

## Clinical Update: December 2021

### Novel Psychoactive Substances Added to Oral Fluid Testing Menu

Aegis' oral fluid testing menu has been expanded to allow providers the option to test for over 90 novel psychoactive substances (NPS), an option previously available only in the urine testing menu. The new additions to the test menu include designer opioids, designer benzodiazepines, synthetic cannabinoids, synthetic stimulants, and hallucinogens/dissociatives, along with xylazine, tianeptine and phenibut. Providers may order tests for each class individually, based solely on their judgement and medical necessity. A brief, introductory discussion of the NPS drug classes is provided below.

#### Designer Opioids

Designer opioids play a role in overdose deaths, with the most commonly observed drug being illicitly manufactured fentanyl (IMF). IMF is analytically similar to prescription fentanyl, but is typically created utilizing different methods, which introduces opportunities for contamination or adulteration. Additionally, fentanyl analogs (fentalogs) have been introduced into the illicit drug supply over the last decade, which may be more or less potent than IMF. Currently, para-Fluorofentanyl is the fentalog most detected via multiple surveillance sources. While IMF and fentalogs have been most prevalent, newer classes of designer opioids are emerging in the global illicit drug supply. One class is nitazenes, of which isotonitazene is the most detected. A recent report from the Washington Post described isotonitazene and protonitazene detection in the District of Columbia drug supply.<sup>1</sup> Aegis has detected nitazenes, including isotonitazene, in patient urine samples from 10 states and fentalogs in 28 states.

#### Designer Benzodiazepines

The first "designer" benzodiazepines widely reported were phenazepam and etizolam, which are/have been legally marketed by pharmaceutical companies in some countries. As countries began to regulate and schedule phenazepam and etizolam as controlled substances, clandestine laboratories began producing and distributing newer designer benzodiazepines such as diclazepam, flubromazepam, pyrazolam, clonazolam, deschloroetizolam, flubromazolam, nifoxipam and meclonazepam; others have continued to emerge. As with the designer opioids, the potency of designer benzodiazepines relative to prescription benzodiazepines is largely unknown and the true contents are unknown to the ultimate user. To date, Aegis has detected designer benzodiazepines in patient urine samples from 34 states.

#### Synthetic Cannabinoids

Synthetic cannabinoid receptor agonists (SCRAs) are structurally related to marijuana but may have very different effects. When SCRAs first appeared in the early 2000s, they were sold as legal replacements for cannabis. Since then, they have gained a reputation for having powerful intoxicating effects. Typically, the synthetic material is sprayed onto herbal plant material and smoked. The ingredients and strength of products containing SCRAs are essentially impossible for the user to know. In the spring of 2018, >470 cases of hypocoagulopathy and bleeding were associated with synthetic cannabinoids that were found to be laced with brodifacoum, a very long-acting anticoagulant commonly used in rat poison. It was thought that the anticoagulant may extend the duration of the drug euphoria or "high." There were at least eight fatalities.<sup>2,3</sup> The most common synthetic cannabinoid detected to date at Aegis is MDMB-4enPINACA, which has been identified in patient urine samples from 24 states.

#### Synthetic Stimulants

The most detected class of synthetic stimulants is the synthetic cathinones. They are derivatives of the naturally-occurring compound cathinone, which is the primary psychoactive component of khat. They are "euphoric stimulants," meaning they have a short acting duration of physical and psychological effects similar to stimulants like amphetamine. The top reasons users choose synthetic cathinones include availability, affordability, and avoidance of legal ramifications. They are often sold as replacements when MDMA, cocaine, heroin, amphetamine, or other stimulants are in short supply.<sup>4</sup> Stimulants can cause an elevated mood, increased energy and alertness, and sociability. Adverse effects can include agitation, combative violent behavior, tachycardia and hypertension, hallucinations, paranoia, confusion, vomiting, hyperthermia, seizures, and death.<sup>5</sup> Eutylone is the most prevalent cathinone in circulation today according to most sources. In addition to the cathinones, new classes of stimulants have been introduced to the illicit market. For instance, Aegis has detected fluorinated analogs of methamphetamine in patient urine samples.

## Other NPS Classes

In addition to the classes mentioned above, Aegis is pleased to offer testing for NPS hallucinogens and dissociatives, which are designed to mimic numerous traditional substances such as LSD, PCP, or ketamine, to name a few. Use of these NPS analogs likely goes undetected with traditional testing. Other testing is available for xylazine, phenibut, and tianeptine. Xylazine is approved as a veterinary tranquilizer and is often identified in overdose death cases along with heroin or fentanyl. Aegis has identified xylazine in patient urine samples from 10 states. Phenibut is available as an over-the-counter supplement in the U.S. and is used for its benzodiazepine-like effects. Tianeptine is structurally an antidepressant, sold over-the-counter in the U.S. as a supplement, but has abuse potential due to its effects at pain receptors. At Aegis, phenibut has been identified in patient urine samples from nine states and tianeptine from three states.

Aegis' NPS offerings are developed to allow providers the ability to identify potentially problematic substance use and afford them the opportunity to provide more informed care and minimize the potential for these unregulated substances to contribute to adverse events, including overdose deaths. This timely testing expansion will increase the utility of oral fluid as an alternative to urine by allowing testing for NPS, which goes undetected in traditional definitive testing.

**NOTICE:** The information above is intended as a resource for health care providers. Providers should use their independent medical judgment based on the clinical needs of the patient when making determinations of who to test, what medications to test, testing frequency, and the type of testing to conduct.

## References:

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2. CDC COCA Clinical Action: Outbreak Alert Update: Potential life-threatening vitamin K-dependent antagonist coagulopathy associated with synthetic cannabinoids use. 23 April 2018. <https://emergency.cdc.gov/newsletters/coca/042318.html>.
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