coma, and death. The primary danger lies in their extreme potency. Microgram quantities can be lethal, and illicitly produced batches often have inconsistent purity and dosage, making accidental overdose highly probable.160 Tolerance and physical dependence develop rapidly with repeated use.160

The extreme potency of many fentanyl analogues means that even minuscule variations in the purity or quantity within an illicitly produced batch can differentiate a psychoactive dose from a fatal one. This lack of precision in clandestine manufacturing makes these substances exceptionally dangerous components of the drug supply. Users face an extraordinarily high risk of accidental overdose, and even first responders handling these substances face potential exposure risks.160 The presence of these analogues in the drug supply necessitates enhanced naloxone availability and preparedness for potentially higher or multiple doses of naloxone to reverse overdoses.

**International Control:** The emergence of numerous fentanyl analogues has posed a significant challenge to international drug control efforts, as new variants are constantly being synthesized.160

##### **3.1.3.2 Nitazenes**

Nitazenes are a class of highly potent synthetic opioids, structurally distinct from fentanyl and its analogues, belonging to the 2-benzylbenzimidazole chemical group.163 They were first synthesized in the 1950s as potential analgesics but were never approved for medical use due to their unfavorable risk profile, including high overdose potential.164 They have re-emerged on the illicit drug market as NPS in recent years.

**Forms and Names:** Nitazenes are typically encountered as powders (white, brown, or yellow) or crystalline solids.164 They have been found in counterfeit tablets (e.g., mimicking oxycodone or benzodiazepines) and as adulterants in other drugs like heroin, ketamine, and synthetic cannabinoids.164 Street names may include "benzimidazole opioids" or "synthetic opioids," though users are often unaware they are consuming a nitazene.165 Specific examples include isotonitazene (the first to be widely identified in Europe in 2019), metonitazene, etonitazene, protonitazene, N-pyrrolidino protonitazene, desnitroclonitazene, and fluetonitazene.163

**Methods of Use:** Nitazenes can be injected, inhaled (snorted as powder), or swallowed (if in tablet form).165

**Mechanism of Action:** Nitazenes are potent mu-opioid receptor agonists, producing effects similar to other opioids like morphine and fentanyl.164

**Acute Effects and Risks:** The effects are characteristic of opioids but are often significantly more potent than fentanyl.163

* **Desired Effects:** Euphoria, pain relief, relaxation, drowsiness.
* **Adverse Physical Effects:** Slowed breathing (respiratory depression, often severe and rapid), slowed heart rate, miosis (pinpoint pupils), nausea, vomiting, constipation, itching, fever, sweating, clumsiness.164 Sudden-onset chest wall rigidity ("wooden chest") has been associated with some potent opioids and may increase mortality risk.164
* **Adverse Psychological/Cognitive Effects:** Decreased consciousness, confusion, anxiety, agitation, hallucinations, paranoia.164

**Long-Term Health Consequences and Risks:** While specific long-term data for nitazenes are limited due to their recent emergence, they are expected to carry similar risks to other potent opioids, including:

* **Addiction and Dependence:** High potential for tolerance and dependence.165
* **Organ Damage:** Potential damage to the lungs, brain (from hypoxia during non-fatal overdoses), and heart.165
* **Withdrawal:** Withdrawal symptoms are likely similar to other opioids (muscle aches, anxiety, insomnia, gastrointestinal distress, cravings) and may be severe.165 Reported effects during withdrawal include excessive sweating, restless legs, fever, dizziness, flu-like symptoms, blackouts, anxiety, and panic attacks.165

**Overdose Risks and Interventions:** Nitazenes pose an extremely high overdose risk due to their potency, which can be many times greater than fentanyl.163 Overdose is characterized by severe respiratory depression, leading to apnea, coma, convulsions, and death.164 Multiple or higher doses of naloxone may be required to reverse nitazene overdoses compared to fentanyl overdoses.164 Nitazenes have been linked to clusters of overdose events and a significant number of fatal toxicology cases.163 Their presence as adulterants in other drugs significantly increases the danger to unsuspecting users.

**Emerging Trends:** The UNODC reported the emergence of 26 different nitazenes by February 2025, identified in 30 countries, with a sharp increase in toxicology cases, predominantly post-mortem.163 This rapid diversification and spread highlight a growing public health threat requiring enhanced surveillance and response capabilities.163

#### **3.1.4 Novel Benzodiazepines ("Designer Benzos")**

Novel benzodiazepines (often called "designer benzodiazepines" or "street benzos") are NPS that are structurally similar to medically prescribed benzodiazepines like diazepam (Valium®) or alprazolam (Xanax®) but are not approved for medical use and are often illicitly synthesized.12 They are a significant concern due to their unknown potency, purity, and potential for severe adverse effects, especially when mixed with other substances like opioids.

**Forms and Names:** These substances are typically found as powders, which can be pressed into tablets or sold in capsules, often mimicking the appearance of legitimate pharmaceutical benzodiazepines.27 They may be marketed online as "research chemicals" or "legal benzodiazepines".27 Examples of novel benzodiazepines that have emerged include etizolam, flualprazolam, clonazolam, flubromazolam, diclazepam, and bromazolam.12

**Methods of Use:** The primary route of administration is oral (tablets or capsules).27 Powders could potentially be snorted or injected, though this is less commonly documented for this specific NPS class compared to stimulants or opioids.

**Mechanism of Action:** Like pharmaceutical benzodiazepines, novel benzodiazepines are CNS depressants that enhance the effects of the inhibitory neurotransmitter GABA at GABA-A receptors.27 This action leads to reduced neuronal excitability, producing sedative, anxiolytic, and muscle-relaxant effects. However, the specific binding affinities and potencies of many novel benzodiazepines are not well characterized, leading to unpredictable effects.

**Acute Effects and Risks:**

* \*\*Desired Effects (similar to prescribed benzodiazepines):

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