**Purpose**: This report provides new information regarding comprehensive drug testing of clinical biological specimens collected after suspected opioid overdoses in various cities across the United States.

**Overview**: Drug use can lead to adverse events and overdose scenarios where individuals present to emergency departments for clinical evaluation and/or treatment. The culprit can be traditional drugs (e.g., heroin, fentanyl, cocaine, methamphetamine) or novel psychoactive substances (NPS); however, proper drug testing methodologies must be employed for accurate identification and characterization. Street-level drug preparations can contain undeclared or unwanted substances, such as toxic adulterants or NPS, which can potentiate effects or lead to adverse reactions. Understanding emerging drug trends and drug testing results can help direct new or revised approaches to clinical treatment and harm reduction efforts.

**Objective**: A partnership between the American College of Medical Toxicology (ACMT) and the Center for Forensic Science Research and Education (CFSRE) was established to comprehensively assess the role and prevalence of synthetic opioids and other drugs among suspected overdose events in the United States.

**Sample Source**: Patients presented to emergency departments within ACMT’s Toxicology Investigators Consortium (ToxIC) experiencing a suspected opioid overdose. Residual, discarded biological samples were obtained for testing against an expansive library of drugs and other substances. Our findings provide a near real-time assessment of the drug market and allude to resulting implications on clinical institutions.

**Testing**: Analysis was performed via liquid chromatography quadrupole time-of-flight mass spectrometry (LC-QTOF-MS). The scope of testing targeted more than 900 drugs, including a vast majority of NPS and metabolites. Drug classes included opioids, stimulants, cannabinoids, and benzodiazepines, among others.

**Key Findings**:

**Location: Los Angeles, CA**
- 100% of samples were positive for at least one opioid
- Fentanyl (100%) was the only opioid detected
- Combined opioid and stimulant use was observed (50%)
- Lidocaine was identified as an adulterant alongside fentanyl (cocaine not present)
- NPS: para-Fluorofentanyl, Etizolam, and Bromazolam

**Location: Pittsburgh, PA**
- 74% of samples were positive for at least one opioid
- Methadone (41%) was commonly detected, followed by fentanyl (33%) and oxycodone (15%)
- Combined opioid and stimulant use was observed (48%)
- Combined opioid and benzodiazepine use was observed (44%)
- No single adulterant was dominant
- NPS: Clonazolam, Etizolam, and MDMB-4en-PINACA

**Summary**:
- Geographical differences were observed, including within state (PA)
- Fentanyl was the most commonly detected opioid nationally (73%)
- Combined opioid and stimulant use was common nationally (59%)
- Several NPS were detected (including benzodiazepines & hallucinogens)

**Location: Bethlehem, PA**
- 100% of samples were positive for at least one opioid
- Fentanyl (94%) was very commonly detected, followed by para-fluorofentanyl (14%), tramadol (12%), and heroin (8%)
- Xylazine was observed alongside fentanyl (20%)
- Combined opioid and stimulant use was common (66%)
- NPS: Clonazolam, 4-MeO-PCP, 3-HO-PCP, para-Fluorofentanyl

**Comparison to Key Findings in Q1 2021**:
- Fentanyl remains the most commonly encountered synthetic opioid in eastern Pennsylvania
- The prevalence of para-fluorofentanyl is increasing
- Opioid and stimulant co-occurrence remained common and increased from 50% to 66%
- Xylazine remained a primary adulterant of fentanyl
- NPS continue to appear within this geographical region and population subset