## K64 Case Report of a Death Involving the Designer Opioid MT-45 Raises the Spectre of Synthetic Opioids in Forensic Casework

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After attending this presentation, attendees will understand the increasing relevance of synthetic opiates in forensic toxicology and death investigation casework and learn about the use of Liquid Chromatography/Tandem Mass Spectrometry (LC/MS/MS) for the detection and quantification of the synthetic opioid "MT-45."

This presentation will impact the forensic science community by introducing the first known case of death due to use of the designer synthetic opioid MT-45, as well as by placing the toxicology results in the context of the autopsy findings, and by explaining the detection and quantification methods used.

Opiates always figure prominently among the most frequently encountered drugs in toxic deaths. Interpretation is often complex due to issues including therapeutic misadventure, tolerance, palliative care, drug-drug interactions, and recreational versus medical use. While the most frequently encountered opioids are morphine (as a therapeutic agent or heroin metabolite), oxycodone, hydromorphone, hydrocodone, and fentanyl, recently illicit "designer opioids" have begun to appear in forensic casework. These include deaths attributed to acetyl fentanyl, a synthetic analog of fentanyl which resulted in a series of deaths in Rhode Island, Louisiana, and North Carolina, and a report of the unrelated synthetic opiate agonist AH-7921, a research chemical linked to deaths in Sweden and the United States. Kratom, a Southeast Asian plant containing the drug mitragynine with opioid-like effects which is currently uncontrolled in the United States, has also been seen in deaths in combination with tramadol. Most recently, much media attention has been paid to "Krokodil" (desomorphine), a synthetic derivative of codeine, although no toxicologically confirmed cases have been documented in the United States. Reported is the first documented incident of a death following use of a novel designer opioid, MT-45 (1-cyclohexyl-4-[(1R)-1,2-diphenylethyl]-piperazine. MT-45 is a substituted 4-(1,2-diphenylethyl)piperazine which is chemically unrelated to other known opioid agonists. It has been demonstrated to have approximately 80% of the potency of morphine in animal studies and is currently uncontrolled in the United States.

The case involved a 35-year-old White male, with a known history of substance abuse, who had not been seen for two days prior to being found deceased. He appeared to have collapsed adjacent to his drug preparation area where a scale, spoon, pipe, lighter, and two packets of white powder were found (syringe not present). One packet tested positive for MT-45 and the other tested positive for etizolam, an illicit thienodiazepine with benzodiazepine-like properties. Neither drug is prescribed in the United States; further investigation determined the decedent had purchased these online from a Canadian company and had been doing so on a monthly basis for quite some time. Autopsy revealed cerebral edema, congested lungs, and a possible old injection site on the dorsum of the foot. The postmortem toxicology panel routinely requested came back positive for diphenhydramine 220ng/mL in whole blood (over-the-counter medication present at scene), while the urine was presumptively positive for benzodiazepines and cannabinoids.

The postmortem blood was subsequently analyzed for MT-45 using LC/MS/MS. Sample preparation involved liquid-liquid extraction following addition of ammonium hydroxide and an extraction solvent of n-butyl chloride and acetonitrile (4:1,v/v). The instrument was operated in positive electrospray, Multiple Reaction Monitoring (MRM) mode. The column used for separation was a BEH C18, 2.1 x 5.0mm with mobile phases of 0.1% formic acid in methanol and 0.1% formic acid in water. The internal standard reference was acetyl fentanyl D5. The transitions for acetyl fentanyl D5 were 328.3>105.1 and 328.3>188.1. The transitions used for MT-45 were 349.3>181.1 and 349.3>169.2. The retention times for acetyl fentanyl D5 internal standard and MT-45 were 1.72min and 2.26min. The calibration curve was 1-100ng/mL, with higher concentrations diluted to bring them within the linear range. Targeted analysis of the MT-45 in the case described above was measured at a concentration of 520ng/mL. The cause of death was determined to be acute opioid (MT-45) intoxication. Target analysis for etizolam in the blood also measured a concentration of 35ng/mL. No specificity or matrix effects experiments were performed due to the unique nature of the targeted analysis for uncommon analytes.

**Synthetic Opiates, MT-45, Etizolam**